

Treatment of stress incontinence secondary to chronic cough caused by gastric atony: a case report

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Background: Coughing, especially when it is persistent, is one of the leading symptoms experienced by millions prior to seeking medical help. Gastroesophageal reflux disease (GERD) and allergic diseases such as asthma and sinusitis are the common culprit for subacute or chronic cough in Europe and the United States. In stark contrast, GERD-related cough is comparatively rare in the East. While gastroptosis is associated with GERD, it is very peculiar to find cases of urinary incontinence on top of GERD-related cough. To the best of our knowledge, we are the first to report a case of stress urinary incontinence secondary to chronic cough caused by gastric atony.

Case Description: We reported a case of a 54-year-old female who was admitted to the clinic due to repeated abdominal spasms accompanied by chronic cough for more than 10 years, with aggravating urinary incontinence for the past 10 months. Physical examination showed no positive signs. Upper gastrointestinal radiography displayed no obvious pathological signs in the esophagus. An elongated stomach with low tension is observed, with the lowest point at the sacroiliac level. Gastroscopy revealed no abnormality in the esophageal mucosa, hyperemia and swelling of gastric antrum mucosa. Three-dimensional color ultrasound scan of the pelvis showed possible pelvic floor dysfunction. She had a past history of thrombotic thrombocytopenic purpura and connective tissue disease. Her diagnosis was gastroptosis, and urinary incontinence secondary to gastroesophageal reflux cough. She was prescribed with esomeprazole 20 mg q12h, domperidone 10 mg t.i.d., compound methoxyphenamine hydrochloride 2 pills t.i.d., compound-codeine 10 mL t.i.d., and cholestyramine powder 5 g t.i.d. for 2 weeks, and her symptoms of urinary incontinence and coughing were significantly relieved.

Conclusions: In this case, we conclude that GERD patients with the symptoms of abdominal spasm, cough and urinary incontinence can be effectively treated with etiological treatments with drugs. However, if medication fails, surgical options are also available.

Keywords: Gastroptosis; gastroesophageal reflux disease (GERD); chronic cough; urinary incontinence; case report

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Introduction

Gastric atony often refers to the lack of gastric motility, and gastric emptying disorders (1). It is easy for patients with atony to develop gastroesophageal reflux disease (GERD) (2). GERD is a common digestive system

disease, which is characterized by acid reflux, heartburn and retrosternal pain. In recent years, more and more studies have found GERD to be closely related to chronic cough, and chronic cough has gradually become one of the most common extraesophageal symptoms (3). The standard of diagnosis and treatment of GERD has become

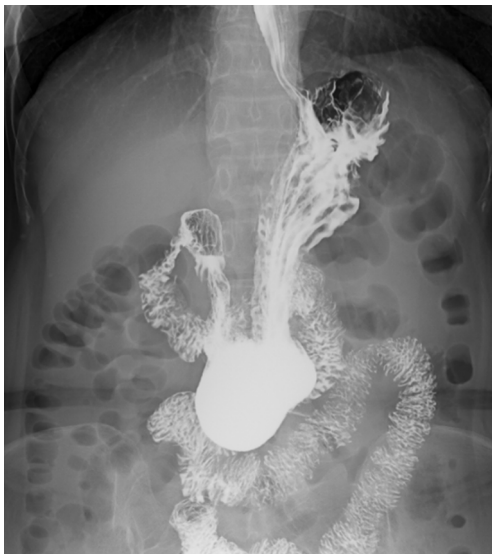


Figure 1 Gastric atony seen on an upper gastrointestinal radiograph.

an important part of the guidelines for the diagnosis and treatment of cough issued by various countries. Similarly, chronic cough can lead to a series of complications, such as chest pain, hernia and urinary incontinence (UI), which can severely impact one's quality of life. However, there are very rare patients affected with the above symptoms simultaneously. According to our literature review, there is no similar cases reported. Therefore, this paper reports a case of stress urinary incontinence (SUI) secondary to chronic cough caused by gastric atony (4), and introduces the process and results of our diagnosis and treatment (5). The purpose of this paper is to provide future references for clinical treatment of similarly afflicted patients. We present the following case in accordance with the CARE reporting checklist (available at <https://dmr.amegroups.com/article/view/10.21037/dmr-22-60/rc>).

