ISSN 2218-6247 (online)

World Journal of *Otorhinolaryngology*

World J Otorhinolaryngol 2015 May 28; 5(2): 37-81

Published by Baishideng Publishing Group Inc

WJO World Journal of Otorhinolaryngology

A peer-reviewed, online, open-access journal of otorhinolaryngology

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2011-2015

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World Journal of Otorhinolaryngology

Contents

Quarterly Volume 5 Number 2 May 28, 2015

World Journal of Otorhinolaryngology
Volume 5 Number 2 May 28, 2015

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NAME OF JOURNAL
World Journal of Otorhinolaryngology

ISSN
ISSN 2218-6247 (online)

LAUNCH DATE
December 28, 2011

FREQUENCY
Quarterly

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PUBLICATION DATE
May 28, 2015

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World Journal of Otorhinolaryngology

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Help Desk: http://www.wjgnet.com/esps/helpdesk.aspx
DOI: 10.5319/wjo.v5.i2.37

World J Otorhinolaryngol 2015 May 28; 5(2): 37-40
ISSN 2218-6247 (online)

EDITORIAL

Deafblindness and dual sensory loss research: Current status and future directions

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Author contributions: Dammeyer J solely contributed to this manuscript.
Conflict-of-interest: The author declares no conflict of interests.

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Received: December 25, 2014
Peer-review started: December 30, 2014
First decision: February 7, 2015
Revised: February 24, 2015
Accepted: April 1, 2015
Article in press: April 7, 2015
Published online: May 28, 2015

Abstract

Deafblindness is more than the addition of hearing impairment plus vision impairment. The absence or impairment of both distance senses gives a condition which is more disabling than the sum of each. Deafblindness is rare among young people but becomes frequent at higher ages. Deafblindness can be either congenital or acquired. The heterogeneity of the population has been reported to be huge. Different levels of vision and hearing loss, different use of language modality, different kinds and severity of additional disabilities, and different medical aetiology are some of the variables splitting the group. Research in deafblindness is still in it is advent due to a number of limitations and a lack of current scientific interest. Some of the challenges in deafblindness research are: lack of consensus on the definition of deafblindness; rareness of the condition which makes it difficult to even gather just a small group to study; heterogeneity of the population; difficulties with using traditional functional assessment procedures; communication barriers; and the difficulties of interpretation of deafblind behavior. This editorial calls for more interest in deafblindness in general and for more international cooperation and innovative studies to overcome existing barriers: Cooperation on data collection to form big enough sample sizes; development of reliable and valid tests and assessment tools; development of new research methods and approaches.

Key words: Deafblindness; Dual sensory loss; Dual sensory impairment; Definition; Methodology

Core tip: Research in deafblindness may have the potential to generate knowledge about several basic questions: How sensory loss affects human development such as mental wellbeing, language development, and cognition. The nature of tactile language and tactile perception. How medical genetics are linked to combined vision and hearing loss. However, research in deafblindness is still in it is advent due to a number of limitations and a lack of current scientific interest. This editorial calls for more interest in deafblindness in general and for more international cooperation and innovative studies to overcome existing barriers.

Dammeyer J. Deafblindness and dual sensory loss research: Current status and future directions. *World J Otorhinolaryngol* 2015; 5(2): 37-40 Available from: URL: http://www.wjgnet.com/2218-6247/full/v5/i2/37.htm DOI: http://dx.doi.org/10.5319/

wjo.v5.i2.37

DEAFBLINDNESS

Deafblindness - otherwise known as dual sensory loss - refers to the combination of vision and hearing impairment. Deafblindness is often researched as two different subgroups - those with congenital vision and hearing impairment and those with acquired dual sensory impairment - because of their different developmental conditions. People with congenital deafblindness have to develop language despite being deaf and blind, while people with acquired deafblindness have to maintain language abilities when becoming deafblind.

Scientific interests in deafblindness have been present throughout history. The scientific interest in deafblindness can in one point be dated back to around 1860 with the case-story of Helen Keller and her teacher Ann Sullivan[1], which shed light on the uniqueness and challenges in being deafblind. Deafblindness is more than the addition of hearing impairment plus vision impairment. The absence or impairment of both distance senses gives a condition which is more disabling than the sum of each. The equation 1 + 1 = 3 illustrates the situation where vision cannot compensate for loss of vision and vise versa. Therefore, people with residual hearing and/or vision are also labeled as deafblind.

Heterogeneity of aetiologies portrays the populations of congenital deafblindness. More than 30 causes of congenital (pre-lingual) deafblindness have been identified in a recent population study[2]. The large number of different aetiologies includes intoxications and infections such as Rubella virus or Cytomegalovirus infection of the fetus or meningitis infection postnatal. A large number of genetic and chromosomal disorders involve vision and hearing impairment such as CHARGE syndrome which is one of the most frequent congenital conditions. CHARGE syndrome is a genetic disorder characterized by coloboma of the eye, heart defects, atresia of the nasal choanae, retardation of growth and/or development, genital and/or urinary abnormalities, as well as ear abnormalities and deafness[3].

Several causes are also known for acquired (post-lingual) deafblindness with Usher syndrome being the most dominant (about half of all cases) among people below 60 years of age[2]. Usher syndrome is an autosomal recessive disorder characterized by congenital or progressive hearing loss and progressive vision impairment due to the eye disease Retinitis Pigmentosa and involve several subtypes[4]. Other causes are head injuries, tumors, blindness following diabetes, as well as hearing impairment caused by noise exposure. In old age, the major causes to vision impairment are age-related macular degeneration, cataracts, and glaucoma[5]. Hearing impairment in old age are often attributed to presbycusis (age-related sensorineural hearing loss)[6].

Research in the field of acquired deafblindness has mainly been concerned with mental health and life outcome consequences among the elderly. Some of the reported findings have been, that acquired deafblindness is associated with a much higher prevalence of depression, cognitive decline, and difficulties with activities of daily living (for a review see Dammeyer[7] 2014).

Research themes with respect to congenital deafblindness have mainly concerned the study of how language and communicative development can be supported by using pre-lingual tactile support. It has, for instance, been explored how the caretaker can sustain and expand the social interaction by responding to the child's expressions of tempo, rhythm, intensity, and emotions within the tactile modality[8]. These studies are mostly case-based studies with a focus on qualifying intervention methods (for a review see Dammeyer[7] 2014).

A number of other research fields are related to people with dual sensory impairment but do not take an explicit focus on deafblindness. Examples are medical research in syndromes which frequently involve dual sensory losses such as Usher Syndrome, CHARGE Syndrome, and Maternal Rubella Syndrome. For instance, one research topic has been the behavioural phenotype in children with CHARGE syndrome[9].

Despite the uniqueness and interest in deafblindness a contradiction exists in scientific research. The number of published research reports with regard to deafblindness is sparse. A search in Pubmed on the terms deafblindness, dual sensory loss, or dual sensory impairment reveals less than 150 hits and the term deafblindness reveals less than 500 hits (November 2014). Most of this research concerns people with acquired deafblindness or specific medical syndromes. Congenital deafblindness has rarely been scientifically explored or reported on. The lack of published research may have at least seven explanations.

First, the rareness of the condition makes it difficult to even gather just a small group to study. Prevalence of congenital deafblindness and acquired deafblindness among people below 60 years of age is below the 0.1 percent level. Acquired deafblindness is more frequent at higher ages (prevalence around 30 percent at age 80) (for a review see Dammeyer[7] 2014), and may therefore be more researched.

Second, the heterogeneity of the population makes it difficult to study people with deafblindness as one single group. Different levels of vision and hearing loss, different use of language modality, different kinds and severity of additional disabilities, and different medical aetiology are some of the variables splitting the group. With regard to additional disabilities mental retardation and developmental disorders have been reported as the most frequent in the congenital deafblind group[10].

Third, due to the dual sensory loss, it is generally very difficult to use traditional functional assessment procedures and psychological tests, since these often require full sensory functioning as a prerequisite. Several researchers have concluded that one cannot rely on visual or auditory test items and interpretation of results from standardized norms is dubious, at best, for cognitive, language, and social assessment[11,12].

Forth, it is often difficult to communicate or even cooperate with a person with congenital deafblindness even for a researcher mastering both the local oral, signed, and tactile languages. Communication form and abilities may be very individual to each person. A mix of oral, visual, tactile and alternative communication systems is often used. Similar communicative challenges, but to a lesser degree, are also the case for individuals with acquired deafblindness.

Fifth, interpretation of "deafblind behaviour" can be very challenging. The communication and behaviour of a person with congenital deafblindness must be understood from the "tactile-bodily being in the world[13]. A congenitally deafblind man who hits his head with his hand may be exemplifying a symptom of a mental or behavioural disorder (for example psychosis, anxiety, frustration), or it may be a means of self-stimulation, or communication (telling the caretaker that he needs help, is hungry or misses someone). The question of validity when interpreting deafblind behaviour is challenging but vital to take into consideration in all deafblind research.

Sixth, deafblind research has for the most part been a sub-discipline to deaf education, service and research. In education and rehabilitation the same methods as used among people with a hearing impairment are applied, just adapted for tactile modality. Often tactile adapted visual sign-language has been used. This may lead to "blindness" for the deafblind person's tactile perception which shapes the communication and mind differently compared to people with hearing loss.

Seventh, last, but not least, there is no consensus on the definition of deafblindness in the literature. Overall two types of definitions are employed; a medical definition in terms of audiological and visual criteria, and a functional definition based on self-report and observation, evaluating the individual impact of vision and hearing loss on everyday life activities and the individual's possibilities for participation in society. The lack of a clear definition in research and practice makes it difficult to compare research results across studies[14].

To overcome these barriers in deafblind research, which cover issues related to definition, methodology, theory, and organization of research, a number of different initiatives need to take place. Some of these may be: (1) The individual researcher needs to use a more thorough definition and description of the study population by using well defined terminology and criteria, building on existing research; (2) Development of standardized tests, questionnaires, and other assessment tools for individuals with deafblindness is important. For example it is important to develop tests which can differentiate symptoms of autism disorder from symptoms related to consequences of dual sensory impairment[15]; (3) Many studies use video observation of tactile behaviour and communication. Studying one modality (tactile) with another modality (visual) is not optimal. The methodological challenge is clear; with reliable methods to measure tactile behaviour more directly and with more validity. New technology has to be applied and developed such as automatic motion tracking technology using infrared markers, neuroimaging methods such as event related potentials, and technology measuring touch; and (4) Because of the different methodological challenges the rareness and heterogeneity of deafblindness, an increased cooperation among international research groups is greatly needed to solve the critical challenges and limitations in deafblind research. Cooperation on data collection to form big enough sample sizes may be one aim. Often many variables have to be controlled, such as medical aetiology, cognitive abilities, and communication mode, which is impossible in small sample sizes.

IN SUMMARY

Research in deafblindness may have the potential to generate knowledge about several basic questions: How sensory loss affects human development such as mental wellbeing, language development, and cognition. The nature of tactile language and tactile perception. How medical genetics are linked to combined vision and hearing loss. However, research in deafblindness is still in it is advent due to a number of limitations and a lack of current scientific interest. This editorial calls for more interest in deafblindness in general and for more international cooperation and innovative studies to overcome existing barriers.

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World Journal of Otorhinolaryngology

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Help Desk: http://www.wjgnet.com/esps/helpdesk.aspx
DOI: 10.5319/wjo.v5.i2.41

World J Otorhinolaryngol 2015 May 28; 5(2): 41-43
ISSN 2218-6247 (online)

EDITORIAL

Diagnosis and treatment of sudden sensorineural hearing loss

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Conflict-of-interest: None.

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Received: January 5, 2015
Peer-review started: January 7, 2015
First decision: February 7, 2015
Revised: February 23, 2015
Accepted: April 16, 2015
Article in press: April 20, 2015
Published online: May 28, 2015

Abstract

Nationwide epidemiological surveys of idiopathic sudden sensorineural hearing loss (SSNHL) have been performed five times by the Research Committee of the Ministry of Health and Welfare or the Ministry of Health, Welfare and Labour in Japan. These surveys included patients who had SSNHL in 1972, 1987, 1993, 2001, and 2012. Using the criteria for the grading of hearing loss in SSNHL or the criteria for grading the degree of hearing recovery after SSNHL established by the Research Committee, we compared the outcomes of SSNHL between the five nationwide surveys. The results revealed that the outcomes of SSNHL have not changed in the past 40 years. In 1972, 88% of patients received steroids, but none received prostaglandin E_1 (PGE_1). The use of PGE_1 has increased since the 1980s, but its effect on SSNHL may not be significant. Intratympanic steroid injection has been introduced recently for the treatment of SSNHL, but it does not seem to be used widely in Japan. Intratympanic therapy that can reduce the total amount of steroids administered will be used more frequently if the true effects and indications for this therapy are known. Elucidation of the etiologies of SSNHL and development of treatments specific for these etiologies are expected.

Key words: Sudden deafness; Grading system; Initial hearing level; Final hearing level; Treatment method; Nationwide epidemiological survey

Core tip: Nationwide epidemiological studies of sudden sensorineural hearing loss (SSNHL) were performed five times between 1972 and 2012 in Japan and have revealed that the recovery rate of SSNHL has not improved for 40 years. Elucidation of the etiologies of SSNHL and development of treatments specific for these etiologies are expected.

Nakashima T. Diagnosis and treatment of sudden sensorineural hearing loss. *World J Otorhinolaryngol* 2015; 5(2): 41-43 Available from: URL: http://www.wjgnet.com/2218-6247/full/v5/i2/41.htm DOI: http://dx.doi.org/10.5319/wjo.v5.i2.41

INTRODUCTION

According to a recent epidemiological study of idiopathic sudden sensorineural hearing loss (SSNHL) in Japan, the outcome of SSNHL has not changed in the

Table 1 Criteria for the grading of hearing loss in sudden sensorineural hearing loss

Grade 1	PTA < 40 dB
Grade 2	40 dB ≤ PTA < 60 dB
Grade 3	60 dB ≤ PTA < 90 dB
Grade 4	90 dB ≤ PTA

Evaluation of the initial audiogram should be performed within 2 wk of onset. PTA: Arithmetic mean of the five frequencies: 250, 500, 1000, 2000, and 4000 Hz.

Table 2 Final grades of initial grade 4 cases in five nationwide sudden sensorineural hearing loss surveys in Japan *n* (%)

	1972	1987	1993	2001	2012
Grade 1	26 (14)	49 (18)	70 (18)	25 (15)	5 (21)
Grade 2	31 (16)	44 (17)	62 (16)	36 (22)	1 (4)
Grade 3	87 (46)	119 (45)	173 (43)	68 (41)	11 (46)
Grade 4	45 (24)	53 (20)	95 (24)	38 (23)	7 (29)
Total	189 (100)	265 (100)	400 (100)	167 (100)	24 (100)

The data for 1972, 1987, and 1993[2], 2001[3], and 2012[1] are summarized.

past 40 years[1]. Table 1 shows the criteria for grading SSNHL established by the Research Committee of the Ministry of Health and Welfare in Japan in 1988.

The grading system is also used to evaluate the final hearing level, which is measured when the hearing level becomes stable[2,3]. Table 2 shows the distribution of the grades of the final audiograms for grade 4 cases at the initial audiogram in five nationwide surveys performed from 1972 through 2012[1-3].

The outcome has not differed significantly between the five surveys. Classification of grades 1 and 2 at the final audiogram as the "good recovery group" and grades 3 and grade 4 at the final audiogram as the "poor recovery group" and analysis using the χ^2 test showed that the ratio of good to poor recovery has not differed significantly between any survey year. This suggests that the treatment results for the worst grade of SSNHL at the initial examination have not improved in the past 40 years.

TREATMENT METHODS

Table 3 shows the percentages of patients with SSNHL who were treated with steroids, vitamins, stellate ganglion block (SGB), hyperbaric oxygen therapy (HBO), or prostaglandin E_1 (PGE_1) in 1972, 1987, and 2001 in Japan[3,4].

The use of PGE_1 has increased since the 1980s, but its effect on SSNHL may not be significant[5-7]. Treatment methods for patients who had SSNHL in 2012 have not been investigated. However, steroids remain the main drugs for the treatment of SSNHL at present throughout the world. Intratympanic steroid injection has been introduced recently for the treatment of SSNHL[8], but it does not seem to be used widely in Japan. Intratympanic steroid injection may be used more frequently if the true effects and indications are known as it can reduce the total amount of steroids administered.

Table 3 Percentages of patients who received steroids, vitamins, stellate ganglion block, hyperbaric oxygen therapy, or prostaglandin E_1 for sudden sensorineural hearing loss

	1972	1987	2001
Steroids	88%	93%	85%
Vitamins	88%	93%	92%
SGB	24%	27%	8%
HBO	3%	12%	11%
PGE_1	0%	11%	33%

Data for 1972 and 1987[4], and 2001[3] are summarized. SGB: Stellate ganglion block; HBO: Hyperbaric oxygen therapy; PGE_1: Prostaglandin E_1.

