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Esophageal Melanoma - A Rare Neoplasm

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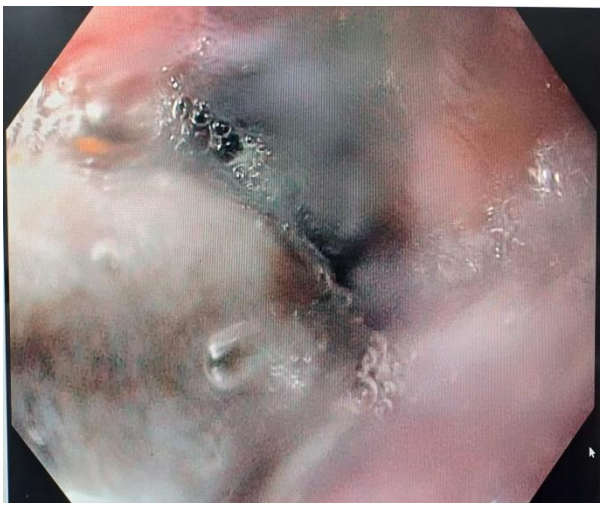
Abstract:- A 70 year old man having progressive dysphagia, coronary artery disease (CAD) with an Ejection Fraction (EF) of 30% was detected to have a poorly differentiated esophageal malignancy. Immunohistochemistry (IHC) was positive for HMB 45 and SOX 10 confirming esophageal melanoma. In view of advanced age and poor cardiac function, surgical treatment was not feasible. Palliative esophageal metallic stenting was performed. Immunotherapy was suggested with ICI. We present this case in view of rarity of esophageal melanoma and to stress the need for evaluation with IHC in subjects with poorly differentiated esophageal malignancy.

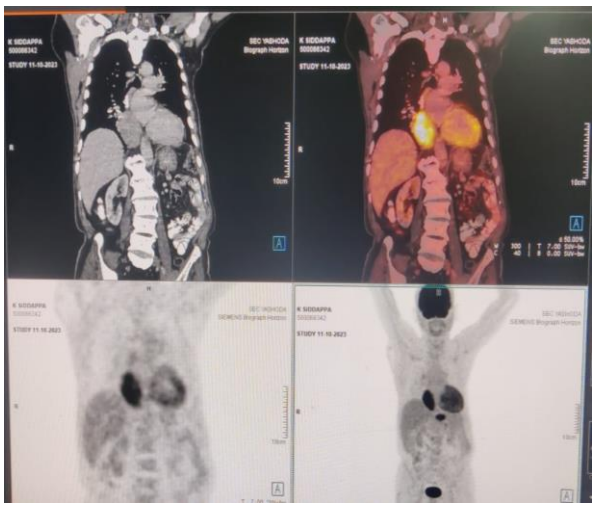
Keywords:- *PMME, Dysphagia, Immunotherapy, SEMS, Melanoma.*

I. INTRODUCTION: CASE REPORT

A 70 year old man presented with progressive dysphagia for solids since 3 months. There was weight loss and weakness. There was no chest pain, abdominal pain, fever, recurrent respiratory infection or any neurological symptoms. He is a smoker and consumes alcohol. There was evidence of osteoarthritis of both knees and eight years ago angiogram documented coronary artery disease (CAD). Physical examination was normal. Cardiac evaluation revealed low ejection fraction (EF) 30%. Endoscopy revealed a large ulcero proliferative friable growth with areas of necrosis and dark pigmentation in esophagus extending downwards from 32 cm. Biopsy of the lesion revealed a tumor composed of discohesive epithelioid cells with scant eosinophilic cytoplasm, increased nuclear cytoplasmic ratio, prominent nucleoli and focal pigmentation within cytoplasm, suggesting poorly differentiated malignancy. On IHC, the tumor cells were diffusely positive for HMB 45 and SOX 10; and negative for CK5/6 and P40. A diagnosis of esophageal malignant melanoma was made. PET scan revealed lower esophageal wall thickening of 3.8 cm and longitudinal involvement of 6-7cms with enlargement of right paratracheal, subcarinal and gastrohepatic lymphnodes (4.3 x 3.8 cm) suggestive of $T_4N_3M^0$. In view of severe left ventricular dysfunction (EF 30%), patient was keen on palliation of dysphagia. He was uninterested in radiochemotherapy or surgical options. A self-expanding metal stent was placed across the esophageal narrowing for relief of dysphagia. The case is reported in view of rarity of esophageal melanoma.



Endoscopic Image



PET Scan Image

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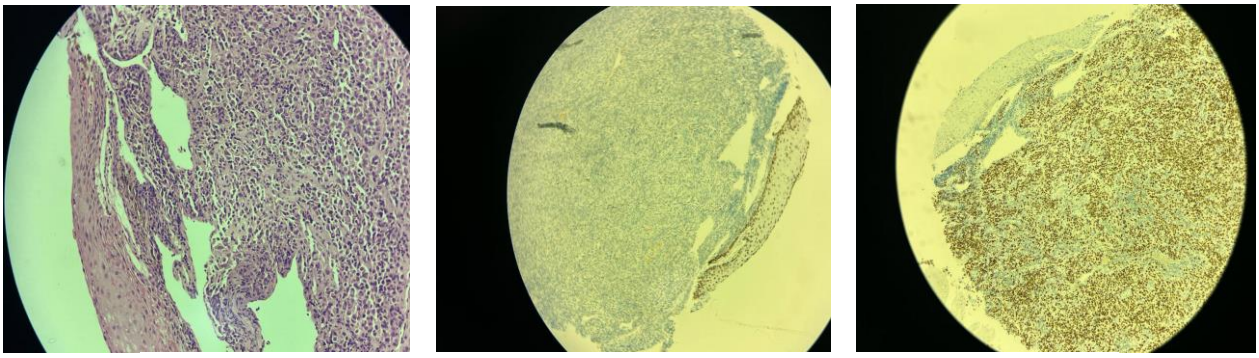