Case presentation

A 54-year-old woman who had presented with “repeated abdominal spasms accompanied by coughing for more than 10 years, with aggravated UI for the past 10 months” was admitted on October 15th, 2018. In the past 10 or more years, the patient had repeatedly suffered from paroxysmal periumbilical spasms, which typically occurred after a change in body position or after a meal. Each spasm was accompanied by paroxysmal cough (mainly dry cough).

White phlegm and vomiting were occasionally seen. The symptoms spontaneously resolved within several minutes. No chest tightness, shortness of breath, or breathing difficulty was noted. The number of attacks was comparable between day and night, and wheezing occasionally occurred at night. Acid reflux and belching were occasionally experienced. Pulmonary function tests in a different facility showed no obvious abnormality, and no specific treatment was applied. In the last 10 months, the patient felt the frequency and severity of the abdominal spasms and cough increased. The cough was accompanied by UI; she had to change to more than 10 times every day.

Physical examination revealed a soft and flat abdomen. No tenderness or palpable mass was detected. She had no shifting dullness, and there were bowel sounds about 4 times per minute.

The upper gastrointestinal radiography after admission showed no obvious abnormality in the esophagus. The atonic stomach had a low tone, with the lowest tone seen at the sacroiliac level (*Figure 1*). Gastrosocopy showed no obvious abnormality in esophageal mucosa, whereas hyperemia of antral mucosa was visible. Pulmonary computed tomography (CT) showed focal fibrosis, proliferation, and calcification in the anterior segment of the upper lobe, right middle lobe, and lower lobe, along with multiple bullae in both lungs. Color Doppler ultrasound of the urinary system showed no obvious abnormality in the kidneys, ureters, and bladder. Three-dimensional (3D) color Doppler ultrasonography of the pelvic floor indicated the possibility of spastic pelvic floor syndrome. She had developed thrombocytopenic purpura and connective tissue disease more than 10 years prior, which were treated with therapeutic plasma exchange and regular hormone therapy. These treatments were discontinued 5 years ago. She denied any history of asthma, hypertension, diabetes, or coronary heart disease. Also, she denied any history of smoking or drinking. As a gravida 2 para 2 (G2P2) woman, she had two spontaneous vaginal deliveries.

The diagnosis of gastroptosis and UI secondary to gastroesophageal reflux-induced chronic cough (GERC) was considered. After oral administration of esomeprazole 20 mg q12h, domperidone 10 mg t.i.d., compound methoxyphenamine hydrochloride 2 pills t.i.d., compound-codeine 10 mL t.i.d., and cholestyramine powder 5 g t.i.d. for 2 weeks, coughs during the daytime were reduced by half and coughs at night effectively disappeared. Accordingly, UI was also declined. Finally, the patient was discharged from our hospital with a significant reduction in symptoms after

2 weeks of medication without significant adverse effects.

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Declaration of Helsinki (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

IMDT discussion

Discussion among the Seventh Affiliated Hospital of Sun Yat-sen University

Gastric atony is often associated with disturbance of gastric emptying. Studies have shown that about 58% of patients with GERD are accompanied by delayed gastric emptying (6). Delayed gastric emptying can dilate the proximal stomach, induce transient relaxation of the lower esophageal sphincter, and lead to gastroesophageal reflux (GER). However, cough is a common extraesophageal symptom of GERD, and GERD with cough as the main manifestation is known as GERC.

In Europe and the United States, GERC is the third most common cause of chronic cough after asthma and postnasal drip syndrome, which together account for 90% of the causes of chronic cough (7). In China, GERC accounts for 5–20% of chronic cough, which is the fifth cause of chronic cough (8).

The pathogenesis of GERC has two theories: reflux theory and reflex theory. The former believes that the gastric contents reflux to the pharynx and larynx due to the abnormal structure and function of the lower esophagus or more severely, inhale into the lung, stimulating the cough receptors of the pharynx and larynx or trachea and bronchi to cause cough. The latter believes that the esophageal stimulation signal produced by distal lower esophageal reflux can be transmitted to the vagus nucleus, the vagus nerve center of the brainstem, and induce airway neurogenic inflammation through the esophagobronchial reflex. An excited cough center or sensitized cough reflex leads to cough (9).

