A 69-year-old man presented to the gastroenterology clinic with a 2-month history of progressive difficulty initiating a swallow, accompanied by nasopharyngeal regurgitation and a sensation of residual food remaining in his throat. Accompanying symptoms included coughing and choking while eating, as well as excessive drooling. He would need to swallow repeatedly for proper passage of food and experienced regurgitation of fluid through his nose while swallowing. He had a 5-lb weight loss that he attributed to poor oral intake in the setting of gradually worsening symptoms during this time. In addition, he experienced lightheadedness when getting out of bed in the mornings. He had never experienced similar symptoms previously. He had healthy dentition and denied any otalgia, dysarthria, diplopia, halitosis, odynophagia, nausea or vomiting, abdominal pain, melena, or hematochezia. His medical history was notable for hypertension, hyperlipidemia, ulcerative colitis, and human papilloma virus (HPV)-positive squamous cell carcinoma of the tongue with lymph-node involvement and extension into the neck 12 years before, status postsurgical resection and radiation without recurrence. Medications on presentation included azathioprine, aspirin, atorvastatin, and lisinopril. He had a previous history of tobacco use, but had quit 12 years before.

At presentation, his vital signs were within normal limits. Physical examination revealed a thin man resting comfortably with no visible oropharyngeal lesions, no palpable head or neck masses, and no cervical or supraclavicular lymphadenopathy. Neurologic examination demonstrated intact cranial nerve examination without any sensory or motor abnormalities. Gait examination was unremarkable. Abdominal examination showed normal bowel sounds without hepatosplenomegaly and tenderness to palpation.

Laboratory testing (reference ranges) revealed the following results: hemoglobin, 14.5 g/dl (13.5 to 17.5); mean corpuscular volume, 94.1 fl (81.2 to 95.1); leukocytes, 5.5x10^9/L (3.5 to 10.5 x 10^9); platelet count, 382x10^9/L (150 to 450x10^9); erythrocyte sedimentation rate, 11 mm per hour (0 to 22); C-reactive protein, 3.0 mg/L (<8); sodium, 141 mmol/L, (135 to 145); potassium, 4.2 mmol/L (3.6 to 5.2); and creatinine, 0.7 mg/dL (1.7-2.3).

1. Which of the following symptoms, if present, would most support the diagnosis of oropharyngeal dysphagia?
   a) Sensation of food sticking in the lower chest
   b) Nasal regurgitation
   c) Heartburn
   d) Weight loss
   e) Odynophagia

The prevalence of dysphagia among individuals ≥65 years of age is common and ranges from 14% to 33%. When evaluating a patient with dysphagia, it is essential to first classify the dysphagia as either oropharyngeal (difficulty initiating a swallow caused by oral and pharyngeal dysfunction) or esophageal (difficulty with swallowing that occurs a few seconds after food intake owing to esophageal etiology). A sensation of food sticking in the lower chest would support esophageal dysphagia secondary to a mechanical cause (ie, stricture or malignancy), or motility disorder (ie, achalasia or esophageal spasm). Nasal regurgitation is a characteristic symptom of oropharyngeal...
dysphagia, with patients experiencing regurgitation of food through their nose while swallowing. Heartburn would be a classic symptom of gastroesophageal reflux disease but not of oropharyngeal dysphagia. Weight loss is a nonspecific symptom that may be seen in many disorders including diminished oral intake secondary to both oropharyngeal and esophageal dysphagia. Finally, odynophagia would be most consistent with esophageal disorders, particularly pill-induced or infectious esophagitis, rather than a nasopharyngeal process.

Normal swallowing consists of 3 main phases: oral preparatory, pharyngeal, and esophageal. Our patient’s symptoms of difficulty initiating a swallow, nasal regurgitation, and a sensation of food being stuck in the neck are all clinical features characteristic of oropharyngeal dysphagia. Nasal regurgitation can occur with swallowing of liquid or solid foods. He specifically described difficulty with initiating transfer of food from the mouth to the pharynx. In contrast, esophageal dysphagia is characterized by difficulty swallowing, occurring after a few seconds of food intake, and often the predominant discomfort can be present in the lower chest. One-third of patients with a distal esophageal etiology of dysphagia may still point to the neck as a localizing site. Aspiration pneumonia is not specific to oropharyngeal dysphagia and can also be seen in certain cases of esophageal dysphagia, most notably achalasia.

