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Room 903, Building D, Ocean International Center,
No. 62 Dongsihuan Zhonglu, Chaoyang District,
Beijing 100025, China
Telephone: +86-10-8538-1892
Fax: +86-10-8538-1893
E-mail: baishideng@wjgnet.com
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Room 903, Building D, Ocean International Center,
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Telephone: +86-10-8538-1891
Fax: +86-10-8538-1893
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Fax: +86-10-8538-1893
E-mail: baishideng@wjgnet.com
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Room 903, Building D, Ocean International Center,
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Current trends in the diagnosis and management of post-herniorraphy chronic groin pain

Abdul Hakeem, Venkatesh Shanmugam

Abdul Hakeem, Department of General Surgery, Aintree University Hospital NHS Trust, Longmoor Lane, Liverpool, L9 7AL, United Kingdom

Venkatesh Shanmugam, Department of General and Colorectal Surgery, Nottingham University Hospital NHS Trust, Queens Medical Centre, Nottingham, NG7 2UH, United Kingdom

Author contributions: Hakeem A did the literature search and wrote the initial draft; Shanmugam V cross-checked the literature search, edited the paper and conceptualised the idea.

Correspondence to: Mr. Abdul Hakeem, MRCS, Department of General Surgery, Aintree University Hospital NHS Trust, Longmoor Lane, Liverpool, L9 7AL, United Kingdom. drhabdulrahman@yahoo.com

Telephone: +44-113-8085924 Fax: +44-132-5490293

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Abstract

Inguinodynia (chronic groin pain) is one of the recognised complications of the commonly performed Lichtenstein mesh inguinal hernia repair. This has major impact on quality of life in a significant proportion of patients. The pain is classified as neuropathic and non-neuropathic related to nerve damage and to the mesh, respectively. Correct diagnosis of this problem is relatively difficult. A thorough history and clinical examination are essential, as is a good knowledge of the groin nerve distribution. In spite of the common nature of the problem, the literature evidence is limited. In this paper we discuss the diagnostic tools and treatment options, both non-surgical and surgical. In addition, we discuss the criteria for surgical intervention and its optimal timing.

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Key words: Hernia; Lichtenstein repair; Chronic groin pain; Inguinodynia; Neuropathic pain; Neurectomy; Nerve block

INTRODUCTION

Mesh inguinal hernia repair is one of the most common operations performed worldwide. Inguinodynia or Chronic Groin Pain following this operation is a potential complication and its incidence can be as high as 62.9%^[1]. A quarter of these patients suffer from severe impairment in carrying out their daily routines^[2-4]. Courtney *et al*^[5] showed the effect of chronic groin pain on physical and social functioning, thereby limiting the individual's ability to participate in any paid employment. The rate of chronic groin pain following both open and laparoscopic hernia repair is vastly underreported^[6,7]. Hindmarsh *et al*^[8] shown that only 1% of patients with chronic groin pain post-herniorrhaphy were referred for further treatment. The main purpose of this review is to look at the available evidence on diagnostic modalities for this chronic problem and to discuss the varied treatment options practised worldwide.

AETIOLOGY OF CHRONIC GROIN PAIN

The exact aetiology of this complex pain is unknown, although various theories have been proposed. Chronic groin pain has been classified empirically as neuropathic or non-neuropathic in origin. Neuropathic pain is con-

sidered to be due to damage to the inguinal nerves and usually develops in the sensory distribution of the injured nerve. Non-neuropathic pain is caused by either mesh-related fibrosis or post-operative fibrosis. The nerves involved are the Ilioinguinal nerve (IIN), the Iliohypogastric nerve (IHN), the genital branch of the Genito-Femoral nerve (GFN) and, rarely, the Lateral Femoral Cutaneous nerve (LFC). These nerves can be damaged either by partial or complete transection, stretching, contusion, crushing, electrical damage or by being caught in the suture used in open repair or the tacks used in laparoscopic repair. Secondary nerve damage can also occur as a result of adjacent inflammatory processes, such as granuloma, or because of excess fibrotic reaction or mesh encasement^[9]. Wantz *et al*^[10] showed that handling of the sensory nerves during surgery leads to chronic residual neuralgia.

Heise *et al*^[11] were the first to describe non-neuropathic pain caused by rolling up of the mesh or mesh-related excess fibrosis. Similarly, another pain syndrome, termed “somatic pain”, has been described secondary to damage to the pubic tubercle while anchoring the mesh^[12]. A small group of patients have been shown to suffer from diffuse pain around the spermatic cord (funiculodynia), resulting in ejaculatory pain^[13]. This has been described as “visceral pain” and is due to venous congestion of the spermatic cord or to mesh encasement of the cord. A combination of neuropathic, non-neuropathic, visceral and somatic pain is common, making clinical or radiological differentiation of the cause extremely difficult.

During laparoscopic repair, the IIN is at risk lateral to the internal ring and the GFN medial to the ring. The IHN is commonly damaged by tacks or staples along its entire length, making it highly vulnerable during laparoscopic mesh fixation^[14-16]. Occasional damage to the LFC nerve^[17,18] and the femoral nerve^[19] have also been shown during laparoscopic repair. Although laparoscopic repair has been shown to result in reduced chronic groin pain, exact reasons for this are unclear^[20-23].

COMPLEX SYMPTOMS OF CHRONIC GROIN PAIN

The complex symptoms of post-herniorrhaphy chronic pain vary depending on the involvement of the nerve or nerves, amount of mesh-related fibrosis and damage to spermatic cord structures. The neuropathic symptoms include pain (neuralgia), burning sensation (paraesthesia), reduced sensation (hypoesthesia) and increased sensation (hyperaesthesia). The pain may radiate to the hemiscrotum, upper leg or back.

Neuropathic pain is usually characterised by the presence of a trigger point, its episodic nature and by being aggravated by walking or sitting. It is variously described as a stabbing, burning, shooting or pricking sensation^[24]. In contrast, non-neuropathic pain is a constant dull-ache over the entire groin area with no specific trigger point and is usually aggravated by strenuous exercise. Patients

commonly describe it as a gnawing, tender, pulling or pounding sensation^[11].

A small group of patients also report numbness over the groin or thigh, with the most common point of maximal tenderness at the pubic tubercle. These patients have inflammation of the pubic tubercle either due to stitches made on the pubic bone during open repair or application of tacks in laparoscopic repair^[13]. Another range of symptoms are related to sexual dysfunction due to vas engulment and inflammatory reaction caused by the mesh. Patients describe ejaculatory pain in the region of superficial ring or testicular or labial pain due to GFN irritation^[25]. Other complaints included diminished quality of life, mood swings and depression^[26,27].

DIAGNOSIS OF CHRONIC GROIN PAIN

The diagnosis of chronic groin pain begins with a comprehensive patient history and good knowledge of the anatomy of inguinal nerves. The history should include the commonly encountered risk factors for chronic groin pain which include age below median, female gender, postoperative complications, recurrent hernia repair, open repair techniques, history of preoperative pain and an interval of less than 3 years from surgery^[28].

Due to the infrequent presentation of chronic groin pain, there is no clear consensus on the diagnosis of this iatrogenic problem. Neuropathic pain is usually distributed along the sensory innervations of the affected nerve(s) and can be reproduced by tapping the skin medial to the antero-superior iliac spine or over an area of local tenderness (Tinel's test). The clinical differentiation of ilioinguinal, iliohypogastric and genitofemoral neuralgia is difficult, frequently resulting in misdiagnosis and inappropriate treatment^[29,30]. This is because of the overlapping sensory innervations of these three nerves, peripheral communication between their nerve twigs and, most importantly, their common roots of origin^[31]. Along with these anatomical factors, fibrosis caused by the procedure and the mesh causes a degree of non-neuropathic pain in most cases, thereby making it difficult to delineate the neuropathic cause clinically.