The core of treatment has three points in this case. The first point is acid suppression. Secondly, motility promotion should be strengthened. At last, cough inhibition also plays an important role. On the one hand, proton pump inhibitor (PPI) can effectively reduce gastric acid secretion, reduce

the acidity and volume of esophageal reflux (10), and reduce pulmonary aspiration or esophagobronchial reflex caused by reflux by inhibiting the last step of H^+-K^+-ATP enzyme (proton pump) secreted by gastric mucosal parietal cells to relieve cough. On the other hand, through the use of gastrointestinal motility-promoting drugs, the emptying of gastric contents can be accelerated and the gastroduodenum motility can be coordinated. In addition, the combined use of antitussive drugs can greatly relieve the symptoms of cough, reduce the abdominal pressure, relieve the intravesical pressure, and reduce the occurrence of UI.

Drug therapy remain the first-line treatment for GERD, and PPI is the first choice (11). For chronic coughs whose acid inhibition treatment is ineffective, the 2016 American College of Chest Physicians (ACCP) guidelines (12) state that gabapentin experimental treatment is recommended and re-evaluated at 6 months after informing patients of complications and benefits such as drowsiness and vertigo. Gabapentin is a neuromodulator, with its mode of action mainly aimed at the nerve hypersensitivity in chronic cough, and its curative effect has been confirmed by randomized controlled trials (13). Therefore, we can consider its use for chronic refractory cough. Botulinum toxin has been used in the treatment of muscle spasm diseases for many years and has achieved satisfactory results. Local injection of botulinum toxin can safely and effectively treat achalasia without causing the occurrence and aggravation of GERD. Sterling *et al.* (14) showed in their research that 11 patients with refractory GERD complicated with gastroparesis were successfully treated with botulinum toxin by local injection of botulinum toxin into the pylorus. After an average reaction period of 5 months, it was found that the reflux symptoms of GERD patients were significantly improved.

For cases of reflux or gastroparesis with poor results from standard drug treatment, surgical treatment can be considered. Anti-reflux surgery is a promising radical therapy for the treatment of intractable or refractory GERC by artificially reconstructing the mechanical barrier of GER (15). The commonly used anti-reflux surgery is laparoscopic gastric fundus mucosal folding, with an efficacy of about 85% (16). However, the curative effect is reduced with time, and the effective rate is about 71% 5 years after operation (17). In recent years, it has been reported that endoscopic radiofrequency ablation of the lower esophageal sphincter, suture, silicone injection or transoral incisionless fundoplication has the advantages of a better short-term effect, simpler operation, less trauma, higher safety and less complications (18). However, its long-

term effect remains to be further clarified, and more clinical feedback is required to definitively conclude whether it can become a widely used treatment. Other surgical methods such as transpyloric stenting (TPS), peroral endoscopic pyloromyotomy (POEP), gastric electrical stimulator (GES), laparoscopic pyloroplasty (LP), and laparoscopic gastrectomy (LG) are available for refractory gastroparesis patients who are ineffective by lifestyle modification and drug treatment as well.

For the treatment principle of SUI secondary to cough, the focus is to identify and treat the causes of cough whenever possible, and secondarily, deal with UI. The management of UI includes non-operative treatment and surgery. As a rule of thumb, non-operative treatment should be first considered. It primarily involves behavioral therapy, pelvic floor muscle training (PFMT), drug therapy, electrical stimulation therapy and electromagnetic therapy. Non-operative treatment has high safety and few complications, and a variety of these methods can be combined to improve the symptoms of UI. Surgical treatment can be performed for mild SUI patients with poor conservative treatment effects or poor compliance, as well as moderate and severe SUI patients whose quality of life have been seriously impacted. Common surgical procedures include mid-urethral slings (MUS), vaginal suspension, autogenous fascia sling, para-urethral injection of fillers and compression implants (19).

Several issues regarding the management of this patient were further discussed below.

Question 1. What is the possible etiology of chronic cough caused by gastric atony?

Expert opinion 1: Shinichi Kinami

Gastroparesis is the abnormal downward displacement of the stomach. Gastroparesis is more common in slim individuals. This condition is likely to occur because of nutritional deficiency and low amount of visceral fat and as a result, the stomach lowers. Alternately, gastric atony is an affliction in which the smooth muscle strength of the stomach is reduced, and it is a condition close to gastroparesis. Gastroparesis refers to a disorder in which gastric emptying is delayed, despite the absence of a mechanical obstruction, such as pyloric stenosis. Gastroparesis is divided into two types, the secondary gastroparesis which may occur after gastrectomy or diabetes mellitus, and the idiopathic gastroparesis. Some cellular abnormalities are observed in patients with gastroparesis, such as loss of Kit expression,

loss of interstitial cells of Cajal, and an increase in CD45 and CD68 immunoreactivity (20). In this case, the individual presents idiopathic gastroparesis.