EVALUATION OF HEARING RECOVERY

Siegel's criteria[9] or criteria determined by the Research Committee of the Ministry of Health and Welfare in Japan[10] are used in the evaluation of hearing recovery after SSNHL. These criteria use both the final hearing level and the magnitude of the hearing gain (in dB). The percentage improvement is also used to evaluate the degree of recovery and is calculated by dividing the difference between the initial hearing level and final hearing level by the difference between the initial hearing level and opposite ear hearing level[5]. Another method is used to obtain the percentage of the final hearing grade for each grade of the initial audiogram (Table 2)[1-3]. Various factors are associated with the degree of hearing recovery including the initial hearing loss, shape of the audiogram, interval between the onset of SSNHL and initial visit to an ENT doctor, age, and other factors. It is recommended to use several methods for the evaluation of hearing recovery.

Future problems

To increase the recovery rate of SSNHL, it is essential to investigate the etiology of SSNHL, which is considered a multifactorial disease. 3-Tesla magnetic resonance imaging can be used to evaluate disruption of the blood-labyrinthine barrier by observing the contrast enhancement of the inner ear after intravenous injection of gadolinium contrast agents[11-13]. Increased permeability of the blood vessels is closely associated with inflammation. Whether the effects of steroids with anti-inflammatory function vary according to the condition of the blood-labyrinthine barrier should be settled in future. Development of intratympanic therapy or drug-placement therapy in the round window niche is expected[14-16].

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P- Reviewer: Abulezz T, Coskun A **S- Editor**: Tian YL
L- Editor: A **E- Editor**: Lu YJ

World Journal of Otorhinolaryngology

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DOI: 10.5319/wjo.v5.i2.44

World J Otorhinolaryngol 2015 May 28; 5(2): 44-52
ISSN 2218-6247 (online)

REVIEW

Relationship between chronic rhinosinusitis and lower airway diseases: An extensive review

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Author contributions: All the authors contributed to this paper.
Supported by JSPS KAKENHI (Grants-in-Aid for Scientific Research), No. 25462642.
Conflict-of-interest: The authors have no conflict of interest to disclose.

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Received: October 4, 2014
Peer-review started: October 5, 2014
First decision: November 14, 2014
Revised: December 4, 2014
Accepted: March 4, 2015
Article in press: March 5, 2015
Published online: May 28, 2015

Abstract

Significant links between allergic rhinitis and asthma have been reported, and the united airway disease hypothesis is supported by numerous findings in epidemiologic, physiologic, pathologic, and immunologic studies. The impact of allergic rhinitis on asthma has been established. On the other hand, the relationship between chronic rhinosinusitis and lung diseases has been under investigation. Chronic rhinosinusitis is a common disease, and the high prevalence of chronic rhinosinusitis in some kinds of lung diseases has been reported. Recent studies suggest that the treatment of chronic rhinosinusitis has beneficial effects in the management of asthma. Here, we present an overview of the current research on the relationship between chronic rhinosinusitis and lower airway diseases including asthma, chronic obstructive pulmonary disease, cystic fibrosis, diffuse panbronchiolitis, primary ciliary dyskinesia, idiopathic bronchiectasis, and allergic bronchopulmonary aspergillosis.

Key words: Chronic rhinosinusitis; Sinusitis; Asthma; Chronic obstructive pulmonary disease; Cystic fibrosis; Diffuse panbronchiolitis; Primary ciliary dyskinesia; Idiopathic bronchiectasis; Allergic bronchopulmonary aspergillosis

Core tip: Chronic rhinosinusitis is a persisting inflammatory condition of the paranasal sinus. A close relationship between chronic rhinosinusitis and lower airway diseases has been suggested. The purpose of this review is to summarize recent findings on the correlation between chronic rhinosinusitis and lung diseases.

Kariya S, Okano M, Nishizaki K. Relationship between chronic rhinosinusitis and lower airway diseases: An extensive review. *World J Otorhinolaryngol* 2015; 5(2): 44-52 Available from: URL: http://www.wjgnet.com/2218-6247/full/v5/i2/44.htm DOI: http://dx.doi.org/10.5319/wjo.v5.i2.44

INTRODUCTION

Chronic rhinosinusitis is a common clinical problem, and is a complex inflammatory disease that is poorly

understood. Chronic rhinosinusitis is defined by the presence for 12 wk or longer of two or more of the following symptoms: (1) nasal blockage/obstruction/congestion; (2) nasal discharge (anterior/posterior nasal drip); (3) facial pain/pressure; and (4) reduction or loss of smell. One of these should either be nasal blockage/obstruction/congestion or nasal discharge (anterior/posterior nasal drip). The presence of endoscopic findings [(1) nasal polyps, and/or (2) mucopurulent discharge primarily from the middle meatus, and/or (3) oedema/mucosal obstruction primarily in the middle meatus] and/or mucosal changes within the ostiomeatal complex and/or sinuses revealed by computed tomography is also required[1].

According to the current consensus, chronic rhinosinusitis is subclassified into chronic rhinosinusitis without nasal polyposis (CRSsNP), chronic rhinosinusitis with nasal polyposis (CRSwNP), and allergic fungal rhinosinusitis[1-3]. Chronic rhinosinusitis has complex pathophysiological features, and the etiology of chronic rhinosinusitis is not fully understood. In immunological characteristics, CRSwNP with interleukin (IL)-5-positive cells in nasal polyps can be differentiated from CRSwNP without IL-5-positive cells by different inflammatory patterns (predominance of eosinophils *vs* neutrophils)[4].

Both pathogen exposure and host condition have significant effects on the onset of chronic rhinosinusitis. The patency of sinus ostia, normal mucociliary function, and healthy immune system are essential factors for the maintenance of normal sinus function. Mucociliary function is remarkably impaired in some diseases such as cystic fibrosis and Kartagener's syndrome (a type of primary ciliary dyskinesia). Allergic diseases and immunodeficiency may induce chronic rhinosinusitis. A close relationship between chronic rhinosinusitis and lower airway diseases has been suggested[5-9]. The purpose of this review is to summarize current understandings regarding the interaction between chronic rhinosinusitis and lower respiratory conditions. Recently, the term "rhinosinusitis" rather than "sinusitis" has been adopted because sinusitis rarely occurs in the absence of rhinitis[10,11]. In this review, rhinosinusitis and sinusitis are used synonymously.

ASTHMA

The relationship between allergic rhinitis and asthma is now established, and numerous clinical, epidemiological, and biological studies recommend integrated management[12,13]. In the past few decades, the association between chronic rhinosinusitis and asthma has come to be recognized. The presence of rhinosinusitis is associated with more severe asthmatic symptoms in patients with asthma[14]. In epidemiological and radiographic studies, 40% to 90% of asthmatic patients presented abnormal findings on CT scans of their sinuses[15-18].

Several explanations for the association of chronic rhinosinusitis and asthma including the naso-bronchial reflex, pharyngo-bronchial reflex, postnasal drainage of inflammatory mediators from the upper to lower airway, inhalation of dry, cold air and environmental pollutants, and the "shared pathogenesis" of chronic rhinosinusitis and asthma are proposed. The naso-bronchial reflex is mediated by afferent pathways involving the trigeminal nerve and efferent fibers causing bronchoconstriction by means of the vagus nerve. The irritant in the nasal cavity has led to efferent bronchoconstriction[16]. However, the exact mechanisms linking chronic rhinosinusitis and asthma are under debate[19,20].

Severe mucosal inflammation with immune dysregulation is a common feature of chronic rhinosinusitis and asthma[21]. The immunological findings including IL-17, IL-18, IL-25, IL-33, toll-like receptors (TLRs), and thymic stromal lymphopoietin (TSLP) are similar in chronic rhinosinusitis and asthma[22-24]. Transforming growth factor (TGF)-β1 is a major participant in the airway remodeling of asthma, and is also known to play an important role in the tissue remodeling processes and enhanced epithelial immunoreactivity involved in chronic rhinosinusitis[25]. Because the enhanced TGF-β signaling in CRSsNP and reduced TGF-β signaling in CRSwNP is compatible with the remodeling patterns observed in the disease subgroups, TGF-β is characterized as a key switch between CRSsNP and CRSwNP[4]. More than 80% of nasal polyps in Caucasians express IL-5 protein, and more than 50% are eosinophilic, whereas in the Chinese group that was studied, less than 20% express IL-5 protein and less than 10% are eosinophilic[26]. The prevalence of allergic rhinitis, a typical immunoglobulin E (IgE)-mediated type Ⅰ allergic disease, has been increasing in African continent[27,28]. Allergic rhinitis is significantly more common among asthmatic subjects (76%) than among nonasthmatic subjects (48%) in urban Ghana[29]. The role of IL-5 and eosinophils in chronic rhinosinusitisin in African subjects has not been reported to date, however allergy is the commonest etiological factors for chronic rhinosinusitisin in Nigeria[30]. Although regional differences have been reported, IL-5, a strong secretagogue for human eosinophils, and IgE, specifically IgE against staphylococcal enterotoxins, are identified as indicators of asthma comorbidity in a group of patients with CRSwNP[31].

Blood and sputum eosinophil levels in patients with asthma are directly correlated with sinus mucosal thickening as assessed by computed tomography (CT) scanning[32]. The link between chronic rhinosinusitis and asthma is not only of academic interest, but also an important factor in diagnostic and therapeutic strategy. Asthma phenotypes are very heterogeneous, and inflammation can be predominantly eosinophilic or neutrophilic[33]. Increasing evidence suggests that patients with chronic rhinosinusitis should be evaluated for possible concomitant asthma, and that patients with asthma should always be evaluated for possible nasal and paranasal disease. Both medical and surgical treatments of chronic rhinosinusitis benefit concomitant asthma[34-37]. Although an opposite opinion

has been held[38], functional endoscopic sinus surgery is suggested for asthmatic patients including children in whom appropriate medical therapy has failed to resolve sinus disease[39-41].

CHRONIC OBSTRUCTIVE PULMONARY DISEASE

Chronic obstructive pulmonary disease (COPD) is one of the most common chronic respiratory diseases. Smoking is the primary risk factor for COPD. The coexistence of upper airway diseases with COPD is not well documented, and only a few authors have studied the role of chronic rhinosinusitis in COPD. Although the available data are limited, a certain relationship between sinonasal disorders and COPD has been suggested[42]. In epidemiological studies, patients with an established diagnosis of COPD have a significantly higher incidence of rhinosinusitis as compared with age-matched control subjects (12.4% *vs* 2.5%; OR = 6.08; 95%CI: 2.87-12.89)[43]. Another recent study supports these findings[44]. The potential hypotheses for interaction between the upper and lower airways in COPD patients are (1) loss of nasal conditioning function; (2) direct passage of inflammatory mediators and/or microorganisms between upper and lower respiratory tracts; (3) nasobronchial neuronal reflexes; (4) stimulation at one point of the respiratory mucosal surface resulting in a pan-airway inflammatory response; and (5) inflammation caused by smoking[42,45].

Numerous cytokines, chemokines, and other inflammatory factors including TGF-β, tumor necrosis factor-alpha (TNF-α), interferon gamma (IFN-γ), IL-1β, IL-6, IL-8, IL-18, chemokine (C-C motif) ligand 2 (CCL2), chemokine (C-X-C motif) ligand 9 (CXCL9), CXCL10, and CXCL11 are involved in COPD[46]. A physiological study using spirometry and acoustic rhinometry showed a significant relationship between nasal patency and pulmonary airflow obstruction in COPD[47]. In immunological studies, COPD has been associated with an increased level of IL-8, a potent neutrophil chemoattractant, in nasal secretion, and patients with COPD have higher nasal concentrations of eotaxin, granulocyte-colony stimulating factor (G-CSF), and IFN-γ than controls[48,49].

Cigarette smoking is the main cause of COPD, and it also induces sinonasal inflammation[50-53]. Smoking is associated with inflammation throughout the airway. The evidence from previous studies provides conflicting data on the relationship between rhinosinusitis and COPD severity. A recent study showed that clinical symptoms, endoscopic score, saccharine test results, cellular profile of nasal lavage, and levels of eicosanoids in nasal lavage in chronic rhinosinusitis patients are not different between COPD stages, and concluded that sinonasal inflammation is not strictly related to COPD severity[54]. Although the coexistence of COPD and chronic rhinosinusitis is frequently observed, further studies are needed to explain the causative role of chronic rhinosinusitis in COPD.

CYSTIC FIBROSIS

Cystic fibrosis is an inherited disease caused by genetic mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene that encodes for an ATP-regulated ion-channel, which is expressed in many tissues. Although several therapeutic agents have been developed in recent years, no curative therapy exists for cystic fibrosis[55]. Gene therapy is an attractive approach, however the difficulty of gene therapy is reflected by the variable results of the 25 gene therapy trials for cystic fibrosis[55]. Gene therapy using non-viral vectors or viral vectors is actively investigated, however no current gene therapy trial is actively enrolling patients. Because the surface fluid in cystic fibrosis patients has a high NaCl concentration due to dysfunction of the CFTR Cl^- channel, cystic fibrosis airway epithelia fail to kill pathogens[56]. Chronic rhinosinusitis with or without nasal polyposis is common in patients with cystic fibrosis[57,58]. Nasal polyps are present in approximately 40% of chronic rhinosinusitis patients with cystic fibrosis, and the polyps exhibit predominantly neutrophilic, rather than eosinophilic, inflammation[59].

Numerous bacteria are frequently isolated from sinus cultures of chronic rhinosinusitis patients with cystic fibrosis; *Pseudomonas aeruginosa* as well as *Staphylococcus aureus* are the most common bacterial species[60]. The same pathogen is commonly found in both the upper and lower respiratory tracts in chronic rhinosinusitis patients with cystic fibrosis, and genotypes of sinus bacteria are shown to be consistent with those in the lower airway, indicating that the nasal cavity and paranasal sinuses may serve as bacterial reservoirs for recurrent lung infection[61].

The management of chronic rhinosinusitis in patients with cystic fibrosis is difficult. Medical management usually consists of daily nasal care, nasal saline irrigations, surfactant lavage, and medications. Oral or intravenous antibiotics, decongestants, antihistamines, topical and/or systemic steroids, dornase alfa, ibuprofen, and N-acetyl cysteine are used as therapeutic agents[62]. Surgical management is indicated for patients who fail medical management. Surgical management of the sinuses in cystic fibrosis patients may improve lower airway outcomes. However, no definitive effect of endoscopic sinus surgery on lung infection has been established[63]. Multiple studies have shown the safety and effectiveness of endoscopic sinus surgery for chronic rhinosinusitis in cystic fibrosis patients. However, overall failure rates requiring revision surgery are high (13% to 89%)[64-70].

Sinus diseases should be routinely evaluated by diagnostic testing (*i.e.*, CT scan) in patients with cystic fibrosis because chronic rhinosinusitis could be a source for lower airway infection[71,72].

DIFFUSE PANBRONCHIOLITIS

Diffuse panbronchiolitis (DPB) is characterized by chronic sinobronchial inflammation, and is a treatable neutrophil-related pulmonary disease. DPB was originally found in Asian populations, and has recently been encountered in Western countries, both clinically and pathologically[73-78]. In DPB, no association with smoking or exposure to fumes or toxic agents has been proven. Human leukocyte antigen (HLA) alleles (HLA-B54 and HLA-A11) are thought to be causal factors for a genetic predisposition to DPB, and these findings suggest a major HLA susceptibility gene for DPB. Untreated DPB generally progresses to bronchiectasis, with resultant respiratory failure and death[79].

Patients with DPB have a history of chronic rhinosinusitis or still have the disease[75,80]. Significant improvement of DPB and concomitant chronic rhinosinusitis has been reported after the use of long-term therapy with macrolide antibiotics[81,82]. Before the 1970s, the prognosis of patients with DPB was poor, with 10-year survival rates of under 40%. However, after the 1980s, long-term erythromycin treatment has increased the 10-year survival rate to over 90%[83].

The mechanisms of the anti-inflammatory properties of macrolides are still being investigated. Macrolides inhibit the production of many proinflammatory cytokines, such as IL-1, IL-6, IL-8, and TNF-β, by suppressing transcription factors including nuclear factor-kappa B and/or activator protein-1[84,85]. It is highly recommended that chronic rhinosinusitis in patients with DPB be treated with 14- and 15-membered macrolides.

PRIMARY CILIARY DYSKINESIA

Primary ciliary dyskinesia is a rare, genetically heterogeneous autosomal recessive disorder characterized by ciliary dysfunction and impaired mucociliary clearance[86]. The clinical effects of primary ciliary dyskinesia include recurrent lower airway infection, bronchiectasis, male infertility, otitis media with effusion, rhinitis, and rhinosinusitis[87-89]. Otitis media with effusion is considered the most common otolaryngologic manifestation of primary ciliary dyskinesia, affecting up to 85% of children with primary ciliary dyskinesia. Chronic rhinitis and chronic rhinosinusitis are found in almost all primary ciliary dyskinesia patients[90,91].

