Pseudoachalasia: A peculiar case report and review of the literature

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Abstract

Pseudoachalasia is a rare secondary achalasia, which accounts for only a small subgroup of patients. We describe a 77-year-old woman with recent onset of dysphagia and typical esophageal manometric findings of achalasia. Moreover, esophageal manometric findings of vascular compression at 36 cm from the nose were associated with dysphagia. An upper endoscopy showed the absence of lesions both in the esophagus and gastro-esophageal junction, whilst a 15-mm ulcer on the gastric angulus was detected. The gastric ulcer resulted in being a diffuse signet ring cell carcinoma at histology, suggesting pseudoachalasia. An abdominal computed tomography scan showed an irregular concentric thickening of the gastro-esophageal junction wall extending for 7 cm and a dilated ascending thoracic aorta with no presence of the inferior vena cava, with an enlarged azygos as the source of vascular compression of esophagus. Moreover, cardia involvement from diffuse signet ring cell carcinoma of the gastric angulus was also recognized as the cause of dysphagia. The cancer was not suitable for a surgical approach in an old patient with cardiovascular comorbidities and support therapy was started. In our ambulatory series, pseudoachalasia was eventually diagnosed in 4.7% of 234 consecutive patients with esophageal manometric finding suggestive of achalasia. We also reviewed cases in the literature and aimed to evaluate the reported causes of pseudoachalasia.

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Key words: Pseudoachalasia; Achalasia; Esophageal vascular compression; Thoracic aorta; Azygos vein

Core tip: Typical esophageal dysmotility can be observed in pseudoachalasia, a secondary form of achalasia mostly due to cancer or even benign tumors, post-operative complications or paraneoplastic syndromes. Dysphagia is frequently observed in subjects with pseudoachalasia. We describe a peculiar case where dysphagia could be due to a vascular compression of the esophagus rather than involvement of the esophagus at the gastro-esophageal junction from gastric neo-plasia. The less invasive therapeutic option should be proposed in an old patient. The reviews of our cases of pseudoachalasia and the literature are included.
INTRODUCTION
Pseudoachalasia is a secondary form of achalasia which accounts for up to 4% of patients with achalasia-like syndrome, with symptoms, radiographic and esophageal manometric findings that mimic primary achalasia. It was first recognized by Ogilvie in 1947 as a form of achalasia due to involvement of the cardia region from gastric adenocarcinoma. Achalasia is a rare esophageal motor disorder with an estimated annual incidence of 1 per 100000 individuals. The pathophysiology of achalasia consists of loss of inhibitory neurons of the myenteric plexus in the esophageal wall. Likely, it is believed to be the result of a slowly progressive process affecting the neural control of lower esophageal sphincter (LES) relaxation, with consequent symptoms, dysphagia, regurgitation, chest pain and weight loss, indistinguishable from those in pseudoachalasia. Patients with idiopathic achalasia or pseudoachalasia are not rarely misdiagnosed as having other diseases, such as gastro-esophageal reflux or stricture. So far, Chaga’s disease, intestinal pseudo-obstruction, amyloidosis, surgery (post vagotomy, post fundoplication), pancreatic pseudocyst and cardia cancer have been identified as types of pseudoachalasia. We describe a peculiar case of pseudoachalasia and review data reported in literature.

CASE REPORT
A 77-year-old woman, with previous acute myocardial infarction, was suffering with hypertensive and mild depression for which she was taking angiotensin converting enzyme inhibitor, serum serotonin reuptake inhibitor and low-dose aspirin. Because of swallowing difficulties of solids and liquids for the last 3 mo, with recent recurrent vomiting episodes and a 9-kg weight loss, she underwent a barium study which showed an enlarged esophagus, with a characteristic tapered narrowing of the lower end, producing a “rat tail” appearance. However, an upper endoscopy showed an absence of lesions, both in the esophagus and gastro-esophageal junction, whilst a 15-mm ulcer on the gastric angulus was detected. While waiting for histological assessment of the gastric ulcer, a conventional esophageal manometric study was performed to rule out achalasia.

Esophageal manometry was done with a 8-lumen pneumo hydraulically infused catheter using external transducers with an ambulatory stationary recording system (Mui Scientific, Ontario, Canada), as previously described. Four distal radially oriented leads were used to identify and measure LES pressure by the use of the station withdrawal method. Peristalsis was considered absent if both extrapolated onsets and the peaks of waves at 5 cm, 10 cm and 15 cm above the LES after swallow of 5 mL water were not in sequence, i.e., simultaneous contractions. The tracing was also examined for evidence of vascular compression, which may be diagnosed when a localized area of elevated intra-esophageal resting pressure of at least 4 mmHg with superimposed cyclic pressure spikes with a frequency of 60-100/min is observed. This segment of vascular compression was also assessed for evidence of relaxation to resting intra-esophageal pressure in response to wet swallows.

