CLINICAL VIGNETTE

Poorly Differentiated Neuroendocrine Tumor of Esophagus

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Case Presentation

A 51-year-old female presented with 3 weeks of persistent abdominal pain. She reported onset flu like illness with diarrhea and sharp abdominal pain. The pain worsened with eating and had a 5-pound weight loss. She denies dark stools, hematochezia, BRPBR, and NSAID use. She has a prior history of amoeba infection treated with metronidazole with resolution. She had tried OTC proton pump inhibitors without improvement.

Physical Examination

On exam, she was a thin woman who was afebrile. Her BMI was 19.4. Blood pressure 100/64. Heart rate 61. Her abdomen was soft and non-distended with normal bowel sounds. There was mild tenderness to palpation in the epigastrium but no organomegaly. Her labs showed normal CMP, ESR, and CRP.

She was referred to Gastroenterology with suspected Peptic Ulcer Disease versus Gastritis and was prescribed sucralfate and dexlansoprazole. H. Pylori blood testing was normal and EGD was scheduled due to persistent symptoms. On EGD the proximal esophagus was normal but a large mid-esophageal ulcer was seen. It was described as a necrotic, 4 cm ulcer extended over half the esophagus circumference, between 28-34 cm from the incisors. This appeared to be consistent with esophageal cancer and multiple biopsies were taken.

The pathology returned as a high-grade neuroendocrine tumor of the mid esophagus. The tumor cells were arranged in microtubular structures, with small round cells containing scanty cytoplasm. Endoscopic ultrasound showed regional lymph nodes, without evidence of any distant metastasis or lymph nodes beyond the regional area and she was referred to Hematology/Oncology.

Staging evaluation included Chest CT, which showed subcarinal right-greater-than-left mid and lower esophageal thickening and a 26 x 22 mm right lower esophageal eccentric mass with central necrosis. No lymphadenopathy was noted. A CT of the neck was unremarkable and there was no cervical lymphadenopathy. Abdominal/pelvic CT showed no evidence of distant metastatic disease.

Body FDG PET/CT showed focal intense FDG activity corresponding to the mid esophageal mass, suggestive of tumor. The imaging also showed multiple gastro hepatic ligament lymph nodes with mild to moderate increased FDG activity concerning for nodal involvement. Brain MRI was negative, and there appeared to be adjacent lymph nodes involvement but no distant metastases.

Discussion

This patient presented with a complaint of stomach pain and was diagnosed with a rare esophageal high-grade neuroendocrine tumor. Based on the limited disease, she was treated similar to a limited small-cell lung cancer with chemo radiation with cisplatin and etoposide. She completed her therapy and underwent repeat endoscopies, scans, and diagnostic tests including biopsies of the esophagus, which showed no evidence of disease.

Based on the complete remission, she was not considered for surgical resection. She remained at high risk for recurrence and therefore started on Atezolizumab maintenance.

The addition of Atezolizumab after initial chemotherapy has been reported to be highly effective for extensive disease in the lung, however, is not given with chemo radiation for more limited case of the disease. Continuing immunotherapy seems to improve the outcome and this patient did well initially with Atezolizumab maintenance. Unfortunately, after four months of maintenance, she developed abdominal pain. Repeat EGD did not identify esophageal recurrence. However, PET CT identified extensive metastatic disease. This was confirmed with a gallium dotatate scan and she was started on Lutetium 177 Dotatate.

Neuroendocrine tumosr (NET) are a rare form of cancer that develops in neuroendocrine cells, which secrete hormone. NET occurs when malignant, unregulated cells grow and can occur in any organ, including lungs, pancreas or gastrointestinal tract. There is no unified neuroendocrine cancer.

Typically, the initial stages present no symptoms. At later stages, depending on the type and location of the cells affected, patients can experience symptoms related to the high hormone levels. The initial clinical manifestations are often the result of regional disease, but NETs have an aggressive history sometimes characterized by widespread, early metastases.

Neuroendocrine tumors characterized by elevated procalcitonin are rare. Increased procalcitonin occurs in neuroendocrine malignancies of the digestive system, including esophageal NET. Procalcitonin elevation is more common in infections but can be associated with tumor status and disease progression.[1,2] The majority of patients with esophageal NET are diagnosed during a routine EGD.[3] Esophageal neuroendocrine tumors are quite rare, very aggressive, and have a poor prognosis. Risk factors include alcohol use and smoking.[4]

The most common symptoms of esophageal NETs are local symptoms including dysphagia, abdominal discomfort, and weight loss and anorexia.[4] The majority of esophageal NETs have already metastasized at the time of diagnosis.[4] Esophageal NET is very aggressive and primarily metastasizes to the liver, lymph nodes but can involve bone marrow and brain.[3]

There is no formal staging for NET of the esophagus. Most clinicians use TNM staging classification to help determine treatment. The prognosis also depends on histological staging.[5] The initial evaluation of patients with NET should include assessment of the primary tumor and regional lymph nodes to determine the extent of regional disease. Prior to treatment, patients should be evaluated for the presence of distant metastases. Treatment options for NET depend on the type and location of the tumor and whether hormone related symptoms are present. Surgery and radiotherapy are commonly used in local disease, but, unfortunately, neither is associated with long term survival.[5] Some patients presenting with local disease can be cured by aggressive therapy, but most relapse and have a poor prognosis. Adjuvant systemic chemotherapy is generally recommended, but most patients will still develop metastatic disease.

The management of systemic disease with chemotherapy is based on the approach used in small cell lung cancer with combination of a platinum compound and etoposide. Unfortunately, most positive responses are partial and of a short duration.

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