Sinonasal disease in primary ciliary dyskinesia is poorly understood[92]. The prevalence of nasal polyps in chronic rhinosinusitis patients with primary ciliary dyskinesia is low (15% to 30%), and nasal polyps are rarely observed in pediatric patients[93-96]. In the management of the lower airway tract, macrolide therapy has no effect in primary ciliary dyskinesia[81]. Saline nasal irrigation, longterm macrolide therapy, and endoscopic sinus surgery may be beneficial for primary ciliary dyskinesia patients with intractable chronic rhinosinusitis[96-98]. Nasal symptoms usually consist of persistent nasal discharge and blockage; sinus surgery may not be effective in reducing nasal discharge[99]. Because of the lack of evidence in the literature, any surgical intervention should be followed by noninvasive management of chronic rhinosinusitis[90].

IDIOPATHIC BRONCHIECTASIS

Bronchiectasis is defined as abnormal and irreversibly dilated bronchi caused by the loss of the elastic and muscular components of the bronchial and peribronchial tree following recurrent lower airway infection. Bronchiectasis is the result of several different etiologies including cystic fibrosis, primary ciliary dyskinesia, immunodeficiency, tuberculosis, graft-*vs*-host disease, and inflammatory bowel diseases. The most common causes of bronchiectasis are idiopathic and post-infective damage[87,100]. Regardless of the underlying cause, inflammation in bronchiectasis is predominantly neutrophil driven[101].

Chronic rhinosinusitis was found in 45% to 84% of the cases of patients with idiopathic bronchiectasis[102,103]. A recent study reported a possible association between bronchiectasis and chronic rhinosinusitis[104]. Because the available data is limited, the clinical, histopathological, and immunological characteristics of chronic rhinosinusitis in patients with idiopathic bronchiectasis are largely unknown.

ALLERGIC BRONCHOPULMONARY ASPERGILLOSIS

Allergic bronchopulmonary aspergillosis (ABPA) is a Th2 hypersensitivity lung disease, and is one of the frequent forms of allergic bronchopulmonary mycosis. ABPA is commonly caused by bronchial colonization with *Aspergillus fumigatus*[105]. *A. fumigatus* affects approximately 0.7% to 3.5% of asthmatic patients and 7% to 9% of patients with cystic fibrosis[106-108]. Up to 50% of patients with acute severe asthma has *A. fumigatus* hypersensitivity, and 7% to 15% of cystic fibrosis patients have ABPA[108-111]. Patients with *A. fumigatus*-mediated chronic asthma or ABPA in cystic fibrosis showed significantly decreased pulmonary function leading to poorer outcomes[112-115]. In addition, antifungal therapy leads to better lung function in *A. fumigatus*-sensitized cystic fibrosis patients[116].

Allergic fungal rhinosinusitis (AFRS) is a noninvasive form of fungal chronic rhinosinusitis, and has IgE-mediated type I hypersensitivity to fungal proteins[117]. Dematiaceous fungi (such as *Bipolaris spicifera* or *Curvularia lunata*) or Aspergillus species (such as *A. fumigatus*, *A. niger*, or *A. flavus*) are commonly detected in allergic mucin, which is the characteristic extramucosal "peanut buttery" viscoelastic, eosinophil-rich material in AFRS[118]. The serological findings of Bipolaris spicifera in AFRS are analogous to those seen with *A. fumigatus* in ABPA[119]. AFRS has similar

clinicopathological features to those in ABPA. However, immunological hypersensitivity is less intense in AFRS compared to that in ABPA[120].

Conflicting opinions have been reported in the incidence of the coexistence of allergic bronchopulmonary fungal disease and AFRS[121,122]. There is a lack of data on the causative and pathophysiologic relationship between ABPA and AFRS, and it has not been proven whether the postnasal drainage of Aspergillus-containing mucus into the lower airways influences the development or severity of ABPA[123]. Postoperative systemic and/or standard topical nasal steroids are recommended in the medical management of AFRS[124]. Further studies are needed to assess relationships in the etiology and management strategy of ABPA and AFRS.

CONCLUSION

To date, numerous studies have been reported about the relationship between upper and lower airway diseases[125]. Chronic rhinosinusitis is frequently coexistent with lung diseases, and has a causative role in the onset and development of chronic lower respiratory diseases. Appropriate assessment and treatment in the upper respiratory tract are necessary to manage united airway diseases.

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P- Reviewer: Berlucchi M, El-Shazly A, Noussios G
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World Journal of Otorhinolaryngology

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DOI: 10.5319/wjo.v5.i2.53

World J Otorhinolaryngol 2015 May 28; 5(2): 53-57
ISSN 2218-6247 (online)

Why use tympanometry in general practice: A review

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Author contributions: Lous J solely contributed to this manuscript.
Conflict-of-interest: No conflict of interest.

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Telephone: +45-86-273471
Received: November 10, 2014
Peer-review started: November 11, 2014
First decision: January 8, 2015
Revised: January 23, 2015
Accepted: February 10, 2015
Article in press: February 12, 2015
Published online: May 28, 2015

Abstract

Otitis media is a frequent problem in preschool children and one of the most common reasons for treatment with antibiotics in children. The exact diagnosis is important for proper management. The diagnosis of otitis media is often difficult. Pneumatic otoscopy, otomicroscopy, and tympanometry can improve the diagnostic quality by indicating fluid or no fluid in the middle ear and thus improve the quality of treatment. The aim of this review is to explain why and how tympanometry can improve the diagnostic quality in otitis media, and to identify some barriers and difficulties encountered when using tympanometry in daily practice. The current literature on tympanometry and own experiences during 38 years are used to elucidate the aim. Tympanometry is difficult to understand and use, when the procedure is not properly trained. The problems are both of a technical nature, and it is difficult to understand and use the information from the curve and the figures on the display. If the use of tympanometry in general practice is increased, the diagnostic quality will improve and hopefully antibiotics will be prescribed on more appropriate indications and less frequently. More demand on tympanometry will hopefully reduce the price of the tympanometer, making it more accessible for GPs. First in that situation the use will be nearly as common as the use of the otoscope.

Key words: Impedance audiometry (Tympanometry); Otitis media; General practice; Diagnosis; Treatment

Core tip: The aim of this review is to explain why and how tympanometry can improve the diagnostic quality in otitis media, and to identify some barriers and difficulties in using tympanometry in daily practice.

Lous J. Why use tympanometry in general practice: A review. *World J Otorhinolaryngol* 2015; 5(2): 53-57 Available from: URL: http://www.wjgnet.com/2218-6247/full/v5/i2/53.htm DOI: http://dx.doi.org/10.5319/wjo.v5.i2.53

INTRODUCTION

Otitis media (OM) is a common disease in children. More than 80% of children have had OM before the age of two years[1]. The presentation of otitis media can have two different forms: either acute otitis media (AOM) or otitis media with effusion (OME), also called secretory otitis media. The two forms are closely related. We often see a development from OME to AOM and from AOM to OME, as well as stages in between often challenging the physicians.

AOM is an acute inflammatory disease in the middle ear with acute symptoms like ear pain, ear tugging, vomiting, sleeping problems and often fever,

the tympanic membrane is changed in structure (opaque) and color (erythema) and often bulging out, and the middle ear cavity contains fluid (purulent)[2]. The tympanic membrane has in children with AOM no or impaired mobility. When culturing, more than ¾ are found to have bacteria in the middle ear fluid. In Denmark, before the era of antibiotics AOM was a serious disease among children with a mortality of about 6%[3]. Even today 127 relevant papers on complications and sequelae have been published between January 2007 and June 2011[4].

OME often has no or minor symptoms like a small hearing loss, some ear discomfort or pain and sleeping problems[5]. The tympanic membrane can be transparent and amber colored or sometimes grey with visible fluid levels or air bubbles behind the tympanic membrane, and the mobility is impaired[6,7]. Or the tympanic membrane can be opaque (not transparent), dull or sometimes edematous. In OME the fluid normally is without living bacteria.

WHY THE DIAGNOSIS IS IMPORTANT IN CHILDREN WITH EAR COMPLAINTS?

In otitis media a correct diagnosis is fundamental to proper management. AOM must be differentiated from OME to avoid unnecessary antimicrobial use[2,7]. Diagnosing AOM requires a history of acute onset in sign and symptoms, and presence of middle ear effusion, and signs of middle ear inflammation[2], whereas OME just is fluid in the middle ear without signs or symptoms of acute ear infection[7].

The diagnosis of OM can be difficult in a crying child with fever in the out-of-hours service in the late evening. Also the differentiation between AOM and OME can be difficult with a normal otoscope, especially in children, because of a narrow and angled ear canal with hair and cerumen. Is the tympanic membrane normal (gray, translucent, with light reflex)? Is the tympanic membrane translucent or with changed color (erythema or amber)? Is it possible to see fluid level or air bubbles behind the tympanic membrane? *etc.*

HOW TO IMPROVE OUR CLINICAL EXAMINATION?

Three important tools can improve our clinical examination. Pneumatic otoscopy improves the diagnostic quality by giving information of the mobility of the tympanic membrane, thus providing an indication about presence or absence of fluid in the middle ear and thereby improving the quality of treatment. Pneumatic otoscopy is recommended in the United States guidelines on OME with the best balanced sensitivity 94% (95%CI: 91%-96%) and specificity of 80% (75%-86%)[7]. The equipment for doing pneumatic otoscopy is not expensive, but the problem is that it is difficult to learn and is therefore seldom used in general practice[8].

Another tool is otomicroscope with better light and bioccular magnification. It can easily be combined with pneumatic examination. A sensitivity of up to 94% and specificity of 94% have been found[9,10]. The otomicroscope requires a lot of space in the surgery, is difficult to move, and is expensive. Therefore it is not recommended for use in normal general practice clinics.

A third technique to improve the diagnostic quality in ear patients is tympanometry (electroacoustic impedance audiometry). Tympanometry is in the guidelines recommended as an alternative or supplement to pneumatic otoscopy[7]. Tympanometry measures the "stiffness" of the tympanic membrane (and middle ear and ear canal). The use can be learned in a few hours course, including understanding of the test results displayed on the screen[11]. The tympanometer is still relatively expensive, but more demand will hopefully reduce the price.

MORE TECHNICAL DETAILS ON TYMPANOMETRY - WHAT IS IT?

As mentioned, tympanometry is an electroacoustic impedance measurement of the tympanic membrane and related structures[12]. A generated sound of 220 Hz is sent into the ear canal, and a microphone measures the reflection of sound energy from the tympanic membrane during a pressure change in the ear canal from +200 to -400 daPa (dekapascal nearly equal to mm water pressure). That means the tympanic membrane will be pressed inwards in the beginning, then gradually become more relaxed, when the pressure in the ear canal is the same as in the middle ear and finally more tense or stiff when the negative pressure in the ear canal sucks the tympanic membrane outwards. During this pressure change the impedance (or actually the admittance) is recorded and displayed on the screen of the tympanometer (low - > high - > low) - normally as a bell-shaped curve called a tympanogram, with a top between +50 and - 99 daPa. This curve is called type A tympanogram according to Jerger/Fiellau-Nikolajsen's modification[13,14]. In ears with negative pressure the curve has the same shape, but is displaced to the left, the negative side of the X-axis. When the pressure is between -100 and -199 daPa it is called a type C1 curve and when between -200 and -400 a type C2 curve. In middle ears filled with fluid the tympanic membrane will act more stiffly, *i.e.*, more sound is reflected (less admittance) and the curve will be very low or flat (a type B tympanogram) (Figure 1). Type B tympanogram has a high predictive value for fluid in the middle ear (97%-93%), and a type A tympanogram signifies a middle ear without fluid[15,16]. The C tympanograms are in a stage between normal and not normal. Often C1 is classified as normal, and often C2 means negative pressure with a mix of fluid and air in the middle ear[15].

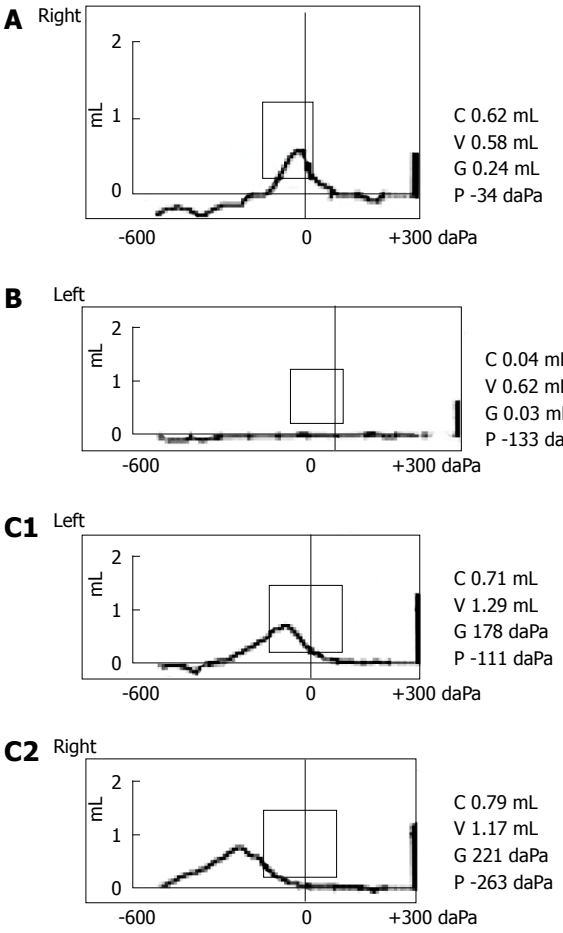

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Figure 1 Tympanogram types. A: Normal; B: Flat, signify fluid in the middle ear; C1: Slight under pressure, normal; C2: Significant under pressure.

WHAT IS THE EFFECT OF USING TYMPANOMETRY IN GENERAL PRACTICE?

The effect of using tympanometry was studied in a group of 40 GPs in the of Region Southern Denmark[17]. They performed otoscopy and made a diagnosis on the basis of history and examination. Subsequently they performed tympanometry successfully in 88% of the children, and in 26% the diagnosis was changed. Their findings indicated that tympanometry and training of the GPs resulted in more relevant cases being referred for treatment by ENT[17]. In another Danish study 20 GPs were randomized to use tympanometry and 20 to usual management. Children under 16 years of age were included when the GP found indication for otoscopy[18]. They found 8.4% with acute otitis in the control group and 2.6% in the tympanometry group. OME was found in 14.2% in the control group and in 25% in the tympanometry group. Antibiotics were prescribed in 7.6% in the control group and in 4.1% in the tympanometry group[18].

WHAT ARE THE PROBLEMS IN USING TYMPANOMETRY?

We asked a group of GPs and practice nurses attending courses on otitis media and tympanometry what problems they had[11]. Of the 197 participants 142 completed the questionnaire (72%), 48 (34%) had not used tympanometry before, and 94 (62%; 95%CI: 52-71) of the participants with experience in tympanometry had frequently one or more problems when performing tympanometry (Table 1). The total number of frequent problems was 172. None of the 94 experienced participants were without problems when performing tympanometry.

The problems were often technical: how to get airtight sealing, or a reliable written curve, and how to handle the tympanometer. The other half of the problems was how to understand the curves and the written figures on the display and how to use the information in the clinical situation[11]. Table 2 gives more detailed answers to these questions. After the course, the number of frequent problems was reduced significantly (Table 1).

The problems in using tympanometry is reflected in a surprisingly skewed use, with many not using at all, a majority using it seldom, and a very few using it more than once daily[11,19] (Figure 2).

WHAT IS RELATED TO THE USE OF TYMPANOMETRY?

Clinic type does not matter. Single-handed GPs in smaller clinics have the same use (mean 24.4, 95%CI: 20.2-28.8) of tympanometry per year as GP in clinics with several GPs (mean 26.3, 95%CI: 22.3-30.4), (*ANOVA*, F = 0.4, *P* = 0.53)[19]. We found no relation to sex and age in the use of tympanometry. We found a difference in use between three regions, representing about half of Danish population, with about 900 clinics and more than 1700 GPs. A total of about 60% (95%CI: 57-63) used tympanometry, even since 2006 it has been reimbursed with about 14 € per examination, and the increase was slow from 56% in 2007 to 60% in 2009. Tympanometry was significantly more used in the Region of Southern Denmark (68%) (64 to 73), than in the North Denmark Region (61%) (54 to 68) and Region Zealand (48%) (42 to 53). Maybe the explanation for this difference is related to early research using tympanometry in both the Region of Southern Denmark[17,18] and the North Denmark Region[20] with participation of several trendsetting GPs in the regions.

WHAT IS AN APPROPRIATE NUMBER OF TYMPANOMETRY TESTS PER GP PER YEAR?