In detail, manometric findings were typical of achalasia with LES pressure of 38 mmHg (range of normal values between 10 mmHg and 30 mmHg), decreased LES relaxation and the absence of peristalsis with simultaneous contractions in the esophageal body. Moreover, elevated intra-esophageal resting pressure of 22 mmHg at 36 cm from the nose with superimposed cyclic pressure spikes with a frequency of 88/min was registered (Figure 1). Absence of relaxation in response to swallows on manometric tracing with evidence of vascular compression of the esophagus was found in our patient and considered to be the cause of dysphagia. The gastric ulcer resulted in being a diffuse signet ring cell carcinoma at histology and a computed tomography (CT) scan disclosed a dilated ascending thoracic aorta with no presence of the inferior vena cava with azygos continuation (Figure 2) as the source of vascular compression of the esophagus. In addition, an irregular concentric thickening of the gastro-esophageal junction wall extending for 7 cm was documented and recognized as the cause of dysphagia from mechanical obstruction in the more distal esophagus. The tumor mass also involved the left diaphragmatic pillar with the adjacent adipose tissue. Such a feature was consistent with diagnosis of pseudo-achalasia, as shown by esophageal manometry. The cancer was not suitable for a surgical approach in an old patient with cardiovascular comorbidities and support therapy was started.

Our ambulatory series
By reviewing medical records of outpatients with dysphagia referred to our ambulatory series to perform conventional esophageal manometry, we computed 234 consecutive patients with achalasia. Of these, 11 (4.7%) patients were eventually diagnosed with pseudoachalasia due to different causes (Table 1). No manometric findings of esophageal vascular compression were detected in the manometric tracings.

Literature review
A computer-assisted search was performed using PubMed, with the limitation of English language and from June 1968 to June 2012, by using the exploded medical subject heading term “pseudoachalasia”. Boolean operators (NOT, AND and OR) also were used in succession to narrow and widen the search. Manual searches of reference lists from identified relevant articles were performed to identify any additional studies that might have been missed. Overall, we identified 155 publications reporting data of 302 patients diagnosed with pseudoachalasia. As shown in Table 2, primary malignancies of the esophagus or esophago-gastric junction accounted for 50% of cases of secondary achalasia. This was followed by secondary malignancies (18%), such as metastases
(12%), which primarily originated from lung and breast. Benign causes, including mesenchymal tumors, secondary amyloidosis and peripheral neuropathy accounted for 14% of patients with pseudoachalasia. In 12%, the motor abnormality occurred as a consequence of gastro-esophageal surgery, namely anti-reflux surgery. Rare causes of pseudoachalasia were neurological disorders (3.5%) or paraneoplastic syndromes (2.5%) in the context of small-cell carcinoma, bronchial carcinoid, gastric carcinoma and pleural mesothelioma. However, none of these paraneoplastic syndromes was associated with mediastinal or esophageal infiltration by the primary tumor.

**DISCUSSION**

Pseudoachalasia is a rare disease which accounts for only a small subgroup of patients with dysphagia. Owing to the lack of a large series, there are no reliable epidemiological data on the incidence and prevalence of the disease. In our series, 4.7% of patients who fulfilled the manometric criteria of achalasia were eventually diagnosed with a malignant disease, directly or indirectly involving the cardia, or following anti-reflux surgery. Two patterns of tumor involvement have been described[19]. The most

| Age (yr) | Sex | Duration of dysphagia (mo) | Etiology | Treatment |
|---------|-----|---------------------------|----------|-----------|
| 83      | M   | 5                         | Esophageal adenocarcinoma | Radiotherapy |
| 82      | F   | 3                         | Cardia adenocarcinoma     | Esophageal metal stent |
| 79      | M   | 7                         | Gastric carcinoma         | Supportive therapy  |
| 77      | F   | 2                         | Gastric carcinoma         | Radiotherapy |
| 75      | M   | 8                         | Cardia adenocarcinoma     | Chemotherapy |
| 74      | M   | 9                         | Gastric carcinoma         | Surgery |
| 71      | M   | 4                         | Mediastinal tumor         | Radiotherapy |
| 69      | F   | 5                         | Cardia carcinoma          | Chemotherapy |
| 69      | M   | 3                         | Pancreatic tumor          | Chemotherapy |
| 68      | M   | 6                         | Lung adenocarcinoma       | Surgery |
| 52      | F   | 12                        | Stricture post-fundoplication | Surgery |