Gastroparesis is associated with aspiration (21). Reflux has been associated with chronic cough and laryngitis. In this situation, GER is expected to be involved in the chronic cough. However, no abnormality is recognized in the esophageal mucosa during the upper-gastrointestinal endoscopic examination. On the other hand, GERC can be divided into two subgroups based on the GER's pH, namely acid GERC or nonacid GERC. Nonacid GERC is less common than acid GERC (22). If this case is of nonacid GERC, there is no discrepancy even if the esophageal mucosa is intact. The endoscopic examination showed hyperemia of antral mucosa, so infection with *Helicobacter pylori* (HP) is suspected in this situation. The attenuation of gastric acid secretion in HP infection may contribute to the normal esophageal mucosa and the absence of pneumonia symptoms.

Expert opinion 2: Derek B. Hennessey

This patient could have GERD in association with or as a result of their gastric atony. If the cough is due to GERD, then listening to the patient and taking a thorough patient history will be enough to diagnose the condition. Patients with GERD often complain of heartburn, belching or regurgitation and patients with a GERD-related cough often have night-time coughs or coughing after meals. When a patient does not have these symptoms, the chances of them having acid reflux as a primary cause of their cough is small.

Question 2. Is the chronic cough in this patient an atypical manifestation of GERD?

Expert opinion 1: Shinichi Kinami

The abdominal pain in this context is paroxysmal and of short duration. The GERD, under this circumstance, may be attributed to transient reflux associated with gastroparesis rather than to anatomical factors such as hiatal hernia. The chronic cough was accompanied by increased abdominal pressure, and the transient GER was exacerbated further, and so it seems to fall into the vicious circle of the aggravation of the nonacid GERC.

Expert opinion 2: Derek B. Hennessey

The most common causes of chronic cough are non-gastrointestinal disorders such as postnasal drip, asthma and

chronic obstructive pulmonary disease (COPD). However, it is estimated that up to 15% of chronic cough cases are related to GERD (23). So I would not consider it an atypical manifestation of reflux.

Question 3. What are the possible mechanisms underlying the effective treatments that are currently available?

Expert opinion 1: Shinichi Kinami

In this case, in addition to antitussives, it may be effective to reduce the frequency of nonacid GER by using enterokinesis-stimulating drugs. Domperidone may be effective.

Expert opinion 2: Derek B. Hennessey

There are two theories for the development of GERD associated cough, the reflux theory and the reflex theory. In the reflux theory, gastric fluid reflux into the oesophagus past the sphincter, this results in micro-aspiration of micro-droplets into the larynx and bronchial tree, directly causing cough as a protective mechanism. In the reflex theory, gastric fluid reflux in the oesophagus leads to an esophagobronchial reflex that causes cough. The standard treatment for patients with GERD-associated cough is a trial of PPI therapy. The patient is given a high dose of PPIs and is monitored for up to 3 months to see if his or her cough improves. It is thought that it takes approximately three months for true GERD-related cough to improve because the nerves involved in the cough reflex take time to return to normal function. Studies suggest that this treatment is effective in up to 70% of patients with chronic cough (24).

Question 4. Are there any alternative treatments? What are the treatments for gastric atony that are currently available?

Expert opinion 1: Shinichi Kinami

Accurate diagnosis of idiopathic gastroparesis is difficult. Thus, there could be many idiopathic gastroparesis cases among those diagnosed for postprandial distress syndrome type of functional dyspepsia (FD). The effective drug for FD seems to be efficient in this case. Acotiamide is a valuable drug which proved its effectiveness for FD in a double-blind clinical trial (25).

On the other hand, some herbal medicines are considered to be effective for gastric atony and GERD, and these drugs are supposed to be potent as an alternative treatment in this

situation. Rikkunshito is one drug to be considered (26).

Expert opinion 2: Derek B. Hennessey

There are some recent reports in the literature demonstrating a benefit with the use of gabapentin in patients with GERD-associated cough (27). An article was published in *Lancet* in which researchers conducted a randomised, double-blind, placebo-controlled study of patients with idiopathic cough who were treated with gabapentin or placebo. These investigators found significant improvement in their patients' cough-related quality of life. However, these patients received high doses of gabapentin with a titration protocol up to 1,800 mg if tolerated, which led to a 31% rate of adverse effects (28). Gabapentin is associated with side effects such as fatigue, drowsiness, and occasionally nausea. Pregabalin is similar to Gabapentin and has fewer side effects and may be an alternative in this regard.