Nobody knows. In the clinics doing tympanometry the

Table 1 Frequent problems when using tympanometry

Type of frequent problems in 94 participants with some experience in tympanometry	Before the course *n* (%)	Six weeks after the course *n* (%)	Absolute improvement (95%CI)
Technical problems			
Getting a reliable curve written	38/93 (40.9)	10/94 (10.6)	30.20% (18 to 41)
Getting airtight sealing	32/92 (34.8)	9/93 (9.7)	25.10% (13 to 36)
Problems handling the tympanometer	21/91 (23.1)	5/92 (5.4)	17.60% (8 to 28)
Getting the children to cooperate	11/91 (12.1)	4/93 (4.3)	7.80% (0 to 17)
Understanding the results			
Understanding the meaning of the displayed figures and using them as quality assurance of the measurement	41/93 (44.1)	6/94 (6.4)	37.70% (26 to 48)
Understanding what the curves mean for the clinical decision	29/93 (31.2)	2/94 (2.1)	29.10% (19 to 39)

Table 2 Key messages about practical use of tympanometry

Airtight sealing between the tip of the tympanometer and the ear canal is important. If there are problems with sealing use a little water or cream on the tip, and more pressure towards the ear canal and at the same time pull the external ear up and backwards to stretch the ear canal. Alternatively use a bigger and more solid tip
In order to perform valid tympanometry the sound signal and air pressure have to pass through the ear canal. That means there must be no earwax blockade and the probe has to point in the direction of the ear canal. Partly ear wax occlusion does not disturb the measurement
The result of the tympanometry is a curve, called a tympanogram. The curve is characterized by the height of the curve (compliance), the flatness of the curve (gradient), and location of the peak on the x-axis (pressure). These three characteristics will be given as figures on the screen of the tympanometer, together with the curve (Figure 1)
The fourth value measured by the tympanometer is the ear canal volume. It is important to compare the volumes of left and right ear canal. Normally they will be nearly the same, if the same size of tip is used in both ears. A very small ear canal volume measurement can occur because of ear wax blockade or because the tip is pointing towards the wall of the ear canal. A high ear canal volume is seen in ears with perforation of the tympanic membrane or ventilation tube (grommet) in function. A blocked grommet gives a normal ear canal volume
The appearance of the curve and the figures has to fit (quality assurance)
Any not-normal curve should be repeated to exclude any artefacts
The curves are often classified according to Jerger/Fiellau-Nikolajsen in Type A = normal peaked curve with pressure between +50 and -99 daPa (decaPascal), Type B is a flat curve without peak, and Type C1 peak curve with negative pressure (-100 to -199), and Type C2 a peaked curve with negative pressure of -200 daPa or less (Figure 1)
Other curve types are also described. Type D is a very high curve (high compliance), meaning a very flexible tympanic membrane, often because of atrophy. Type P is a peaked tympanogram with positive pressure above +50 daPa, often because of acute otitis media with a bulging tympanic membrane
The tympanogram has to be compared with the history and objective findings
A flat tympanogram (Type B) means a stiff tympanic membrane and predicts fluid in the middle ear (a positive predictive value of more than 90%)
A normal tympanogram (Type A) means a middle ear without fluid and an intact tympanic membrane (a negative predictive value of more than 95%)
Types C1 and C2 tympanograms are often seen in children with a runny nose. These types are a stage "in between", *i.e.*, they can develop into a Type B or A tympanogram. In daily clinical practice C1 is often classified as normal. Some of the ears with Type C2 tympanograms have a mixture of air and effusion in the middle ear

median value was 28 tympanometry tests per year (interquartile range 13 to 53) per GP. The increase in the use of tympanometry was only between 1% and 4% per year. The variation in the use of tympanometry was surprisingly high, from none, to a maximum of more than 500 tympanometric examinations per GP per year. There may be several reasons for this variation. Education seems to be important.

No official recommendation on when to perform tympanometry has been made in Denmark, but a reasonable use could be whenever you are in doubt of the otoscopic findings, and that is very common. The 5% most frequent users of tympanometry seem to use it in about 2%-3% of their consultations, just the same number of ear diseases in most registrations in general practice[21]. This means that the tympanometer should be used more than 100 times per GP per year and in order to do that, a tympanometer within arm's reach is required in the clinic.

WIDEBAND ACOUSTIC IMMITTANCE (MULTIFREQUENCE TYMPANOMETRY)

Multi-frequency and multicomponent tympanometry added useful extensions to simple low-frequency tympanometry. They permitted the clinician to use probe tones that were higher in frequency than 226 Hz. This addition to the simple tympanometry proved useful for neonates and for any patient who did not produce obvious low-frequency tympanograms. Only a few of tympanometers used in general practice in Denmark can change probe tone to a higher frequency[22].

The next technical step is wideband tympanometry measurements provide a view of the acoustic response properties of the middle ear over a broad range of frequencies and ear-canal pressures. More research

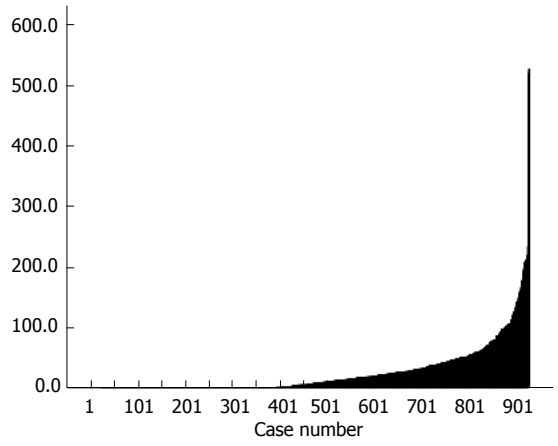

Figure 2 Number of tympanometries per GP in 2009. Figures from three Region with more than 900 GPs[19].

is need before the clinical implication of this technic can be outlined[23]. The price of the wideband acoustic immittance equipment of about 15000 € is a barrier for use in general practice.

PERSPECTIVE

An increased use of tympanometry in general practice will improve the diagnostic quality in children with middle ear problems and also improve the use of antibiotics, resulting in more appropriate antibiotic prescribing. More demand for tympanometry will hopefully reduce the price of the tympanometer, making it more accessible to GPs. That means that the use of tympanometry will be nearly as common as the use of otoscopy.

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P- Reviewer: Lee DH, Xu Z **S- Editor**: Ji FF **L- Editor**: A
E- Editor: Lu YJ

World Journal of Otorhinolaryngology

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DOI: 10.5319/wjo.v5.i2.58

World J Otorhinolaryngol 2015 May 28; 5(2): 58-64
ISSN 2218-6247 (online)

MINIREVIEWS

Tongue dysfunction in neurological and neuromuscular disorders: A narrative literature review

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Author contributions: Umemoto G solely contributed to this manuscript.
Conflict-of-interest: I certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

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Received: September 28, 2014
Peer-review started: September 29, 2014
First decision: December 27, 2014
Revised: February 18, 2015
Accepted: March 16, 2015
Article in press: March 18, 2015
Published online: May 28, 2015

Abstract

Evaluation of oral function is useful for tracking longitudinal changes in swallowing function. Using videofluoroscopic (VF) images, we can evaluate swallowing function, but it is extremely difficult to quantitatively evaluate the oral phase. Recently, several studies have tried to quantitatively assess tongue function by analyzing tongue movement on VF images, to measure tongue thickness by ultrasonography, and to measure tongue pressure as surrogate for tongue strength. In this review article, the current state of quantitative assessments of tongue function for identification and management of dysphagia in patients with neuromuscular and other neurological disorders (NNMD) has been outlined. Disturbed bolus transport in patients with NNMD has been quantitatively measured on VF images by analyzing tongue base movement and bolus transport from the mouth to the pharynx. Enlarged tongue in Duchenne muscular dystrophy patients were observed by measuring the transverse width of the tongue on ultrasound. Tongue pressures that were measured using a handheld probe in NNMD patients were less than half of those in healthy subjects. More studies are needed to develop guidelines what types of tongue dysfunction give an indication of adjusting diet and introducing tube feeding to NNMD patients.

Key words: Videofluoroscopy; Swallowing pressure; Tongue thickness; Tongue pressure; Neuromuscular and other neurological disorders

Core tip: Several studies have tried to quantitatively assess tongue function by analyzing tongue movement on videofluoroscopic images, to measure tongue thickness by ultrasonography, and to measure tongue pressure as surrogate for tongue strength. In this review article, the current state of quantitative assessments of tongue function for identification and management of dysphagia in patients with neuromuscular and other neurological disorders (NNMD) has been outlined. In the future, more studies are needed to develop guidelines what types of tongue dysfunction give an indication of adjusting diet and introducing tube feeding to NNMD patients.

Umemoto G. Tongue dysfunction in neurological and neuromuscular disorders: A narrative literature review. *World J Otorhinolaryngol* 2015; 5(2): 58-64 Available from: URL: http://

www.wjgnet.com/2218-6247/full/v5/i2/58.htm DOI: http://dx.doi.org/10.5319/wjo.v5.i2.58

INTRODUCTION

Evaluation of oral function is useful for tracking longitudinal changes in swallowing function. We performed a review of videofluoroscopic (VF) evaluation of swallowing to determine whether incomplete lingual range of motion corresponds to difficulties with bolus clearance, propulsion, and containment. There are various assessment tools for clinical practice of dysphagia, such as the Sydney swallowing questionnaire[1] and the MD Anderson dysphagia inventory[2] which were self-administered questionnaires, but it is extremely difficult to objectively and quantitatively evaluate the oral phase in swallowing function, because a self-administered questionnaire have difficulty in assessing symptoms of dysphagia in patients who are not consciously aware of swallowing dysfunction or aspirate silently. Especially, there is a high incidence of silent aspiration in patients with neuromuscular and other neurological disorders (NNMD)[3-7]. On the other hand, Han *et al*[8] proposed a 100-point VF dysphagia scale and established some subscales, such as "bolus formation" and "mastication," for oral phase. However, the grading standard for the subscales in the oral phase is vague, because of the complexity of masticatory or tongue function. In recent years, depending on development of image analyzing software, some studies tried to analyze kinematic swallowing movements. van der Kruis *et al*[9] reviewed researches biochemically analyzing hyoid bone displacement in VF. The tongue has an important role in mastication and swallowing because it transports food to the molars, initiates mastication, mixes foods with saliva, and propels a food bolus into the pharynx. Clinically, tongue function consists of various factors, including mobility, shape variation, and variable posture of the tongue[10]. Several recent studies have tried to quantitatively assess tongue function quantitatively by analyzing tongue movement based on VF images[11], to measure tongue thickness by ultrasonography[12], and to measure tongue pressure as surrogate for tongue strength[13,14].

In dysphagia in patients with NNMD, tongue dysfunction is an important factor, particularly in the oral phase. Parkinsonian patients exhibit tongue movement problems, and patients with muscular disorders show tongue weakness. These symptoms can cause aspiration or suffocation which may produce serious complications. Therefore, patients with NNMD need appropriate long-term follow-up for swallowing function in prevention of aspiration pneumonia and management of nutrition. However, because most of research studies concerning dysphagia have been conducted on patients with stroke, there is an absolute lack of information on dysphagia in patients with NNMD who have a chronic course.

In this review article, the current state of quantitative assessments of tongue function for identification and management of dysphagia in patients with NNMD has been outlined on the basis of some studies.

Methods

A literature review was completed on MedLine using the following search terms: tongue movements, tongue thickness, and tongue pressure in NNMD. A search for these words yielded 22 results from 1994 to 2014. The specific term "tongue function" search combined with "parkinsonian syndromes" yielded 31 results, "tongue movements" 28, "tongue thickness" 0, and "tongue pressure" 3. The specific term "tongue function" search combined with "neuromuscular diseases" yielded 58 results, "tongue movements" 39, "tongue thickness" 2, and "tongue pressure" 17. Of these articles 22 were considered relevant and included in this review.

EVALUATION OF TONGUE FUNCTION BY USING VF IMAGES

Bradykinesia and muscle rigidity observed in Parkinson's disease (PD) are considered causes of dysphagia. In most PD patients, swallowing dysfunction is related to abnormal movements associated with oropharyngeal dysfunction. In the oral phase in PD patients, related movement abnormalities include labial bolus leakage, incomplete or hesitant mastication, tongue tremor, tongue pumping, prolonged tongue elevation, and slowed and small mandibular excursion[15-18]. Troche *et al*[19] evaluated the swallowing function in the oral phase of PD patients using bolus transit time and the number of tongue thrusts on VF images, but only a few studies have quantitatively assessed mandibular and tongue movements in PD patients.

Nilsson *et al*[20] described that prolongation of the oropharyngeal transit time may reflect dysfunction caused by rigidity and motor deterioration and that rigidity and bradykinesia influence the motility function of the tongue. Johnston *et al*[21] suggested that the oral phase of swallowing is under voluntary control, and Nagaya *et al*[17] indicated that its alterations are related to bradykinesia and rigidity.

To perceive the tongue movement accurately, Steele *et al*[22] attached three transducer coils to the dorsal surface of the tongue. However, we tried to more conveniently demonstrate a relationship between food transportation and abnormal movements of the tongue by analyzing VF images of 30 PD patients[23]. Measurements of bolus transit and movements of the mandible and tongue were completed by analyzing the images of swallow trials frame-by-frame or in slow motion using dynamic image analysis software (Dipp-Motion Pro; Ditect, Tokyo, Japan). The movement of the point where the tongue line and the mandible line intersected was calculated on the Y-axis, which was based on two optional points on the cervical vertebrae, for evaluating the tongue

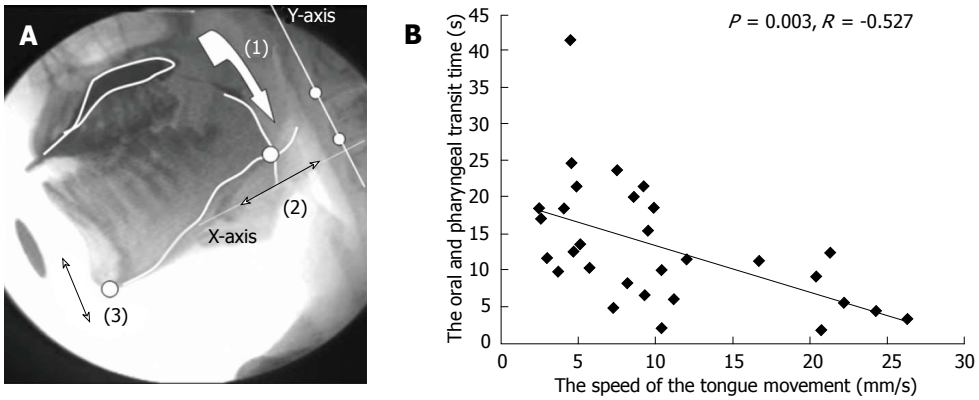

Figure 1 Analysis of tongue movement by using videofluoroscopic images. A: Analysis of videofluoroscopic (VF) images: (1) Oropharyngeal transit time, (2) Distance of tongue movement along the X-axis, (3) Distance of mandibular movement along the Y-axis; B: Distribution and relationship between the oropharyngeal transit time and speed of tongue movement[23].

movement (Figure 1 reproduced from Ref. [22]). The tongue movement distances (mm) were divided by the oropharyngeal transit time (s), which was obtained from a measurement of the speed of tongue movements. The average tongue movements were 15.4 ± 9.2 mm/s in the mild/moderate PD group (Hoehn and Yahr stages Ⅱ and Ⅲ) and 11.0 ± 7.2 mm/s in the advanced PD group (Hoehn and Yahr stages Ⅳ and Ⅴ). The oropharyngeal transit time of the advanced group was significantly longer than that of the mild/moderate group (P = 0.045). The speed of tongue movement negatively correlated with the oropharyngeal transit time (P = 0.003, r = -0.527). These results indicated the importance of the mandibular and tongue function in patients with PD.

Kitashima *et al*[24] also compared the swallowing function in PD patients quantitatively between DBS ON and OFF states after DBS surgery analyzing the speed of tongue movement in VF images and suggested that STN-DBS may influence the tongue movement.

Steele *et al*[22] also investigated tongue movement in patients with moderate PD[25] and reported that PD participants even in early stages showed smaller and more variable movements in the horizontal movement plane.

With regard to other types of NNMD patients, Higo *et al*[26] used VF images to assess swallowing function on the basis of parameters, such as tongue base movement and bolus transport from the mouth to pharynx, in patients with multiple system atrophy with a clinical predominance of cerebellar systems (MSA-C), myasthenia gravis (MG)[7], and amyotrophic lateral sclerosis (ALS)[27]. They observed disturbed bolus transport in patients with these NNMDs quantitatively in the studies. Patients in the early stage of MSA-C showed disturbance in bolus transportation from the oral cavity to the pharynx which will be caused by progression of cerebellar dysfunction and overlapped parkinsonism[26]. In patients with MG, a significant correlation between disturbance of laryngeal elevation and aspiration was found[7]. Most of ALS patients preserved normal upper esophageal sphincter relaxation, however some patients showed upper esophageal sphincter dysfunction[27].