Clinicians must take a careful patient history with close attention to the different phases of swallowing to classify the dysphagia properly and exclude alternative diagnoses. A bedside swallow study with water can illustrate the difficulties a patient may experience when swallowing while highlighting adaptive maneuvers (ie, double swallow, forceful swallow, head posturing). We discussed with the patient that his history of difficulty swallowing with accompanying nasal regurgitation best supports a diagnosis of oropharyngeal dysphagia, and we recommended additional tests.

2. What is the next best test for the patient’s constellation of symptoms?

a) Computed tomography (CT) scan of the neck
b) Magnetic resonance imaging (MRI) of the brain
c) Esophagogastroduodenoscopy (EGD)
d) Video swallow study
e) Laryngoscopy

Although it is crucial to rule out recurrent malignancy in patients with previous head and neck cancer, he did not have any palpable masses or lymphadenopathy of the head and neck to warrant an evaluation of the soft tissues with CT of the neck. An MRI of the brain would be indicated if he had focal neurologic deficits or any other abnormality on neurologic examination to suggest a central nervous system process, such as stroke, for his dysphagia. An EGD would be the best next test for esophageal dysphagia. However, in our patient case, the video swallow study is the best diagnostic test in order to detect abnormalities in the oropharyngeal phase and to assess the severity of disease. This study provides valuable information regarding the mechanics and musculature of the upper esophageal sphincter and pharynx. It can help detect potential structural causes of oropharyngeal dysphagia, demonstrate oral and pharyngeal transit times, and highlight aspiration. An esophagram is an important adjunct for further evaluation of structural etiologies of dysphagia. In sum, the video swallow study can illustrate structural conditions such as Zenker diverticulum, which are important to know before performing endoscopy, and show the function of the oropharyngeal musculature, which can be weak in conditions such as amyotrophic lateral sclerosis (ALS). Finally, nasopharyngeal laryngoscopy is ideal for evaluating structural lesions of the oropharynx, hypopharynx, larynx, and proximal esophagus and less likely to be helpful in this case.

Given that our patient’s symptoms were most concerning for oropharyngeal dysphagia, he underwent a video swallow study.
that demonstrated moderate oropharyngeal dysfunction with the presence of aspiration. He had diminished epiglottic movement and penetration of thin liquids into the laryngeal vestibule with piriform retention and decreased hypopharyngeal constriction. Clinicians should also have a high index of suspicion for recurrence of malignancy in those with a history of radiation. Laryngoscopy was performed with visualization of the nasopharynx, oropharynx, and hypopharynx, demonstrating no evidence of recurrent malignancy, in addition to a normal CT chest scan.

3. Based on the patient’s evaluation thus far, which is the most likely cause of his oropharyngeal dysphagia?
   a) Past radiation exposure
   b) Recurrence of malignancy
   c) Amyotrophic lateral sclerosis (ALS)
   d) Stroke
   e) Zenker diverticulum

There are numerous causes of oropharyngeal dysphagia, ranging from structural to neurologic to infectious etiologies. He had a history of squamous cell carcinoma of the head and neck—caused by HPV as well as previous smoking—treated with surgery and external beam radiation. His xerostomia and oropharyngeal dysphagia was most likely a result of previous exposure to radiation. Increased duration and dose of radiotherapy are associated with a higher likelihood of developing oropharyngeal dysphagia. Radiation-induced oropharyngeal dysphagia can occur as a result of functional disorders, secondary to muscle weakness, or structural causes such as stricture. Recurrence of malignancy is also less likely in this patient owing to the absence of systemic symptoms such as significant weight loss and absence of any masses of the head and neck or lymphadenopathy noted on examination.

Although both ALS and stroke can result in oropharyngeal dysphagia, it is unlikely, based on his history and physical examination. More specifically, he had no focal neurologic deficits and had a gradual—rather than acute—onset of symptoms. In stroke, symptoms may appear rather acutely, whereas ALS can present with gradual symptoms. Other neurologic conditions commonly associated with oropharyngeal dysphagia include myasthenia gravis, multiple sclerosis, and Parkinson disease. Finally, Zenker diverticulum is a false diverticulum, containing only the mucosa and submucosa of the esophagus. It commonly occurs at the upper part of the esophagus, called Killian triangle, which is an area of muscular weakness. Zenker diverticulum is less likely in this patient, given its relative rarity, the history of radiation, and the absence of dysphagia to solid foods as the predominant symptom.

