CASE REPORT

Mediastinal granuloma: a rare cause of dysphagia

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SUMMARY

Dysphagia is commonly attributed to disorders arising from dysfunction of the oesophageal mucosa or oesophageal motility. Mediastinal structures causing compression of the oesophagus remain a rare presenting cause of dysphagia. We report a case of a woman presenting with dysphagia to solid foods and associated symptoms of weight loss. Traditional evaluation for dysphagia was unrevealing until cross-sectional imaging suggested a mediastinal obstructive process. The finding of a mediastinal granuloma, distinct from mediastinal fibrosis, as the aetiology of dysphagia is a rare finding, with specific treatment implications. The patient was treated with itraconazole antifungal therapy with an improvement in her symptoms.

BACKGROUND

Symptoms of dysphagia are commonly attributed to disorders arising from dysfunction of oesophageal motility. Initial diagnostic evaluations commonly include contrasted barium radiographic studies as well as oesophagogastrroduodenoscopy (OGD) for evaluation of obstructive processes or mucosal processes such as Schatzki's rings, webs and malignancy. Manometry is reserved for cases without determined aetiology to assess for underlying motility disorders such as scleroderma and achalasia. Extraoesophageal compression by mediastinal structures remains a rare presenting cause of dysphagia. The differential diagnosis of mediastinal granulomas includes histoplasmosis, tuberculosis and sarcoidosis. Our case highlights the importance of evaluation of the mediastinal structures in individuals presenting with persistent dysphagia and weight loss. Accurate assessment of the underlying aetiology can lead to tailored treatment, as in this case, leading to an improvement in clinical symptoms.

CASE PRESENTATION

A 33-year-old woman with no significant medical history and no history of smoking was referred for evaluation of dysphagia. The patient had, 6 months prior to initial consultation, reported the onset of dysphagia to solids at the level of the suprasternal notch, associated with regurgitation and without a history of heartburn. The patient denied difficulty in swallowing liquids and denied odynophagia. Associated symptoms included weight loss associated with decreased oral intake in the setting of dysphagia without a history of fevers or night sweats. The patient lived in the Midwestern USA and denied a history of recent travel.

On physical examination, the patient was afebrile with a demonstration of neither cervical

lymphadenopathy nor thyromegaly. An examination of her chest, heart and lungs was without abnormality. Empiric proton-pump inhibitor therapy led to an improvement in regurgitation without improvement in her dysphagia.

INVESTIGATIONS

Initial studies included an oesophogram, with identification of neither an oesophageal stricture nor narrowing, and with OGD demonstrating a 2 cm hiatal hernia. Oesophageal manometry was performed demonstrating normal resting lower oesophageal sphincter pressure and 7/11 wet swallows demonstrating normal peristalsis of the oesophageal body.

Initial laboratory investigation demonstrated a normal complete blood count: white cell counts $7.3 \times 10^3/\mu\text{L}$, haemoglobin 14.5 g/dL and platelet count $245 \times 10^3/\mu\text{L}$.

The patient did not have improvement in symptoms with empiric oesophageal dilation. She subsequently described symptoms of chest pain and dyspnoea, therefore a non-contrast CT scan of the chest was performed demonstrating ill-defined mediastinal subcarinal and hilar lymphadenopathy with calcification (figure 1).

The patient was referred to pulmonary medicine and underwent a diagnostic endobronchial ultrasound bronchoscopy with subcarinal transbronchial lymph node needle aspiration. Cytological examination demonstrated inflammatory debris and Gömöri methenamine silver stain demonstrated yeast elements suggestive of histoplasmosis (figure 2). Histoplasma urinary antigen was negative and a screening antibody assay was positive.

DIFFERENTIAL DIAGNOSIS

In a patient presenting with dysphagia to solid foods but not to liquids, an obstructive process must initially be ruled out. Although rare in a patient of this woman's age range, given her associated symptom of weight loss, ruling out malignancy was required with an OGD. Furthermore, performance of an OGD allowed for mucosal inspection and biopsy to rule out eosinophilic oesophagitis. Although the patient denied difficulty in swallowing liquids, oesophageal manometry ruled out abnormalities of oesophageal motility such as achalasia or absent peristalsis associated with scleroderma.

TREATMENT

The patient was referred to an infectious diseases specialist and treatment with itraconazole was begun with planned treatment duration of 12 months.

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Figure 1 (A) Axial and (B) coronal computed-tomography of the chest, demonstrating subcarinal lymphadenopathy with calcification.

OUTCOME AND FOLLOW-UP

Over the course of 4 weeks, the patient noted a resolution in her clinical symptoms of dysphagia. She continued to report a persistent cough. Repeat CT of the chest was performed 5 months after initial diagnosis, showing calcified mediastinal lymph nodes smaller in size compared with those in the original investigation.

