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ABOUT COVER

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ORIGINAL ARTICLE

Retrospective Study

Recurrent oropharyngeal cancer: Analysis of surgical treatment outcomes

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Abstract

BACKGROUND

The main goal of our research is to introduce transoral robotic surgery and laser resection (TLR) as a considerable way of treating patients with recurrent oropha-

ryngeal malignancies.

AIM
To develop a foundation of minimally invasive transoral surgical technique for patients with oropharyngeal recurrence.

METHODS
This study prospectively and retrospectively included patients with recurrent tumors from 2003 to 2018. Subjects were allocated into two groups: (1) Group I; underwent TLR; and (2) Group II (control); underwent open surgeries of varying volume. Evaluation was done with intraoperative blood loss, postoperative infection incidence, and quality of life using the scale for patients with head and neck tumors known as the Functional Assessment of Cancer Therapy-Head & Neck Scale.

RESULTS
One-hundred and forty one patients were included (103 males and 38 females), in 82 cases (85.4%), a recurrent tumor developed earlier than a year after primary tumor therapy; forty-six were in group I and 69 in group II, age ranging from 18 years to 86 years (average: 57.6 years). The first group showed a statistically significant less amount of blood loss and a decreased incidence of infectious complications ($P < 0.05$). Additionally, there was a significant difference in functional outcomes (quality of life scores) but no significant difference in survival curves.

CONCLUSION
In properly elected patients, TLR is not just reasonable but tends to be a favorable alternative for recurrent oropharyngeal cancers compared to the outcomes of the open surgery group.

Key Words: Oropharyngeal cancer; Transoral laser resection; Open surgery; Recurrent tumor; Oropharyngeal squamous cell carcinoma

Core Tip: Our study included a large retrospective part and compared two prospective groups of patients, who were subjected to open surgery or transoral robotic surgery and laser resection (TLR). The results show that in properly elected patients, TLR is not just reasonable but has a tendency to be a favorable alternative for recurrent oropharyngeal cancer compared to the outcomes of the open surgery group. The use of TLR in our study was associated with shorter operating times, lower blood loss counts, lower postoperative complication rates, a higher quality of life and a proportionate 2-year survival when compared with open surgery performance rates. As open surgery was thought for decades to be the mainstream treatment approach for recurrent tumors of the oropharyngeal zone, considerable experience has accumulated which indicates that this management bears unfavorable functional outcomes. The results of our comparative study defined a higher quality of life in patients who underwent TLR.

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INTRODUCTION

Malignant tumors of the oral cavity and oropharynx compose around 2%-5% of all malignancies. The current mainstream, first-line treatment for oropharyngeal squamous cell carcinoma (SCC) is function preserving chemoradiation. Neoadjuvant chemoradiotherapy salvage surgery for local recurrent tumor is widely deemed as the only possible treatment strategy that may establish curative effect. The possibilities of life-saving operations in such cases are limited by the complexity of surgical access, high probability of serious complications, proximity to vital organs and structures, and the general health of patients during relapse. Unfortunately, salvage interventions which incorporate open surgical access to the head and neck region are associated with prolonged hospital stays, high intraoperative blood loss counts, decreased survival prognosis, and quality of life. These interventions also may require additional bone resection and/or a reconstructive component, which incorporates a regional pedicle flap or a microsurgical flap.

Recently evolving transoral robotic surgery and transoral laser microsurgical resection (TLMR) have a potential to overcome the morbidities associated with open surgery. Published academic data suggests that a considerable fraction of subjects with recurrent oropharyngeal cancers may benefit from performance of TLMR. Currently very limited data is available on the comparison of surgical, oncological and functional results in patients with recurrent oropharyngeal SCC treated with TLMR and with those treated by traditional open surgical approaches. The purpose of this study was to

compare surgical, functional and oncological outcomes in patients undergoing open surgery *vs* TLMR, and to determine the role of minimally invasive surgical techniques in the management of recurrent oropharyngeal tumors.

MATERIALS AND METHODS

All study participants provided informed written consent prior to study enrollment for the surgical procedure

According to the medical archive, from 2003 to 2018, 141 patients with recurrent oropharyngeal tumors were observed at the N.N. Blokhin National Research Center of Oncology (BNRCO). The clinical data of the patients were analyzed retrospectively and prospectively.

The following clinical parameters were evaluated in all patients: Sex, age at the time of diagnosis, localization of the primary tumor, method of treatment of the primary tumor, morphological properties of the primary tumor, presence of adjuvant therapy, date of the first progression after treatment of the primary tumor, localization of metastases, systemic chemotherapy for recurrence of the primary tumor and realized metastases, both regional and long-term, overall survival and progression-free survival on the background of treatment. The date of death and disease progression was estimated according to the data provided by the out-patient monitoring department. The date of the visit was established by analyzing outpatient records of the patient's visit to the out-patient department of BNRCO.

To conduct a comparative analysis of the effectiveness of TLMR compared to salvage surgery, a comparison group was identified and included 25 patients. To assess operative outcomes, intraoperative blood loss counts, and postoperative infection incidence were compared between the two study groups. Functional results were evaluated by comparative assessment of the quality of life by the Functional Assessment of Cancer Therapy-Head & Neck Scale in the groups of TLMR and open surgery.