Radiation-induced dysphagia is a late complication of head and neck cancer treatment and was the likely cause of his symptoms. Although it can be difficult to predict which patients will develop swallowing difficulties from radiation therapy, clinicians should have a high index of suspicion for treatment-induced dysphagia in those with previous radiation, as in the case of our patient. Radiation can cause dysphagia via a combination of muscle weakness in addition to esophageal stricture. Given the absence of a stricture on video swallow study, his dysphagia was believed to be secondary to radiation-induced muscle weakness. Dysphagia can occur many years afterward, as in this patient, even though he did not experience any dysphagia while undergoing radiation treatments or immediately thereafter. Another likely contributing factor included previous surgical resection of his head and neck cancer.

4. What is the next best step in management of the patient’s oropharyngeal dysphagia?
   a) Nasogastric (NG) tube insertion with bolus tube feeds
   b) Initiation of total parenteral nutrition (TPN)
   c) Referral to speech therapy
   d) Referral to surgery
   e) Trial of proton pump inhibitor

Management of oropharyngeal dysphagia includes treating the underlying etiology when possible and preventing complications.
secondary to aspiration. In patients with severe symptoms who are at high risk of aspiration, enteral nutrition may be recommended. Regardless, an NG tube would not be appropriate as it is mainly used for short-term duration up to 3 months. If this patient required enteral nutrition, it would be likely needed long term. Enteral feeding is preferred to TPN because of increased risk of complications associated with TPN such as bloodstream infections, metabolic derangements including hyperglycemia, serum electrolyte alterations, macro- or micronutrient excess or deficiency, and hepatic dysfunction. For moderate oropharyngeal dysphagia, including with our patient, swallowing rehabilitation with speech therapy is first-line therapy. Referral to surgery would only be indicated in the setting of a mechanical obstruction such as recurrence of malignancy causing oropharyngeal dysphagia or in the setting of a symptomatic Zenker diverticulum. Proton pump inhibitors have no role in the management of oropharyngeal dysphagia.

Our patient underwent swallowing rehabilitation with speech therapy, which consisted of swallowing exercises, postural adjustments, facilitative swallowing strategies, and dietary modifications. Adaptive swallowing behaviors included prolonged chewing, chin-tuck against resistance, and avoidance of dry particulate foods. He was monitored for malnutrition, weight loss, and dehydration. Despite treatment with swallowing rehabilitation and speech therapy for several months, he continued to experience significant nasopharyngeal regurgitation of both solids and liquids and developed aspiration pneumonia, requiring hospitalization and antibiotics.

5. Given the patient’s continued oropharyngeal dysphagia, despite the treatment discussed thus far, what is the next best step in management?
   a) Therapeutic endoscopy
   b) Initiation of TPN
   c) Percutaneous endoscopic gastrostomy (PEG) placement with bolus tube feeds
   d) Percutaneous jejunostomy (PEJ) placement with continuous tube feeds
   e) Mirtazapine

Therapeutic endoscopy would be indicated for mechanical causes of esophageal dysphagia (ie, dilation of esophageal strictures or webs) and not for treatment of oropharyngeal dysphagia. As discussed previously, enteral feeding is preferred to TPN, as it is more physiological, associated with fewer potential complications and risks, and requires less frequent monitoring. Percutaneous endoscopic gastrostomy is the preferred next step in management for this patient; PEG tubes are relatively well tolerated, can be used at home, and allow bolus feeds that mirror normal physiological meal patterns. Percutaneous jejunostomy is not the preferred form of enteral nutrition, as feeding directly into the small intestine requires longer continuous feeds, has increased possibility of side effects (ie, diarrhea), and greater potential difficulties with medication administration; PEJ is used in situations in which a PEG is not possible: for example, in a patient with a gastric malignancy leading to gastric outlet obstruction. Finally, mirtazapine is an antidepressant associated with weight gain, but this would not treat his underlying problem of oropharyngeal dysphagia.