Deysine *et al*^[32] and Starling *et al*^[33] used IIN block and recommended IIN neurectomy if the block relieved pain. If pain persisted after IIN block, L1-L2 plexus block was carried out and, if this relieved pain, GFN neurectomy was then performed. If pain was partially relieved by both blocks, groin exploration of both nerves was then carried out. There is no consensus on how these nerve blocks should be performed and how the results should be interpreted. Bower *et al*^[34] showed that after an unspecified nerve block, 13 out of 15 patients had pain relief and went on to have their IIN, IHN and/or LFC nerve excised. Again, there were no clear criteria for putting the patient through neurectomy.

Heise *et al*^[11] suggested that nerve block neither predicts nor changes outcome. They suggested that if hernia is done without mesh, then nerve blocks are needed to

identify nerve involvement. However, if a mesh is present, the sensitivity of the test is poor due to lack of spread of anaesthetic agent because of mesh-related fibrosis. Though peripheral nerve blocks or paravertebral blocks have been tried, they lack the ability to differentiate the involved nerve and are only helpful temporarily as a means of relieving pain.

CT or MRI scans are helpful in identifying non-neuropathic causes of chronic groin pain by identifying mesh-related pathologies, recurrent hernias and occasionally neuromas^[35,36]. A few studies have used MR Neurography to differentiate the involved nerves by studying the water content of the inguinal nerves^[37]. Kim *et al*^[38] carried out electromyograms on all patients, specifically looking for denervation of the pyramidalis muscle which is supplied by the IIN nerve. They showed that 91% of IIN neurectomies and 90% of combined neurectomies were successful, although there was no mention of the rate of pain recurrence.

TREATMENT OPTIONS FOR CHRONIC GROIN PAIN

The treatment of chronic groin pain can be a difficult ordeal for both the patient and the clinician. Many algorithms have been put forward for management of chronic groin pain^[2,39], but none of them has been proved in randomised trials. Pain related to neuropraxia (intact axon and myelin sheath), is usually temporary and may resolve itself in around 6 mo post-herniorraphy. As time progresses, chronic groin pain disappears without treatment in 30% of the patients, remains mild in 45% and in 25% of them it persists as severe pain affecting their everyday life^[5].

NON-SURGICAL TREATMENT

Lifestyle modification

Chronic groin pain has been shown to be aggravated by walking, stooping or hyper-extension of the hip and relieved by recumbent position and flexion of the hip and thigh^[35]. Hence, some clinicians have advised lifestyle changes, advocating sedentary lifestyle or sedentary occupations to negate the neuropathic pain caused by movement. This leads to poor quality of life and loss of productivity^[5] and is not now recommended because of the availability of better medical and surgical modalities.

Analgesics

Many clinicians use pharmacologic agents to manage chronic groin pain. These include non-steroidal anti-inflammatory drugs (NSAIDs), opioids, muscle relaxants, antiepileptics and antidepressants. However, these drugs may not prove helpful in relieving all types of chronic groin pain. The anti-depressants and antiepileptics are helpful in neuropathic pain whereas opioids or NSAIDs are usually minimally effective or ineffective for neuropathies^[40]. In most studies, NSAIDs were used as the first

line analgesic treatment. Kim *et al*^[38] used gabapentin or oral steroids as second line agents following the failure of NSAIDs. The steroids work by reducing the inflammation and oedema surrounding entrapped nerves. The efficacy of these treatment regimens has not been proven and majority of patients suffer recurrence with worse pain due to development of resistance to analgesics.

Physical and psychological therapies

Physical therapies including massage, physiotherapy and acupuncture have been tried^[24]. Keller *et al*^[41] used thermotherapy to temporarily negate the painful stimulus. Ferzli *et al*^[42] tried Capsaicin cream applied topically as a counter-irritant to desensitize painful stimulus. These physical techniques may reduce pain temporarily but few, if any, can prevent the recurrence of pain.

Nerve blocks

Nerve blocks reversibly interfere with neuronal transmission, leading to temporary pain relief. This can, therefore, be both diagnostic and therapeutic. The ideal nerve block would specifically anaesthetise the nerve proximal to the injury but this is technically challenging. Various chemical agents used for blockade are shorter- or longer- acting local anaesthetics, steroids and glycerol as well as neurolytic solutions such as alcohol or phenol^[11]. Commonly, these agents prevent neuronal transmission through nerve fibres either by blocking membrane ion channels or by denaturation of axon proteins. They can also be used with non-pharmacologic techniques like cryoanalgesia and transcutaneous electrical nerve stimulation, depending upon the response to the anaesthetic agents. All these therapeutic modalities have their own risks, therefore a positive diagnostic block should guide the further use of therapeutic blocks.

There is little published information on the success rate of nerve block as this depends on the experience of the surgeon or the anaesthetist performing the procedure. There is no consensus on approach or the type of anaesthetic agent to be used for therapeutic inguinal nerve blockade. Previously, blind injection of local anaesthetics was practiced, based on knowledge of the anatomy of the nerves. Recently Ultrasound guided blocks have been shown to be highly accurate and selective for blockade of either the IIN or the IHN, thereby increasing success rates^[43]. In a case reported by Hartrick, GFN block was attempted through a trans-psoas approach using the L3-L4 vertebral space as a guide^[44]. This anecdotal evidence cannot be generalised to the population and more extensive controlled trials are needed.

Alcohol or phenol injection has been tried for reducing chronic inflammation caused by mesh or post-operative fibrosis^[45]. Neuro-destructive procedures, such as cryo-ablation which destroy the nerve fibres by coagulation at very low temperatures (-40°C), have been shown to give some temporary pain relief^[46]. Following cryo treatment pain recurred due to axonal regeneration. Radiofrequency pulses, working by thermo-coagulating

nerves at very high temperatures, have been shown to cause temporary pain relief in ilioinguinal neuralgia^[47]. Again, definite evidence for their effectiveness is lacking.

SURGICAL TREATMENT

The surgical treatment of chronic groin pain was first described by Stulz *et al*^[48] in 1982. They performed IIN neurectomy on 5 patients with chronic groin pain following inguinal hernia repair, achieving a 100% success rate. However, surgical explorations and neurectomy carried out by other groups during this period were quite unsuccessful. Hameroff *et al*^[49] performed IIN neurectomy on 2 patients with 100% recurrent pain after few months. Harms *et al*^[30] reported similar problems, also in two patients. The first patient had 2 unsuccessful explorations, followed by successful GFN block and 3rd exploration leading to GFN neurectomy. Second patient had IIN neurectomy on 1st exploration and, due to recurrence of pain further, exploration and GFN neurectomy. Since then a number of studies have shown success rates ranging from 70%-100%^[11,12,24,27,29,30,32-34,38,41,48-59] (Table 1).

Principles of surgical treatment

Removal of the foreign body (mesh) alone has not been shown to relieve chronic groin pain. It is thought that it is due to chronic inflammation around the nerves from the mesh-induced reaction and the consequent degenerative nerve damage. Traditionally, surgical treatment of chronic groin pain includes groin exploration, mesh removal and neurectomy. Open chemical neurolysis has been tried, but does not resolve the problem of neuromas and secondary scarification^[33]. Freeing the nerve alone (physical neurolysis) has been tried but with high failure rates^[27,53]. Similarly simple division of the nerves without resection is not recommended. The entire length of the nerves should be excised, in order to involve all the neural connections between the nerves. Neurectomy with or without mesh excision is usually the preferred surgical treatment but there are no current consensus on which surgical approach should be chosen and which nerve should be excised. Heise *et al*^[11] found that 62% of patients who had mesh removal plus neurectomy achieved excellent results in comparison with the mesh-removal-alone group where the success rate was 50%. They concluded that concurrent neurectomy affords better results than mesh removal alone. Recently radio-frequency ablation of inguinal nerves have used with the aim for ablating the painful impulses transmitted by injured nerves. Rozen *et al*^[60] found that after radio-frequency ablation at T12, L1, L2 root level 4 out of 5 patients showed complete resolution of pain 4 to 9 mo later. Again, there is a lack of systematic evidence to support these findings.

The IIN can be identified lateral to the internal ring and then traced towards the external ring and resected as distally as possible. The IHN can be identified by the separation of the external oblique aponeurosis from the underlying internal oblique muscle as proximally as possible. With the IHN, dissection should include the intra-

muscular section, in order to look for nerve entrapped by sutures, mesh plugs or tacks. The GFN is usually identified through a retro-peritoneal (flank) approach. In a very rare case of LFC nerve involvement, decompression was performed by releasing the inguinal ligament on the anterior superior iliac spine and the lateral fibres of internal oblique aponeurosis^[27].