MEASUREMENT OF TONGUE THICKNESS BY USING ULTRASONOGRAPHY

It is possible to assess tongue thickness of healthy persons or mild-stage neuromuscular patients by inspection or palpation to a certain extent, but it is difficult to evaluate tongue atrophy of patients with severe-stage disease because they have difficulty protruding their tongues. Furthermore, there are differences in tongue thickness between the rest and protrusion positions. During mouth opening, which results in contraction of tongue muscles to a certain extent, tongue muscles will waste away or become paralyzed. Liégeois *et al*[10] measured the lingual volume in healthy subjects using magnetic resonance imaging (MRI) and suggested significant correlations between tongue volume and body height, weight, and the body mass index (BMI)[10], but MRI technique is tedious and expensive. Therefore, to assess the thickness of an atrophied and paralyzed tongue in detail in patients who have difficulty protruding or moving their tongue, ultrasound examination is more convenient[12] and effective than is inspection or palpation alone.

The so-called "pseudohypertrophy" (enlargement) in Duchenne muscular dystrophy (DMD) patients was found in a former study that measured the transverse width of the tongue[28], but no reports have shown a relationship between weakness and pseudohypertrophy of the tongue. A previous study of Van Den Engel-Hoek *et al*[29] showed the possibility of ultrasound examination to differentiate patients with DMD from healthy persons measuring tongue thickness in five DMD patients. The tongue thickness of the DMD patients ranged from 43.9 mm to 68.4 mm, whereas the one in healthy individuals was 47.3 ± 20.1 mm. They again have recently reported on the convenience and good reproducibility of quantitative muscle ultrasound to measure tongue thickness in DMD patients[30], and that tongue thickness

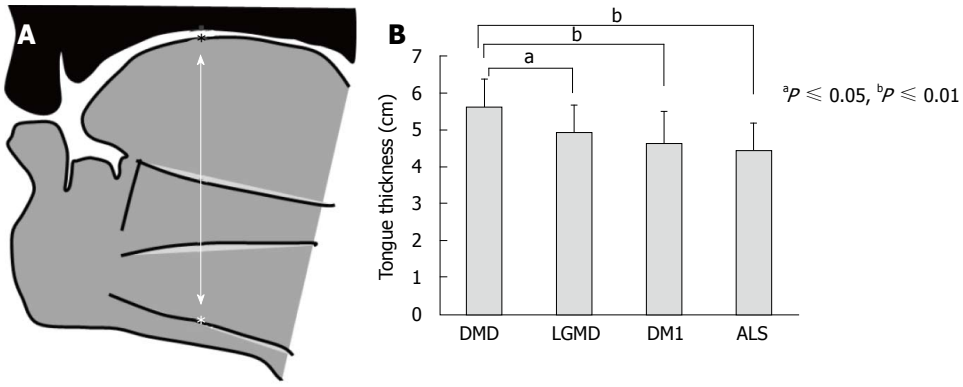

Figure 2 Measurement of tongue thickness by using ultrasonography. A: Measurement of tongue thickness, the upper boundary of the mylohyoid raphe, and the upper surface of the tongue; B: Comparison of tongue thickness among the four groups[31]. DMD: Duchenne muscular dystrophy; LGMD: Limb girdle muscular dystrophy; DM1: Myotonic dystrophy type 1; ALS: Amyotrophic lateral sclerosis.

increased in advanced stages. However, they have only evaluated patients with muscular dystrophy.

We also compared tongue thickness among 130 patients with DMD, limb girdle muscular dystrophy (LGMD), myotonic dystrophy type 1 (DM1) and ALS (Figure 2 reproduced from Ref. [31])[31]. The DMD group showed a tongue thickness of 56.3 ± 7.3 mm, which was significantly higher than those of other groups. The ALS group had a tongue thickness of 44.4 ± 7.2 mm, which was significant correlated with maximum tongue pressure.

"Tongue pseudohypertrophy" in DMD patients could be predicted to cause limited tongue movement because of the lack of space. We tried to describe the distinctive relationship between tongue thickness and tongue movement function in NNMD patients[31]. However, the increased tongue thickness was associated with a tendency towards an increase rather than a decrease the mobility of tongue root (P = 0.062, r = 0.414). The limitation of tongue movement may require several small movements of the tongue to transport the bolus through the oral cavity and pharynx.

EVALUATION OF TONGUE STRENGTH BY MEASURING TONGUE PRESSURE

Hayashi *et al*[32] measured tongue pressure by a method that used a handheld probe (JMS Co., Ltd., Hiroshima, Japan) (Figure 3B reproduced from Ref. [32]). The probe was assembled with a small balloon and pressurized with air at 19.6 kPa. Patients were asked to compress the balloon onto the palate for approximately 7 s using maximum voluntary effort of the tongue. The increase in the inner pressure of the balloon was taken to be the as tongue pressure. The average maximum tongue pressure in healthy people by age group was 41.7 ± 9.7 kPa for those in their twenties, 40.4 ± 9.8 kPa for those in their forties, and 37.6 ± 8.8 kPa for those in their sixties[33].

Using the JMS system, the average maximum tongue pressure was reported to be 15.3 ± 6.4 kPa in patients with spinal and bulbar muscular atrophy (SBMA) by Mano *et al*[34], and 11.8 ± 5.3 kPa in patients with SBMA and 15.0 ± 14.1 kPa in patients with ALS by Morimoto *et al*[35]. Using the Iowa oral performance instrument (IOPI)[13], Easterling *et al*[36] showed that tongue pressures ranged from 22.1 ± 11.8 kPa to 13.5 ± 10.9 kPa in patients with ALS, and Palmer *et al*[37] reported pressures that range from 19.5 ± 0.7 kPa to 26.9 ± 7.8 kPa in patients with oculopharyngeal muscular dystrophy (OPMD)[37]. These values were less than half of the ones of healthy people matched by age.

We compared dysphagia between 20 patients with DM1 and 24 patients with DMD on the basis of the maximum tongue pressure and the range of hyoid bone excursion during pharyngeal transit time, and the area of pharyngeal residue after the first swallow on VF images[38]. The range of hyoid bone excursion and area of pharyngeal residue of the DM1 group were significantly larger than those of the DMD group (P = 0.001, P < 0.001). However, there was no significant difference in maximum tongue pressures measured by JMS system between the DM1 group (12.0 ± 6.9 kPa) and the DMD group (13.6 ± 8.0 kPa).

Hori *et al*[14] used a tactile sensor system in the palatal plate to measure tongue pressure. This system could be useful for measuring tongue pressure and activity during oropharyngeal swallowing. Hamanaka-Kondoh *et al*[39] measured tongue pressure in DMD patients while they swallowed water and reported that the subsequent order of tongue-palate contact disappeared and the maximal magnitude and value of tongue pressure on the mid-anterior palate were smaller.

With regard to the relationship between tongue thickness, tongue pressure, and VF findings, we detected significant correlations between tongue thickness and maximum tongue pressure in the ALS group[31], and between range of hyoid bone excursion and maximum tongue pressure in patients with DMD but not with DM1[38]. These results suggest that the type of NNMD

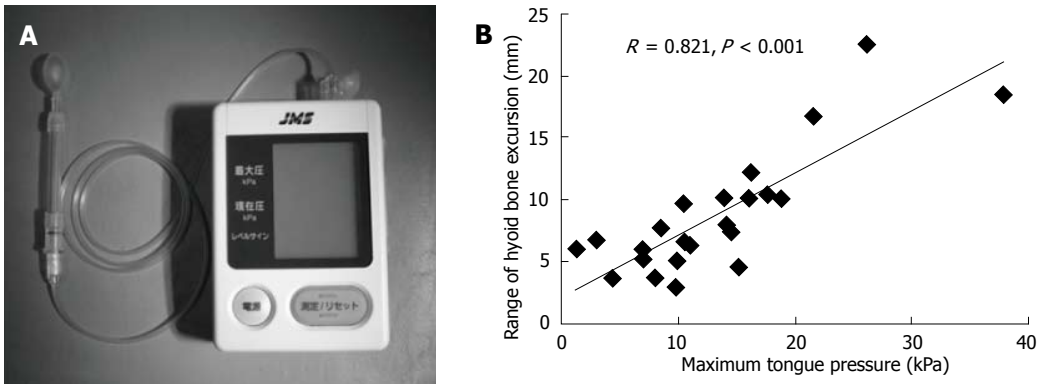

Figure 3 Measurement of tongue pressure as tongue strength. A: The tongue pressure measuring device (a handy probe) is shown; B: Correlation between the maximum tongue pressure and range of hyoid bone excursion in the Duchenne muscular dystrophy group[30].

may affect the relationship among these factors.

RELATIONSHIP BETWEEN TONGUE PRESSURE AND SWALLOWING PRESSURE

Finally, we can conveniently predict swallowing pressure from the data of tongue pressure data. The average values of swallowing pressure measured using manometry in the oropharynx were 131.4 mmHg in patients with PD in a study by Sung *et al*[40], 53.3 mmHg in patients with ALS in a study of by Higo *et al*[26], and 24 mmHg in patients with DM1 in a study by Modolell *et al*[41]. The swallowing pressures were lower in the PD patients than in the control group, and those in patients with ALS and DM1 were less than half of those in control group.

We analyzed the relationship between tongue and swallowing pressure in patients with NNMD. We measured the largest change of swallowing pressure in the hypopharynx and the upper esophageal sphincter (UES) of 24 DM1 patients during several swallowing events. In the DM1 group, the maximum tongue pressure (13.4 ± 6.8 kPa) significantly correlated with maximum swallowing pressure (53.3 ± 27.0 mmHg). This result suggests that reduced tongue and swallowing pressure may induce pharyngeal residue and increase the risk of aspiration and chocking on large pieces of solid food.

Certainly, an indication for an oral feeding tube should not merely depend on outcomes of the VF or the other assessments of tongue function. However, we expect to apply the data acquired by assessing tongue function to establishing a standard for introduction of tube feeding to patients. To develop such convenient guidelines, more data concerning tongue function and analysis of the relationship between tongue dysfunction and symptoms in the pharyngeal phase are needed.

DISCUSSION

There are few reviews that include extensive data on tongue movements, tongue thickness, and tongue pressure in NNMD. Through this review of the current literature, it is obvious that the data collected on tongue dysfunction in NNMD is limited in quality and quantity.

Despite the development of image analyzing software, there are few studies which analyze tongue movements in VF images of NNMD patients. However, to understand the progress of dysphagia in patients with NNMD for long periods, it is necessary to conveniently assess tongue movements at regular intervals. Although the method used by Umemoto *et al*[23] is thought to be useful for quantifying rigidity or bradykinesia of tongue movements in patients with parkinsonian diseases, more attempt to facilitate the method is requested in order to diffuse the analysis of tongue movements onto the daily clinical practice.

A change in volume of tongue in patients with DMD or ALS with progression of diseases is well known. However, we have not had such an objective data regarding the change. Although the previous study of van Den Engel-Hoek *et al*[30] showed that tongue hypertrophy was found 70% of 18 patients with DMD[30], they did not mention the relationship between tongue hypertrophy and tongue strength. More studies are needed to test the hypothesis that tongue muscle tissue is replaced with connective tissue or fat under a tongue hypertrophy. Regarding tongue atrophy in ALS patient, we could show a significant correlation between tongue thickness and maximum tongue pressure[31].

There are two methods of tongue pressure measurement, a balloon system for compression onto the palate[32,33] and a tactile sensor system in the palatal plate[6,39]. The balloon system is so convenient that many data of tongue pressure based on each NNMD have been collected[34-37], but the data are not reflected in dynamic water or food swallow. In the other hand, the tactile sensor system in the palatal plate is available during swallowing water or food. However, the penetration rate of the system is not sufficient and the number of report regarding NNMD using the system remain is just only one[39]. In the future, based on each NNMD and each stage of disease, more data is expected and the meaning

of data of each channel of the tactile sensor system should be clearly understood.

All data of analysis of VF images, tongue thickness, and tongue pressure are insufficient. In the future, to establish a better way of managing dysphagia in patients with NNMD, we should collect such data and draft a guideline on methods to adjust diet or introduce tube feeding for the patients. In the process of producing the guideline, we need to clarify the characteristic in tongue dysfunction of each NNMD and the relationship between the degree of tongue dysfunction and appropriate nutrition management.

CONCLUSION

Through some studies outlined in this article, changes in tongue movements, thickness, and tongue pressure with progression of NNMD have been suggested. More studies are needed to develop guidelines what types of tongue dysfunction give an indication of adjusting diet and introducing tube feeding to NNMD patients.

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DOI: 10.5319/wjo.v5.i2.65

World J Otorhinolaryngol 2015 May 28; 5(2): 65-70
ISSN 2218-6247 (online)

ORIGINAL ARTICLE

Retrospective Study

Nasopharyngeal carcinoma: Long term follow-up of 83 patients

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Author contributions: All authors contributed to the collection of data, the redaction of the manuscript and had approved this final version of the article.
Ethics approval: The study has been approved by the medical ethics committee of the military hospital, Tunis, Tunisia.
Informed consent: All the study participants provided informed written consent prior to study enrollment.
Conflict-of-interest: None.
Data sharing: Technical appendix, statistical code, and dataset available from the corresponding author at alimardassi@gmail.com.

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Telephone: +216-22-552252
Received: September 27, 2014
Peer-review started: September 28, 2014
First decision: January 8, 2015
Revised: February 13, 2015
Accepted: March 5, 2015
Article in press: March 9, 2015
Published online: May 28, 2015

Abstract

AIM: To analyzes the clinical, paraclinical, therapeutical and evolutive features of nasopharyngeal carcinoma (NPC).

METHODS: All the patients treated for a nasopharyngeal carcinoma between 2000 and 2013 in the Ear-Nose-Throat Department of the Military Hospital of Tunis, Tunisia were collected in this study. Eighty-three patients signed a written consent prior to study enrollment. The gender ratio (M/W) was 6.5 with a median age of 49 years (range 16-85). The median follow up time was 37 mo (18 to 108 mo). The evolution, during and after the end of therapy, was assessed on clinical biological and radiological exams. Different parameters were analyzed and compared to other series: complications of chemo and radiotherapy, recurrence of the disease, metastasis and overall survival rate.

RESULTS: Of the 83 patients of our study, 15% had T1 tumors, 20% had T2, 23% had T3 and 41% had T4 disease. At the time of diagnosis, 14% of the patients had a cranial nerve deficit. Only 12 patients had exclusive radiotherapy and the remaining of our patients had concomitant radio chemotherapy. Iatrogenic complications were diagnosed in 53% of the cases: radioepithelitis (28%), radiodermatitis (9%), xerostomia (17%), osteoradionecrosis (3%), cerebral radionecrosis (1%) and a pancytopenia (17%). The follow-up period varied from 18 to 108 mo (average: 37 mo). During the first six months after treatment, a persistence of the disease was found in 11% of patients, while a recurrence of the cancer was diagnosed in 6% and distant metastasis developed in 14% of the patients. Fifteen patients needed remedial chemotherapy for a relapse or metastasis and five had palliative chemotherapy for very advanced cases. We report 3 cases of death during the follow-up.

CONCLUSION: Despite its excellent radio-chemotherapy response, and general good prognosis, a careful follow-up of patients with NPC is necessary to detect and manage

any iatrogenic complication, locoregional recurrence or metastasis of the disease.

Key words: Nasopharyngeal carcinoma; Cranial nerve; Radiotherapy; Chemotherapy; Metastasis

Core tip: The carcinoma of the nasopharynx (NPC) is a particular form of cervico-facial cancers by its anatomic location, distinct pathologic features, ethnic pathogenesis and specific clinical outcome. This tumor is thought to have a good prognosis especially in undifferentiated and locally noninvasive forms. In this paper, we report our experience in the management of NPC and we report our results and complications during and after the end of therapy.

Mardassi A, Mathlouthi N, Hlila N, Halouani C, Mezri S, Zgolli C, Chebbi G, Ben Mhamed R, Akkari K, Benzarti S. Nasopharyngeal carcinoma: Long term follow-up of 83 patients. *World J Otorhinolaryngol* 2015; 5(2): 65-70 Available from: URL: http://www.wjgnet.com/2218-6247/full/v5/i2/65.htm DOI: http://dx.doi.org/10.5319/wjo.v5.i2.65

INTRODUCTION

Nasopharyngeal carcinoma (NPC) has unique epidemiological, clinical and evolutive features that differentiate it from other cervico-facial cancers[1]. It's known to be a multifactorial disease, most probably involving viral (EBV), genetic, dietary and environmental factors[1]. NPC can vary also histologically and the most frequent type remains the UCNT (undifferentiated carcinoma of the nasopharyngeal type). Every entity has similar endemic features with different incidences throughout the world[1]. Different studies found that this type of carcinoma is rare in Europe where the annual incidence doesn't exceed 1/100000. North African countries (Tunisia, Algeria, Morocco) have a higher incidence than Northern Europe (8 to 12 per 100000). The highest incidence is noted in South East Asia and in China with an annual incidence of 40 to 120 per 100000[2]. NPC differentiate itself from other head and neck carcinomas by its particular anatomic limits, viral carcinogenesis, remarkable radio and chemo sensitivity[3] and clinical outcome[4].

