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Case Report

Plummer-Vinson syndrome presenting as squamous cell carcinoma of esophagus

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Abstract

Plummer-Vinson syndrome (PVS) also known as Paterson-Brown-Kelly syndrome is a rare syndrome which comprises iron deficiency anemia, dysphagia, and esophageal webs. The pathogenesis of PVS is not clear. Iron deficiency anemia is essential for diagnosis of PVS. If left untreated, there is an increased risk of developing pharyngeal or esophageal cancer in about 10% of patients. There are no strict guidelines for endoscopic surveillance in patients with PVS. Iron replacement can improve dysphagia and potentially lead to regression of esophageal webs. In this case report, we present a patient who had long-standing dysphagia for years which progressed to squamous cell cancer of esophagus by the time she sought medical treatment.

Key words

Dysphagia, esophageal cancer, iron deficiency anemia, Paterson-Brown-Kelly syndrome, Plummer-Vinson syndrome, risk factors, squamous cell cancer

Introduction

Plummer-Vinson syndrome (PVS) is a clinical syndrome which comprises iron deficiency anemia, dysphagia, and esophageal webs. It was very common in countries with high prevalence of iron deficiency; however, with improvement of nutritional status, it is extremely rare.[1] It is more common in females than males because of inadequate dietary intake of nutrients, multiparity, and menstrual blood loss. The pathogenesis of PVS is unclear, but there is association of iron deficiency anemia with dysphagia.[2,3] Manometric studies show low amplitude contraction and low swallowing pressures at pharyngeal level in iron deficient patients likely from myasthenic changes in esophageal muscle fibers which lead to dysphagia.[4] Some studies have shown that replacement with iron improved dysphagia in PVS.[2] Esophageal web formation is thought to be a result of tissue injury resulting in mucosal changes and abnormal peristalsis in the esophagus.

Case Report

A 37-year-old female of South Asian/Pakistani descent who had no significant past medical history was referred to our center for dysphagia and weight loss. On close questioning, she had intermittent solid food dysphagia at the level of the sternal notch for 3 years without any other alarming or progressive symptoms for which she never sought medical care. However, for last few months, she developed progressive severe solid and liquid food dysphagia associated with significant loss of appetite and weight and at this point she sought medical care. She had no history of smoking cigarettes, chewing tobacco, alcohol use, or drinking hot liquids. There was no family history of esophageal cancer. Physical examination was remarkable for the patient being cachectic with conjunctival pallor but no cheilosis or koilonychia.

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Laboratories showed iron deficiency anemia (hemoglobin 8.5 g/dl, mean corpuscular volume 71 [82–98] femtoliter, iron 12 (37–170] μg/dl, ferritin 12 [13–150] ng/dl, transferrin 243.5 [188–341] mg/dl, and total iron binding capacity 340.9 [250–450] μg/dl). Liver function tests and B12 and folate levels were all normal.

Her esophagogastroduodenoscopy showed friable mass in the distal esophagus/gastroesophageal junction (GE), and pathology revealed invasive moderate to poorly differentiated keratinizing squamous cell cancer (SCC) [Figure 1]. There was also an esophageal web and multiple constricting rings below the upper esophageal sphincter [Figure 2] in the proximal esophagus. Computed tomography (CT) of the chest, abdomen, and pelvis showed large, partially exophytic stenotic tumor involving the distal esophagus/GE junction, proximal stomach, and lesser curvature. Positron emission tomography-CT showed extensive regional tumoral invasion and perigastric nodal metastatic disease, but no distant metastases were seen. She was diagnosed with esophageal cancer stage T3 N2 M0 (stage 111 B). Carboplatin and paclitaxel were started along with radiation therapy. Due to poor intake and severe malnutrition, laparoscopic jejunal feeding tube was placed.

She had good response from chemoradiation. Tumor mass decreased from 9 cm to 2.5 cm, and there was resolution of perigastric and regional lymphadenopathy. After discussion with the patient and family, it was decided to do exploratory laparotomy, resection of stomach and distal esophagus. However, intraoperatively, she was found to have extensive involvement of the left lateral aspect of liver, body, and tail of pancreas. Surgery was aborted and palliative G-J tube was placed. Patient unfortunately expired after a couple of months.

Discussion

PVS or Paterson-Kelly syndrome comprises dysphagia due to upper esophageal web and iron deficiency anemia. It is more common in middle-aged women and rarely seen in childhood and adolescents.[5,6] Dysphagia is usually painless, intermittent, limited to solid foods and is associated with weight loss. Anemia can manifest as fatigue, weakness, and other features such as glossitis, angular cheilitis, and spoon-shaped fingernails (koilonychia) can be present. Splenomegaly and thyroid enlargement are occasionally seen.[7]

The incidence of PVS has decreased because of advanced health care, improved care for pregnant women, and decreased number of pregnancies and nutritional improvement. Iron deficiency is hypothesized to play an important role in PVS. Tissue iron helps in the proliferation of epithelial layer and with iron deficiency, upper alimentary tract is particularly susceptible because of high cell turnover. Atrophic mucosal changes in the upper alimentary tract are initially reversible with iron treatment; however, without treatment, malignant degeneration can occur at hypopharynx, mouth, tongue, and upper gastrointestinal tract. Autoimmune conditions such as rheumatoid arthritis, pernicious anemia, and thyroiditis have been associated with PVS.[8] There are case reports which showed association between Crohn's disease, celiac disease, and PVS.[9,10]