Statistics (was performed by Microsoft Excel 2022, SPSS 22 StatSoft Inc)

Life expectancy and time to progression were evaluated using the Kaplan-Mayer method and compared by a log-rank test. The χ^2 tests and Fisher's exact criterion were used to verify the validity of differences in the values of features in the groups. The differences were considered statistically significant at $P < 0.05$. The correlation was carried out using the Pearson correlation coefficient and Spearman's rank correlation coefficient. The Cox proportional regression analysis model was used to assess the independence of traits and calculate comparative risk.

RESULTS

Patient population

The study included 141 patients who underwent treatment at BRNCO and underwent surgery for recurrent oropharyngeal tumors. Twenty-one (14.9%) patients received primary treatment at our institution and 120 (85.1%) patients were treated in other medical institutions. Of the examined patients, 38 (27.0%) were women, 103 (73.0%) were men. The mean age of the enrolled patients was 57.6 (52.0; 66.5) years, minimum 18, maximum 86 years (Table 1).

DISCUSSION

Chemoradiotherapy, as the initial function preserving treatment mode for oropharyngeal cancers, has shown good effect, however, up to one third of cases demonstrate locoregional relapses. Until recently, the only way to treat such cases was open access surgery. However, oncologic results of such interventions are modest. Five-year survival rate was reported to range between 26% and 49.1% for patients who underwent salvage surgery[1,2].

Advancements in endoscopic surgery have led to the development of minimally invasive techniques that enable transoral surgery as an alternative to transmandibular and or transcervical approaches. Transoral microsurgery laser resection (TLRM) was the first minimally invasive technique to be applied to the oropharynx. High-volume TLRM surgeons have reported favorable oncologic outcomes using TLRM in cases of oropharyngeal recurrence. However, the technical challenges of this method have limited widespread adoption outside of select large academic centers. The target of a transoral approach is different in patients with recurrent tumors of the oropharynx. In these cases, surgery may be the only available means of treatment or a method for treatment intensification. Small-volume recurrent tumors can be managed by a transoral approach without reconstruction. Hence, considering the effect of prior radiation on wound healing and the risk of life threatening complications (bleeding) after transoral surgery, large-volume recurrent oropharyngeal tumors may require simultaneous microvascular reconstruction (Table 2) (Figures 1 and 2A).

Our study included a large retrospective part and compared two prospective groups of patients, who were subjected to open surgery or TLRM. The results show that in properly elected patients, TLRM is not just reasonable but has a tendency to be a favorable alternative for recurrent oropharyngeal cancers compared to the outcomes of the open surgery group. TLRM in our study was associated with shorter operating time, lower blood loss counts, lower postoperative complication rates, higher quality of life and proportionate 2-year survival when compared with open surgery performance rates. Since open surgery was the mainstream treatment approach for recurrent tumors of the oropharyngeal zone for decades, considerable experience has accumulated which indicates that this management bears

Table 1 Distribution of patients by sex and age

Age in years	Woman, *n* = 23	Men, *n* = 73	Total
30-40	2 (5.3)	9 (8.7)	11
41-50	7 (18.4)	12 (11.7)	19
51-60	10 (26.3)	43 (41.7)	53
61-70	13 (34.2)	35 (34.0)	48
> 70	6 (15.8)	4 (3.9)	10
Me [25%; 75%]	59.7 ± 2.1 [52.0; 67.0]	56.8 ± 1.9 [52.0; 66.0]	57.6 ± 2.0 [52.0; 66.5]

Data are *n* (%).

Table 2 Surgical approaches used depending on the volume of soft tissue surgery (resection)

Surgical approach	Transoral laser resection	Median mandibulotomy	Segmental resection	Total
Resection of the lateral wall of the pharynx	1 (3.0)	7 (20.0)	4 (15.4)	12 (17.4)
Resection of the base of the tongue	1 (3.0)	2 (5,7)	0 (0.0)	3 (4.3)
Resection of the lateral wall of the pharynx and soft palate	1 (3.0)	8 (22.9)	1 (3.9)	10 (14.5)
Resection of the base of the tongue and the lateral wall of the pharynx	3 (9.1)	9 (25.7)	13 (50.0)	25 (36.2)
Resection of the root of the tongue, lateral wall of the pharynx and cheek	1 (3.0)	1 (2.9)	4 (15.4)	6 (8.7)
Resection of the lateral wall of the pharynx and hard palate	0 (0.0)	1 (2.9)	0 (0.0)	1 (1.4)
Resection of the base of the tongue, lateral wall of the pharynx, cheeks and soft palate	1 (3.0)	3 (8.6)	1 (3.9)	5 (7.2)
Resection of the base of the tongue, resection of the lateral wall of the pharynx, cheeks, soft palate and hard palate	2 (6.1)	2 (5.7)	3 (11.5)	7 (10.1)
Total	10 (14.5)	33 (47.8)	26 (37.7)	69 (100)

Data are *n* (%).

