CASE REPORT

A tenebrous tale: malignant melanoma of the oesophagus

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SUMMARY

A 57-year-old man presented with a 4-month history of worsening symptoms of oesophageal obstruction. The physical examination was unremarkable. An oesophagogastroduodenoscopy revealed an exophytic tumour in the distal oesophagus. A biopsy demonstrated malignant melanoma. Staging of the melanoma showed disseminated lymph node and bony-spine metastases. He had no prior history of cutaneous or ocular melanoma. Following full multidisciplinary team input, he was palliated with a metal mesh stent and immunotherapy. He died 3 months later following community management.

BACKGROUND

Malignant melanoma of the oesophagus (MME) is extremely uncommon. MME can arise from the oesophagus itself (primary) or from distant metastases to the oesophagus (secondary). It is essential to distinguish between Primary melanoma of the oesophagus (PME) and secondary as the management and prognosis differs greatly between the two. According to the American Joint Committee on Cancer, metastatic melanoma of the oesophagus is considered a grade IVc melanoma. It is associated with a very poor prognosis, with a median survival of 4–6 months.

CASE PRESENTATION

A 57-year-old man presented with a 4-month history of 12.7 kg weight loss, epigastric discomfort, progressive dysphagia, odynophagia and anorexia. His background history included a 60-pack-year history of smoking, and he consumed 28 units of alcohol per week. His physical examination was unremarkable. Of note, he had no prior history of cutaneous or ocular melanoma.

INVESTIGATIONS

An oesophagogastroduodenoscopy revealed a 5 cm malignant exophytic tumour in the distal oesophagus, 25 cm from the incisors, and a biopsy was taken (figure 1). Histological analysis showed an oesophageal squamous mucosa with ulceration. The immunohistochemistry was positive for S100 protein HMB 45, melan A and focally positive for CD117 and negative for CD34 and DOG1 (stains for gastrointestinal stromal tumour (GIST)). The appearance was consistent with malignant melanoma. No BRAF mutation was detected (figures 2

and 3). A total skin survey and funduscopy showed no evidence of any cutaneous/ocular lesion.

Staging CT of thorax, abdomen and pelvis (CT TAP) and subsequent positron emission tomography (PET) CT showed a large obstructing midoesophageal mass, disseminated lymph node metastases and bony-spine metastases.

DIFFERENTIAL DIAGNOSIS

1. Adenocarcinoma
2. Squamous cell carcinoma
3. GIST

TREATMENT

Following full staging and MDT input, a diagnosis of metastatic PME was made. Given the patient's poor prognosis, systemic chemotherapy and radiation therapy were not advocated. He was commenced on a trial of immunotherapy. However, this was discontinued due to poor treatment response. Therefore, the decision was made to manage him with oesophageal stenting to palliate the oesophageal obstruction and to facilitate discharge to his home (figure 4). He received palliative therapy in the community.

OUTCOME AND FOLLOW-UP

The patient subsequently passed away 3 months after the initial diagnosis of metastatic melanoma of the oesophagus.

DISCUSSION

Melanomas of the gastrointestinal (GI) tract are very uncommon tumours that comprise 1.5%–2.0% of all melanomas.¹ They are however considered to be the extraintestinal malignancy most likely to metastasise to the GI tract.² Mucosal melanoma is an exceptionally aggressive kind of melanoma.³ In a study carried out by John Hopkin's university, they examined the post mortem of 56 cadavers with metastatic melanoma. They found that there was GI involvement in 56% of cases.⁴ In another study of 41 patients presenting with metastatic melanoma of the GI tract between 1954 and 1989, the oesophagus was the least common site of metastases (5%). When pathologists examine GI metastases, they may either be pigmented or amelanotic. They are most commonly ulcerated. It is very uncommon to find them as a solitary mass.⁵

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Figure 1 Exophytic mass in the oesophagus, as seen by oesophagogastroduodenoscopy.

