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A Woman with Progressive Dysphagia

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The following is an unusual case of dysphagia from the monthly clinicopathological conference (CPC) of the University of Illinois College of Medicine. At this conference a clinical faculty member is presented with a case (of which he or she has no prior knowledge) and then proceeds to describe the clinical reasoning involved in reaching a final diagnosis. This case was discussed in February 2009.

DISCUSSANTS

Chief Discussant: Sumuk Sundaram, MD
Gastroenterology: Andrew Batey, MD
Pathology: Ike Uzoaru, MD

CASE PRESENTATION

A 70-year-old woman initially presented to her primary care physician for nonproductive cough of a few weeks’ duration. Cardiopulmonary examination and chest plain films were unremarkable. The patient was treated symptomatically with dextromethorphan; lisinopril was discontinued. After eight weeks she reported no improvement in her cough and had additional concerns about “food getting stuck in the chest.” The patient had difficulty swallowing both solids and liquids; she coped by eating small bites and limiting her meal portions. She had no trouble chewing or initiating a swallow. The dysphagia was slowly progressive. The patient denied odynophagia, regurgitation, loss of appetite or weight, halitosis, stridor or change in her voice.

DISCUSSION

Dysphagia is a frequent problem in the elderly. Up to 10% of the population aged 50 years or older experience dysphagia. Dysphagia should always be investigated. Although aging is associated with mild esophageal dysmotility, it is not typically symptomatic.

Dysphagia is caused by either oropharyngeal or esophageal disorders. It is important to get an accurate history and do a detailed physical examination to distinguish between these two general categories of disorders. Oropharyngeal dysphagia is caused by conditions that affect the transfer of food bolus from the oral cavity past the upper esophageal sphincter. The most common cause for this disorder is stroke. Other important causes include neurological disorders such as Parkinson’s disease, multiple sclerosis and amyotrophic lateral sclerosis. Mechanical obstructive causes include oropharyngeal neoplasms, Zenker’s diverticulum, upper esophageal webs and anterior mediastinal masses. Esophageal dysphagia is caused by disorders affecting passage of food from the upper esophageal sphincter into the gastric cavity. Common neuromuscular etiologies include achalasia, diffuse esophageal spasm and scleroderma. Mechanical causes include lower esophageal rings like Schatzki’s ring, esophageal strictures and webs, foreign bodies, esophageal tumors, and extrinsic compression from an enlarged aorta, enlarged left atrium, mediastinal lymphadenopathy or substernal extension of a goiter. Cancer of the gastric cardia can occasionally present with dysphagia to both solids and liquids (pseudoachalasia) as the cancer infiltrates the myenteric plexus or the vagus nerve. Weight loss usually indicates the duration and severity of dysphagia. Odyphagia, if present, is usually an indicator of inflammation or malignant process.

CASE PRESENTATION

Past medical history was significant for left vocal cord paralysis five years ago resulting in a chronically and mildly hoarse voice. Diagnostic workup at that time included la-
ryngoscopy and computerized tomography (CT) scan of neck but failed to identify an etiology of the vocal cord paralysis. Esophagogastroduodenoscopy (EGD) performed six years ago for evaluation of gastroesophageal reflux disease (GERD) showed moderate esophagitis. Other pertinent health history included Type 2 diabetes mellitus with peripheral neuropathy, coronary artery disease managed by coronary artery bypass grafting, hypertension, hyperlipidemia, hypothyroidism, osteoporosis, degenerative joint disease and an episode of rheumatic fever at age 15 years. Surgeries included cholecystectomy, appendectomy, tonsillectomy and tubal ligation.

The patient was prescribed atenolol, calcium with vitamin D supplement, gabapentin, insulin, hydrochlorothiazide, levothyroxine, metformin, omeprazole, pravastatin, raloxifene and valsartan. Family history was significant for coronary artery disease, hypertension, hypothyroidism and lymphoma. The patient had a 26 year pack a day smoking history and consumed caffeinated beverages daily. There was no history of alcohol or drug use.

DISCUSSION

GERD affects roughly 40% of the US population. Long-standing GERD is a risk factor for esophageal strictures and Barrett’s esophagus. Untreated GERD is reported to cause strictures with frequency ranging from 7–23% and is responsible for 70–80% of all esophageal strictures.4 Barrett’s esophagus is the replacement of the normal stratified squamous epithelium of the distal esophagus by a specialized intestinal columnar metaplasia which happens as a result of chronic exposure to gastric contents. The presence of BE predisposes to development of esophageal adenocarcinoma which can cause mechanical dysphagia. Anatomically, the patient’s history of vocal cord lesion five years ago is probably unrelated to her current dysphagia symptom. It is unlikely that her previous cardiothoracic surgery is a contributing factor.