MATERIALS AND METHODS

We retrospectively reviewed the medical records of 83 patients with NPC diagnosed and treated at the Ear-Nose-Throat department of the Military Hospital of Tunis Tunisia between 2000 and 2013. The patients who weren't followed in our department and those who didn't sign the written consent were excluded from the study. The median follow up time was 37 mo (range: 18-108 mo). Parameters recorded were the clinical, paraclinical, therapeutical and evolutive features of the disease. The follow-up started by the detection of the complications of radio-chemotherapy and was prolonged during many months after the end of treatment.

Statistical analysis

In this retrospective and descriptive study, 83 patients have been reported. For quantitative data, the mean and the standard deviation have been obtained. For qualitative data, the percentage of each sub-group has been calculated. The statistical method is adequate because there was no comparison between the variables. *P*-value was not calculated since no hypotheses are tested in the study.

RESULTS

The main presenting symptom was epistaxis (50%), followed by a neck mass (43%), serous otitis media (38%) and headache (14%). Fourteen per cent of the patients had a cranial nerve deficit at the time of diagnosis: cranial nerve Ⅵ (40%), Ⅲ (38%), Ⅸ (4%), Ⅺ (4%) and Ⅶ (4%). Clinical cervical adenopathies were diagnosed in 36 patients (43%). A bilateral neck adenopathy was seen in 23% of the cases and 17% had neck nodes > 6 cm (N3). The diagnosis was made in all the cases through a nasal endoscopy with a histopathological exam that confirmed the type of the tumor. The histological type was an undifferentiated carcinoma (UCNT) in all the cases. All the patients benefited from a radiological exam to explore the tumor location and its extensions (Figure 1). A CT-scan was done in all the cases associated to MRI for 2 patients. Bony scintigraphy was indicated only in locally advanced tumors and in case of bone pain. Our patients were staged conforming to the American joint committee on cancer staging system 1997. Thus, 15% had T1 tumors, 20% had T2, 23% had T3 and 41% had T4 disease (Table 1).

The therapeutical approach was decided upon a multidisciplinary committee. Only 12 patients had exclusive radiotherapy (50-70 Gy delivered to the nasopharygeal region and the cervical node areas). The remaining of our patients had concomitant radio-chemotherapy consisting of 3 cycles of cisplatin and 5-Fluorouracil (5-FU) along with a total radiation dose of 70 Gy over 7 wk.

Complications due to the treatment (radiotherapy/chemotherapy) were diagnosed in 53% of the cases. After radiotherapy, 28% of patients developed a radioepithelitis, 9% developed a radiodermatitis, 17% a xerostomia, 3% an osteoradionecrosis and 1% cerebral radionecrosis (Figure 2).

During chemotherapy, a pancytopenia associated with fever was noted in 17% of the cases however, a toxic renal failure was diagnosed in one patient (Table 2).

The median follow-up period was 37 mo (18-108

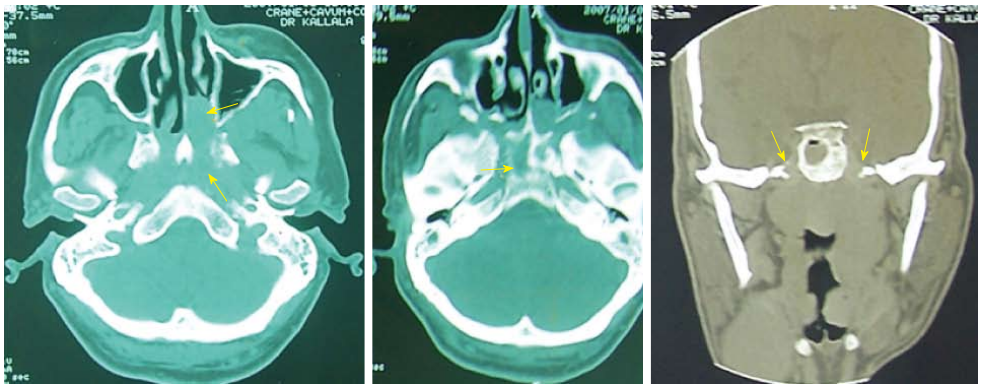

Figure 1 Undifferentiated carcinoma of the nasopharyngeal type of the nasopharynx T4 with lysis of the skull base.

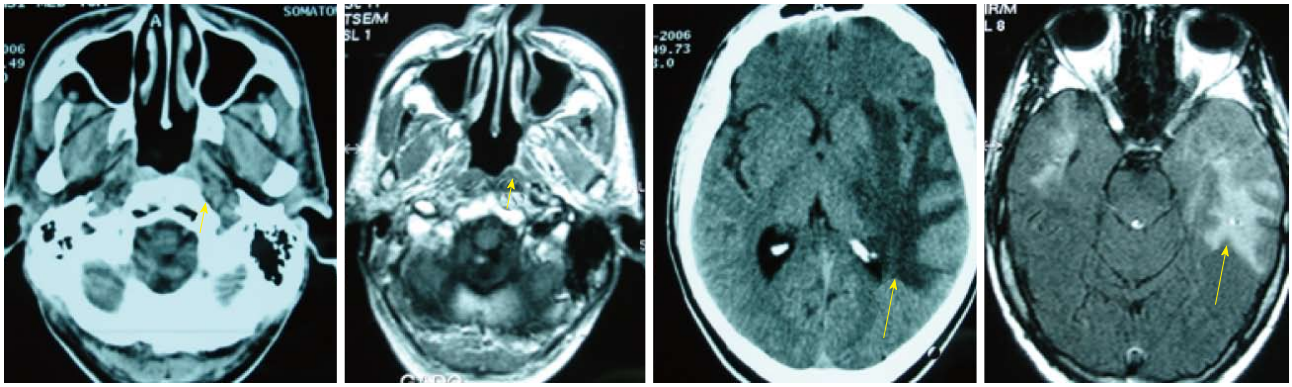

Figure 2 Cerebral osteonecrosis of the nasopharynx 3 mo after the end of radiotherapy.

Table 1 Distribution of tumor and nodal status

Stage	T1	T2	T3	T4	Total
N0	3	3	7	7	20
N1	5	5	5	7	22
N2	5	6	7	12	30
N3	0	3	0	8	11
Total	13	17	19	34	83
%	15.6	20.5	22.9	41	100%

Table 2 Iatrogenic complications of the treatment

Treatment	Complications	Nb	%
Radiotherapy	Radioepithelitis	23	28.4
	Radiodermatitis	7	8.8
	Xerostomia	14	17.64
	Osteoradionecrosis	2	2.9
	Cerebral radionecrosis	1	1.2
Chemotherapy	Pancytopenia	14	17.64
	Renal failure	1	1.2

mo). During this period, 10 patients were lost. The follow-up let us to seek in time the occurrence of a relapse of the disease or the appearance of distant metastasis.

After completion of treatment course, a persistence of the disease was found, at the first 6 mo in 11% of patients (4/9 received exclusive radiotherapy and 5/9 received concomitant radio-chemotherapy). A recurrence of the cancer was diagnosed in 6% of the patients after an average duration of 24 mo. All of them had received concomitant radio-chemotherapy.

Distant metastasis developed in 14% of the patients (Figure 3). The sites of these second localizations are resumed in Table 3. A concomitant radio-chemotherapy was indicated in all the cases. One patient had loco regional failure at the time of distant metastasis. The average time for the occurrence of metastasis was 27 mo (24 to 36 mo).

Fifteen patients needed remedial chemotherapy for a relapse or metastasis and five had palliative chemotherapy for very advanced tumors.

Two of the patients treated with remedial chemotherapy received a course of Capecitabine (Xeloda) used as rescue treatment. One patient died after a severe pancytopenia and one is still alive at the time of the study. During the period of follow-up, two other patients died after massive and multifocal metastasis.

DISCUSSION

NPC is a rare neoplasm that affects countries with different incidences. Its distribution on the world shows a high incidence in China[5] and a low incidence in

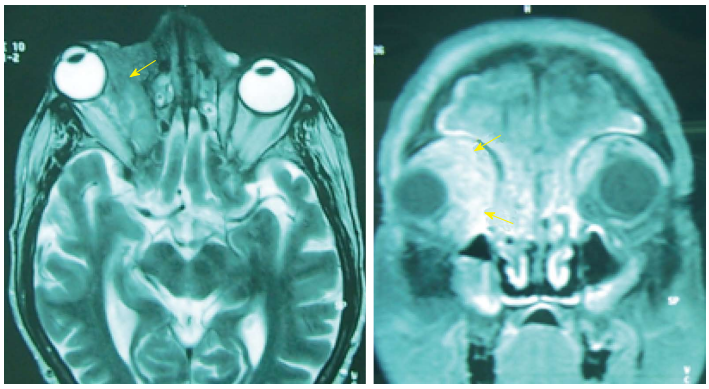

Figure 3 Orbital metastasis diagnosed 2 years after the end of chemotherapy for a T4 undifferentiated carcinoma of the nasopharyngeal type of the nasopharynx.

Table 3 The sites of metastasis

Site of the metastasis	*n*	%
Bone	3	3.6
Bone + liver	4	4.8
Orbit	1	1.2
Liver	2	2.4
Brain	1	1.2
Bone + liver + lung	1	1.2
Total	12	14.40

Table 4 Comparison with some southern Asian nasopharyngeal carcinoma series

	Our study	Wang *et al*[20] (a)	Goto *et al*[21] (b)	Kawashima *et al*[22] (c)
Stage T1	15.6	10	37	30
Stage T2	20.5	14	30	18
Stage T3	22.9	20	15	18
Stage T4	41	56	18	35
Overall survival rate	97%	88%	78%	87%
Metastasis	14%	18%	11%	24%

Western Europe and in the United States[6]. Concerning our country and in North Africa in general, the incidence of the tumor is nearly 4/100000[1].

In our study, the average age of the patients was 49 years with a sex-ratio of 6.5. These findings are not usually found in other countries since age distribution of NPC is different from one geographic region to another[7,8]. In Asian series, it is observed that cases occur mostly in the fifth and sixth decade of life[9]. However, a bimodal distribution is observed in North African series: a first peak around 20 years and a second one at 50 years of age[10,11].

Most times, the diagnosis of NPC is based on nasal symptoms: epistaxis and/or unilateral nasal obstruction. The disease is clinically obvious by the association to cervical lymph nodes, serous otitis, tinnitus, or signs of cranial nerve involvement[12]. However, these symptoms are not specific to NPC and atypical clinical manifestations are noted in aggressive or extensive forms of the tumor[1]. Therefore, it is imperative to have an accurate initial clinical exam of the cervical lymph node groups and the cranial nerve functions.

The staging and the accurate evaluation of NPC extension are based mainly on magnetic resonance imaging (MRI) and cervico-facial CT-scan[13]. Both imaging methods complement each other. In fact, CT detects better the lytic bone lesions, while MRI provides an accurate visualization of the tumor limits and the soft tissue extension[14].

NPC is considered as a radiosensitive tumor and, therefore, radiotherapy is the main treatment in almost all the cases. The local control rates in patients treated by radiotherapy remains generally acceptable with good results (80%-90%) in T1 and T2 stages, whereas worse outcomes are observed in locally advanced diseases with a higher risk of local recurrence and metastasis[15]. At a 5 year follow up, the authors reported various results with regard to the rate of relapse noted especially in locally extensive tumors[15-17]. In our study, the average period for the occurrence of recurrence was 24 mo and for distant metastasis was 27 mo.

When it comes to acute radiotoxicity, oral mucositis is the most frequent complication, followed by dermatitis and alterations in taste. The most frequent late toxicities are hyposialosis, xerostomia and dental complications which may be prevented by oral hygiene measures and fluoride use[18].

Regional recurrences and distant metastasis are not uncommon with NPC, even after completing the therapeutic approach[19]. Thus, a long term follow-up is mandatory for many years after treatment.

While comparing our results with the southern Asian NPC series, we noted that we had in our group better results in term of overall survival rate. The rates of metastasis were quite similar to those reported by Wang *et al*[20] and Goto *et al*[21] but lower than the results of Kawashima *et al*[22] (Table 4).

In case of recurrent and metastatic NPC, different protocols of chemotherapy have been used[23]. The most active chemotherapeutic agents include Cisplatin, Bleomycin, Doxorubicin and 5-Fu[24]. Chemotherapy can be neoadjuvant, adjuvant or concomitant to radiotherapy[1]. In our study, most of our patients were treated by concomitant chemo radiotherapy. This approach mainly aims to provide a much better control of the disease[25].

Bone and pulmonary metastases from nasoph-

aryngeal carcinoma are the most common type of distant metastasis and represent the main etiology of fatal outcome in these patients[26].

A second radiation therapy is often indicated in case of local relapse[1]. However, second-line chemotherapy with Cisplatin seems to be the most effective protocol to treat the NPC metastatic lesions even if this therapy doesn't improve significantly the long-term mortality[27].

New drugs are actually in trial stage for treating recurring and metastatic nasopharyngeal carcinoma: gemcitabine, capecitabine and paclitaxel[23,28]. A chinese study has shown that a monotherapy with capecitabine (Xeloda) has shown a significantly better survival rate[29].

NPC is a particular type of head and neck cancer characterized by a specific therapeutic approach and outcome. The most important issue with this tumor remains the high risk of relapse and/or distant metastasis especially in advanced stages of NPC. A long term follow-up is mandatory to detect early these complications.

COMMENTS

Background

Nasopharyngeal carcinoma is distinct from other head and neck carcinomas because of its particular anatomic location, distinct pathologic features, ethnic pathogenesis and specific clinical outcome.

Research frontiers

The study describes the results of the follow-up of patients treated for a nasopharyngeal carcinoma (NPC) in term of iatrogenic complications and long-term recurrence or metastasis of the disease.

Innovations and breakthroughs

The follow-up, during and after the end of treatment for NPC, must be careful and prolonged since locoregional recurrences or metastasis may occur after many years.

Applications

The authors must retain that despite its excellent radiochemotherapy response and general good prognosis, a careful follow-up of patients with NPC is necessary to detect and manage any iatrogenic complications, locoregional recurrence or metastasis of the disease.

Terminology

NPC: Nasopharyngeal carcinoma; UCNT: Undifferentiated carcinoma of the nasopharyngeal type; EBV: Epstein barr virus; CT: Computed tomography; MRI: Magnetic resonance imaging.

Peer-review

The author's present work showing the relationship of local recurrence or distant metastasis and the duration the treatment of chemotherapeutic drugs and radiation in NPC patients. They show a treatment failure in advanced stages of NPC patients with a high risk of local recurrence and distant metastasis. The findings are interesting.

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DOI: 10.5319/wjo.v5.i2.71

World J Otorhinolaryngol 2015 May 28; 5(2): 71-73
ISSN 2218-6247 (online)

CASE REPORT

Rare complication: Tapia's syndrome following shoulder surgery under endotracheal general anesthesia

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Ethics approval: Instution stated that it was not nececssary due to the retrospective nature of the report, therefore not obtained.
Informed consent: All study participants, or their legal guardian, provided informed written consent prior to study enrollment.
Conflict-of-interest: The authors certify that they have no affi liations with or involvement in any organization or entity with any fi nancial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affi liations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

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Received: September 26, 2014
Peer-review started: September 28, 2014
First decision: January 8, 2015
Revised: March 4, 2015
Accepted: April 10, 2015
Article in press: April 12, 2015
Published online: May 28, 2015

Abstract

Tapia's syndrome is a rare disorder, characterized with paralysis of extracranial part of Nervus Vagus and Nervus Hypoglossus, effecting the ipsilateral vocal cord and the tongue. This complication is usually related to intubation and head positioning during surgery. In this study, we report a case with Tapia's syndrome under general anesthesia, following arthroscopic shoulder instability surgery. Patient recovered as short as 3 mo, following complication.

Key words: Tapia's syndrome; General anesthesia; Shoulder arthrocopy; Complication

Core tip: Tapia's syndrome is a rare postoperative disorder. It is directly related to traction and hyperflexion of the head during surgery. Patients complain from dysarthria and hoarseness on the first post-operative day, which is related to traction and compression injury to N. Vagus and N. Hypoglossuss. Early diagnosis and treatment is the most important factor in the success of the treatment.

Şimşek E, Eren İ. Rare complication: Tapia's syndrome following shoulder surgery under endotracheal general anesthesia. *World J Otorhinolaryngol* 2015; 5(2): 71-73 Available from: URL: http://www.wjgnet.com/2218-6247/full/v5/i2/71.htm DOI: http://dx.doi.org/10.5319/wjo.v5.i2.71

INTRODUCTION

Tapia's syndrome is a rare disorder with simultaneous paralysis of N. Laringeus Recurrens (branche of N. Vagus) and N. Hypoglossus, affecting ipsilateral tongue and vocal cord. It was first described in 1904 by

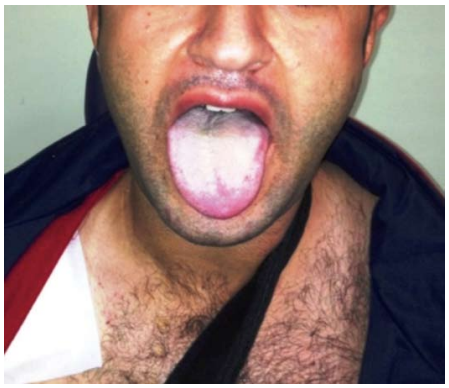

Figure 1 Tongue deviation due to left hypoglossal nerve paralysis.