Our patient underwent placement of a PEG tube without complications and tolerated bolus feeds at home. His weight improved to his previous baseline before the onset of the oropharyngeal dysphagia. He was counseled on the continued risk of aspiration, even with a PEG. He was monitored for tube dysfunction, local infections, and peristomal leakage at subsequent clinic visits.

DISCUSSION

This patient was diagnosed with oropharyngeal dysphagia as a late complication of radiation therapy that he had received 12 years previously for HPV-positive squamous cell carcinoma of the tongue with nodal disease and extension into the neck. Our case
highlights the importance of differentiating oropharyngeal dysphagia from esophageal dysphagia, as this has important implications for the diagnostic and management approach. In general, patients with oropharyngeal dysphagia present with difficulty initiating a swallow, nasopharyngeal regurgitation, and sensation of residual food in the neck. The best test for work-up of suspected oropharyngeal dysphagia is videofluoroscopy. Management strategies vary, in part depending on the underlying cause and severity of the dysphagia. For those with mild-to-moderate symptoms, swallowing rehabilitation with speech therapy is first-line therapy. Enteral nutrition is reserved for those with refractory symptoms despite speech therapy or severe dysphagia at high risk of aspiration. In contrast, esophageal dysphagia can present with a sensation of food sticking in the lower chest. Evaluation may include endoscopy and esophagram, and in cases in which no etiology is found, esophageal manometry ultimately may be required.

Oropharyngeal dysphagia caused by exposure to radiation arises through a variety of mechanisms including neuropathy and fibrosis of the oral, laryngeal, and pharyngeal musculature. Some patients can develop mandibular osteoradionecrosis, laryngeal chondroradionecrosis, and cranial nerve dysfunction. The time to onset of osteoradionecrosis is variable, with some patients developing symptoms shortly after treatment, whereas others are diagnosed years later. Symptoms of osteoradionecrosis include jaw pain, dysgeusia, dysesthesia or anesthesia, speech difficulties, fistula formation, or pathological fracture. Older age, primary malignancy involving the larynx or hypopharynx, advanced stage at cancer diagnosis, and post-treatment neck dissection are risk factors for oropharyngeal dysphagia. In addition to radiation-induced oropharyngeal dysphagia, radiation can also result in esophageal toxicity. Proximal esophageal strictures can develop in about 2% to 16% of patients treated with radiation therapy for head and neck cancer. Despite treatment with esophageal dilation, some strictures can be refractory or recur frequently. Although radiotherapy is important for organ preservation in the treatment of many pharyngeal and laryngeal cancers, it can lead to impaired quality of life from complications of severe oropharyngeal or esophageal dysphagia that can develop or progress years after therapy.

Our patient presented with oropharyngeal dysphagia in the setting of previous radiation to the head and neck region for a malignancy. Despite adequate enteral nutrition and hydration after PEG placement, he continued to experience episodes of light-headedness and dizziness. Orthostatic hypotension caused by volume depletion was thus a less likely etiology of these symptoms. Radiotherapy can also result in dysfunction of the carotid baroreceptors, with resultant autonomic dysfunction including orthostatic hypotension, as seen in our patient. Autonomic dysfunction is associated with cranial, neck, and mediastinal radiation therapy. Given the significant overlapping clinical findings between radiation-induced and stroke-associated oropharyngeal dysphagia (ie, drooling, nasopharyngeal regurgitation, autonomic dysfunction), a thorough neurologic evaluation must be conducted. In this patient, his baroreflex failure was a consequence of his previous neck irradiation that led to inflammation and subsequent fibrosis of the carotid arterial walls, which damaged the carotid sinus baroreceptors. His arterial baroreflex response was thus attenuated to changes in blood pressure. He had a severely abnormal autonomic reflex screen. As in our patient, autonomic dysfunction can develop many years after radiation therapy. Treatment is primarily supportive with lifestyle changes including use of compression stockings and medications such as midodrine.

In conclusion, clinicians should be aware of delayed complications of head and neck radiation including oropharyngeal dysphagia and baroreceptor dysfunction.
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CORRECT ANSWERS: 1. b. 2. d. 3. a. 4. c. 5. c.