

Photoclinic

Figure 1. Lesion found during the upper gastrointestinal endoscopy.

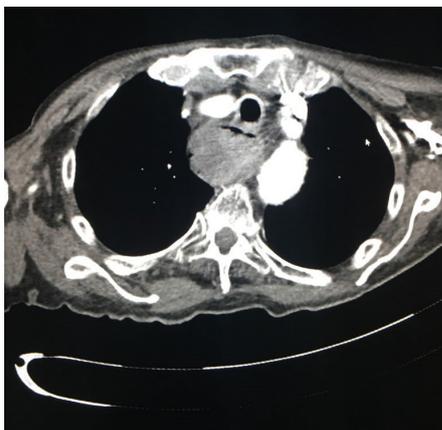


Figure 2. CT Scan Thorax- a Bulky Mass Lesion in Upper Thoracic Esophagus Infiltrating the Posterior Tracheal Wall but not Eroding Into it.

An 85-year-old man presented with complaints of difficulty in ingesting, epigastric discomfort during 3 weeks and intermittent vomiting of blood for 1 week and was admitted in the emergency department.

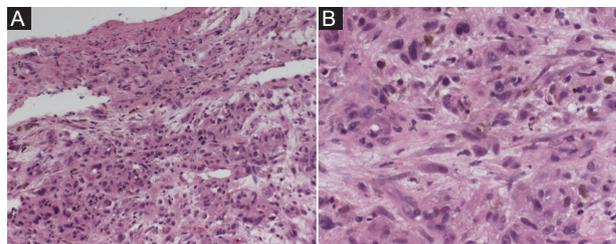


Figure 3. (A) Necrotic superficial Stratified Squamous Epithelium with underlying pleomorphic neoplastic cells with brown melanin pigment in some areas (H&E x200). (B) Hyperchromatic pleomorphic cells with conspicuous nucleoli and melanin pigment in some cells (H&E x400).

He had medical history of hyperplasia of prostate. The physical examination was unremarkable except for epigastric pain.

An upper gastrointestinal endoscopy revealed a necrotic, ulceropolypoid mass involving the middle third of the esophagus (Figure 1). No pigmentation was noted grossly and it was thought to be malignant.

Computed tomography (CT) of neck, thorax and abdomen was done, revealing a bulky mass lesion in upper thoracic esophagus measuring about 30 mm (Figure 2). The upper thoracic vertebrae were not eroded. No fistula or significant lymphadenopathy were seen. No lung lesion or pleural effusion were apparent. A whole body nuclear medicine (NM) scan was done and it was unremarkable elsewhere.

The biopsy material was reported back as necrotic, with poorly preserved squamous lining and a cellular tumor with clusters of atypical pleomorphic rounded and spindle cells with prominent nucleoli with scanty brown intracytoplasmic pigment (Figure 3). The nuclei were enlarged and contained prominent nucleoli and nuclear pseudoinclusions. The mitotic count was 3/10 HPF.

**What is your diagnosis?
See the next page for your diagnosis.**

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Photoclinic Diagnosis

Primary Melanoma of Esophagus Mimicking a Carcinoma

The lesion was negative for cytokeratin AE1/AE3 and the atypical cells showed prominent melan-A staining pointing towards junctional activity and supporting the case to be the primary one from histological point of view. The cells were also positive for S-100, but negative for CK7, CK20, TTF-1, synaptophysin, CD-117 and LCA (Figure 4). The negativity for CK7 and CK20 helped to rule out adenocarcinoma, that of cKit ruled out GIST and LCA negativity ruled out lymphoma.

It was diagnosed as PMME after a thorough search for a primary from dermal, ocular and mucosal sites failed to reveal any such.

Additional laboratory tests were performed, including renal function, hepatic function and the tumor markers CEA, enolase, and CA125, and the levels were within the normal range.

It was still possible to perform a study for BRAF. However, the case was negative for this mutation. The patient was planned to receive chemotherapy but within a week, he suffered a total anterior circulation stroke. The patient succumbed to it in the next week.

Melanoma of the gastrointestinal tract is an uncommon entity, representing 1–3% of all the malignant tumors of the digestive system.¹ In the gastrointestinal tract, it most commonly metastasizes to the liver tissue (68%) and small bowel (58%) and rarely to esophagus (4%) and anus (1%).²

Primary malignant melanoma of esophagus (PMME) is very rare, constituting 0.1%–0.2% of all esophageal

tumors and 5.9% of all the primary melanomas of the gastrointestinal tract.³ It is derived from melanocytes that have aberrantly migrated in the esophageal mucosa.⁴

PMME occurs predominantly in males, with a 2:1 male-to-female ratio, and the prevalent age is 60.5 years.⁵ Most patients complain of dysphagia (73% of patients),^{5,6} similar to any other esophageal malignancy. Other symptoms are weight loss, retrosternal pain, and upper GI bleeding.^{6,7}