Amid adopted an anterior approach, where the nerve could be identified within the lateral crus of the internal ring, within the internal ring or between the spermatic cord and the inguinal ligament. He showed that complete resection might not be possible with this approach, but that even partial resection is sufficient if the other 2 nerves are resected completely^[54]. He devised a single stage procedure, where simultaneous IIN, IHN and GFN neurectomies were performed under local anaesthetic with proximal end implantation of these nerves. Amid also devised a technique of implanting the cut end of the IIN and IHN within the fibres of the internal oblique, reducing the risk of adherence with aponeurotic structures and thereby reducing the chance of recurrent pain^[36]. For GFN, the nerve was cut under tension in order to retract the nerve into the internal ring. In a retrospective review of 225 patients who underwent surgery for neuropathic and non-neuropathic pain, 11% had traumatic neuroma, 32% had nerve entrapment by suture, staple or mesh and 57% had perineural fibrosis^[36]. They showed complete improvement in 85% of their patients, while 15% of them had transient insignificant pain with no functional impairment. Four of the 225 patients showed no benefit from this triple neurectomy^[36]. Krähenbühl *et al*^[55] performed laparoscopic triple neurectomies using a retro-peritoneal approach and showed complete cure in three patients. Ducic *et al*^[56] adopted an open inguinal approach to identify the GFN postero-lateral to the cord, traced the nerve from there all the way to the pre-peritoneum and resected under tension. They showed 100% pain relief in 4 patients treated with GFN neurectomy.

Resected tissue from neurectomy should be sent for histology to confirm the removal of the involved nerve. Most importantly, there should be an informed decision about post-neurectomy numbness in the area of corresponding nerve innervation.

Criteria for surgical treatment

Surgical treatment is required if refractory pain persists after treatment with oral analgesics and/or local nerve(s) blockades. Nerve block must have resulted in a complete or substantial decrease in pain before neurectomy can be recommended. There are no defined limits on how often nerve blocks can be carried out and the practice has varied among surgeons worldwide. Deysine *et al*^[32] employed IIN block and if it was effective on first use, IIN neurectomy was then considered. No information is given on the success rate of nerve blockade from this study or the reasons for selecting successful IIN block alone as an indication for surgical treatment. Kim *et al*^[38] also relied on nerve blocks alone as an indication for neurectomy. They concluded that the nerve blocks were sensitive enough if

Table 1 Studies showing neurectomy performed by open, laparoscopic or a combination of both open and laparoscopic approach

Author	Country	No. of pts	Surgical approach	Which nerve excised?	Was mesh excised?	Follow-up duration	Recurrence/Persistent pain	Complications	Remarks
Hameroff <i>et al</i> ^[49] , 1981	USA	2	Open	IIN	N/A	NM	2/2	Nil	Only temporary pain relief following neurectomy
Stulz <i>et al</i> ^[48] , 1982	Switzerland	5	Open	IIN	N/A	NM	No separate data for inguinal hernia patients	Nil	Out of 22 patients who underwent neurectomy, 5 had previous inguinal hernia repair. In all inguinal hernia cases, IIN was entrapped within the scarred tissue and was excised
Harms <i>et al</i> ^[30] , 1984	USA	2	Open	GFN, IIN + GFN	N/A	18 mo (patient 1), NM in other patient	2/2	Wound infection (2)	First patient had 2 unsuccessful exploration, followed by successful GFN block and 3rd exploration with GFN neurectomy. Second patient had IIN neurectomy on 1st exploration and due to recurrence of pain further exploration and GFN neurectomy
Starling <i>et al</i> ^[33] , 1987	USA	26	Open	IIN or GFN	N/A	NM	2/13 in IIN group and 3/13 in all GFN group patients	Nil	No differentiation possible in GFN group to establish only patients with previous hernia repair. Overall 10 out of 13 with GFN neurectomy were pain free
Starling <i>et al</i> ^[29] , 1989	USA	31	Open	IIN or GFN	NM	NM	2/19 in IIN 4/12 in GFN	Nil	Selective nerve blocks used to identify involved nerve(s). In GFN group, no data was given to differentiate those patients who had hernia repair and those who had other abdominal operations
Bower <i>et al</i> ^[34] , 1996	USA	15	Open	IIN, IHN, GFN or LFC	No	66 mo	3/12	Nil	Three patients had persistent pain following redo exploration. Redo explorations could not identify involved nerve in two patients and identified a recurrent hernia in the other patient
Nahabedian <i>et al</i> ^[51] , 1997	USA	2	Open	IIN, IHN or GFN	NM	21 mo	0/2	Nil	In one of the patients, no nerve was identified intra-operatively and on the tissue excised, but pain relief was noted post-operatively
Heise <i>et al</i> ^[11] , 1998	USA	20	Open	IIN or IHN or GFN	Yes	16 ± 3 mo	8/20	Haematoma (1), Testicular atrophy (1)	4 patients had only mesh excised and 6 patients underwent selective neurectomy based on operative findings plus mesh excision
Lee <i>et al</i> ^[53] , 2000	USA	11	Open	IIN, IHN, GFN or LFC	Yes	10 mo	NM	Haematoma (1) and recurrent hernia (1)	History and clinical examination alone was done for pre-operative assessment. Mesh removal alone did not relieve pain in any patients. IIN was commonly excised. Majority of patients had excellent pain relief, no differentiation could be done to identify those with hernia repair
Deysine <i>et al</i> ^[32] , 2002	USA	22	Open	IIN	No	NM	0/22	Nil	Diagnostic nerve blocks were attempted in all patients. 8 out of 30 patients responded to conservative treatment and the rest were subjected to IIN neurectomy alone. No follow-up data was available and complications were not mentioned
Ducic <i>et al</i> ^[56] , 2004	USA	4	Open	GFN + IIN	No	9 mo	0/4	Nil	All patients had failed medical treatment. No clear information on diagnosis of nerve entrapment, One patient had previous unsuccessful GFN resection and another patient had previous failed IIN resection
Kim <i>et al</i> ^[38] , 2005	USA	16 (33 total)	Open	IIN, IIN + IHN	NM	12-46 mo	3/33, 10% had recurrent pain, but no clear mention about hernia patients	NM for hernia patients	33 patients were operated for CGP, but only 16 had previous hernia repair. Diagnostic nerve blocks done on all patients. Of all 33 patients operated, 91% of IIN neurectomies and 90% of combined IIN + IHN neurectomies were successful