The most common symptoms of MME are dysphagia, substernal or epigastric discomfort and weight loss.⁶ In one particular study, the median length of symptoms prior to diagnosis was 1 month.⁷ The physical examination may be unremarkable. In 26% of cases of intestinal melanomas, no extraintestinal primary lesion can be identified.⁸ In those circumstances, regression of the primary site can explain the lack of primary lesion. Regression of melanoma is a well-described phenomenon, occurring in 10%–35% of cases.⁹ Immunological processes have been postulated as the cause of regression.¹⁰

When an oesophageal cancer is suspected, endoscopy and biopsy are performed. Endoscopy confirms the presence of mass. To diagnose melanoma of the oesophagus, a biopsy is taken^{11–13} and stained with the immunohistochemical stains used in the diagnosis of cutaneous melanoma. The presence of melanosome (HMB45), melan-A and S100 protein are obligatory for the diagnosis of melanotic melanoma.¹⁴ If an oesophageal melanoma is detected an extensive examination must be performed for synchronous melanoma at cutaneous and ocular sites.¹⁵ To diagnose PME, there must be no prior history of melanoma.¹⁵ The prognosis is better for PME relative to secondary melanoma of the oesophagus.¹⁶ Staging is performed with CT TAP, fluorodeoxyglucose PET to detect the presence of locoregional and distant metastasis and MRI where indicated to detect bony or brain metastasis. Unlike staging cutaneous melanoma, sentinel lymph node biopsy has no role in melanoma of the GI tract.

In case report series all 10 of the patients with metastatic melanoma of the oesophagus were dead within 10 months. Metastatic melanoma of the oesophagus seems to be an indicator of widespread disseminated malignant melanoma.¹⁷ According to the American Joint Committee of Cancer, metastatic melanoma of the oesophagus is classified as stage IV.¹⁸ The metastatic site of the

Figure 2 H&E stain of oesophageal specimen.

Figure 3 S100 stain of oesophageal specimen.

melanoma may be divided into M1a (skin, soft tissue and distal nodal), M1b (lung) and M1c (all other visceral sites).¹⁹ In a study carried out it was found that the median survival rates were 1 year for those with metastases to distant lymph nodes or the GI tract and just 4 months for patient with metastases to bone.²⁰

Due to the rarity of the metastatic melanoma of the oesophagus, there is no optimal treatment paradigm in the literature for the palliative management of this condition. The largest, recently published case series identified a mere 19 patients with metastatic PME in North America, over an 8-year period. The 3-year survival in patients with metastatic PME was 0%, and the median survival was only 3.7 months. On multivariate analysis, radiotherapy was not associated with any survival benefit. Due to the inclusion of only two patients in the immunotherapy treatment arm, it is not possible to assess for a meaningful benefit with immunotherapy. To our knowledge, the role of palliative stenting of the oesophagus has not been addressed in MME. It may improve the quality of life during the short median survival.²¹

The key determinant for the appropriate management of MME is whether, or not the disease is present elsewhere. If the disease is widespread, the therapy should include palliation of the symptoms, especially dysphagia and chemotherapeutic regimens.¹⁷ In isolated PME, an oesophagogastric resection may be performed in selected cases.¹⁷ There is no standard chemotherapeutic regimen for MME, either in a treatment or a palliative context. The chemotherapeutic and immunotherapy drugs suggested for patients with stage IV melanoma are ipilimumab, vemurafenib, high-dose interleukin 2 or dacarbazine.²² In another study, 17 patients with MME underwent extensive programmes of resection of all intra-abdominal disease. They have a considerable survival advantage of 23.5 months compared with the patients who underwent palliative therapy or partial resection.²³ For palliative treatment several procedures can be carried out. The

Figure 4 Palliative oesophageal stent insertion.

procedures may include oesophageal dilatation, laser resection or an endoesophageal prosthesis.¹⁷ In the future, more fruitful therapeutic options may include the development of improved immunotherapy.

Learning points

- Malignant melanoma does not only affect the skin.
- Malignant melanoma of the oesophagus is rare and carries a poor prognosis.
- Differentiating between primary and secondary melanoma of the oesophagus is paramount for management and prognosis.
- Regression of the primary site can explain cases where a primary site cannot be identified.
- Mainstay of metastatic melanoma of the oesophagus is palliation. Oesophageal stenting can be used to improve a patient's overall quality of life.

Contributors JOS collected the clinical data and coperformed the literature review. JMH coperformed the literature review and formatted the images. PM stained the histological specimens and gave pathology input on the case. DBOC obtained the endoscopy images. DBOC and KC were responsible for writing and editing the final draft.

Competing interests None declared.

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