

## Primary Malignant Melanoma of Oesophagus: A Case Report with Review of Literature.

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**Abstract:** Primary malignant melanoma of the oesophagus is a rare tumour. It is a biologically aggressive tumour and the prognosis is poor with limited life expectancy. Surgery is the only hope to improve survival and even with radical surgery the 5-year survival is an exception. We report a 61-year-old patient who was diagnosed with malignant melanoma of the oesophagus when he was investigated for dysphagia.  
**Key words:** Malignant melanoma, oesophageal cancer

### INTRODUCTION

The lower end of oesophagus contains melanocytes and hence it is one of the sites that has a potential to develop primary melanoma. Less than 270 cases of primary oesophageal melanoma have been reported in the English literature. Primary oesophageal melanoma accounts for 0.1-0.2% of all oesophageal malignancies and there is paucity of data regarding this condition. It is common in elderly male patients; metastases are common and lead to mortality.

### CASE REPORT

A 61 year old male patient was admitted to our hospital with the complaint of dysphagia over a four week period. The dysphagia was progressive and associated with abdominal discomfort and loss of appetite. There was no history of hematemesis or melena. This patient had a history of high blood pressure, ischaemic heart disease with atrial fibrillation and hyperlipidemia. He had stopped smoking 40 years ago and did not consume alcohol. There was no family history of any malignancy. The physical examination was unremarkable. There were no cutaneous lesions. His blood investigations were all within the normal range.

The patient underwent an upper gastrointestinal endoscopy which revealed an exophytic pigmented tumour at the gastro-oesophageal junction (Fig. 1). Histology of the tumour was oesophageal melanoma. A computerized tomography (CT) scan of the thorax and abdomen showed a long segment circumferential wall thickening involving the mid to distal oesophagus causing significant luminal compromise (Fig. 2). The scan also demonstrated an enlarged perigastric lymph node, a tiny hypodense lesion in the liver and a gallstone. A diagnosis of primary oesophageal melanoma was made. patient underwent an Ivor Lewis oesophagectomy. His post-operative course was uneventful and he was discharged on the ninth post-operative day. Macroscopic pathology revealed a 11cm x 11cm x 2.5cm polypoidal mass with multiple tan brown nodules and blue-gray areas (Fig. 3). Microscopic pathology revealed squamous epithelium with an extensive underlying cellular tumour composed of nests, islands and sheets of cells. Intra and extra cytoplasmic melanin pigment was also noted. There was high mitotic activity. There were focal junctional lentiginous components noted in the overlying squamous epithelium (Fig. 4). The tissue was positive for Melanin A and S100 proteins. The tumour had infiltrated into the muscle layers and was present at the circumferential resection margin. The tracheo-oesophageal groove node showed evidence of metastases. The perigastric lymph node however was negative for metastases.

Adjuvant radiotherapy was he declined by the patient. A follow-up CT scan at 2 months revealed liver and right adrenal metastases. He

was offered palliative chemotherapy this time which he refused. He was readmitted with dysphagia four months after surgery. Endoscopy revealed a food bolus proximal to a stricture and CT scan confirmed loco-regional recurrence of the tumour. He underwent palliative oesophageal stenting. Six months after the surgery he presented with seizures and a CT scan brain revealed multiple brain metastases. He has been alive with metastatic disease for seven months after surgery and is currently undergoing radiotherapy and palliation.



Figure 1: OGD demonstrates a pigmented intraluminal tumour



Figure 2: Circumferential oesophageal tumour with luminal narrowing

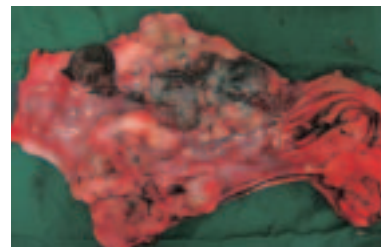


Figure 3: Pigmented and polypoidal intraluminal tumour with multiple tan brown nodules and blue-gray areas

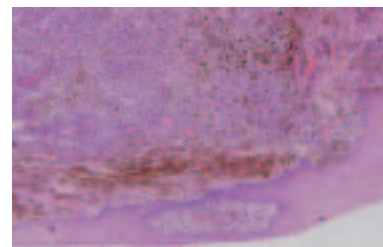


Figure 4: The sections show squamous epithelium with an extensive underlying cellular tumour composed of nests, islands and sheets of cells. The tumour cells are predominantly epithelioid with focal spindle celled areas and exhibit prominent eosinophilic nucleoli. Focal junctional lentiginous component is noted in the overlying squamous epithelium. The tumour also infiltrates the muscle layer.

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## DISCUSSION

Melanocytes originate from the neural crest and migrate to skin and squamous epithelium. Melanocytes do not usually migrate to oesophageal epithelium hence primary melanoma of the oesophagus was controversial until De la Pava et al first described scattered melanocytes at the junction of the squamous epithelium and lamina propria of the oesophagus<sup>1</sup>. Oesophageal melanocytosis is a normal condition and found in up to 2% of oesophagoscopies. It is usually associated with chronic oesophagitis or gastro-oesophageal reflux disease<sup>2</sup> and may be precursor to malignant lesion<sup>3</sup>.