Diabetes mellitus can be associated with dysphagia.5,6 Candida esophagitis occurs with higher frequency in diabetics than nondiabetics, and severe autonomic neuropathy can result in abnormal esophageal contractions, spontaneous contractions and impaired lower esophageal sphincter tone leading to heartburn and dysphagia. However, diabetes-related autonomic neuropathy should not be considered the sole contributor to symptomatic dysphagia. In our patient there was a history of peripheral neuropathy but no other findings to suggest severe autonomic neuropathy.

Hypothyroidism by itself is not commonly associated with esophageal dysmotility. However, literature review reveals hypothyroidism may be linked to achalasia,7 lower esophageal sphincter hypotension and aperistalsis,8 and at least one case of myxedema causing dilated esophagus.9 These cases are extremely infrequent. Also, there is no other history to suggest symptomatic hypothyroidism in our patient.

Osteoporosis has been reported to cause dysphagia only as a late complication when a patient develops severe kyphosis.10 More recently, therapy for osteoporosis has been linked with esophageal disorders. Pill esophagitis is a well-known adverse effect of bisphosphonate therapy.11 There is also recent literature suggesting an increased incidence of esophageal cancer with this class of medication.12,13 Several other medications have been directly linked with esophageal injury. Some common medications include antibiotics like doxycycline and clindamycin, nonsteroidal anti-inflammatory drugs (NSAIDs), ziduvudine, iron supplements, calcium channel blockers, nitrates and medications that may cause xerostomia including anticholinergics, angiotensin converting enzyme (ACE) inhibitors and antihistamines.14 The link between tobacco and alcohol use giving rise to esophageal injury through esophagitis and malignancy has already been well established. Review of symptoms should gather information to focus on the etiology and conditions discussed so far.

CASE PRESENTATION

Review of systems was positive for generalized weakness, fatigue, and intermittent dyspnea after coughing and eating. There was no history of nausea, vomiting, abdominal pain, diarrhea, constipation, hematochezia or melena. The patient denied any changes in bladder habits, incontinence, dysuria or hematuria. No wheezing, chest pain, palpitations, tingling or numbness was reported.

DISCUSSION

A general physical examination and focused symptom/organ specific examination will provide good etiologic clues. General factors such as body habitus, drooling and mental status should be noted. A thorough neurologic examination is required as stroke is a common etiology. Special attention should be focused on cranial nerve examination. Thyroid masses and neck lymphadenopathy contributing to swallowing difficulty can usually be easily palpated. Abdomen should be well evaluated for any palpable masses. A positive test for blood in the stool may provide clues for malignancy and esophagitis.
Initial laboratory workup is usually dependent on the differential diagnosis. In general, a complete blood count may be helpful in screening for infections, inflammation or chronic blood loss. Thyroid testing can screen for thyroid dysfunction-related dysphagia which may be the case in goiter or malignancy.

CASE PRESENTATION

Vital signs were unremarkable and the patient did not appear in acute distress. No goitrous thyroid enlargement, lymphadenopathy or cervical masses were noted. Hoarseness and decreased lower extremity sensation were unchanged from previous examinations. No obvious neurological deficits were noted. Stool hemoccult test was negative. Screening laboratories including electrolytes, markers of liver function, TSH, C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) were unremarkable.

DISCUSSION

When no obvious etiology is detected, initial workup generally starts with evaluation of esophageal anatomy. Studies that are commonly used include modified barium swallow, complete esopahgram and upper endoscopy. Special studies such as esophageal pH monitoring, esophageal double contrast study and manometry are utilized as indicated by the findings on initial evaluation.

CASE PRESENTATION

A modified barium swallow revealed a 2 cm left lateral and flexible pharyngeal diverticulum consistent with a Zenker’s diverticulum. Mild to moderate aspiration was also noted during the pharyngeal phase of the study.

DISCUSSION

Zenker’s diverticula are usually due to defects in the weak muscular wall of the hypopharynx known as “Killian’s triangle.” It is formed by the oblique fibers of the inferior pharyngeal constrictor muscle and the cri-copharyngeal sphincter. Lesions usually occur in males. Zenker’s diverticula slowly enlarge over time. Common clinical features include pulmonary aspiration, halitosis, regurgitation of food into the mouth, and dysphagia. In our patient, a diagnosis of Zenker’s diverticulum was made with a modified barium swallow study. Mild cases of dysphagia can be managed conservatively through dietary changes. Surgical resection is the mainstay of treatment in moderate to severe cases. Minimally invasive techniques such as endoscopic diverticulectomy are increasingly being used.