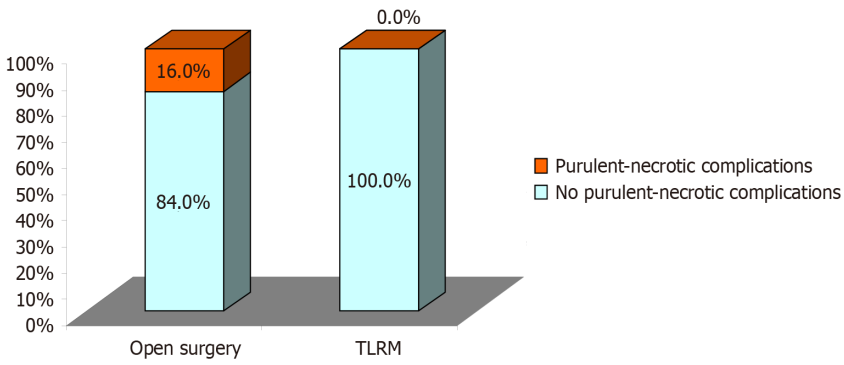

Figure 1 Development of purulent-necrotic complications depending on the type of operation. TLRM: Transoral microsurgery laser resection.

unfavorable functional outcomes. The results of our comparative study defined higher quality of life in patients who underwent TLRM. (Figures 2B and 3).

Postoperative surgical complications are observed occasionally after salvage open surgery of recurrent oropharyngeal cancers, these may include infectious complications as well as wound healing problems. This was supported by our observations. The complication rate seen in the TLMR group was lower than for open surgery. Such parameters as blood loss counts, operative time and occurrence of postoperative infectious complications were all lower in the TLRM study

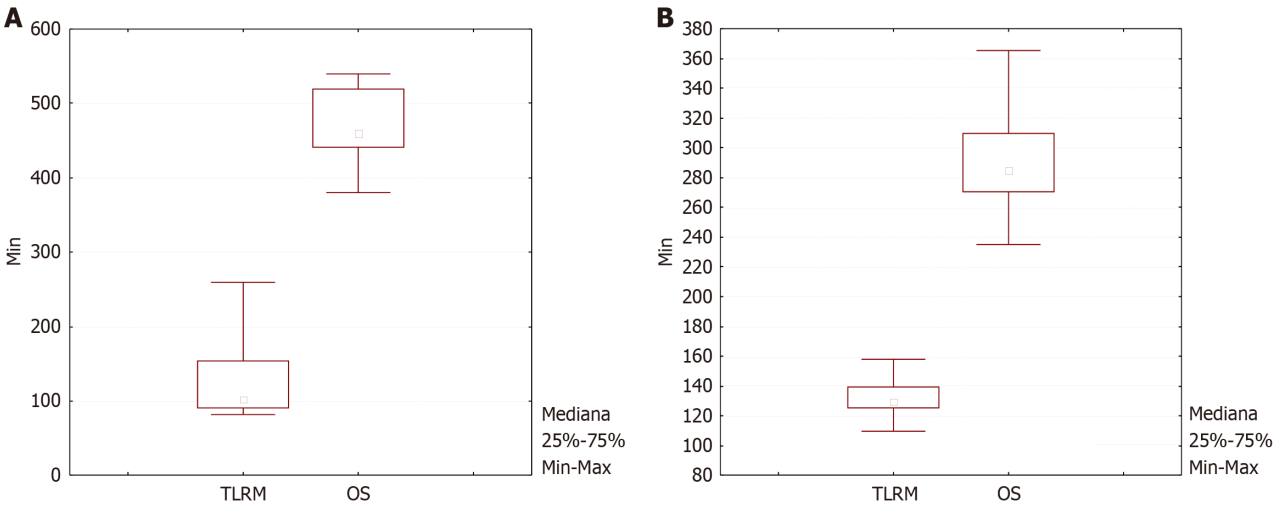

Figure 2 Blood loss and operation duration in transoral robotic surgery and laser resection and open surgery. A: Blood loss; B: Operation duration. TLRM: Transoral microsurgery laser resection; OS: Overall survival.

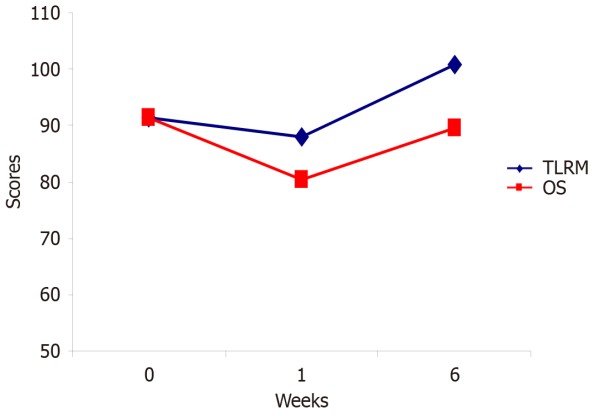

Figure 3 Quality of life assessment on the QLQ-C30 H&N35 scale (total score). TLRM: Transoral microsurgery laser resection; OS: Overall survival.

group. Considerations that are to be taken in account when planning TLRM as treatment for recurrent oropharyngeal cancers are: The size and exact location of the lesion and personal operator's experience with this technique (Table 3) (Figure 1, Figure 2A, Figure 3).

Surgical treatment alone or in combined approaches are main methods of choice for the treatment of recurrent tumors, if surgery is possible to perform. Many authors pointed out better survival rates in surgical treatment of relapses compared to those in conservative treatment.

Koo *et al*[3] analyzed the effectiveness of treatment in 23 patients with recurrent oral cancer. Of these, 13 underwent surgery and 10 received chemotherapy or radiation therapy. The median overall survival in patients who have been undergoing surgical treatment significantly exceeded that in conservative treatment.