Brown Pigmentation P40 Negative SOX10 Positive

Fig 1: Histopathology of Esophageal Neoplasm

II. REVIEW OF LITERATURE

Moles or nevi are common, harmless skin lesions, which may be found in normals and number about 10-45 on the human body. They appear anywhere on the body including scalp and armpits during childhood or teenage; may be colored black, brown, blue, red or pink; flat and/or raised, oval or round, measures less than 6 mm and may grow hair.

Moles which change color, grow to a large size, become asymmetric and itchy, may take a neoplastic transformation (melanoma). Although melanoma usually grows on the skin, it can also grow in mucosal membrane like mouth, nose, sinuses and pelvic organs like rectum, anus, vulva and urinary tract. Primary malignant melanoma (MM) is a rare disease, accounting for 0.1-0.8% of all malignant tumors of the esophagus[1,2,3]. Esophageal melanoma occurs most commonly in middle or lower third of esophagus, appears as an elevated lesion with ulceration, mostly pigmented but sometimes present as white or grey lesion called amelanotic melanoma (Table No. 1). Prognosis of esophageal MM is generally poor, but can be improved with the present standard of care. Factors that may lead to poor prognosis include age ≥ 60 years, invasion depth (T_2 or deeper), lymph node metastasis and distant metastasis [4].

Surgery is the treatment in all possible cases; other treatments include chemotherapy (DAV: Dacarbazine, Nimustine, Vincristine), radiotherapy and/or immunotherapy (Nivolumab) [5,6].

Esophageal melanosis is development of pigmentation in the esophagus which may or maynot be a precursor lesion of primary malignant melanoma of esophagus (PMME). Esophageal melanosis has been reported 0.1% in Japan, 2.1% in India (Endoscopic screening), 2% in UK [8,9,10]. It has been proposed that when esophageal melanosis like lesion is detected, follow up endoscopic screening should be performed at periodic intervals[7].

Table No. 1: Clinicopathological Comparisons of PMME

Features	Kim et al [11] 2022 n= 17	Wang et al [1] 2019 n=76	Dai et al [12] 2020 n=70
Symptoms	Dysphagia	Dysphagia	Dysphagia
Mass Forming	88%	-	-
Infiltrative	12%	-	-
Melanotic	76%	-	-
Amelanotic	24%	-	-
Location	Upper 17% Middle 17% Lower 66%	Upper 8% Middle 34% Lower 58%	Upper 4% Middle 41% Lower 55%
Lymph-node Metastasis	30%	37%	45%
Surgical Treatment	58%	77%	100%
Role of Radiation	-	-	2%
Role of Chemotherapy	41%	63%	75%
Survival	10 mo	19 mo	13.5 mo

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➢ *PMME: Primary Malignant Melanoma of Esophagus*

Because of marked variability of histology of esophageal melanoma, all poorly differentiated esophageal tumors (especially amelanotic type) should be subjected to IHC. The differential diagnosis of esophageal poorly differentiated tumors include basaloid squamous cell carcinoma, lymphoma, sarcoma and neuroendocrine carcinoma. Broad panel of IHC markers for diagnosis include S100, HMB45, SOX10, P40, LCA, Synaptophysin and Chromagranin. In our case, the tumor had focal cytoplasmic brown pigment and was positive for SOX10 and HMB45 suggesting esophageal melanoma.

Primary malignant melanoma of esophagus (PMME) is a rare tumor. Any esophageal growth diagnosed as poorly differentiated cancer on endoscopic biopsy, needs evaluation by immunohistochemistry for diagnosing PMME. A significant proportion of PMME are amelanotic but it is suggested that there may not be any difference in the prognosis between melanotic and amelanotic varieties. Certain mutations like C-KIT, NRAS, BRAF, HER2 and predictive markers like PD-L1 may have a role in selection of chemotherapeutic or immunotherapeutic agents. The main treatment of PMME is surgical, and the tumors are generally considered to be chemotherapy resistant. A combination of immunotherapeutic agents like nivolumab and/or pembrolizumab with chemotherapeutic agents may yield better survival rates than conventional chemotherapy alone.

III. CONCLUSION

PMME is a rare neoplasm and the diagnosis needs to be confirmed by characteristic IHC findings. The disease is more common in men and elderly age groups. Lower third of esophagus is commonly affected. Surgery is the treatment of choice in operable patients and majority usually require adjuvant chemotherapy. Immunotherapy may be considered in advanced cases especially when PD-L1 expression is present. Overall the outcome of PMME is not encouraging, but an early diagnosis may be able to improve the outcome.

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