CASE PRESENTATION

Dietary modifications were recommended by a speech pathologist and the patient was fully compliant. However, six weeks later she presented to the emergency room “gasping for air.” The patient reported gradual worsening dyspnea over the past month with exacerbations. The current episode began the day before presentation and worsened to the point that she could barely breathe. Vital signs and oxygen saturation were unremarkable, but stridor was noted. No cervical lymphadenopathy or goiter was palpable.

DISCUSSION

In the presence of dyspnea and stridor, a neck lesion should be suspected. CT imaging studies of the neck and upper mediastinum will be helpful. Laryngoscopy may be considered in relevant cases.
CASE PRESENTATION

Since the stridor appeared to predominate in the expiratory phase, CT of the neck and chest was obtained to evaluate for an intrathoracic lesion. An anterior mediastinal mass (5.7 cm x 5.3 cm) encircling and compressing the trachea to approximately 30% of normal lumen diameter was noted. The mass seemed to extend superiorly to the thyroid with no clear demarcation from thyroid tissue. Posteriorly, it extended to the paraesophageal and retroesophageal area, most extensively on the left. Right tracheal deviation was observed. There was no extension below the aortic arch or above the sternal notch. Some mediastinal lymphadenopathy and numerous non-calcified bilateral lung nodules were also noted. Given the history of unilateral vocal cord paralysis, flexible fiberoptic laryngoscopy was performed, though no lesions of the nasopharynx, oropharynx or hypopharynx were visualized. The left true vocal cord was immobile and near the midline in the paramedian position, while the right true vocal cord was freely mobile. The glottic airway was adequate and no abnormalities of the glottis or supraglottic larynx or hypopharynx were identified.

DISCUSSION

A substernal thyroid mass causing dysphagia and stridor in the absence of palpable thyroid enlargement is rare. According to one study that did not account for mass size, about 90% of all substernal goiters were palpable and more than one third caused tracheal deviation.15 Less than 2–3% of these were malignant.

CASE PRESENTATION

Ultrasound guided biopsy of the anterior mediastinal mass was done by interventional radiology.

PATHOLOGY

The biopsy revealed a poorly differentiated malignancy consistent with anaplastic thyroid carcinoma. There were micro-follicles present which showed significant atypia, and cells stained positive for thyroglobulin, TTF-1, and CK 19. Special stains for cytokeratin and CK 7 were weakly positive, and cells stained diffusely positive for vimentin. Tumor cells were negative for HMB-45, CD 45 and CK 20.

Final diagnosis: Anaplastic thyroid carcinoma originating from the left lobe and extending into the superior mediastinum and the tracheoesophageal groove with notable lymphadenopathy and possible pulmonary metastasis.

CASE PRESENTATION

During the hospitalization the patient’s respiratory distress was managed non-invasively by positive pressure ventilation. Intravenous glucocorticoids were administered following biopsy with only partial and transient relief of dyspnea. The patient clearly expressed her wishes against mechanical ventilation and understood the poor prognosis of her disease. She chose palliative treatment and expired shortly after diagnosis.

CONCLUSION

Anaplastic thyroid carcinomas are undifferentiated tumors of thyroid follicular epithelium. These tumors
typically affect older adults and account for only 2–5% of all thyroid cancers. Fewer than 10% occur in people under age 50 years and nearly 70% of all affected patients are women. Approximately 20–30% of patients are discovered to have a coexistent differentiated thyroid carcinoma at time of diagnosis suggesting that anaplastic carcinomas may arise from transformation of initially well differentiated tumors.

Anaplastic carcinomas typically present as a rapidly enlarging neck mass. The enlarging mass may cause neck pain, and involvement of the upper airway and esophagus may result in dyspnea, dysphagia, hoarseness, and cough. The mass is usually irregular and firm to hard in consistency. There may be associated tenderness to palpation. There is evidence of local or distant metastasis in about 90% of patients at the time of diagnosis, with lung the most common site of distant metastasis, age, male gender and presence of dyspnea. Given the very rapid progression of anaplastic thyroid carcinoma and poor treatment response, comfort care measures and end of life planning should be part of early management. This case illustrates that if an initial finding fails to fully explain a patient’s symptoms, consider additional workup for other potential etiologies.

Surgery is generally not recommended given rapid local growth and presence of distant metastasis at diagnosis. Radiotherapy does not prolong survival, and there is high rate of local recurrence in patients who experience initial benefit. Paclitaxel is the preferred chemotherapeutic agent, but there is also no significant survival benefit of chemotherapy. Mean survival is less than six months after diagnosis. Prognostic factors include tumor size, distant metastasis, age, male gender and presence of dyspnea. Given the very rapid progression of anaplastic thyroid carcinoma and poor treatment response, comfort care measures and end of life planning should be part of early management. This case illustrates that if an initial finding fails to fully explain a patient’s symptoms, consider additional workup for other potential etiologies.

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REFERENCES