Zafereo *et al*[4] noted that the 3-year overall survival for patients who underwent salvage surgery, radiotherapy, palliative chemotherapy, or replacement therapy was 48.7%, 31.6%, 3.7%, and 5.1%, respectively[5-9].

According to Choe *et al*[9], 2-year survival rates in patients treated with chemoradiotherapy alone were significantly lower compared to those in patients undergoing salvage surgery (10.8% and 28.4%, respectively). The authors conclude that, due to the high risk of severe toxicity, repeated chemoradiotherapy should be performed only in a strictly select group of patients[10-14].

Kano *et al*[1], in an analysis of 11 patients who underwent salvage surgery and 24 who underwent conservative treatment, showed statistically significant differences in 5-year survival (49.1% and 16.3%, respectively).

Kropotov *et al*[5] points out that due to the emergence of new effective techniques for the surgical treatment of patients with oropharyngeal cancer, the chemoradiation approach is no longer considered as the method of choice in the treatment of such patients. However, further randomized trials are needed to individualize the treatment approach and choose the optimal treatment tactics for a particular patient[15-17]. The specific medical literature sources possess a considerable number of studies describing the effectiveness of surgical treatment of primary oropharyngeal cancers. Little attention is paid to exploring the process of therapy of relapsed tumors. In addition, as noted by Jayaram *et al*[6], the quality of many studies should not be considered good enough[18-22]: all studies were retrospective, some had an extremely small sample size (29 patients, 39 patients)[23-30]. The greatest hindrance to an adequate assessment is caused

Table 3 Predictors of the occurrence of postoperative purulent-necrotic complications

Surgery type	τ Kendall	*P* value
Operations on the mandible	0.36	< 0.001[a]
Reconstruction of bone defect	0.30	< 0.001[a]
"Open" operations	0.30	< 0.001[a]
Reconstruction of a soft tissue defect	0.28	< 0.001[a]
Operation volume (total score)	0.26	< 0.001[a]
Radiation therapy of the primary tumor	0.20	0.005[a]
Early recurrence tumor	0.19	0.007
Operations on the lymph drainage area	0.14	0.042[a]

[a]Reached a statistically significant level.

by the heterogeneity of the groups and the lack of adjustment of the result to possible predictors of effectiveness. Thus, the association of a tumor with the human papillomavirus was considered only in one clinical study[31]. Adams *et al*[7] reported that 74% of patients had a second relapse on average 9 months after salvage surgery[32-34], according to Zafereo *et al*[4] the recurrence rate was 66%, the onset time was 8 months on average[35,36].

Jayaram *et al*[6], based on meta-analysis of recurrent oropharyngeal malignancies, treatment showed the mean effect value for 3-year overall survival to be 26% with moderate heterogeneity (I^2 = 40.7%), the mean effect value for 5-year overall survival was 23%, with high heterogeneity (I^2 = 73.9%)[37,38]. However, it should be noted that this meta-analysis is based on studies conducted during the period 1976-2014, and the above indicators describe the effectiveness of rescue operations over the entire period.

At the same time, the authors indicate that there was a significant positive trend in 5-year survival over this period: 20% for studies conducted before 2000 and 35% after 2000 (P < 0.001). Such a phenomenon may be associated both with an improvement in the technique of surgical intervention, an increase in the quality of the algorithm for assessing the possibility of surgical treatment, and an increase in the relative frequency of tumors associated with the human papillomavirus.

This literature review considers the results of studies conducted in 2006-2016. Hamoir *et al*[7], considering the effectiveness of salvage operations in 29 patients with recurrent oropharyngeal cancer, determined 2-year survival rates of 64.5%, 5-year survival rates of 43.4%[39].

Fakhry *et al*[27] conducted a comparative analysis of the effectiveness of surgical treatment of recurrent oropharyngeal cancer in patients associated (49 patients) and non-associated (29 patients) with human papillomavirus. The overall 2-year survival rate for p16-positive patients was 72%, for p16-negative patients it was 45% (P = 0.004)[40-43].

CONCLUSION

In conclusion, we would like to point out that despite the impressive success of surgery as the best way of treatment for patients with oropharyngeal recurrent tumors, we strictly assume that this cohort of patients should be carefully stratified, managed and thoroughly discussed with multidisciplinary teams of specialists before surgery.

FOOTNOTES

Author contributions: Ilkaev K, Gvetadze SR, Azizyan RI, and Mudunov AM developed the design of the research and performed the research and the analysis of the data; Roshchina EA, Bolotin MV, Larinov D, and Yang X took part in the clinical data collecting and its analysis; Ilkaev K and Gvetadze SR wrote and edited the manuscript; All the contributing authors have read the text and approved the final copy of the article. Zhao Ilkaev K and Gvetadze SR contributed equally to this work as co-first authors.

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CASE REPORT

Recovery of hearing loss in atypical Meniere's disease after treatment with orofacial and neck massage: A case report

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Abstract

BACKGROUND

A 48-year-old female presented with sudden-onset right-sided aural fullness, low-frequency hearing loss, and tinnitus. Medical history included right-sided temporomandibular joint disorder (TMJD) with crepitation, and retro-orbital headaches. The patient was diagnosed with atypical Meniere's disease (MD) and received intratympanic steroids, prednisone, betahistine, and began a low-sodium diet; however, the patient's symptoms worsened.