Amid <i>et al</i> ^[54] , 2004	USA	225	Open	Triple neurectomy	Yes	6 mo	15% had transitional incisional pain with no functional impairment	Nil	Proposed 1-stage procedure of simultaneous neurectomy of all three nerves without mobilisation of spermatic cord. The nerve ends were implanted proximally into the fibres of internal oblique muscle
Murovic <i>et al</i> ^[50] , 2005	USA	1	Open	GFN	No	NM	0/1	Nil	Ten patients with Genitofemoral neuralgia were analysed, but only one patient had previous hernia repair. Diagnostic nerve blocks were used prior to GFN neurectomy by lateral extraperitoneal approach
Ducic <i>et al</i> ^[27] , 2008	USA	18	Open	IIN, IHN, GFN or LFC	NM	12-24 mo	3/18	Nil	Nerve blocks not routinely done. Patients selected for surgical intervention based on history and physical findings
Delikoukos <i>et al</i> ^[12] , 2008	Greece	6	Open	IIN	Yes	28 mo	0/6	Nil	No nerve blocks were utilised. Persistent pain in spite of analgesics were indication for surgery in this study. IIN were either excised or freed from the mesh, if entrapped
Vuilleumier <i>et al</i> ^[24] , 2009	Switzerland	43	Open	IIN + IHN	Yes	12 mo	2/43	Recurrent hernia (1)	Diagnosis of neuropathy was done using clinical findings and positive Tinel's sign. All patients had failed conservative treatment with systemic analgesics, injection of local anaesthetics and steroids, and physiotherapy. Radical neurectomy done in all cases. GFN not excised in any case
Zacast <i>et al</i> ^[58] , 2010	USA	27	Open	IIN, GFN	Yes	35 mo	6/19 (followed-up patients)	Nil	Diagnosis was made using selective nerve blocks. Only 19 of the 27 patients responded to telephone follow-up and 67% mentioned either complete pain relief or pain lesser than before
Loos <i>et al</i> ^[52] , 2010	Netherlands	54	Open	IIN, IHN, GFN	Yes	18 mo	24%	Haematoma (1), wound infection (1), haemorrhage (1), ischaemic orchitis (1)	Diagnostic nerve blocks were used in majority of them (78%) and some patients underwent CT or MRI (22%). Tailored neurectomy performed depending on intra-operative findings
Krähenbühl <i>et al</i> ^[55] , 1997	Switzerland	2	Laparoscopic (Retro- peritoneal)	GFN and IIN	No	3 mo	0/2	Nil	No information given about the diagnosis of CGP and indication for laparoscopic neurectomy. Retroperitoneal neurectomy done, but no clear mention about how the nerves were identified intra-operatively
Wong <i>et al</i> ^[59] , 2001	Canada	1	Laparoscopic (pre-peritoneal approach, under fluoroscopic guidance)	Nerve not excised	Yes (mesh and staples)	NM	0/1	Nil	Single patient report with 5 month history of groin pain following laparoscopic hernia repair. Mesh and tackers were found to entrap the IIN and were removed laparoscopically aided by fluoroscopy
Rosen <i>et al</i> ^[57] , 2006	USA	12	Combined open and laparoscopic	IIN + IHN	Yes	6 wk	0/12	Nil	All patients had previous open hernia repair and 2 failed percutaneous nerve blocks to treat CGP. TAPP repair done initially, followed by groin exploration, mesh removal and nerve transection. Too short follow-up
Keller <i>et al</i> ^[41] , 2008	USA	21	Combined open and laparoscopic	Triple neurectomy	Yes	6 wk	1/19 (followed up patients)	Nil	Percutaneous nerve block was unsuccessful in all patients. Initially transabdominal diagnostic laparoscopy was performed irrespective of the route of initial surgery. Mesh was placed in the opposite location to the first mesh (laparoscopic if the first was open and <i>vice-versa</i>). Too short follow-up

NM: Not mentioned; IIN: Ilioinguinal neurectomy; IHN: Iliohypogastric neurectomy; GFN: Genitofemoral neurectomy; LFC: Lateral femoral cutaneous neurectomy; CGP: Chronic groin pain; N/A: Not applicable; Triple Neurectomy: IIN + IHN + GFN neurectomy; TAPP: Trans-abdominal pre-peritoneal repair; CT: Computed tomographic; MRI: Magnetic resonance imaging.

carried out by an experienced anaesthetist. Bower *et al*^[34] showed temporary pain relief in 13 of their 17 patients following unspecified nerve block. These patients went on to have IIN, IHN or LFC neurectomy depending on operative findings. Failure or recurrence of pain following at least two attempted nerve blocks is the criterion for choosing surgery followed in most units worldwide.

Loos *et al*^[52] showed that previous pain treatment is a predictor of poor operative treatment result. Kehlet *et al*^[61] studied factors for persistent post-surgical pain and found that a few patients suffer from central nervous system sensitisation, making them refractory to any form of treatment and poor candidates for surgical exploration. Nerve blocks and TENS are effective treatments for such patients and surgery should be avoided^[52]. Currently there is no consensus on the type of assessment tool for patients needing neurectomy and, as a result, there is no definitive protocol available for selecting patients for surgical exploration.

Timing of surgical intervention

Differences in the assessment of chronic groin pain, and variations in diagnostic practice and in the length of trial period with nerve blocks, have meant that the timing of surgical intervention has been widely varied. The timing of surgical intervention should ideally be at least 6 mo after herniorrhaply to give adequate time for any neuropraxia to settle and time to try medical management^[62].

Surgical approach

A combined open and laparoscopic approach has been proposed by two groups^[41,57]. Keller *et al*^[41] used a protocol where after removal of mesh from the previous hernia repair, further mesh was placed in the opposite location to the first mesh (laparoscopic, if previously open repair and *vice versa*). Twenty of 21 patients reported significant resolution of symptoms at 6 wk follow-up. Results showed that an initial laparoscopic approach aids examination of the inguinal areas to rule out a recurrent hernia or any other inguinal pathology. At the same time if a previous laparoscopic repair was performed, the mesh was excised and triple neurectomy plus re-do repair carried out using an open approach. Conversely, if an open repair was done previously, the inguinal areas were checked initially using laparoscopy and a TAPP repair performed, followed by mesh removal plus triple neurectomy through the previous open incision. These authors also found that one patient with testicular pain and a previous plug-and-patch repair, had the vas engulfed by mesh. Removal of the plug with the vas cured his symptoms, thereby avoiding an unnecessary neurectomy which would have been performed if open approach alone was applied.

Rosen *et al*^[57] took a similar approach in patients with previous open inguinal hernia repair, using initial laparoscopic evaluation and TAPP repair, followed by open exploration, removal of mesh and then IIN and IHN neurectomy. They believed that removal of GFN was not needed, as none of their patients had any ejaculatory or other sexual symptoms. In one patient with chronic or-

chalgia following previous plug and patch repair, the initial diagnostic laparoscopy showed plug mesh engulfing the vas deferens, and the resection of both led to permanent relief of pain. The other 11 patients showed significant improvement in their pain following neurectomy. To date, there are no randomised studies comparing the open and laparoscopic approaches for neurectomy. The majority of the available results are from individual case series and are, therefore, biased by individual surgeon's laparoscopic abilities and the small number of patients reported.

Which nerve should be excised?

A review of surgical treatment for chronic groin pain carried out by Aasvang *et al*^[63] showed that the details of surgical treatments used were not evidence based and varied between different published studies. There was no clear explanation in most studies of why only one or two nerve were resected, rather than all three. Neurectomy should ideally resect the entire length of the nerve as far proximally as possible, to leave a smoothly cut end. There is still no consensus on whether only the affected or the entrapped nerve should be removed, or whether three nerves should be removed on the basis that remaining nerve branches may still transfer pain stimuli^[35]. Resection of the three nerves, IIN, IHN and GFN, has been shown to permanently relieve chronic groin pain at the expense of inguinal numbness.

Ilioinguinal neurectomy alone has also been shown to be an effective treatment for relieving chronic groin pain in several studies^[29,32,38]. Starling *et al*^[29] performed IIN neurectomy alone in 17 patients and showed complete pain relief in 15 of them. Kim *et al*^[38] showed similar results, with 19 of their 21 patients showing considerable pain relief following isolated IIN neurectomy. In a retrospective review of 19 patients, Keller *et al*^[41] showed that triple neurectomy was performed in 7, dual neurectomy in 9 and at least one nerve was excised in 18 patients. Of 19 patients only one had recurrent pain a year after neurectomy.

Loos *et al*^[52] followed a tailored neurectomy approach where, depending on intra-operative findings of nerve involvement or mesh pathology, the nerve was excised with or without mesh. According to these authors, this protocol avoids the removal of all three nerves, as proposed by Amid, avoiding the consequent chronic numbness^[56]. In a retrospective review of 68 patients who underwent tailored neurectomy, 12 patients (17.6%) needed further operation because of persistent pain. This study showed a complete pain relief in 52%, partial pain relief in 24% and pain unchanged in 24% at 1.5 years median follow-up.

Vuilleumier *et al*^[24] in a prospective cohort study of neuropathic groin pain patients, defined a radical neurectomy where the inguinal canal was explored through an anterior approach and mesh, IIN and IHN were removed radically by sharp dissection, ends of the nerves being tied with prolene sutures. They showed that median pain score (VAS) decreased significantly post-operatively, with 41 (95%) reporting complete relief and 2 (5%) having partial relief from pain. There had been a median of 6 mo

work incapacity in these patients but all of them returned to work 6 wk post-operatively. Vuilleumier *et al*^[24] suggested that as GFN is a small nerve and neurectomy of GFN can cause damage to spermatic blood vessels, the procedure should not be recommended. Overall, there is no consensus on which nerve should be excised for the treatment of chronic groin pain.