Allen and Spitz⁸ have described the diagnostic criteria for primary mucosal melanoma. The criteria include:

- i) A typical morphological pattern of melanoma and presence of melanin granules inside the neoplastic cells.
- ii) The development of the lesion must be in an area of junctional change within the esophageal squamous epithelium.
- iii) There must be junctional activity with melanoma cells in the adjoining esophageal epithelium.⁸

Besides these criteria, previous medical history of cutaneous melanoma has to be ruled out, and a complete systematic clinical investigation is required for a definitive diagnosis of PMME.⁸

Other authors establish the diagnosis of PMME through several different approaches.⁵ Thorough physical examination of the skin and mucosae must fail in identifying any superficial metastatic or primary malignant melanoma. Additional tests are needed in order to rule out that a tumor in the esophagus is possibly a metastasis. The blood tests include tumor markers, as well as hepatic and renal function. Besides, further endoscopic

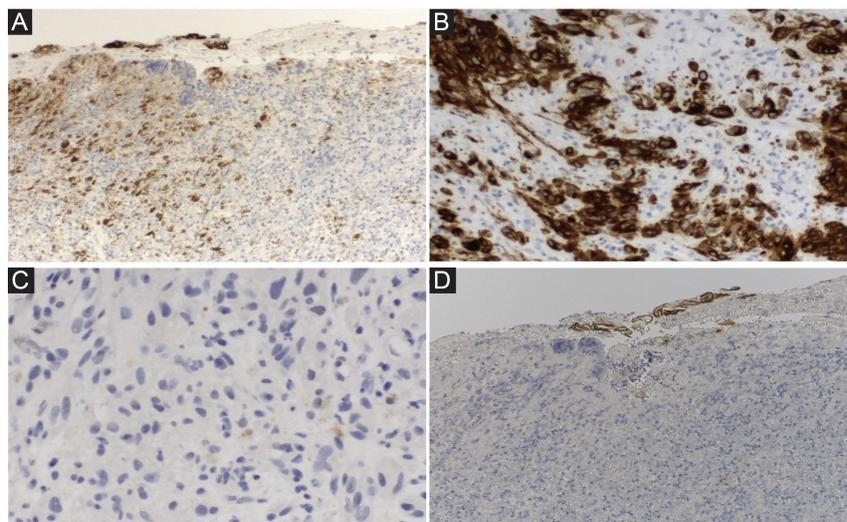


Figure 4. (A) Necrotic squamous epithelium with Melan A positive cells at the junction and luminal surface layers of the epithelium (Melan A IHC x100). (4B) Melan A positive cells in the deeper layers of esophagus (Melan A IHC x200). (4C) Cells are negative (TTF 1 IHC x400). (D) Superficial squamous cells are positive but neoplastic cells are negative (CKAE1/AE3 IHC x100).

and radiological examinations are compulsory for accurate diagnosis.⁵

Mucosal melanomas have worse prognosis than cutaneous ones, apparently due to delay in diagnosis.⁷ The entity masquerades as carcinoma in imaging as well as endoscopically, due to less pigmentation but it has a different management approach. PMME is highly aggressive also because of its nature to grow vertically and invasion of lymphovascular channels, resulting in higher rate of metastatic disease at presentation.^{6,9} The earliest organ to get involved is the liver.⁶ The other organs involved in decreasing frequency of involvement are the mediastinum, lungs and brain.⁹

A poorly differentiated carcinoma can be often a mistaken identity. Besides, mucosal melanomas often present in advanced stage. Therefore, accurate diagnosis and timely resection are the main prerequisites. In our case, although the patient presented late, an unrelated set of events made it fatal. There was quick histological diagnosis and brisk clinical and imaging search to confirm the entity with a whole panel of markers clearly ruling out other mimics.

The therapeutic approach to PMME should be individualized, taking into account the size and location of the tumor, age, presence or lack of metastases, and comorbidities.¹⁰ The appropriate treatment approach for a PMME would be surgical resection with regional lymph node dissection. Total or near total esophagectomy presents the best survival outcome of five years compared to nine months for local resection.⁶ However, even after complete excision by surgical resection as the standard treatment, the prognosis is poor, with a 5-year survival rate of 30.7%.⁵ Other options like immunotherapy, chemotherapy and radiotherapy can also be administered but with limited benefits.⁵ In our case, this could not be evaluated due to the early demise of the patient for a different unrelated cause.

In conclusion, the entity of PMME, although it is rare and often metastatic or mimicking carcinoma, must be borne in mind, as early and correct diagnosis in early stage of the disease could offer the patient a better repertoire of treatment modalities.

Authors' Contribution

All authors contributed equally to this manuscript.

Conflict of Interest Disclosures

The authors have declared that no competing interests exist. Besides, no funding or other financial support was received.

Ethical Statement

Written informed consent was obtained from the patient / relatives of patient who participated in this study.

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