CASE SUMMARY

The patient sought physical therapy for TMJD; testing revealed reduced motion and dysfunction with vertical opening, lateral excursion of the mandible to the right, and tenderness to palpation. Treatment included soft tissue mobilization of right facial structures and temporal fossa, intraoral massage of the right pterygoid musculature, and massage of right neck structures. After 4 weeks, the patient noticed subjective improvement in hearing and decreased headaches. After 11 weeks, an audiogram showed that the hearing loss had recovered. The patient has continued the daily at-home intraoral/neck massage therapy and maintained normal hearing over 4 years to date. The temporal relationship between physical therapy and recovery of hearing loss suggests muscular or inflammatory etiology as at least partially causative of this patient's symptoms. The mechanism of healing may have been due to decreased inflammation, improved blood flow, restored function of cranial nerves, or some combination of these and other unknown factors.

CONCLUSION

This report suggests that orofacial physical and massage therapy may be an

effective treatment for the cochlear symptoms associated with MD.

Key Words: Meniere's disease; Temporomandibular joint disorder; Cochlear migraine; Cochlear hydrops; Low-frequency hearing loss; Case report

Core Tip: A patient who experienced right-sided symptoms of Meniere's disease (MD) with comorbid right sided temporomandibular joint disorder (TMJD) and mid-face/retro-orbital headaches experienced no relief from traditional MD treatments. The patient sought out physical therapy for TMJD, which included soft tissue mobilization of right facial structures and temporal fossa, intraoral massage, and massage of right neck structures. The patient recovered from the right-sided hearing loss and associated MD symptoms and had decreased headaches after 1 month. Physical and massage therapy for the cochlear symptoms associated with MD may be an important adjunctive treatment, though confirmatory studies are needed.

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INTRODUCTION

The underlying etiology of Meniere's disease (MD) is not fully understood[1], with a variable clinical presentation that includes spinning vertigo with tinnitus, fluctuating hearing, and/or fullness of the ear. Current medical treatment recommendations include diuretics, a low-sodium diet, and intratympanic steroid therapy[2], but outcomes are unpredictable and there is no cure.

The following is a report of a patient diagnosed with atypical MD (cochlear symptoms and periodic disequilibrium without spinning vertigo) who showed no improvement over one year while receiving conventional recommended therapeutics. However, the patient rapidly improved and recovered full hearing with reduction of aural fullness and tinnitus after receiving physical therapy of the neck, face, and jaw (including intraoral massage) over an 11-week interval.

CASE PRESENTATION

Chief complaints

A 48-year-old female presented with sudden-onset right-sided ear fullness, tinnitus, and sound distortion. The patient denied having spinning vertigo, but had experienced periodic brief episodes of disequilibrium.

History of present illness

The patient had no history of present illness.

History of past illness

The patient had no history of past illness.

Personal and family history

The patient's medical history included panic disorder, right-sided temporomandibular joint disorder (TMJD) with crepitation, and infrequent mild-to-moderate mid-face/retro-orbital headaches. There were no other comorbidities, and the patient did not use alcohol or tobacco. Current medications were venlafaxine 18.75 mg daily and alprazolam 0.25 mg as needed for management of panic attacks. The patient noted that the aural symptoms began after a recent emotionally traumatic event. She initially presented to her primary care physician who prescribed Flonase and referred her to an otolaryngologist.

Physical examination upon admission

Her head and neck examination, including otologic and cranial nerve examination, was unremarkable. Pure tone audiometry showed a right-sided low-frequency hearing loss (Figure 1A) with normal hearing in the left ear, and word recognition scores of 92% in the right ear and 100% in the left. Tympanometry showed bilateral type A configuration. The patient was initially diagnosed with low-frequency sudden sensorineural hearing loss (SSHL) and cochlear hydrops.