Dealing with neurectomized nerve ends

The transected nerve can be ligated, cauterised or buried within the muscle fibres. Keller *et al*^[41] did not ligate the cut nerve ends until bleeding occurred, because of the risk of neuroma formation at the tied end. Majority of surgeons usually tie the nerve end with absorbable suture and tuck it under the internal oblique muscle.

Mesh excision

Currently there are no long-term results available from large studies on the safety of surgical mesh removal with or without neurectomy.

Pubic periosteal reaction or osteitis

If there is pubic periosteal reaction or osteitis, then possible causative agents such as suture materials, staples or rolled up meshes should be removed. Steroid injection can be useful when used intra-operatively or post-operatively if pain persists^[62].

CONCLUSION

Chronic groin pain is not uncommon. It is particularly common in patients with pre-operative pain due to hernia and in patients who are of younger age. Diagnosing chronic groin pain is difficult and needs a high level of patient co-operation. Pain severity is subjective and will remain difficult to evaluate until better scoring systems are developed. In most studies pain is measured subjectively prior to initiation of medical or surgical treatment. Occasionally, objective assessment tools like VAS are used or there is correlation with pre-operative pain scores before treatment is given. There is currently a lack of consensus on the appropriate transition from medical to surgical management of these patients.

The role of surgery in patients with chronic groin pain is controversial and due to various surgical methodologies adopted by surgeons worldwide, data are highly confusing and difficult to interpret. Moreover, the current treatment regimens for chronic groin pain have limited success and their long-term benefits and quality of life effects are still uncertain. A randomised clinical trial comparing nerve blocks *vs* surgical neurectomy is currently being undertaken^[64] to obtain a definitive answer to this difficult problem.

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Successful treatment of esophageal metastasis from hepatocellular carcinoma using the da Vinci robotic surgical system

Wiroon Boonnuch, Thawatchai Akaraviputh, Carnivale Nino, Anusak Yiengpruksawan, Arthur Andrew Christiano

Wiroon Boonnuch, Thawatchai Akaraviputh, Minimally Invasive Surgery Center, Division of General Surgery, Department of Surgery, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, 10700, Thailand

Carnivale Nino, Anusak Yiengpruksawan, Department of Surgery, the Valley Hospital, Valley Health System, NJ 07652, United States

Arthur Andrew Christiano, Department of Pathology, the Valley Hospital, Valley Health System, NJ 07652, United States

Author contributions: Boonnuch W originated the idea and drafted up the manuscript; Nino C collected the data; Yiengpruksawan A and Christiano AA wrote a portion of the manuscript; Akaraviputh T critically reviewed and edited the manuscript.

Correspondence to: Thawatchai Akaraviputh, MD, Minimally Invasive Surgery Center, Division of General Surgery, Department of Surgery, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, 10700, Thailand. sitak@mahidol.ac.th

Telephone: +66-2-4198006 Fax: +66-2-4121370

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Abstract

A 59-year-old man with metastatic an esophageal tumor from hepatocellular carcinoma (HCC) presented with progressive dysphagia. He had undergone liver transplantation for HCC three and a half years previously. At presentation, his radiological and endoscopic examinations suggested a submucosal tumor in the lower esophagus, causing a luminal stricture. We performed complete resection of the esophageal metastases and esophagogastronomy reconstruction using the da Vinci robotic system. Recovery was uneventful and he was been doing well 2 mo after surgery. α -fetoprotein level decreased from 510 ng/mL to 30 ng/mL postoperatively. During the follow-up period, he developed a recurrent esophageal stricture at the anastomosis site and this was successfully treated by endoscopic esophageal dilatation.

INTRODUCTION

The incidence of metastatic esophageal tumor (MET) is low, ranging from 0.3%-6.1% in autopsy series^[1-3], with hepatocellular carcinoma (HCC) was accounting for less than 0.4% of primary lesions^[4]. The majority of METs are associated with diffuse metastases or with mediastinal carcinomatosis, and thus are not candidates for aggressive local treatments. Recently, we performed a robot-assisted local resection of an isolated partially obstructing MET using the da Vinci surgical system in a patient who had undergone liver transplantation for cirrhotic liver associated with HCC. The case is reported herein.

CASE REPORT

The patient was a 59-year-old man who underwent liver transplantation for cirrhotic liver associated with a solitary HCC. Three and a half years later, he developed progressive dysphagia. Esophagography showed severe narrowing of the distal esophagus. Computed tomography (CT)

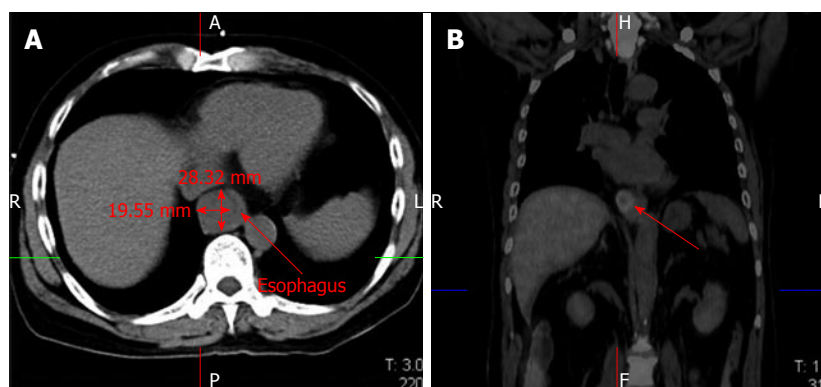


Figure 1 Computed tomography scan demonstrated marked thickening of the esophageal wall (A). Positron emission tomography scan showed marked uptake by the esophageal lesion without any recurrence of hepatocellular carcinoma at other sites (B).

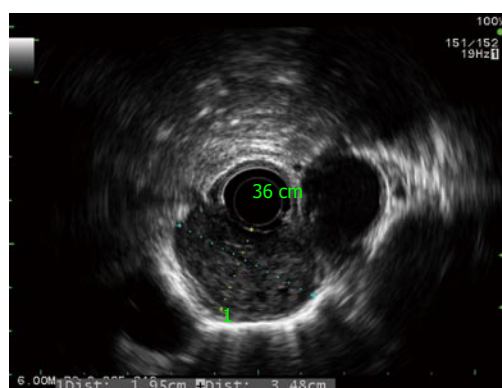


Figure 2 Radial echoendoscopy showed a heterogeneous submucosal tumor about 2 cm × 3.5 cm in diameter without periesophageal lymph node.



Figure 3 Intraoperative finding of the da Vinci S Robotic surgical system (A), the dense adhesion was resected using endoGIA staple (B).

scan demonstrated marked thickening of the esophageal wall around the stricture (Figure 1A). Endoscopic study revealed an extrinsic compression at 35 cm from the incisors, causing severe stenosis but without any mucosal irregularity. Positron emission tomography (PET) scan showed marked uptake by the esophageal tumor without any recurrence of HCC at other sites (Figure 1B). Endoscopic ultrasonography revealed a large submucosal tumor of 1.9 cm × 3.5 cm in diameter in the lower esophagus (Figure 2). Laboratory analysis revealed an elevated α -fetoprotein level of 510 ng/mL. The patient was diagnosed with MET from recurrent HCC. Since his general condition was excellent, we decided to perform surgical resection.

Surgical technique

After induction of general anesthesia with a single-lumen endotracheal tube, the patient was placed in the lithotomy position. An arterial line, a central venous catheter, and a Foley catheter were placed. Pneumatic compression stockings were placed on both legs. Preoperative antibiotics were administered. The abdomen was prepared and draped in the usual sterile fashion. After placing the trocar, the abdomen was insufflated to 14 mmHg. The abdominal cavity was inspected for any evidence of carcinomatosis. Lysis adhesion was performed using standard

laparoscopy. Part of the dense adhesion of the omentum was transected using endoGIA staples for prevention of intra-operative bleeding. Laparoscopic ultrasonography of the liver demonstrated no recurrence of HCC.

