Spontaneous Regression of Malignant Melanoma of the Gastro-Oesophageal Junction

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Abstract

Introduction: Both esophageal melanoma and regression of malignant melanoma are rare occurrences and exist in the literature mainly in the form of case reports. There have been no reported cases of complete regression of primary malignant melanoma of the esophagus.

Presentation of the Case: A 57 year old family doctor was found on routine blood tests to have an iron deficiency anaemia. Upper gastrointestinal endoscopy revealed a tumor of the gastroesophageal junction (GEJ) and biopsies confirmed a malignant melanoma. Staging investigations were performed and the patient proceeded to have a primary open Ivor-Lewis esophagectomy. Histopathological examination of the resected specimen showed no active tumor.

Conclusion: Regression of melanoma is a rare occurrence and may be related to the immunogenic nature of the cancer. It has been associated both favourably and negatively in the literature with prognosis. There are no reported cases of complete regression of disease where the primary tumor has been in the esophagus.

Keywords: Oesophageal Melanoma; Melanoma Regression

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Consent: We confirm that the patient has given the informed written consent for the case report to be published.

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Introduction

The following report outlines a case of malignant melanoma of the gastroesophageal junction (GEJ), managed surgically without neo-adjuvant chemotherapy. Histopathological examination of the resected specimen showed complete tumoral regression.

Case presentation

A 57 year old gentleman was referred to the upper gastrointestinal surgical team after presenting to his family doctor with an episode of haematochezia. His past medical history included obstructed sleep apnoea and chronic pain for which he had a sacral nerve stimulator. His past surgical history included a right total hip replacement, a previous open appendectomy and a laparoscopic fundoplication for gastro-oesophageal reflux disease in 2010. His initial blood tests demonstrated iron deficiency anaemia with a haemoglobin of 96g/L, a mean corpuscular volume, 81.7 fl, a haematocrit of 0.31 L/L and a serum ferritin of 2 ug/L.

An esophago-gastro-duodenoscopy (EGD) revealed a large fleshy polypoid lesion, 39-44cm from the incisors, which bled easily on contact (Fig. 1). Histology of multiple biopsies suggested a tumor mass with poorly differentiated cells and immunohistochemistry showed that the tumor was positive for S100, HMB 45, Melan A and focally for CD117 but was negative for SMA. It was confirmed as a malignant melanoma.

Staging computer tomography (CT) showed a thickened distal esophagus with a 3x3x3cm mass extending into the GEJ but with no evidence of other lesions (Fig. 2). Proton emission tomography (PET) scan showed a highly active primary lesion with no further avid areas. An endoscopic ultrasound scan was performed which suggested the stage of the tumor at T3N2MX. A staging laparoscopy and peritoneal washings did not demonstrate any evidence of peritoneal malignancy.

Figure 1 Tumor at initial OGD.
Figure 2 Specimen demonstrating a pigmented black lesion at the GOJ

Figure 3 Extensive lymphohistiocytic infiltrate (H&E 20x)
After discussion at a multidisciplinary team meeting, the patient proceeded to primary surgery and underwent an Ivor-Lewis esophagectomy. At the time of surgery a large melanotic node was noted within lymph node station 10, this was removed en bloc. Post operatively the patient recovered well and was discharged home 8 days post procedure. At his 6 week follow-up appointment he was recovering well and subsequently at 5 months post operation he continued to be well.
Macroscopic histological review showed a pigmented lesion 35 x 20 mm predominantly in the proximal stomach, the epicentre of which lay 10mm from GEJ (Fig3). Sections from the lesion revealed extensive lymphohistiocytic infiltrate and mild fibrosis (Fig 4). Numerous melanin laden histiocytes were also appreciated (Fig 5). No viable tumor cells were seen in the entirety of the surgical specimen. Melanoma cocktail immunostain was also negative (Fig 6). Sixty-two lymph nodes were recovered which also did not reveal any viable tumor cells.

Given that this specimen showed no active malignancy the initial biopsy was re-reviewed and was confirmed to demonstrate malignant melanoma with no evidence of regression. The interlude between the biopsy and the operation was 8 weeks. A dermatology opinion was sought in light of these findings, and despite thorough examination and investigation, no evidence of melanoma was identified. A repeat PET scan and oncology review at 3 months post operation did not demonstrate any evidence of malignancy.

This patient had primary malignant melanoma of the GEJ which regressed spontaneously.

Discussion

This case highlights two unusual entities; the first being primary melanoma of the GEJ, the second being spontaneous regression of the primary lesion.

Primary malignant melanoma of the gastro-intestinal tract is rare; metastatic disease from a distant primary is more common[1]. Bauer first described primary melanoma of the esophagus in 1906 [2] and subsequently there have been many reported cases, although it accounts for less than 0.1% of all oesophageal cancers[3]. The prognosis is poor with a median survival of 10 months and 5 year survival of 4.2%[4]. Primary malignant melanoma of the stomach is less common than oesophageal melanoma.

Postulated theories for the origin of melanocytes with the gastro-intestinal tract include migration of neural crest cells during embryogenesis [5] and the differentiation of amine precursor uptake and decarboxylation (APUD) cells into melanocytes [6]. A literature review of Medline and EMBASE identified only 4 reported cases of primary melanoma affecting the GEJ, [7-10] and one of these patients showed evidence of spontaneous regression.

Spontaneous regression of tumors is a well-recognised phenomenon that has been described in renal cell carcinoma, head and neck cancer, and leukaemia as well as melanoma [11]. Stewart described the criteria that must be satisfied in order to consider spontaneous regression; clinical and histological diagnosis of malignancy, lack of therapeutic manipulation sufficient to account for regression, clinical evidence of regression, significant period of follow-up and, if possible, histological examination of tissue sites where regression has occurred [12]. For the case herein described; there was clinical and histological confirmation of malignancy from the initial biopsies, no therapeutic intervention, clinical evidence of regression and follow-up with a CT PET scan. The final criteria are not applicable in this case as the site in question has been resected. We can be confident in the diagnosis of complete regression. The mechanism for regression is poorly understood but may be related to the highly immunogenic nature of melanoma [13].

An alternative explanation for the findings described would be that the GEJ melanoma was not a primary but rather a metastasis from an occult primary. Malignant melanoma can present with metastasis from an unknown origin, this is the case in 2-3% of all melanomas [14]. The reasons for this include; a concurrent unrecognised melanoma, a previously excised melanoma and an antecedent spontaneously regressed primary [15]. In this case our patient did not have a history of melanoma, was reviewed by a dermatologist and had a post-operative PET scan. Despite this, there remains a possibility that this GEJ tumor represents a metastasis from an occult or regressed primary melanoma.
Given the unusual pathology and natural history to date it is difficult to provide accurate prognostication. However, given the poor outcome of patients with esophageal and GEJ melanoma and reports of recurrence when spontaneous regression is seen [16], it would seem prudent to provide regular and intensive follow-up.

**Conclusion**

Gastro-esophageal melanoma and spontaneous melanoma regression have both been described in the literature. Their occurrence together is a unique finding.

**Abbreviations**

HMB 45: Human Melanoma Black 45  
CD117: Mast/stem cell growth factor receptor  
SMA: Smooth Muscle Actin

**References**