Antonia Gracia, an otorhinolaryngologist[1,2]. Although the symptoms and findings may change according to the extent of the damage, common symptoms are: hoarseness, dysarthria and dysphagia[3]. Most common cause of this rare disorder is general anesthesia, however it may be encountered following trauma, tumors, surgery and infections affecting head and neck[4,5]. Pressure on the nerve due the intubation tube's cuff, hyperextension or excessive lateral positioning of the head are possible mechanisms[2]. Neuropraxy of the nerve usually resolve with medical therapy. Tapia's syndrome is mainly encountered unilateral[2,6].

CASE REPORT

Twenty-five years old, male patient was diagnosed as right shoulder anterior instability, due to multiple dislocations. Arthroscopic bankart repair was performed under general anesthesia with orotracheal intubation, in a beach-chair position (with a 50° of flexed table) without any external traction or positioning device. Head was secured with straps with proper supports. Surgery was performed in 2 h without any event. Patient complained dysarthria and hoarseness on the first postoperative day. Oropharyngeal examination revealed left hypoglossal nerve palsy (Figure 1). There was no uvula deviation or abnormality of the soft palate elevation. On endoscopic laryngeal examination with 70° rigid laryngoscope, there was left vocal cord palsy. There was no laryngeal or hypopharangeal edema or hematoma. No other pathological findings were observed on neurological, otorhinolaryngological, head and neck examination. No intracranial or vascular pathology was observed on cranial and cervical magnetic resonance (MR) imaging and MR angiography. Patient was diagnosed as peripheric type Tapia's syndrome and medical therapy was indicated. Intravenous prednisolone was initiated at a dose of 1 mg/kg per day and gradually decreased in a 10 d period. B1-B6 vitamin complex was admitted orally. There was no dysphagia or aspiration complaint, therefore a nasogastric tube wasn't utilized. We observed recovery starting on the 3rd day, and full recovery on the 10th week postoperatively.

DISCUSSION

Tapia's syndrome is a rare disorder effecting ipsilateral tongue and vocal cord, due to injury of N. Vagus and N. Hypoglossuss simultaneously. It may be presented as central type with contralateral hemiplegia in addition to effected 10th and 12th cranial nerves intracranially, or as peripheric type where related nerves are effected extracranially[1].

N. Laryngeus reccurrens and N. hypoglossuss are in close proximity at upper hypopharynx and lateral of lower hypopharengeal region, and N. Hypoglossus cross N. Vagus at the anterior surface of the transvers process of the 1st cervical vertebra. These anatomical locations are possible injury sites for both nerves[1,3,7].

Syndrome possibly occur with neuropraxy of the nerve due to compression, traction or disorders in vascularity. Compression of the intubation tube's cuff or laryngeal mask, traction related to anterior or lateral positioning of the head during surgery are possible neural injury mechanisms. Other causes are traumatic carotid artery injury, tumors located at submandibular or lateral cervical area and chronic infections[2,3,7-9].

Although it is commonly encountered unilateral, there are rare bilateral cases reported[6]. Orotracheal intubation is present in most of the cases in the literature. Syndrome encountered more frequently following rhinoplasty and septoplasty and less frequently following shoulder surgery, thoracotomy and cardiac surgery, osteosynthesis of the mandibula fracture and lateral cervical laminoplasty[2,3,5,7,10].

Symptoms vary according to the extent of the neural damage. Hoarseness, dysarthria dysphagia and aspiration are most common symptoms[3,5]. It is diagnosed with laryngeal and neurological examination. MRI and MRI angiography are required to exclude intracranial and other pathologies.

Treatment is supportive, with systemic corticosteroids, B vitamin complexes and speech therapy. As the reason for Tapia's Syndrome following anesthesia or surgery is neuropraxy, full clinical recovery is obtained in 3-4 mo. Faster recovery is also reported[3,5]. We observed fast recovery following medical therapy starting at the 3rd day.

Hoarseness, sore throat, dysphagia are common complications of general anesthesia. However, these complaints particularly following surgeries with cervical hyperextension or lateral positioning, may be related to Tapia's syndrome and medical therapy has to be initiated as soon as possible following diagnosis.

COMMENTS

Case characteristics

Common symptoms of Tapia's syndrome are hoarseness, dysarthria dysphagia and aspiration in the early post operative period.

Clinical diagnosis

Presented case complained of hoarseness and dysarthria in the first postoperative day. Patient did not have dysphagia or aspiration.

Differential diagnosis

In the selected cases, intracranial pathologies has to be assessed for central

type Tapia's syndrome.

Laboratory diagnosis

Patient was diagnosed using endoscopic laryngeal examination with 70° rigid laryngoscope. There was left vocal cord palsy.

Imaging diagnosis

No intracranial or vascular pathology was observed on cranial and cervical magnetic resonance (MR) imaging and MR angiography. No other radiological assessment was performed.

Pathological diagnosis

There was left vocal cord palsy. There was no laryngeal or hypopharangeal edema or hematoma. No other pathological findings were observed on neurological, otorhinolaryngological, head and neck examination.

Treatment

Intravenous prednisolone was initiated at a dose of 1 mg/kg per day and gradually decreased in a 10 d period. B1-B6 vitamin complex was admitted orally.

Experiences and lessons

Hoarseness, sore throat, dysphagia are common complications of general anesthesia. However, these complaints particularly following surgeries with cervical hyperextension or lateral positioning, may be related to Tapia's syndrome and medical therapy has to be initiated as soon as possible following diagnosis.

Peer-review

The case report is very interesting and offers to the reader useful information.

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P- Reviewer: Hatzopoulos S, Marandola M **S- Editor**: Ji FF
L- Editor: A **E- Editor**: Lu YJ

World Journal of Otorhinolaryngology

Submit a Manuscript: http://www.wjgnet.com/esps/
Help Desk: http://www.wjgnet.com/esps/helpdesk.aspx
DOI: 10.5319/wjo.v5.i2.74

World J Otorhinolaryngol 2015 May 28; 5(2): 74-77
ISSN 2218-6247 (online)

CASE REPORT

Synchronous carcinoma of head and neck: 2 cases report

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Author contributions: All authors contributed to the collection and the analysis of the data and to the redaction of the manuscript.
Ethics approval: The case report was approved by the medical committee of ethics of the Military Hospital Tunis, Tunisia.
Informed consent: The patient provided informed written consent prior to study enrollment.
Conflict-of-interest: Nothing to declare.

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Received: September 25, 2014
Peer-review started: September 25, 2014
First decision: January 8, 2015
Revised: January 23, 2015
Accepted: February 9, 2015
Article in press: February 11, 2015
Published online: May 28, 2015

Abstract

Multiple primary cancers are becoming an increasingly frequent situation and are often the source of many diagnostic and therapeutic difficulties. We report the case of two patients diagnosed with head and neck synchronous carcinomas. The first case is a 33-year-old man with a history of a keratinizing squamous cell carcinoma of the eye lid and who was operated 4 mo later from a mucoepidermoid carcinoma of the submandibular salivary gland. The second case is a 71-year-old woman who underwent a total parotidectomy for a mucoepidermoïd carcinoma of the left parotid gland and who consulted 2 mo later for epistaxis. The explorations concluded to a squamous cell carcinoma of the nasopharynx. The patient had a complementary radiotherapy. No local neither distant recurrence of the two tumors has been detected after a follow-up of 36 mo in the first case and 24 mo in the second one.

Key words: Carcinoma; Submandibular gland; Parotid gland; Nasopharynx; Radiotherapy

Core tip: Patients with head and neck cancer have a high risk of developing a simultaneous locoregional tumor. At the time of cancer diagnosis and during the follow-up, the clinician must search carefully for a second neoplasm which may reduce significantly the survival expectancy and have to be managed accurately. This paper describes and discusses, over two observations, the clinical and therapeutic features of these multiple primary cancers.

Mardassi A, Mathlouthi N, Hlila N, Halouani C, Mezri S, Zgolli C, Chebbi G, Ben Mhamed R, Akkari K, Benzarti S. Synchronous carcinoma of head and neck: 2 cases report. *World J Otorhinolaryngol* 2015; 5(2): 74-77 Available from: URL: http://www.wjgnet.com/2218-6247/full/v5/i2/74.htm DOI: http://dx.doi.org/10.5319/wjo.v5.i2.74

INTRODUCTION

Nowadays multiple primary cancers (MPC) are becoming an increasingly frequent situation, especially with the increased recovery rate of the first cancer and with the progress in diagnosis and therapeutic techniques in oncology, but also given an aging population

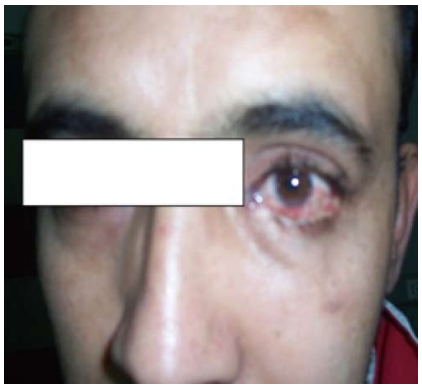

Figure 1 A keratinizing squamous cell carcinoma of the left lower eye lid after surgery.

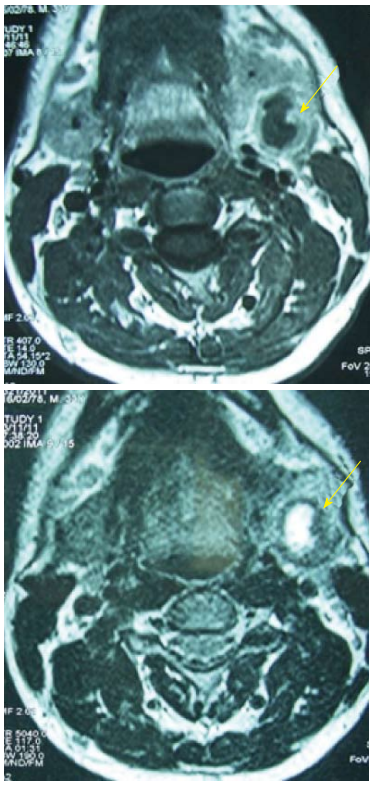

Figure 2 Magnetic resonance imaging showing a tumoral mass of the left submandibular gland with a heterogeneous signal in T1 and hyper signal in T2.

worldwide[1]. Billroth was the first to announce, in 1869, the upcoming of MPC. Then, it was Warren and Gates[2] in 1932, who established the criteria defining MPC. Thereby, the coexistence of multiple primary cancers in a single patient has been described in oncology literature with a frequency varying from 5.5% to 8.5% for all cancers combined[1]. We report in this article, the case of two patients diagnosed each with 2 different head and neck carcinomas.

CASE REPORT

Observation 1

A 33-year-old man was operated 4 mo ago for a keratinizing squamous cell carcinoma of the left lower eye lid T2aN0M0 (Figure 1). He presented to our ENT department with a one month history of a painless left submandibular swelling without salivary colic. Clinical examination found a 3 centimeter left submandibular firm mass, with no signs of inflammation and with no lymphadenopathy. Nasal endoscopy and the examination of the oral cavity didn't revealed abnormalities. The magnetic resonance imaging (MRI) showed an oval mass of the left submandibular gland, well defined, presenting with a heterogeneous signal in T1, hyper signal in T2 with both solid and liquid components and a raising signal after injection (Figure 2). The patient underwent a left submandibulectomy and a triangular lymphadenectomy of the same side. Histopathology concluded to a mucoepidermoid carcinoma of the submandibular salivary gland. The lymph nodes were not invaded. The staging of the tumor was completed by a CT-scan of the cervicofacial and thoracoabdominal region. The classification of the tumor was T2N0M0. After a follow-up of 3 years, no recurrence of the two tumors has been noted.

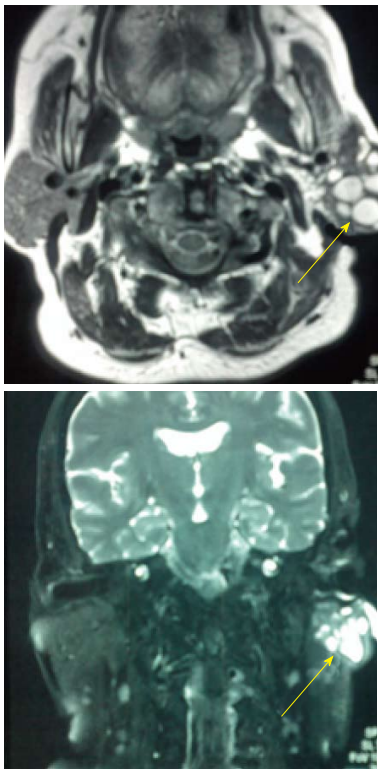

Figure 3 Magnetic resonance imaging in coronal and axial planes showing a multilocular tumor of the left parotid gland.

Observation 2

A 71-year-old woman, with a medical history of asthma and hypertension, underwent a total parotidectomy for a tumoral mass of the left parotid gland (Figure 3). The histopathological exam concluded to a mucoepidermoïd carcinoma (T2N0M0). She consulted 2 mo later for epistaxis, head ache and bilateral tinnitus. The endoscopic examination showed a burgeoning formation

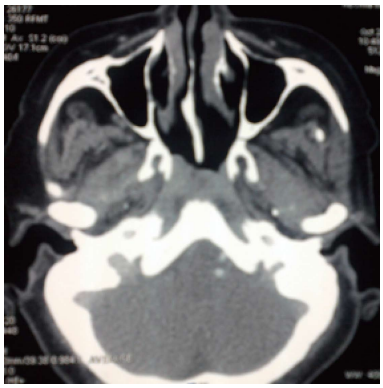

Figure 4 Computed tomography-scan in axial plane showing a tumoral mass of the right side of the posterior wall of the nasopharynx.

of the nasopharynx. The CT-scan showed a tumoral mass at the level of the right side of the posterior wall of the nasopharynx extending to the parapharyngeal fat (Figure 4). A biopsy of the mass was made under local anesthesia. The histological exam confirmed a moderately differentiated squamous cell carcinoma of the nasopharynx. The staging of the tumor was made after clinical examination: (cervical lymph node palpation, nasal endoscopy and examination of the oral cavity), CT-scan of the thoracoabdominal region and endoscopy of the upper digestive and respiratory tracts under general anesthesia. The tumor was classified as T2bN0M0. The patient was then treated by complementary radiotherapy (65 Gy). No local neither distant recurrence of the two tumors has been detected after a follow-up of 24 mo.

DISCUSSION

Multiple primary cancers (MPCs) represent 5.5% to 8.5% of all cancers described in english literature[3], whereas it only represents 7.5% of cancers in the head and neck[4]. According to the International Agency for Research on Cancer (IARC), MPCs are defined as two or more primitive cancers occurring within the same individual[2]. They can occur within the same organ or tissue, as they can affect different tissues or organs. They can correspond neither to an extension, nor to a relapse nor to a metastasis of the same primitive cancer[1].

According to Kilciksiz, MPCs can be divided into synchronous and metachronous tumors. Synchronous cancers are defined as the occurrence of a second primitive cancer within the first six months following the detection of the first cancer, whereas metachronous cancers appear within more than six months[3]. Both cases reported in our study correspond to synchronous cancers.

Within the past few decades, MPC's incidence has known a significant growth given the improvement of the general population survival rate, the improvement of the long term remission of patients suffering from cancer, and of course given the considerable development in the field of medical diagnosis and therapeutic techniques[1,5].

In this light, it is important to establish a complete initial assessment of each apparently isolated cancer in order not to miss out on a second metachronous or synchronous cancer. It is also important to conserve certain therapeutic methods such as radiotherapy to second primitive cancers[6,7]. For our second patient, a complementary radiotherapy was administrated after the diagnosis of the nasopharyngeal carcinoma. This therapy couldn't be used if the patient had been irradiated initially.

A meticulous clinical examination must be conducted to search for a second tumor near or far from the first tumor. In the case of head and neck cancers, cervical palpation, nasal endoscopy and accurate examination of the oral cavity must be undergone. Radiological exams and a biopsy must be done for each doubtful lesion[8].

A panendoscopy of oral cavity, pharynx, larynx, esophagus and bronchi must be performed to analyze and search for other lesions of the upper aerodigestive tract as well as to detect possible second malignancies[9].

Many cancers of the oral cavity, pharynx and larynx are related to tobacco intoxication. That's another argument justifying the investigations looking for a second localization of each primary tumor diagnosed in these sites.