The da Vinci surgical system was then brought into position, cephalad to the patient, and the arms of the system were attached to the trocars. The robotic camera and the two operating robotic instruments were secured in their ports. Transabdominal dissection of the distal esophagus and stomach was started and continued in a cephalad direction along the circumferential borders of the esophagus. The articulated hook cautery was used for this maneuver, allowing precise circumferential dissection of the esophagus, and division of each individual periesophageal attachment with minimal blood loss and trauma. The tumor of the lower esophagus was mobilized so esophageal metastectomy and esophagogastrostomy were performed using the robotic system (Figure 3). The esophagogastrostomy anastomosis was created by the robotic hand-sew technique with vicryl #3/0 interrupted stitches.

Pathological study confirmed the resected specimen was a HCC, suggesting metastatic lesions from the liver (Figure 4). The patient was discharged 14 d later with no apparent symptoms after the surgery. The α -fetoprotein level decreased to 30 ng/mL. Two months later, he devel-

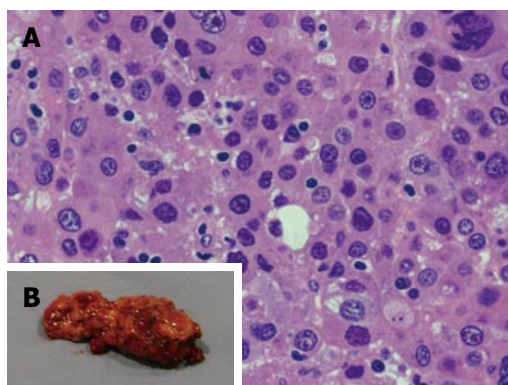


Figure 4 Pathological result of the resected specimen confirmed metastasis from hepatocellular carcinoma.

oped anastomosis stricture causing dysphagia which was successfully treated by endoscopic esophageal dilatation.

DISCUSSION

Since Gross firstly reported a case of metastatic esophageal cancer from the prostate^[5], many reports have shown the esophagus to be a frequent metastatic site from a variety of malignancies including breast^[6], lung^[7], ovary^[8], liver^[9], rectum^[10] and others^[11-14]. In autopsy studies, the overall incidence of esophageal metastases is 0.3%-6%^[1-3]. The most common primary tumor-bearing organs are breast and lung^[6,7]. Esophageal metastasis from HCC has only been described in one previous report^[9]. Our case was diagnosed as an esophageal metastasis from HCC, which is extremely rare especially post liver transplantation.

The possible routes of esophageal involvement are direct extension from adjacent organs, mediastinal nodes or hematogenous spreading from a distant primary^[15]. In this case it is most likely that the HCC developed secondary metastasis in the esophageal wall through hematogenous spread.

METs are usually located in the submucosal layer and cause progressive dysphagia^[3,16]. Esophagography and endoscopy show severe luminal stricture with normal overlying mucosa, often making histological diagnosis difficult^[16]. CT scan demonstrates concentric thickening of the esophageal wall over the stricture without an apparent extrinsic mass^[16,17]. In our patient, the diagnosis was confirmed by PET scan which showed marked uptake by the tumor (SUV - MAX = 4.5) and by an increase in α fetoprotein level to 510 ng/mL. Standard treatment for metastatic esophageal cancer has not yet been established. However, as the majority of such patients already have advanced malignant disease or metastases at multiple sites, systemic chemotherapy and/or local radiation are usually considered as the first choice of treatment. Unfortunately, when the symptoms appear, the majority of the patients already have distant metastases^[9]. Therefore, treatment has been directed toward palliation, for which a variety of options exist, including endoscopic di-

lation and stent placement or esophagectomy^[7]. As metastatic HCC shows poor response to chemo-radiation, we discussed with the patient that surgical removal is the optimal treatment. However, recent reports have shown that esophagectomy can provide excellent palliation and long-term survival in certain cases without metastases to other sites^[3,6-8,11,18-21]. The prognosis varied from 7 mo to 14 years after esophagectomy, depending on the biological characteristics of the primary malignancy.

The use of the da Vinci Robotic Surgical System (Intuitive Surgical, Sunnyvale, California) provides the advantages of three-dimensional visualization through a stereo endoscope, tremor reduction, motion scaling, and wristed instrumentation with additional degrees of freedom compared to standard laparoscopic instruments^[22,23]. It may be that advanced robotics will be reserved for only the most complex operations, such as esophagectomy and reconstruction. The system allows the surgeon to work in the narrow space of the mediastinum, overcoming spatial limitations experienced while using thoracoscopic or laparoscopic techniques. The robotic system is of tremendous help in accessing remote areas through a small esophageal hiatus. The extent of lymphadenectomy and the total operative time were not issues in this procedure, but might be improved on with further experience^[24]. In authors' opinion, robotic surgery can ameliorate the technical difficulties encountered laparoscopically and may allow surgeons to perform this and other delicate procedures without increased operative time, because of the maneuverability and increased length of the instruments as well as the excellent three-dimensional operative view. From our experience with this new robotic system, aggressive surgery might be considered as a therapeutic procedure for metastatic HCC of the esophagus, as long as the primary tumor is satisfactorily controlled.

In conclusion, we report a rare case of pre-mortem-diagnosed esophageal metastasis from HCC in a patient who had previously undergone liver transplantation. We performed what is possibly the first reported successful esophageal metastatectomy and reconstruction esophagogastrectomy using the da Vinci robotic system.

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Pneumatosis intestinalis and pneumoperitoneum on computed tomography: Beware of non-therapeutic laparotomy

Kuan-Chun Hsueh, Shung-Sheng Tsou, Kok-Tong Tan

Kuan-Chun Hsueh, Shung-Sheng Tsou, Kok-Tong Tan, Department of Surgery, Tungs' Taichung MetroHarbor Hospital, Taichung City 435, Taiwan, China

Author contributions: All authors wrote this case report.

Correspondence to: Kok-Tong Tan, MD, Department of Surgery, Tungs' Taichung MetroHarbor Hospital, No. 699, Chung-Chi Rd, Sec 1, Wuchi District, Taichung City 435, Taiwan, China. ericktan@gmail.com

Telephone: +886-4-26581919-4300 Fax: +886-4-26582193

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Abstract

Pneumatosis intestinalis (PI) is defined as gas within the gastrointestinal wall and is associated with a variety of disorders. As a concurrent occurrence with pneumoperitoneum, it can easily be mistaken for bowel ischemia with perforated peritonitis. In fact, air dissection or rupture from subserosal cysts may be the cause of intraperitoneal and intraluminal free air, with clinical symptoms such as abdominal pain and fullness occurring as a result. We hereby report a case of an 82-year-old male with a history of chronic obstructive pulmonary disease who was diagnosed with bowel ischemia and received emergency laparotomy because of the appearance of PI and pneumoperitoneum on abdominal computed tomography scan. However, no perforated hollow organ or necrotic bowel segment was found, only diffusely distributed massive intraperitoneal air and PI of gastrointestinal tract. The laparotomy seemed non-therapeutic for this patient. This is significant warning for clinicians to differentiate the associated conditions of PI, and to evaluate whether or not emergency surgery is necessary.

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Key words: Pneumatosis intestinalis; Pneumoperitoneum; Computed tomography

INTRODUCTION

Pneumatosis intestinalis (PI) is indicated, radiologically or pathologically, as gas within the gastrointestinal wall. Air dissection or rupture from subserosal cysts may be the cause of intraperitoneal and intraluminal free air, which causes clinical symptoms such as abdominal pain and fullness^[1,2]. In the past, this was regarded as a sign of intestinal ischemia, which was indicated for surgical intervention, especially when it coexisted with the presence of pneumoperitoneum. However, new evidence indicates that a conservative approach may be sufficient in certain cases presenting with PI^[3,4].