M: Male; F: Female.
common type consists of malignant stricture of the cardia which acts as a physical barrier to the passage of food. A less frequent type is strictly related to the malignant submucosal infiltration with secondary impairment of inhibitory neurons of the esophageal myenteric plexus by tumor cells, which let the manometric pattern of achalasia be stable even after any treatment. Indeed, many malignancies as common causes of pseudoachalasia directly involve the esophageal myenteric plexus by neoplastic cells infiltrating the mucosa at the cardia as the main pathogenetic mechanism. Moreover, neuronal degeneration distant from the primary tumor site with reduction in ganglion cells in the dorsal nucleus of the vagal nerve or in the vagal nerve itself has been also proposed. This interaction of tumor factors with the esophageal neuronal plexus without a direct infiltration of the esophago-gastric junction, even infrequently, and serological antineuronal nuclear antibody can be detected in these patients, suggesting a paraneoplastic syndrome. Another form of pseudoachalasia occurs following anti-reflux surgery. Three explanations have been proposed: misdiagnosed idiopathic achalasia with evidence of dysphagia just after surgery, achalasia occasionally developing for the underlying gastro-esophageal reflux, and development of scar tissue and/or an overly tight fundic wrap.

Pseudoachalasia needs to be excluded in old patients (> 60 years) with a short duration of symptoms (< 1 year) and substantial weight loss. It might be difficult to diagnose in an early phase because of the low diagnostic yield of either barium and endoscopy studies, with a false-negative rate up to 25% for endoscopic biopsies to diagnose cancer being reported. Moreover, even although the role of the CT scan has been described as useful, the normal findings of either biopsy or CT scan results should not lead to complete reassurance of a benign etiology. Endoscopic ultrasound can provide the level of tumor invasion and possible spread to regional lymph nodes, but shows a low accuracy in differentiating mucosal from submucosal lesions at the lower esophagus or gastro-esophageal junction and only repeated studies or even surgical exploration may point to the diagnosis of pseudoachalasia. Esophageal manometry remains the current gold standard to diagnose esophageal motor disorder, both in idiopathic achalasia and pseudoachalasia, which includes an abnormal relaxation of the LES and absence of peristalsis in the esophageal body.

Since the major mechanism producing pseudoachalasia is undoubtedly a mechanical obstruction of the distal esophagus which causes esophageal dilation, the removal of this obstruction either by surgery and/or chemotherapy and/or radiation can be the goal of treatment in some cases. It often allows the return of normal peristalsis into the esophagus. However, in many patients with pseudoachalasia, the esophageal motor abnormalities have been found to be stable even after a radical treatment of the neoplasia. Recently, the use of expandable metal stents has been proposed as an additional therapeutic option in selected cases of pseudoachalasia when palliation is required in patients not suitable for surgery.

We report a case of pseudoachalasia in an old woman with recent onset of symptoms with substantial weight loss. Barium study, esophageal manometric findings typical of achalasia and manometric findings of vascular compression at 36 cm from the nose were observed. Abdominal CT scan showed a dilated ascending thoracic aorta with no presence of the inferior vena cava with enlarged azygos. Moreover, an irregular concentric thickening of the gastro-esophageal junction wall from diffuse signet ring cell carcinoma of the gastric angulus was also documented, suggesting secondary achalasia.

Our patient represents a typical case of pseudoachalasia due to a gastric tumor. We considered it peculiar because dysphagia could be due to esophageal vascular compression with an elevated intra-esophageal resting pressure of 22 mmHg at 36 cm from the nose with absence of relaxation to resting intra-esophageal pressure in response to swallows. However, cardia involvement from the tumor mass originating from the gastric angulus, which resulted in being diffuse signet ring cell carcinoma, could also cause dysphagia. Moreover, no cases of pseudoachalasia have been described in the literature associated with esophageal vascular compression.

In conclusion, a secondary form of achalasia may diagnose a small subgroup of patients with dysphagia. Esophageal manometric study must be considered in conjunction with a careful barium study, CT scans and an accurate endoscopic examination in these subjects as diagnostic tests. A vascular compression of the esophageal body could cause dysphagia, which in our case was associated with mechanical obstruction of the cardia from a tumor mass originating from the angulus in the stomach. The less invasive therapeutic option should be proposed in an old patient with comorbidities with a short life expectancy in terms of acceptable quality of life and low risk procedure in respect to other more invasive and complex, even more appropriate treatments.

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