Treatment for gastric atony should begin with dietary modification. Low fat, low fibre diet should be encouraged. If the patient has diabetes, control should be improved. Oral prokinetic medications can then be introduced such as metoclopramide, erythromycin and domperidone. Antiemetics may also be helpful. If these options fail, there are some surgical options available. These include pyloric injection of Botulinum toxin, venting gastrostomy, pyloroplasty, partial gastrectomy, feeding jejunostomy and GES.

Question 5. What are the treatments for stress incontinence secondary to coughing?

Expert opinion 1: Shinichi Kinami

Antitussive therapy is most important for the treatment of stress incontinence secondary to chronic cough. However, flaccid pelvic floor is partly responsible for this incontinence in female patients. Pelvic floor muscle group relaxes due to aging and birth history, successively, bladder neck drops, and abdominal pressure transmission to the urethra becomes poor. In this condition, when the abdominal pressure rises, only the internal pressure of the bladder rises, resulting in the leakage of urine. The supplemental therapies, other than antitussive therapy, may include bladder training, phenylpropanolamine, and surgical treatments.

Expert opinion 2: Derek B. Hennessey

When assessing a female patient with UI, it is essential to take an accurate history to categorise the woman's UI and

determine if it is SUI, urgency UI/overactive bladder (OAB) or mixed UI. It is also important to seek to identify relevant predisposing and precipitating factors and other diagnoses. In this case, the chronic cough is the precipitating factor for the UI. Physical examination should be performed to assess for pelvic organ prolapse (POP) and identify atrophic changes, infection and excoriation. Digital assessment to confirm pelvic floor muscle contraction should also be performed. Validated incontinence-specific quality of life scales and questionnaires should be used to quantify the impact of UI and response to treatment. In cases of clear SUI like this, multi-channel filling and voiding cystometry is not indicated.

In this case, every effort should be made to treat the cough as this is a clear precipitant factor for the UI. The patient should also be offered a trial of supervised PFMT of at least three months duration. The PFMT programme should comprise of at least eight contractions performed three times a day. If correction of the chronic cough and conservative management fails, the patient should be offered surgical treatment. The use of a multi-disciplinary team (MDT) meeting is increasingly being used to discuss to correct treatment for patients with SUI before surgical intervention. Furthermore, it has become clear that treatments for SUI should be centralised to maximise outcomes for the patients.

Surgical options open to this patient include intramural bulking agents, synthetic mid-urethral tapes, autologous fascial sling surgery and colposuspension. The patient should be counselled about the advantages and disadvantages of each procedure and be given time to decide which option they want. They should be told that intramural bulking agents are the least effective procedure. That in some countries, mid-urethral tapes are currently out of favour to the potential complications related to mesh erosion. That autologous fascial slings are associated with good outcomes and produce a continence rate of approximately 80% and an improvement rate of 90% which is similar to mid-urethral tapes and better than colposuspension. However, that autologous fascial sling has higher rates of complications such as urinary tract infections, voiding difficulty, and postoperative urge incontinence.

Conclusions

To sum up, GERD plays a very important role in causing chronic cough both at home and abroad. GER caused by gastropothesis may be the most likely cause of chronic cough

in this case. It further induced the symptoms of SUI in this patient. Drug treatment is the first choice, and in the case of poor outcome of drug treatment, surgical treatment can be later considered. However, in view of its invasiveness, the effect of the operation cannot be guaranteed when the causal relationship between GERD and cough is not clear, so it is necessary to strictly identify the cause and carefully select the appropriate surgical candidates.

This is a special case that the symptoms of cough, UI were presented simultaneously in a patient with Gastropothesis. We have treated her effectively with drugs and the clinical symptoms have been significantly relieved. However, the exact conclusion still needs to be confirmed by more cases.

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Footnote

Reporting Checklist: The authors have completed the CARE reporting checklist. Available at <https://dmr.amegroups.com/article/view/10.21037/dmr-22-60/rc>

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <https://dmr.amegroups.com/article/view/10.21037/dmr-22-60/coif>). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Declaration of Helsinki (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

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