We hereby report a case of an 82-year-old male with a history of chronic obstructive pulmonary disease (COPD) who presented with abdominal pain. The computed tomography (CT) scan showed intramural gas of the gastrointestinal (GI) tract and massive pneumoperitoneum, which mimicked intestinal ischemia and perforation. The diagnosis of PI with pneumoperitoneum was confirmed *via* exploratory laparotomy and subsequent pathological analysis, though the etiology remained uncertain. An operation was probably unnecessary for this patient as there are other ways to determine the possible need for laparotomy, such as repeated laboratory and radiological tests. Conservative treatment is probably more suitable for the relief of PI.

CASE REPORT

An 82-year-old man with a past medical history of COPD visited our emergency department because of generalized abdominal pain with fullness and intermittent vomiting for three days. Physical examinations revealed tenderness over the whole abdomen and his hemodynamic status was relatively stable. C-reactive protein was 1.0 mg/dL, marginally elevated from the normal upper limit of 0.8 mg/dL, but other laboratory data were all within normal limits. The abdominal CT scan revealed generalized bowel distention, intramural air within stomach, small and large intestines, and massive intraperitoneal free air (Figure 1). Laparotomy was performed due to the suspected diagnosis of bowel ischemia and hollow organ perforation. Pneumoperitoneum, bowel wall congestion and edematous cystic changes were identified in a CT scan, whereas no bowel perforation was detected. The most prominent pneumatosed jejunal segment around 50 cm in length was resected with primary anastomosis because of the suspicion of bowel ischemia and necrosis. In addition, loop ileostomy was conducted for decompression of the dilated large bowel. Pathologically, the sections of intestinal wall showed diffuse gas-filled cysts of variable size (Figure 2A and B), leading to the diagnosis of PI. Autoimmune or rheumatological diseases were excluded by unremarkable results from laboratory analysis of markers including rheumatoid factor, antinuclear antibody and subtypes (antibodies to dsDNA, Sm, Ro, La), anti-cardiolipin antibody, and serum immunoglobulins, as well as normal results from physical examinations. The possible cause of PI may be associated with underlying COPD. In the following days, the patient received chest physical therapy and medications including bronchodilators and mucolytics for exacerbated COPD and superimposed pneumonia. Repeated abdominal CT scan 2 mo later confirmed the resolution of PI. The patient was discharged uneventfully with no further complaints.

DISCUSSION

Conventional PI has been classified as primary (idiopathic) and secondary^[5]. Primary PI is referred to as the cystic collection of air in the colonic wall with an unknown cause. Secondary PI has been associated with numerous clinical conditions. The most common sources of PI possibly are intraluminal GI gas, bacterial production of gas, and pulmonary gas^[1,6]. The increase in the intraluminal pressure and extent of mucosal injury, as seen in intestinal obstruction, endoscopic exam, trauma, mucosal injury incited by autoimmune diseases, acquired immunodeficiency, immunosuppressive therapy, and cytotoxic therapy^[1,2], may lead to intraluminal gas dissection into the injured GI tract intramurally. The invasion of gas-producing bacteria into the injured GI mucosa may be responsible for the bacterial theory of PI. Pulmonary gas formation may arise from alveolar rupture, which results in the dissection of air along vascular channels in the mediastinum, tracking caudally to the retroperitoneum and

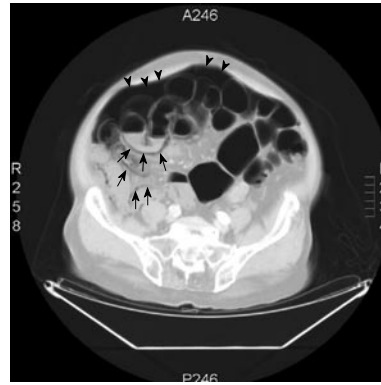


Figure 1 Use of lung window setting in abdominal computed tomography scan revealed massive intraperitoneal free air (arrowheads) and diffuse air collected within the bowel wall (arrows).

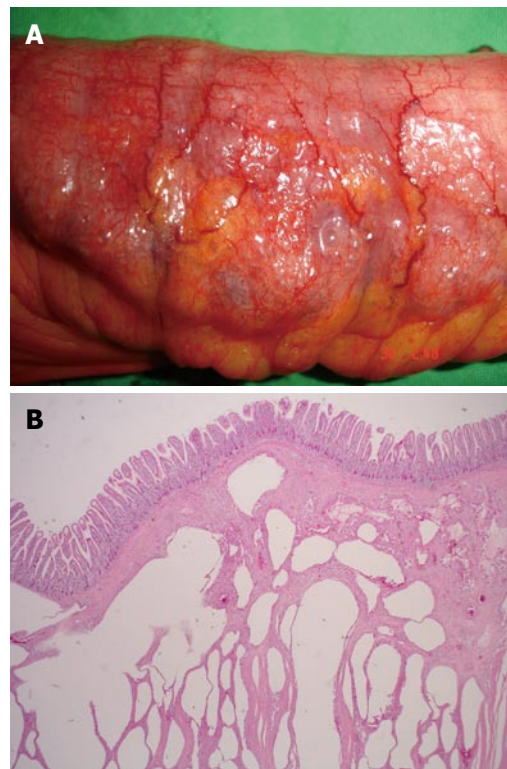


Figure 2 Intestinal wall was grossly thickened, congested, with bubbles on the surface (A) and microscopically the section of small intestine showed diffuse variable sized gas-filled cysts in the submucosa and serosa (B).

then to the vascular supply of the viscera^[1,6]. A review from Boerner and colleagues revealed that 20% out of the 123 patients have had COPD^[7].

The overall incidence of PI may be as low as 0.03%, according to an autopsy series^[8]. In recent times, due to the increased use of the CT scan, the reported incidence of PI has increased to 0.3%^[9]. Of those patients diagnosed with PI, 30%-40% have bowel ischemia/necrosis, and another 30% have bowel obstruction^[3,9]. In another study, of 97 patients diagnosed with PI by CT scan, approximately 50% could have been successfully managed non-operatively, indicating that CT scan is non-specific

and should not be used as the sole indicator for laparotomy^[4]. Conventionally, exploratory laparotomies were performed for patients with PI and pneumoperitoneum because the CT scan indicated possible bowel necrosis and perforation, although the appearance of pneumoperitoneum on CT scan may be attributed to the rupture of PI-associated subserosal cysts^[10-12]. However, there are no large-scale reports of the incidence of pneumoperitoneum in patients with PI.

For patients diagnosed radiologically with PI and a complete history should be taken and physical examinations carried out, especially where there are pulmonary diseases such as COPD^[1,2], systemic diseases as scleroderma, AIDS and inflammatory bowel diseases^[1,2] or medications such as chemotherapeutics, steroids or immunosuppressive agents^[1,2,13]. Appropriate medical treatment should be adopted according to pre-existing illness. In fact, around 50% of patients with PI can be successfully managed non-operatively^[4].

Nonetheless, following the identification of PI urgent surgery may be essential, especially in conditions such as strangulated bowel obstruction or ischemia. Abdominal rebound tenderness, sepsis and failure to respond to conservative treatment are clear clinical indications for surgical treatment. The presence of metabolic acidosis, higher APACHE II score and serum lactic acid level > 2.0 mmol/L at the time of diagnosis are indicators of poor prognosis^[2,4,9]. The appearance of PI on abdominal CT scan gives a definitive diagnosis of bowel ischemia in only 60% of cases^[14]. Signs of the appearances of intramural gas, thromboembolism in the mesenteric vessels, portal venous gas, absence of bowel wall enhancement, or ischemic signs in other organs are considered more specific indications of bowel ischemia^[15]. A broad spectrum of conditions appear as PI on CT scan, and it is reported that patients with PI and other CT findings of ischemia are more likely to have gangrenous bowel^[14], especially where there is portal venous gas, or portal mesenteric gas, which is associated with 81% of patients with transmural bowel infarction^[16].

Meticulous integration of the laboratory data, the appearance on abdominal CT scan and clinical presentations permit clinicians to distinguish benign from life-threatening PI and to decide whether or not urgent surgical intervention is necessary. As described in this case report, it is sometimes difficult to deal with ambiguous findings. For example, the coexistence of PI and intraperitoneal free air on CT scan can be easily mistaken for bowel ischemia and perforation peritonitis^[17]. Since normal laboratory results are not typically consistent with the symptoms of bowel ischemia, surgical intervention would be non-therapeutic, in such cases. To manage patients

with uncertain diagnoses, diagnostic peritoneal lavage or laparoscopy could be performed as an adjunct to confirm bowel necrosis or hollow visceral perforation.