The continued use of tobacco and alcohol gives rise to the risk of metachronous MPC. It may be critical for patients to limit their alcohol and tobacco use after the first head and neck cancer treatment to expect better prognosis by preventing additional metachronous MPC[6]. Mucoepidermoïd carcinoma is by far the most common type of second salivary gland tumour. The vast majority occurred in the parotid gland; only exceptionally have such tumours been reported in the submandibular gland or minor salivary glands[5].

According to many studies, the prognosis of patients with MPC is significantly poorer than those without MPC. This may reflect that these patients with multiple malignant tumors had restricted therapeutic options and in some cases the second tumor is much more aggressive than the first one[1,4].

After a diagnosis of a primary carcinoma of the cervicofacial region, a careful long-term surveillance is mandatory to detect, not only the complications of therapy or a local recurrence of the primary cancer, but also the appearance of a synchronous or metachronous locoregional carcinoma[5,8].

Multiple primitive cancers are an increasingly frequent clinical situation, thanks to the rise of the recovery rate of the first cancer, to the progress in the fields of diagnostic and therapeutic medicine and to the reinforcement of the long term surveillance of cancer patients. The clinician should always keep in mind the possibility of being confronted to multiple primitive cancers. A rigorous assessment of the disease and a regular follow-up of the patient are mandatory in order

to detect in time a second localization.

COMMENTS

Case characteristics

Case 1: He presented with a one month history of a painless left submandibular swelling without salivary colic. Case 2: She consulted for epistaxis, head ache and bilateral tinnitus.

Clinical diagnosis

Case 1: He has a 3 centimeter left submandibular firm mass, with no signs of inflammation and with no lymphadenopathy. Case 2: The endoscopic examination showed a burgeoning formation of the nasopharynx.

Differential diagnosis

Benign associated lesions.

Imaging diagnosis

Case 1: The magnetic resonance imaging showed an oval mass of the left submandibular gland, with a heterogeneous signal in T1, hyper signal in T2 with both solid and liquid components and a raising signal after injection. Case 2: The CT-scan showed a tumoral mass at the level of the right side of the posterior wall of the nasopharynx extending to the parapharyngeal fat.

Pathological diagnosis

Case 1: Histopathology concluded to a mucoepidermoïd carcinoma of the submandibular salivary gland. The lymph nodes were not invaded. Case 2: Histology concluded to a moderately differentiated squamous cell carcinoma.

Treatment

Case 1: The patient underwent a left submandibulectomy and a triangular lymphadenectomy of the same side. Case 2: The patient was treated by complementary radiotherapy.

Related reports

A second simultaneous tumor may be associated to a primary cancer of head and neck and may be searched initially and during the follow-up.

Term explanation

MRI: Magnetic resonance imaging.

Experiences and lessons

Through this case report, we retain that in front of cervicofacial cancers, we must not be focused only on the primary tumor but we must do an accurate clinical examination to search for simultaneous lesions which may change the therapeutic protocol and the life expectancy of these patients.

Peer-review

This study is clearly presented.

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P- Reviewer: Coskun A, Gouveris H **S- Editor**: Ji FF **L- Editor**: A **E- Editor**: Lu YJ

World Journal of Otorhinolaryngology

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Help Desk: http://www.wjgnet.com/esps/helpdesk.aspx
DOI: 10.5319/wjo.v5.i2.78

World J Otorhinolaryngol 2015 May 28; 5(2): 78-81
ISSN 2218-6247 (online)

CASE REPORT

Infrathyroidian hydatid cyst: Diagnostic difficulties and therapeutic management, a case report

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Author contributions: All authors contributed to the collection and the analysis of the data and to the redaction of the manuscript.
Ethics approval: The case report was approved by the medical committee of ethics of the military hospital Tunis, Tunisia.
Informed consent: The patient provided informed written consent prior to study enrollment.
Conflict-of-interest: Nothing to declare.

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Telephone: +216-22-552252
Received: September 27, 2014
Peer-review started: September 28, 2014
First decision: December 17, 2014
Revised: December 28, 2014
Accepted: February 9, 2015
Article in press: February 11, 2015
Published online: May 28, 2015

Abstract

Hydatidosis is a cosmopolitan anthropozoonose common to humans and many mammals. The cervical localization is rare even in endemic countries. We report a case of cervical hydatidosis located in the infra-thyroidian region. The diagnosis was suspected on clinical and radiological examinations (Ultrasonography, computed tomography-scan). The surgical removal of the cyst was difficult because of the inflammatory tissue around the mass. The confirmation of the diagnosis was obtained by the histopathological examination. During the follow-up, a local recurrence of the disease was diagnosed after 9 mo treated successfully by surgery.

Key words: Hydatidosis; Anthropozoonose; Cervical localization; Ultrasonography; Surgery; Histopathology

Core tip: Cervical hydatidosis is a rare clinical form of the anthropozoonose. The clinical presentation is nonspecific and may be diagnosed only after locoregional complications which can be life-threatening. This paper describes and discusses the clinical and therapeutic features of this disease. Imaging allows an adequate characterization of the mass and helps to planify the surgical approach. The prognosis is generally good provided regular and careful follow-up.

Mardassi A, Mathlouthi N, Mbarek H, Halouani C, Mezri S, Zgolli C, Chebbi G, Ben Mhamed R, Akkari K, Benzarti S. Infrathyroidian hydatid cyst: Diagnostic difficulties and therapeutic management, a case report. *World J Otorhinolaryngol* 2015; 5(2): 78-81 Available from: URL: http://www.wjgnet.com/2218-6247/full/v5/i2/78.htm DOI: http://dx.doi.org/10.5319/wjo.v5.i2.78

INTRODUCTION

Hydatidosis is a parasitic disease caused by the development in humans of the larval form of Taenia Echinococcus. It occurs predominantly in rural regions characterized by a significant development of sheep farming and humid climate favoring the survival of parasite eggs[1]. The cervical localization is rare even in

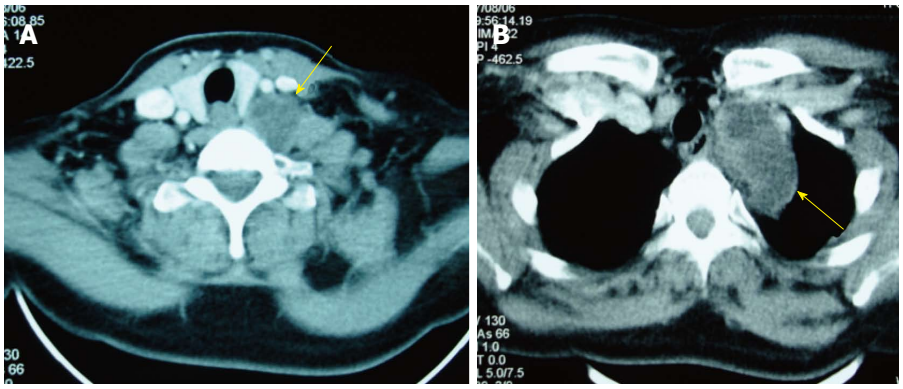

Figure 1 Computed tomography-scan showing a poly-lobulated mass developed at the base of the neck intimately to the thyroid gland and extending into the superior mediastinum.

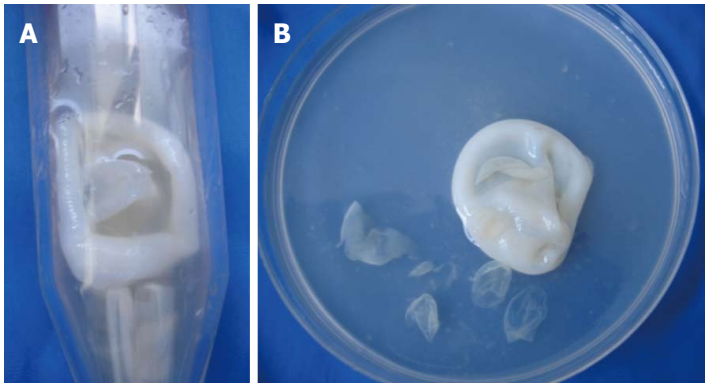

Figure 2 Hydatid vesicles obtained by an aspiration of the cystic mass.

endemic countries[1,2].

CASE REPORT

A 53-year-old woman, with a history of hypertension and depressive syndrome, presented with a cervical mass appeared one year ago, slowly growing, without pain, fever or weight loss. Neither rural origin nor contact with dogs has been reported. Physical examination found a 55 mm × 30 mm swelling located at the base of the neck. The mass was painless, mobile with no local inflammatory response or spasm of cervical muscles. Laboratory tests did not found an inflammatory syndrome and the chest X-ray was normal. Ultrasonographic examination showed two masses of 24 and 32 mm, with a necrotic center. The cervico-thoracic computed tomography (CT)-scan showed a pseudo-tissular mass poly-lobulated developed at the base of the neck intimately to the thyroid gland and extending into the superior mediastinum (Figure 1). Exploratory cervicotomy was performed and, preoperatively, we discovered a cystic mass, surrounded by a fibrous hull, in contact but independent of the thyroid gland, which extended inferiorly behind the sternum. Puncture of the mass brought translucent vesicles suggesting a hydatid cyst (Figure 2). The removal of the cyst with its fibrous hull was difficult because of the inflammatory reaction around the cyst. A cleaning by a hypertonic saline solution has been done to remove all the vesicles. The thyroid gland was not removed since it seemed normal. Post-operatively, the patient has received Albendazole: 400 mg orally twice a day for 3 mo. An abdominal ultrasound was done and revealed no evidence of other involvements. The evolution was marked by a local recurrence of the hydatid cyst 9 mo later. The patient has been reoperated in collaboration with a cardiovascular surgeon. Histopathological examination of the surgical specimen confirmed the diagnosis. The outcome was favorable after a follow-up of 2 years.

DISCUSSION

Hydatidosis is a cosmopolitan anthropozoonose common to humans and many mammals. It occurs mainly in some Mediterranean countries, South America, Australia and Central Asia[1]. The sheep is the intermediate host and the dog is the definitive one. Humans are accidently infected by oral ingestion of tapeworm eggs in contaminated food or water or direct contact with host (licking, caressing)[2]. The parasite borrows the portal system, arrested in 80% of cases in the liver or lung[3]. Once these two filters (liver and lung) exceeded, it may be located in any other region of the body[4]. Cervical hydatid cyst is a rare entity whose frequency does not exceed 1% of all hydatid localizations[1,2]. In Tunisia, two studies on hydatidosis have been reported, those of Ben Ayed *et al*[5] and Zargouni *et al*[6], they estimated the incidence of head and neck localizations at 1.06% and 0.75% respectively. Cervical hydatid cyst presents as a firm, painless mass, slowly growing, in a patient whose general condition is retained[1]. Palpation should be cautious because of the risk of rupture[7]. It is a rarely

evoked diagnosis, even in endemic areas, especially in the absence of other associated localizations. Signs of irritation or compression of adjacent organs may be seen[7]. Zerhouni *et al*[8] reported a case of cervical hydatidosis revealed by laryngeal dyspnea. Signs of cracking or rupture may also occur[1]. Laboratory tests are often negative, apart from a non-specific hypereosinophilia. Serological tests could be contributing when positive[4].

The place of imaging is important in cervical hydatidosis not only to approach the diagnosis, but also in search of other involvements, especially the liver, lung or spleen[9]. Cervical ultrasound is most often the diagnostic key[4,10]. It specifies the fluid nature of the swelling and its place[4,10]. Sensitivity is about 95% and may reach 100% in the forms with vesicles[4]. It shows a similar sonographic appearance to the other hydatid cysts, especially the hepatic one, corresponding to the classification of Gharbi[4,7]. Toward such masses, we can also discuss a cystic hygroma, a cold abscess, a chronic hematoma or an epidermal cyst. The contribution of CT scan is considerable especially in these cases. It contributes to the positive diagnosis by specifying the nature of the mass, its topography, its size and its relation with adjacent structures[4,10]. It shows a fluid density mass, with net and regular limits, unmodified by the contrast[7]. MRI provides better locoregional anatomical study and a detailed analysis of the cystic walls because of its multiplanar character and highest contrast resolution[10]. Hydatid cyst is hypointense on T1 and hyperintense on T2-weighted sections[7]. Daughter vesicles are more hypointense than the rest of the cystic fluid on T1-weighted images and hypo- or hyperintense on T2, according to the presence or absence of scolex[10] which are the features of hydatid cysts but are present in only 30% of cases[11]. The cyst wall appears on T2-weighted images divided into two layers of different signal. The peripheral layer, corresponding to the pericyst is hyperintense on T2 and takes Gadolinium contrast. The inner layer is T2 hypointense without contrast enhancement and corresponds to the fibrous tissue[7,10]: that's the "Rim sign" described by Von Sinner[7].

A chest-X-ray and abdomino-pelvic ultrasound should be performed to look for other involvements[2]. In our patient, no other localization was found.

The fine needle aspiration cytology (FNAC) can contribute to the diagnosis by showing a crystal clear fluid, feature of hydatidosis. However, this review is contested by some authors because of the risk of cracking, dissemination, anaphylactic reaction and sometimes fatal infectious inoculation[2]. It was not performed in our case.

Only histopathological examination allows diagnosis. It shows three layers of hydatid cyst. The inner most germinal layer is thin and translucent on gross. The embryonic tape worm, scolices, develops from an out pouching of the germinal layer and form hydatid sand, settling into the dependent parts of the cyst. The cyst fluid is crystal clear, as it is transudate of serum containing proteins and is therefore antigenic. The middle laminated membrane is white 2 mm thick and is easily ruptured. The outer layer or pericyst is a rigid protective layer with a few millimeters thickness, representing response of the host to the parasite[12]. Surgical removal is the single effective treatment of cervical hydatidosis[12]. It is recommended to protect the operative field with a scolicidal solution to avoid the spread of scolex in case of cyst's accidental rupture[13]. Some authors recommend intracystic injection of scolicidal agents such as hypertonic saline[8,14]. The complete removal carrying away the closed cyst (without rupture) is the method of choice[2,7]. Subtotal pericystectomy or the protruding dome resection are indicated when intimate contact between the cyst and neurovascular axes[7]. Medical treatment with albendazole is reserved for multifocal cysts, non-removable ones, non-operable patient, or per-operatory cyst rupture[2,13]. Rigorous postoperative monitoring at short and long term is necessary. It is mainly based on ultrasound at the rate of 3 to 6 mo to a year to examine the state of the residual cavity[15]. CT scan is reserved for doubtful cases of recurrence and monitoring of large residual cavities[15]. Serology is practiced 6 mo to one year after surgery. The persistence of high levels of antibodies and especially ascension 6 mo to 1 year after surgery testifies to the existence of other unknown cysts, a recurrence or a secondary infection[4]. In our case the monitoring was clinical and ultrasonographic and revealed a recurrence of the disease after 9 mo.

Cervical hydatid cyst is a rare entity even in endemic countries. It is a benign disease but a potentially serious affection by its possible complications. It must be considered in any cystic cervical mass especially in the presence of other associated localizations. Imaging is of a considerable interest in the diagnostic orientation, but the confirmation is obtained by histopathological examination. The basic treatment remains surgical. The prognosis is generally good provided regular and careful monitoring.

COMMENTS

Case characteristics

A 53-year-old woman, with a history of hypertension and depressive syndrome, presented with an isolated cervical mass appeared one year ago.

Clinical diagnosis

Physical examination found a 55 mm × 30 mm swelling located at the base of the neck. The mass was painless, mobile with no local inflammatory response.

Differential diagnosis

Congenital cysts of the neck, malformations, thyroid nodules.

Laboratory diagnosis

Laboratory tests did not found an inflammatory syndrome.

Imaging diagnosis

Ultrasonographic examination showed two masses of 24 and 32 mm, with a necrotic center. The cervico-thoracic computed tomography-scan showed a pseudo-tissular mass poly-lobulated developed at the base of the neck

intimately to the thyroid gland and extending into the superior mediastinum.

Pathological diagnosis

Puncture of the mass brought translucent vesicles suggesting a hydatid cyst. Histopathological examination of the surgical specimen confirmed hydatidosis.

Treatment

Cervicotomy was performed by removing the cystic mass with its fibrous hull. A cleaning by a hypertonic saline solution has been done to remove all the vesicles. Post-operatively, the patient has received Albendazole: 400 mg orally twice a day for 3 mo.

Related reports

In countries with high incidence of hydatidosis, people with cervical cystic masses may be tested for hydatidosis serology in order to assess the diagnosis preoperatively.

Term explanation

FNAC: The fine needle aspiration cytology is an inexpensive and safe technique that contributes to the diagnosis of disease sites.

Experiences and lessons

Through this case report, we retain that hydatidosis must be evoked as a differential diagnosis in front of cystic masses of the neck. Surgery must be accurate to remove all the cystic membrane to avoid the recurrence and the locoregional complications of the disease.

Peer-review

Good.

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P- Reviewer: Ghartimagar D **S- Editor**: Ji FF **L- Editor**: A
E- Editor: Lu YJ

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