Malignant melanoma of the oesophagus is rare and can be primary or secondary. Dysphagia is the commonest mode of presentation and such was the presentation of our patient. The spectrum of presentations include asymptomatic patients diagnosed on routine barium swallow, anorexia, abdominal pain and massive melena with hypovolaemic shock<sup>4</sup>. C Germer et al have reported a case of primary oesophageal melanoma diagnosed in a patient subjected to oesophagoscopy in a search for the cause of extremity phlebothrombosis.<sup>5</sup>

Oesophagoscopy reveals the diagnosis most of the times. Malignant melanoma usually appears as an intraluminal, irregular, polypoidal, pigmented and solitary lesion at the lower end of the oesophagus; multiple, ulcerative and amelanotic lesions have also been reported<sup>6</sup>. Non pigmented melanoma can be difficult to diagnose unless routine immunohistochemistry staining of the biopsy specimens is done. Satellite lesions when found, may be seen as tiny brownish patches adjacent or distal to the polypoidal growth. reported in 12% cases<sup>7</sup>. Malignant melanoma tends to grow intraluminally location of the tumour, the biopsy may be negative. The diagnostic criteria for typical melanomas include a typical melanoma structure, presence of melanin, origin from the squamous epithelium with junctional activity or junctional activity with melanotic cells in the adjacent epithelium<sup>8</sup>. Epithelioid melanoma cells contain large nuclei with irregular contours, nuclear grooves, and nuclear pseudoinclusions. Chromatin is characteristically clumped at the periphery of the nuclear membrane. Prominent red nucleoli are present. Mitoses, including atypical ones, are often abundant. Cells grow as poorly formed nests or as individual cells. Spindle cell melanomas have cohesive cells, which may be arranged in interlocking bundles. Nuclei are spindle-shaped with pleomorphic nuclei and prominent nucleoli. Immunohistochemical staining is positive for S100, HMB – 45, Melanin A, MITF (Microphthalmia-associated transcription factor) and neurone specific enolase. HMB-45 is widely used for detection of melanoma. This method uses monoclonal antibodies to a glycoprotein that is present in cytoplasmic premelanosomes and reacts with melanoma cells, junctional nevus cells, and foetal melanocytes. Melanin-A is a differentiation antigen expressed in all melanocytic cytoplasm. S-100 protein is a homodimeric low molecular weight calcium binding protein, which is mostly distributed in the cytoplasm. This antibody recognizes S-100 and stains melanoma tissues. MITF is located in the nucleus of melanocytes and it plays a key role in melanocyte development, survival and differentiation. MITF staining can also help in the diagnosis of melanoma. Neurone specific enolase is elevated in tumours of neural crest origin (e.g. melanoma) and neuroendocrine tumours. The role of steroid receptor proteins and p53 gene overexpression / mutation is unproven.

Approximately half of the patients will have distant metastases (both haematogenous and lymphatic) at the time of presentation. The liver, mediastinum, lungs, pleura, supraclavicular nodes, bones and brain are the common organs to harbour metastases.

CT scan, endoscopic ultrasonography (EUS) and positron emission

tomography (PET) scan have been useful in the assessment of loco-regional and distant metastasis and even microstasri. PET scanning has 100% sensitivity in lesions more than 10 mm and is able to change the clinical management plan in one fifth of patient with primary malignant melanoma of the oesophagus<sup>9</sup>.

Resectional surgery is the standard of care and is usually possible in most of the cases despite local spread. Resection is the best form of palliation even if the disease is advanced. A resectability rate of 67 to 87% has been reported. Despite the high resectability rate, mean survival reported by two large series is less than 13 months and the five year survival less than four percent<sup>10</sup>. Due to the longitudinal spread of the tumour along the vertical axis of oesophageal mucosa, it is recommended that more tissue be sacrificed in the interest of margin clearance. The results of radical surgery are better than limited local resection or non-surgical therapies. Oesophagectomy can be performed safely with a low morbidity and mortality and hence there is little role for primary chemotherapy, radiotherapy or biological therapy.

The main role of bio-chemo-radiotherapy is adjuvant or palliative and the evidence is based on extrapolation of data from published literature for cutaneous melanoma. Anecdotal cases of good response to adjuvant treatment for oesophageal melanoma have been reported by Japanese authors<sup>11,12</sup>. Kawada K et al from Japan have reported a 7-year survival with local injection of interferon beta on top of systemic pre and postoperative DAV (DTIC - dacarbazine, ACNU – nimustine hydrochloride, VCR - vincristine) chemotherapy<sup>13</sup>. Combination biochemotherapy using cisplatin, interleukin -2 and interferon alfa was reported as having approximately 50% response rate in metastatic melanoma<sup>14</sup>. Wayman J et al has reported the role of intraluminal brachytherapy with laser photoablation<sup>15</sup>.

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