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Ned Abraham, MBBS, FRACS, FRCS, PhD, Coffs Colorectal and Capsule Endoscopy Centre, University of New South Wales, 187 Rose Avenue, PO Box 2244, Coffs Harbour, NSW 2450, Australia

Chapel Alain, PhD, Department of Men Radioprotection, Laboratory of Radio Pathology and Innovative Therapy, Institute of nuclear Safety and radioprotection, PO Box 17, Far 92262, France

Vollmar Brigitte, MD, Professor, Institute of Experimental Surgery, University of Rostock, Schillingallee 69a, Rostock 18057, Germany

Chien-Hung Chen, MD, PhD, Department of Internal Medicine, National Taiwan University Hospital and National Taiwan University College of Medicine, No. 7, Chung-Shan South Road, Taipei 100, Taiwan, China

Stavros J Gourgiotis, MD, PhD, Department of Second Surgical, 401 General Army Hospital of Athens, 41 Zakinthinou Street, Papagou, Athens 15669, Greece

Helena M Isoniemi, MD, PhD, Professor, Transplantation and Liver Surgery Clinic, Helsinki University Hospital, box 263, Helsinki 00029-HUCH, Finland

Chen-Guo Ker, MD, PhD, Professor, Department of Surgery, Kaohsiung Medical University, No. 100, Tz-You 1st Rd, Kaohsiung, Taiwan, China

Adnan Narci, Professor, Department of Pediatric Surgery, Afyon Kocatepe University School of Medicine, Izmir Street, 7km, Afyonkarahisar 03200, Turkey

Marcelo AF Ribeiro, MD, PhD, TCBC, TCBCD, FACS, Department of Surgery, Santo Amaro University, Alameda Gregorio Bogossian Sobrinho, 80/155, Santana de Parnaíba, SP 06543-385, Brazil

Sukamal Saha, MD, FACS, FRCS, FICS, Department of Orthopedics, 3500 Calkins Rd, Suite A, Flint, MI 48532, United States

Manuela Santos, PhD, Associate Professor, Department of Medicine, University of Montreal, Montreal Cancer Institute, CRCHUM/Notre-Dame Hospital, Pavillon De Seve Y5625, 1560 Sherbrooke Est, Montreal, QC, H2L 4M1, Canada

Christian Max Schmidt, MD, PhD, MBA, FACS, Departments of Surgery and Biochemistry/Molecular Biology, Indiana University School of Medicine, 980 W Walnut St C522, Indianapolis, IN 46202, United States

Gregory Peter Sergeant, MD, Department of General Surgery, University Hospital Leuven, Herestraat 49, Leuven B-3000, Belgium

Douglas S Tyler, MD, Department of Surgery, Duke University Medical Center, Box 3118, Durham, NC 27710, United States

Marcus VM Valadao, MD, Instituto Nacional de Cancer, Hospital do Cancer Unidade I, Hc2., Rua do Equador 831, Santo Cristo, Rio de Janeiro 20220-410, RJ, Brazil

Caroline S Verbeke, MD, PhD, Department of Histopathology, Bexley Wing Level 5 St James's University, Hospital Beckett Street, Leeds LS9 7TF, United Kingdom



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Surgery Course, Cairo, Egypt

January 20-22, 2011

Gastrointestinal Cancers Symposium
(ASCO GI), San Francisco, CA,
United States

January 26-30, 2011

5th UK Alpine Liver and Pancreatic
Surgery Meeting, Carlo Magno
Zeledria Hotel, Madonna di
Campiglio, Italy

February 01-03, 2011

6th Annual Academic Surgical
Congress, Huntington Beach, CA,
United States

February 21-26, 2011

Minimally Invasive Surgery
Symposium 2011, The Grand
America Hotel, Salt Lake City, Utah,
United States

March 03-06, 2011

The Society of Surgical Oncology

63rd Annual Meeting, San Antonio,
TX, United States

March 10-13, 2011

The American Hepato-Pancreato-
Biliary Association Annual Meeting,
Miami Beach, FL, United States

March 14-17, 2011

British Society for Gastroenterology
Annual Meeting, International
Convention Centre, Birmingham,
United Kingdom

March 25-27, 2011

NZAGS Conference 2011 GI Surgery,
New Plymouth, New Zealand

March 30-April 02, 2011

The Society of American
Gastrointestinal and Endoscopic
Surgeons 2011 Annual Meeting, San
Antonio Convention Center, San
Antonio, TX, United States

April 02-06, 2011

The American Association for
Cancer Research 102nd Annual
Meeting, Orlando, FL, United States

April 10-12, 2011

The American Association of
Endocrine Surgeons 32nd Annual
Meeting, Houston, TX, United States

April 14-16, 2011

The American Surgical Association
131st Annual Meeting, Boca Raton,
FL, United States

May 07-10, 2011

Digestive Disease Week, Chicago,
IL, United States

May 07-10, 2011

45th Annual Meeting of the Pancreas
Club, Chicago, IL, United States

June 15-18, 2011

19th International Congress of
the European Association for
Endoscopic Surgery, in collaboration
with and incorporating the 15th
National Congress of the Italian
Society of Endoscopic Surgery,
Torino, Italy

September 10-14, 2011

International Congress of
Endoscopy, Los Angeles, CA,

United States

September 22-24, 2011

5th joint EAES and ESGE, European
Workshop on NOTES, Frankfurt,
Germany

September 23-25, 2011

The New England Surgical Society
92nd Annual Meeting, Breton
Woods, NH, United States

September 23-27, 2011

ECCO-European Society for Medical
Oncology Congress, Stockholm,
Sweden

October 23-27, 2011

The American College of Surgeons
97th Annual Clinical Congress, San
Francisco, CA, United States

November 02-05, 2011

American Pancreatic Association
42nd Annual Meeting, Chicago, IL,
United States

November 13-16, 2011

The Western Surgical Association
119th Scientific Session, Tucson, AZ,
United States



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- 3 **Tian D**, Araki H, Stahl E, Bergelson J, Kreitman M. Signature of balancing selection in Arabidopsis. *Proc Natl Acad Sci USA* 2006; In press

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- 5 **Vallancien G**, Emberton M, Harving N, van Moorselaar RJ; Alf-One Study Group. Sexual dysfunction in 1, 274 European men suffering from lower urinary tract symptoms. *J Urol* 2003; **169**: 2257-2261 [PMID: 12771764 DOI:10.1097/01.ju.0000067940.76090.73]

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- 6 21st century heart solution may have a sting in the tail. *BMJ* 2002; **325**: 184 [PMID: 12142303 DOI:10.1136/bmj.325.7357.184]

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- 9 Outreach: Bringing HIV-positive individuals into care. *HRS-A Careaction* 2002; 1-6 [PMID: 12154804]

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- 10 **Sherlock S**, Dooley J. Diseases of the liver and biliary system. 9th ed. Oxford: Blackwell Sci Pub, 1993: 258-296

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- 11 **Lam SK**. Academic investigator's perspectives of medical treatment for peptic ulcer. In: Swabb EA, Azabo S. Ulcer disease: investigation and basis for therapy. New York: Marcel Dekker, 1991: 431-450

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- 12 **Breedlove GK**, Schorfheide AM. Adolescent pregnancy. 2nd ed. Wicczorek RR, editor. White Plains (NY): March of Dimes Education Services, 2001: 20-34

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- 15 Morse SS. Factors in the emergence of infectious diseases. *Emerg Infect Dis* serial online, 1995-01-03, cited 1996-06-05; 1(1): 24 screens. Available from: URL: <http://www.cdc.gov/ncidod/cid/index.htm>

Patent (list all authors)

- 16 **Pagedas AC**, inventor; Ancel Surgical R&D Inc., assignee. Flexible endoscopic grasping and cutting device and positioning tool assembly. United States patent US 20020103498. 2002 Aug 1

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Write as mean \pm SD or mean \pm SE.

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