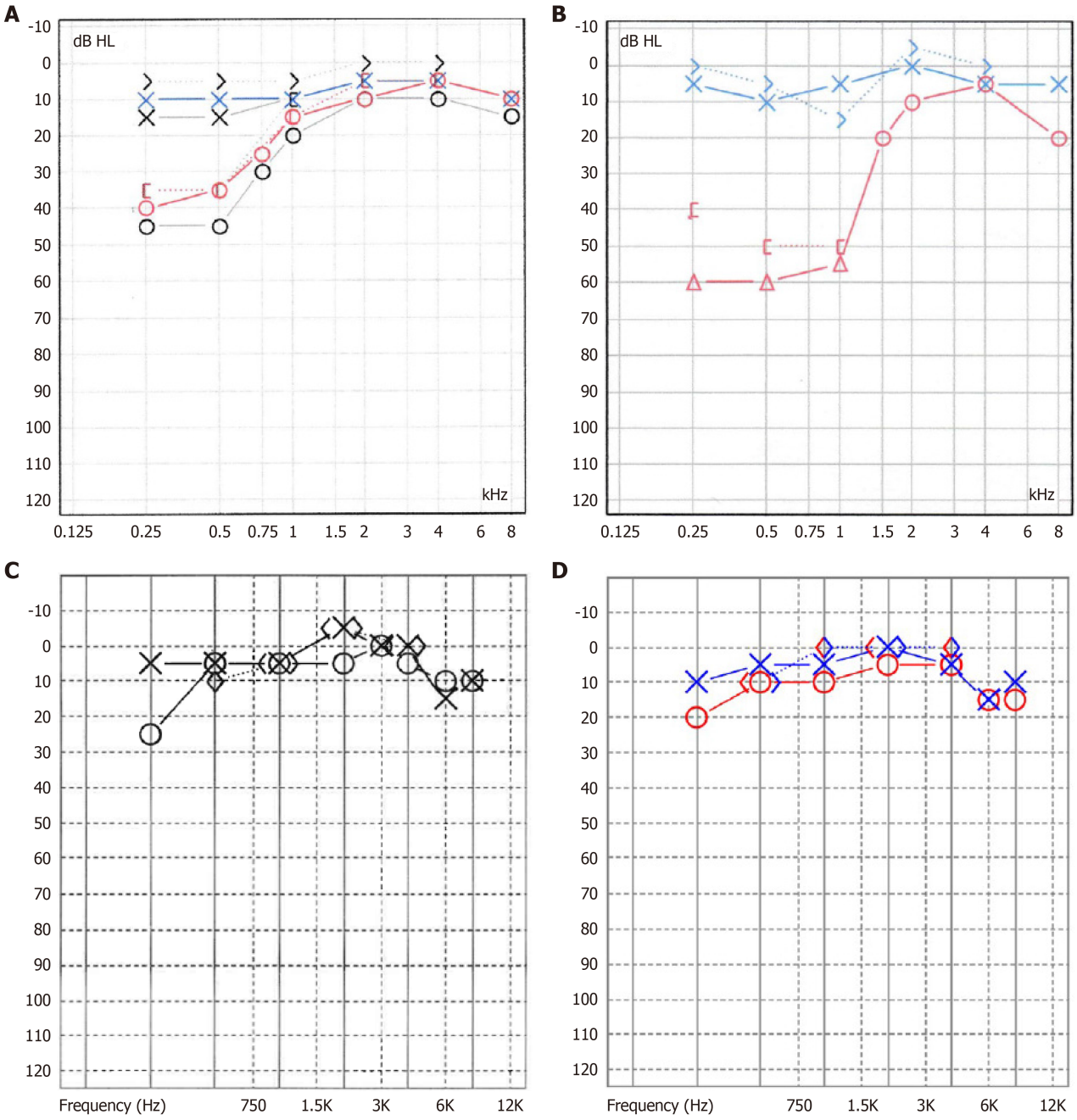

Figure 1 Patient's audiograms prior to and after starting physical therapy and massage. A: Audiogram at time of initial diagnosis of sudden sensorineural hearing loss and cochlear hydrops; B: Audiogram 5 months after diagnosis and treatment with oral steroids, intratympanic steroids, and a low-sodium diet; C: Audiogram 1.25 years after diagnosis and 12 weeks after beginning physical therapy of the jaw and neck; D: Audiogram 3 years after recovery of hearing loss and associated symptoms of atypical Meniere's disease.

Electrocochleography showed normal results for both ears. She was referred to a neurotologist and treated with a tapering course of oral prednisone with no improvement in symptoms or recovery of right-sided hearing loss.

Laboratory examinations

An autoimmune inner ear disease test (heat shock protein 70, immunoglobulin G antibodies) was negative.

Imaging examinations

Magnetic resonance imaging of the internal auditory canals and cerebellopontine angle was unremarkable.

FINAL DIAGNOSIS

Initial diagnosis

The patient was diagnosed with atypical MD, as the symptom complex and hearing loss configuration met all criteria for MD except for spinning vertigo[2] though the hearing loss and aural symptoms were constant and not episodic.

TREATMENT

Treatment for MD

The patient received intratympanic steroid therapy, started a low-sodium diet (less than 1800 mg sodium/day), and began taking betahistine 16 mg per day. After several months, the patient's right-sided hearing loss worsened despite treatment (Figure 1B).

The patient then tried several alternative therapy regimens including several weeks of oral valacyclovir, the John of Ohio supplement regimen for MD, acupuncture, and various splints to treat the pre-existing history of TMJD. Her aural symptoms and hearing loss did not improve in response to any of these alternative therapies, and after 9 months she abandoned these therapies and diets, although she continued to take betahistine daily. Right-sided ear symptoms and hearing loss failed to improve and did not worsen after discontinuation of these treatments.

OUTCOME AND FOLLOW-UP

One year following the initial diagnosis, the patient was placed on a trial of gabapentin 100 mg BID, but treatment was discontinued due to excessive daytime drowsiness even at much lower doses (25 mg every night at bedtime).

Treatment for TMJD

The patient then sought out physical and massage therapy for TMJD and aural symptoms. Computed tomography (CT) imaging of the mandible showed flattening of the super anterior condylar surface on the right side with volume loss of the superior aspect of the condylar head and an osseous projection at the anterior surface of the condyle. The condylar eminence was flattened and congruent with the temporomandibular fossa. The left side temporomandibular joint (TMJ) showed normal anatomy and cortication.

The physical therapist noted decreased static/dynamic functional balance, diminished ambulatory balance (functional gait assessment = 20/30 points) and dizziness with activities of daily living (dizziness handicap inventory = 50/100 points). TMJ testing revealed reduced motion and dysfunction with vertical opening, lateral excursion of the mandible to the right, and protrusion. The physical therapist noted that the patient was tender to palpation throughout the cervical and craniofacial regions. The patient demonstrated pain and reduced active range of motion with cervical rotation and upper cervical flexion and bilateral rotation. She reported symptoms of dizziness during saccades, head thrust to the right, and gaze stabilization activities.