DISCUSSION

Exposure to *Histoplasma capsulatum* is exceedingly common for persons living in endemic areas, but symptomatic infection is uncommon. In endemic areas such as the Mississippi and Ohio River valleys, acute infections with histoplasmosis are commonly asymptomatic. The rate of seroconversion in persons with previously negative serologic tests who move to regions where the disease is endemic is as high as 17.8% after less than 3 months of residence.¹

Granulomatous mediastinitis, or mediastinal granuloma, involves infection of the mediastinal lymph nodes that occurs with pulmonary infection by histoplasmosis. Instead of enlargement of mediastinal lymph nodes that recede and ultimately calcify, granulomatous mediastinitis is characterised by enlargement of multiple nodes, become matted together and undergo caseation necrosis.² Mediastinal lymph node calcifications, typically seen more than 10 years after the initial fungal infection, tend to be focal and scattered in a so-called mulberry pattern.¹ In general, mediastinal calcifications imply a more chronic process such as chronic infection, slow growing neoplasm or granulomatous lymphadenitis secondary to tuberculosis, histoplasmosis or sarcoidosis.¹

While granulomatous mediastinitis is commonly asymptomatic, individuals can experience symptoms related to impingement of the nodal mass around mediastinal structures to include the

superior vena cava, bronchi, pericardium and oesophagus.² Granulomatous mediastinitis is differentiated from mediastinal fibrosis, a potentially lethal condition characterised by excessive fibrosis of the mediastinum with encasement of the vital structures of the mediastinum.² While the pathogenesis of mediastinal fibrosis involves an uncontrolled fibrotic response to the caseous nodes, there is no convincing evidence that patients with granulomatous mediastinitis go on to develop mediastinal fibrosis.³

Oesophageal involvement in reported series of cases of histoplasmosis is reported to occur in 5–13% of patients, typically in the subcarinal region.¹ Among 95 cases of mediastinal granuloma at the Mayo Clinic, 10 (10.5%) demonstrated oesophageal involvement, with dysphagia the primary clinical symptom.⁴ Associated manifestations included weight loss, melena, haematemesis, dyspnoea with exertion and low-grade fever. Six of the 10 patients underwent exploratory thoracotomy with confirmation of a mediastinal granuloma, however, five of the six had negative silver stains on histology.⁴

Evaluation with endoscopic ultrasonography (EUS) has also been described with findings of matted mediastinal lymph nodes and a focally thickened oesophageal wall.⁵ Among 11 patients presenting to Indiana University Medical Center, for dysphagia and endoscopy findings concerning for oesophageal mass or stricture, five of the eight patients who underwent a barium oesophogram demonstrated submucosal or extrinsic compression. On EUS, 7 of the 11 lymph node masses had hyperechoic foci with shadowing consistent with calcification. Among six patients who underwent fine needle aspiration, none had fungal elements detected, however, two patients had increased histoplasmosis antibody titres and six had negative tuberculin-purified protein derivative skin testing.⁴

Diagnosis of histoplasmosis can be made using a variety of testing methods to include: culture, histopathology, antigen detection and antibody assays.² On histopathology, findings of 2–4 µm, oval, narrow-based budding yeasts allows for a tentative diagnosis of histoplasmosis. Yeasts are typically found within macrophages, but can be found also within free tissue. Urinary antigen detection methods, as performed in this case, have increased sensitivity in the setting of disseminated histoplasmosis, with the greatest experience in the population with acquired immune deficiency syndrome and a large burden of organisms. Among patients with granulomatous mediastinitis, *Histoplasma* antigen is commonly not detected in the urine.²

Treatment of symptomatic granulomatous mediastinitis generally consists of itraconazole for a period of 6–12 months, with therapy directed against the ongoing inflammatory process.² While treatment has not been proven to be beneficial, anecdotal reports of successful therapy have been described.⁶ In cases refractory to medical management, surgical debulking of the lymph node mass can be attempted.²

This case highlights the rare description of an extraoesophageal aetiology for dysphagia secondary to granulomatous mediastinitis due to exposure and infection from *H. capsulatum*. Alternative aetiologies of granulomatous lymphadenitis include

Figure 2 Pathological review of subcarinal transbronchial lymph node needle aspiration demonstrating yeast elements on Gömöri methenamine silver stain (100× view).

tuberculosis and sarcoidosis. Infection due to *H. capsulatum* is suggested in this case due to cytological examination findings of yeast elements in needle aspirates of the mediastinal lymphadenopathy, as well as response to medical therapy. Extraesophageal manifestations of dysphagia secondary to mediastinal obstructive processes should be considered among individuals with manifestations that include weight loss, pulmonary symptoms or fever.

Learning points

- ▶ Extraesophageal compression remains a rare cause for dysphagia.
- ▶ The differential diagnosis of mediastinal granulomas includes histoplasmosis, tuberculosis and sarcoidosis.
- ▶ Extraesophageal manifestations of dysphagia should be considered among individuals with manifestations that include weight loss, pulmonary symptoms or fever.

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