Other causes of dysphagia such as achalasia, GE reflux disease, diverticula, and neuromuscular and skeletal muscle disorders should be excluded. Other risk factors for SCC esophagus include smoking, alcohol, foods containing N-nitroso compounds, chewing of areca nuts or betel-quid, red meat, human papilloma virus, and tylosis. Diagnosis of esophageal webs can be done by barium X-ray or videofluoroscopy. Endoscopy not only helps in detecting the webs but also helps in identifying suspicious lesions of the esophagus to exclude malignancy as PVS is considered to be a precancerous condition. Esophageal webs are seen as smooth, annular or semilunar covered with pink mucosa on endoscopy. Webs can also be seen in the absence of PVS and they appear as thin horizontal membranes on the anterior wall consisting of squamous epithelium.

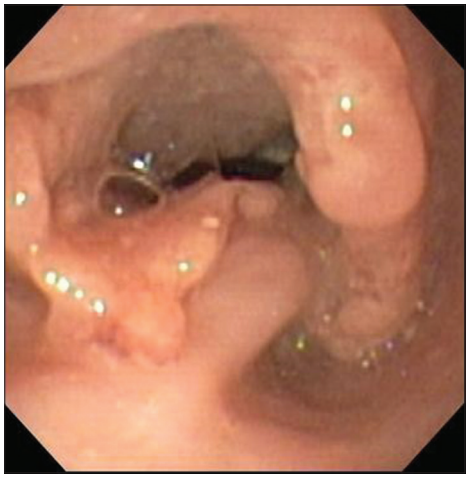

Figure 1: Squamous cell cancer of the distal esophagus

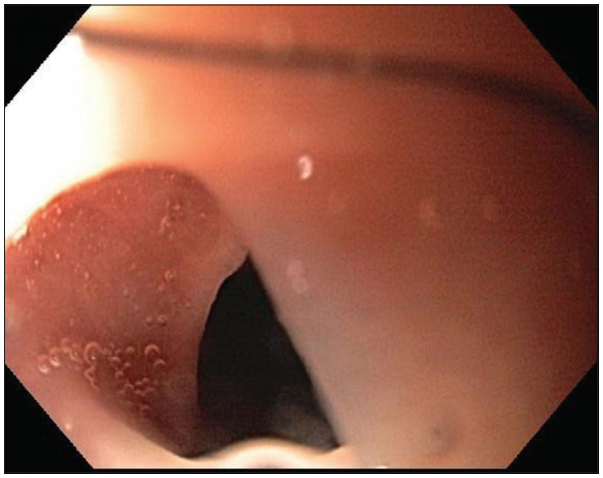

Figure 2: Proximal esophageal web

Owen followed 34 patients with PVS for 15 years and he showed that there was 15% incidence of postcricoid carcinoma. Five patients developed postcricoid cancer.[11] Shamma and Benedict followed 58 patients for 1–46 years and they showed that there was 16% incidence of upper GI cancer. Six patients developed buccal mucosa cancer and 3 patients developed esophageal cancer.[12] Jones followed 76 patients for 15 years and showed that there was 4% incidence of upper GI cancer. One patient had esophageal cancer, one patient had postcricoid carcinoma, and 1 patient had stomach cancer.[13] Chisholm *et al*. followed 72 patients for 6 years and he showed that there was 8% incidence of upper GI cancer: Three patients had postcricoid cancer, 1 patient had esophageal cancer, 1 patient had stomach cancer, and 1 patient had piriform fossa cancer.

Treatment with iron replacement improves anemia and dysphagia.[7] If dysphagia is not improved with iron replacement, then dilatation of the stenosis and rupture of the web with endoscopy is helpful.[14] Close monitoring of patients with upper GI endoscopic surveillance is recommended as there is increased risk of SCC of esophagus, pharynx, and stomach.[2] There is no consensus on the surveillance guidelines for the upper endoscopy for PVS. Prognosis is usually good with PVS, but with SCC of esophagus, the 5-year mortality increases to 85–90%.[15]

Conclusion

We present a rare case report of PVS presenting with SCC of the esophagus as initial presentation. In retrospect, if this patient had presented earlier when she had intermittent nonprogressive dysphagia due to the web, her PVS with the esophageal webs could have been potentially treated and we could have closely followed her. Although we cannot say for sure if her cancer of esophagus might have been prevented by treating her iron deficiency anemia, we could have potentially diagnosed it at an early stage (with a better outcome) due to periodic endoscopy for treatment of webs or surveillance. It is important to consider the differential diagnosis of PVS in patients with dysphagia and iron deficiency anemia. Early endoscopic evaluation, treatment of iron deficiency, and periodic follow-up should play a key role in the management of patients with PVS along with the understanding that it is a risk factor for SCC of the esophagus.

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Conflicts of interest
There are no conflicts of interest.

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