The treatment plan included soft tissue mobilization of right facial structures (particularly the masseter) and right temporal fossa, intraoral massage of the right pterygoid musculature, and massage of right neck structures including the sternocleidomastoid muscle and scalene musculature from the occipital and retromandibular region to the level of the clavicle. Treatment was performed in-clinic weekly for a total of 11 visits, and a concurrent home therapy regimen of daily intraoral and neck massage. Clinical intervention and the home exercise program included strengthening of postural stability muscles to improve postural alignment during function. The treatment program also consisted of stretching exercises for sternocleidomastoid, upper trapezius and levator scapulae to address mobility dysfunction with cervical rotation and side-bending. The patient was educated in a program for intraoral release for the right TMJ region to address dysfunctional movement patterns. The patient was also instructed to perform controlled opening activity of the lower jaw with mirror feedback to emphasize neutral positioning during opening and closing motion. In addition, the patient performed a dynamic balance program and gaze stabilization activities to facilitate improved function of the vestibular system.

Resolution of symptoms

After the first 4 weeks, the patient noticed subjective improvement in right-sided hearing and a decrease in the intensity of right aural fullness and tinnitus. A phone-based audiogram app showed some improvement in the right low-frequency hearing loss. Headaches were also less frequent and less intense. Physical and massage therapy continued for another 7 weeks with further subjective improvement of all symptoms. A follow-up audiogram showed significant improvement in the right low-frequency hearing loss (Figure 1C) to near-normal levels, with word recognition at 100% for both ears.

The patient continued the daily at-home intraoral and neck massage therapy and has maintained normal hearing in the right ear over 4 years to date. A recent audiogram showed normal hearing in all frequencies (Figure 1D). The patient has not taken or pursued any other therapies outside of daily betahistine (16 mg/day) and the at-home physical and massage therapy program. The only residual symptom of atypical MD is mild right-sided tinnitus which is exacerbated by emotional stress or caffeine consumption.

DISCUSSION

This patient's unexpected recovery from acute low-frequency hearing loss, aural fullness, and tinnitus after receiving physical therapy may be attributable to a number of factors, however the temporal relationship between receiving physical therapy on the neck, face and jaw and the rapid resolution of symptoms suggests a muscular, inflammatory, and/or TMJD etiology as at least partially causative. The physical therapy treatment was initiated for the improvement of the muscular and inflammatory issues associated with the patient's right-sided TMJD, and produced a parallel rapid improvement and ultimate resolution of the patient's right-sided low-frequency hearing loss, aural fullness, and a decrease in tinnitus intensity.

The surmised link between TMJD and otologic symptoms is not new, and has been explored in prior research. Given the anatomical proximity between the TMJ, the muscles innervated by the trigeminal nerve, and structures of the ear[3,4], otologic symptoms (particularly aural fullness and tinnitus) are common in patients with TMJD, with prevalence estimates as high as 87%[3]. Research has also shown increased prevalence of TMJD in patients with MD compared to healthy controls[5]. Pekkan *et al*[6] reported that TMJD patients with otological complaints tend to have hearing impairment at low frequencies, and Kitsoulis *et al*[7] reported that moderate and severe TMJD was associated with hearing loss of median and low tones.

The patient in this report had both TMJD and MD. There are several theories as to how TMJD can produce similar and overlapping otologic symptoms as seen in MD. It has been hypothesized that TMJD can influence activation of the auriculotemporal nerves[3] or alter inner ear pressure equilibrium[8]. Alternatively, pain from TMJD can be caused, in part, by the pathological contraction of the masticatory muscles which can stimulate an extravascular inflammatory process and potentially aural fullness[7,9]. Neurogenic inflammation (including release of pro-inflammatory factors) can be caused by injury to the TMJ[10,11], thus sensitizing the trigeminal and facial nerves, leading to vasospasm or tonic spasm of middle ear muscles[7]. It has been theorized that altered trigeminal nerve input caused by TMJ dysfunction may cause activity changes in the dorsal cochlear nucleus that might affect the central auditory pathway, with resulting otologic symptoms [12].

The collective innervation (and irritation) of the tensor tympani, tensor veli palatini, tympanic membrane, and masseter, temporalis, and pterygoid muscles by way of the trigeminal nerve, or the potential contraction of the blood vessels supplying the cochlea, or bruxism leading to microtraumas, can all be contributors to otologic symptoms[13,14]. At the time of the abrupt hearing loss, the patient in this report had moderate-to-severe TMJD (on the same side), as evidenced by CT imaging showing a flattened condyle and signs of joint degeneration, in addition to the patient's symptoms of morning headache, crepitus, and deviation of the mandible to the affected side upon opening. The combination of moderate-to-severe right-sided TMJD may have been a contributing factor to the symptoms of atypical MD, given that her symptoms resolved with TMJD-focused physical therapy that included massage and soft tissue mobilization of the jaw, face, and neck.

