Primary Malignant Melanoma of the Oesophagus

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Abstract
Primary malignant melanoma of the oesophagus (PMME) is a very rare disease with poor prognosis. The median survival is about 10 months. PMME are highly aggressive biologically and metastasize early via haematogenic and lymphatic pathways. Treatment outcome is poor because malignancy is very advanced at the time of presentation. Here, we present the endoscopic features and management of PMME case.

Case Report
A 5 year old female with no comorbidities presented with a 3 month history of non-progressive dysphagia to solids only, retrosternal discomfort, with no significant weight loss and anorexia. Physical examination revealed no skin, ocular lesions or palpable lymph nodes. Complete hemogram with liver and renal function tests were within normal limits. EGD evaluation (with tissue biopsies) showed a 3-4 cm polypoidal growth from 22 cm to 28 cm with multiple black colored melanotic patches overlying the surface of growth with no ulcers or bleed. CT scan evaluation of chest and abdomen revealed a homogeneously enhancing, nodular, 2.5 x 1.8 x 3.6 cm sized subcarinal mass, eccentrically arising from the left lateral wall of the mid-thoracic esophagus causing luminal narrowing and indenting the posterior wall of left bronchus with enlarged right paratracheal lymph nodes with no pulmonary or hepatic lesions (Figure 1). Histopathology revealed uniform round cells with thin rim of cytoplasm and fine nuclear chromatin, arranged in diffuse sheets (Figure 3). Few tumour cells had prominent nucleoli with brown pigment (Figure 4). Immunohistochemical studies were compatible with malignant melanoma: positive for HMB 45, Melan A, S 100 and immunonegative for cytokeratin, EMA, LCA and CD 30.

Three field total radical esophagectomy with end-to-side esophago-gastrostomy and feeding jejunostomy was done. Anatomopathologic examination showed a brownish-black nodular mass of 3 x 1.5 x 1.7 cm with few satellite nodules. Submucosal and lymphovascular invasion was present with normal muscularis propria. Majority of tumour cells were amelanotic. 0/2 hepatic group nodes, 1/10 recurrent laryngeal nodes were positive with perinodal infiltration with R0 resection (T3N1M0, Stage III). Started on chemo-immunotherapy (DTIC 220 mcg, cisplatin 30 mg weekly and interferon 5 million units thrice weekly) after 5 wks of surgery. Follow up at 16 weeks after surgery (3rd cycle of chemo-immunotherapy) with CT scan of chest and abdomen revealed small, well demarcated, hypoenhancing lesions of 1.2 x 1 cm in segments 5 and 6 of the liver, which were suggestive of benign hepatic lesions on whole body FDG PET scan (Figure 2). Decision to continue with chemo-immunotherapy was taken.

The course was complicated with peripheral vein thrombosis and metastases to liver (multiple heterogeneous mass lesions, largest two measure 3.7 x 3.1 cm and 3.7 x 3.2 cm) resulting in discontinuation of immunotherapy (after 40 interferon injections) before her 6th cycle of chemotherapy and substituted with Paclitaxel (120 mg/m2 weekly). CT evaluation of chest and abdomen after 32 weeks of surgery (12th cycle of chemotherapy) showed multiple small, well demarcated, hypoenhancing lesions in whole of the liver and right middle lobe of the lung.

At 40 weeks post-surgery (12 chemotherapy cycles) she succumbed to extensive lung, liver and brain metastasis.

Discussion
The first case of PMME was described by Baur in 1906.1 A total of 337 cases are reported up to the year 2011.2,3 Primary malignant melanoma of the oesophagus (PMME) accounts for less than 0.1%- 0.2% of all primary oesophageal tumours.4 PMME occur mainly in the sixth and seventh decades of life, but may develop at any age, with a male-to-female ratio of 2:1.2 The most frequently reported site for oesophageal malignant melanoma is the distal part of the esophagus.1 PMME are diagnosed at a late stage, when mechanical obstruction develops, and the patients present with symptoms of dysphagia, odynophagia, and weight loss. The patients usually have a symptomatic history lasting a mean of 3.5 months before a diagnosis is established.3 Although radiological studies such as computed tomography and magnetic resonance imaging can identify and locate the tumor, the diagnosis can only be established by upper digestive endoscopy with biopsy and immunohistochemical studies.4 PMME typically reacts positively to HMB-45 and S100 protein and negatively to cytokeratin.2

PMME is clinically confirmed when no other skin lesions (e.g., in the eyes or anal mucosa) are found. Some published studies suggest some criteria for differentiation between primary and metastatic disease.7 Surgical resection with re-establishment of gastrointestinal continuity is
The median survival time is 28 months (range: 11 months to 6 years). Sabanathan et al, reported an average survival rate of 10 months and a five-year survival after surgical treatment of 4.2%. Five-year survival rates have been achieved in 37% recently, while adjuvant therapy has not been proven to increase overall survival but plays a palliative role.

A metaanalysis (18 RCT, 2625 patients of metastatic malignant melanoma) compared the use of chemotherapy versus chemoimmunotherapy, evidence of an increase of objective response rates was found in people treated with chemoimmunotherapy in comparison to chemotherapy, with no difference in survival and a hazard ratio of 0.89 (95% CI 0.72 to 1.11, p=0.31), with increased hematological and non-hematological toxicities in people treated with chemoimmunotherapy.

**References**