While the TMJD causation model seems biologically plausible, central mechanisms could also be contributory or overlapping with TMJD and MD in this patient and others; specifically, this patient could also be afflicted with cochlear migraine. Migraine is associated with inner ear pathologies, including vertigo and tinnitus[15]. Two types of migraine with inner ear symptoms–vestibular migraine and cochlear migraine–have been proposed as distinct entities; vestibular migraine includes migraine with vertigo symptoms, and cochlear migraine includes migraine and auditory symptoms. It has been theorized that MD and migraine inner ear disorder may instead exist on a spectrum, with some patients having only vestibular symptoms (*e.g.*, vertigo, motion sensitivity), termed vestibular migraine on one end, and patients who have only cochlear symptoms (*e.g.*, fluctuating hearing loss, aural pressure, tinnitus) on the other[15]. When experienced together, they form a symptom complex termed cochleovestibular migraine that is similar in presentation to MD[15]. In fact, patients with vestibular migraine are sometimes misdiagnosed as having MD[16]. Of note, it has been hypothesized that migraine and MD share a common etiology[11]. Past research has shown that up to 51% of individuals with MD experience migraine compared to 12% in the general population[15].

According to the diagnostic criteria newly proposed by Lai and Lui[17] in 2018, the patient in this report would meet the criteria for cochlear migraine, though the diagnosis of cochlear migraine is largely still a theoretical concept. While the overlap between vestibular migraine and MD has been well-described, there are limited data published in reports on cochlear migraine. Hwang *et al*[18] conducted one large population-based study in Taiwan, and found that the incidence of cochlear disorders (defined as tinnitus, sensorineural hearing loss, and/or SSHL) was found to be significantly higher among patients with a history of migraines, providing some population-based evidence that migraine can impact the auditory system[19].

A widely accepted model of migraine revolves around the trigeminovascular system[11]. Similar to the TMJD model of otologic symptoms, it is thought that innervation and sensitization of the cochlea and cochlear blood vessels by the trigeminal nerve contribute to the vascular effects of migraine and may impact the inner ear[15,16,20], and that the cochlea is susceptible to injury from vascular dysfunction[21]. It has been shown that the trigeminal nerve directly affects blood flow to the inner ear through innervation of cochlear vasculature[11]. It is possible that the trigeminovascular system in migraine patients causes perfusion deficits in the inner ear; *e.g.*, involvement of the spiral modiolar artery leading to the historically described "cochlear" MD with low-frequency hearing loss[11], similar to the patient described in this report. Reduction in blood flow to the cochlea due to vasospasms would affect the apical turn of the cochlea and has been proposed to describe why the hearing loss is in the low frequencies[16,22].

Multiple studies have found an association between stress levels and migraine occurrence; similarly, physiologic stressors can also provoke MD symptoms[15] potentially *via* activation of afferent pathways through the trigeminal nerve. Given that the patient in this report experienced hearing loss abruptly in the morning after an emotionally traumatic event, it is plausible that this traumatizing event and subsequent physiologic stress changed and compromised

the functional dynamics of the inner ear. It is also possible that intense emotional stress stimuli caused an increase in TMJD behaviors in the patient (bruxing or clenching) and led to the symptoms associated with MD. Alternatively, an overlap of factors between processes related to both TMJD and central processes occurred. For example, it has been shown that patients with TMJD have greater electromyographic activity in the neck and trunk, potentially sensitizing the autonomic nervous system and potentially leading to migraine *via* the trigeminal nerve[7]. Taken together, an overlap of symptoms may exist amongst TMJD, MD, and migraine[18,23-26] and all 3 disorders can be exacerbated by emotional and psychological stress.

For the patient in this report, it appears that with enough stressors (whether mechanical, muscular, vascular constriction, or central biochemical processes) the patient's right ear showed the symptoms of cochlear hydrops and was resistant to conventional medication, unconventional medications, and dietary protocols. The mechanism of healing from the physical therapy intervention may have been based in reduction of inflammation, increased blood flow to injured tissues or muscles, restored function of cranial nerves, or some combination of these and possibly other unknown factors. Past research has reported that myofascial treatments have been shown to alleviate certain types of tinnitus[27,28] and the symptom of aural fullness related to TMJD[9,29], but there are very limited data reported to show that physical therapy can improve the cochlear symptoms in MD. This report suggests that physical and massage therapy of the face, jaw, and neck may be an effective treatment for the cochlear symptoms associated with MD, and merits further study.

It's important to consider that this patient's rapid recovery after receiving physical therapy may be attributable to another cause, such as spontaneous recovery that occurred simultaneously to receiving physical therapy, the fluctuating nature of MD, or due to the use of betahistine. Though the patient had been taking betahistine for several months prior to receiving physical therapy without improvement, the use of this daily medication could be a potential confounder in this patient's recovery. Additionally, the patient may have been misdiagnosed with atypical MD but instead has one of the atypical variants of migraine.

CONCLUSION

The complementary treatment of the cochlear symptoms of MD by a physical therapist may be beneficial for patients. Although physical therapy has been shown to be effective for vestibular disorders, less is known regarding efficacy for cochlear symptoms and disorders. Integrating physical therapy treatment may be particularly effective for patients with cochlear disorders who have comorbid TMJD or migraine, as choosing therapeutic options that target both auditory and musculoskeletal symptoms can potentially yield improved outcomes. Given that the pathophysiology associated with MD is unknown, and that current conventional treatments are limited and have unpredictable outcomes, physical and massage therapy for the cochlear symptoms associated with MD may prove to be an important adjunctive treatment, though confirmatory studies are needed.

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FOOTNOTES

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