Malignant Melanoma of Oesophagus: A Rare Entity

Özofagus Malign Melanomu: Nadir Bir Hastalık

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ABSTRACT

We are discussing a case of malignant melanoma of esophagus, initially presented to us with very atypical presentation. On further history, patient claim having dysphagia for few months, initially to solid then followed by liquid, progressively worsening over few months. On further examination, OGDS reveal pedunculated growth at 30cm and 32 cm with skip free intact mucosa in between. Subsequently, we optimize his nutritional status and performed open tranhiatal total esophagectomy with cervical anastomosis and feeding jejunostomy. Post-operative recovery was uneventful, and patient was well upon discharge. Histopathology of the specimen revealed malignant melanoma of the esophagus. On subsequent follow up. PET scan was also done and shows stable disease with no evidence of tumor recurrence.

Keywords: Melanoma, Esophagus, Dysphagia

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ÖZET

Başlangıçta çok atipik bir sunumla bize sunulan bir özefagus malign melanomu vakasını tartışıyoruz. Daha fazla öyküde, hasta birkaç aydır disfajisi olduğunu iddia ediyor, başlangıçta katı, ardından sıvı, birkaç ay içinde giderek kötüleşen. İleri incelemede OGDS, 30 cm ve 32 cm'de pedinküle büyüme ve arada atlamasız intakt mukoza gösterir. Daha sonra beslenme durumunu optimize ettik ve servikal anastomoz ve beslenme jejunostomisi ile açık tranhiatal total özofajektomi yaptık. Ameliyat sonrası iyileşme olaysızdı ve hasta taburcu olduktan sonra iyiydi. Örneğin histopatolojisi yemek borusunun malign melanomunu ortaya çıkardı. Sonraki takipte. PET taraması da yapıldı ve tümörün nüksetmesine dair hiçbir kanıt olmadan stabil hastalık gösterdi.

Anahtar Sözcükler: Melanom, Özofagus, Disfaji

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INTRODUCTION

Melanoma is more frequently found in sun-exposed areas, however it can appear in other sites including the mucosal surfaces, like the esophagus, however the occurrence is rare(1). Melanocytes are present in small amounts in the squamous epithelium or basal membrane of the esophagus and can be the precursors of melanocytosis, leading to primary malignant melanoma of esophagus. Primary malignant melanoma of esophagus (PMME) is relatively rare tumor, representing approximately 0.1% to 0.2% of all esophageal malignant tumors(2). PMME is characterized by aggressive local invasion and early metastasis. PMME often presents as polypoid lesion and usually causes dysphagia to both solid and liquid progressively, retrosternal and/or epigastric pain. Over the years, the detection rates have improved due to early detection through numerous screening program. The tumour is often located from the middle to lower thoracic oesophagus and the characteristic endoscopic finding of PMME is a polypoid lesion that is usually pigmented, in which these both characteristics were seen in our case. The prognosis of PMME is poor relatively because of its highly malignant biological behavior and its tendency to frequently dissemination. The recently reported 5-year survival after surgical resection is 37.5%(3), which is lower than that of esophageal cancer.

CASE REPORT

67 years old gentleman, with no known co-morbidities, presented with history of dysphagia for almost 6 months duration. Dysphagia is associated with constitutional symptoms. He visited general practitioner multiple times but was treated as gastritis before he come to us. He is an otherwise fit with general body built and denies any family history of malignancy running in the family. He also occasionally complains of on and off vomiting secondary to dysphagia. OGDS reveal pedunculated growth at 30cm and 32 cm with skip free intact mucosa in between, bleeding on touch, occupying 3/3 of the esophageal lumen, able to pass through scope.

We admitted patient straight away after OGDS for nutritional assessment and build up, prior to operation. Once optimize, we proceeded with operation, open Transhiatal total esophagectomy with cervical anastomosis and feeding jejunostomy. Patient recovered well from operation and upper gastrointestinal study at day 5 post operation revealed no evidence of anastomotic leak.

Histopathology (HPE) of the specimen revealed malignant melanoma of esophagus. Cut sections of the specimen revealed two polypoidal growths measuring 40×30×14mm and 30×23×27mm. The masses are 15mm apart and there is another small raised lesion measuring 8×5×3mm, 10mm away from polypoidal masses. The masses surfaces are hemorrhagic with ulceration and slough, cut sections shows they are confined within the submucosa and are well-demarcated from the underlying muscularis propria. Microscopically, sections of the polypoidal masses and a raised lesion show well-circumscribed hypercellular tumors beneath the mucosa. The cells are large and moderately pleomorphic, displaying round nuclei with vesicular chromatin, prominent nucleoli and abundant cytoplasm. Spindle-shaped tumor cells are also present in areas with melanin pigments seen within the cytoplasm. Immunohistochemical studies show the malignant cells are strongly positive for HMD45 with focal positivity for S100, Melan A and CD117. One out of 11 lymph nodes were positive, it is situated at the posterior surface measuring 20×15×14mm with hemorrhagic tan cut surface.

He was seen by Oncologist and Dermatology team as well. Dermatology team ruled out malignant melanoma of the skin, in view of same pathology noted on the esophagus. Subsequently CT scan were performed about 6 months post operation which revealed stable disease with no local recurrence or distant metastasis with stable lung nodule and liver cyst. One-year post operation PET scan were done and shows stable disease with no evidence of tumor recurrence. His recovery has been speedy and uneventful. We are continuing our assessment for this patient together with oncology team.

Following are the cut section of computed tomograpy of our patient discusss in this case with comparison of pre-operation and post-operation CT

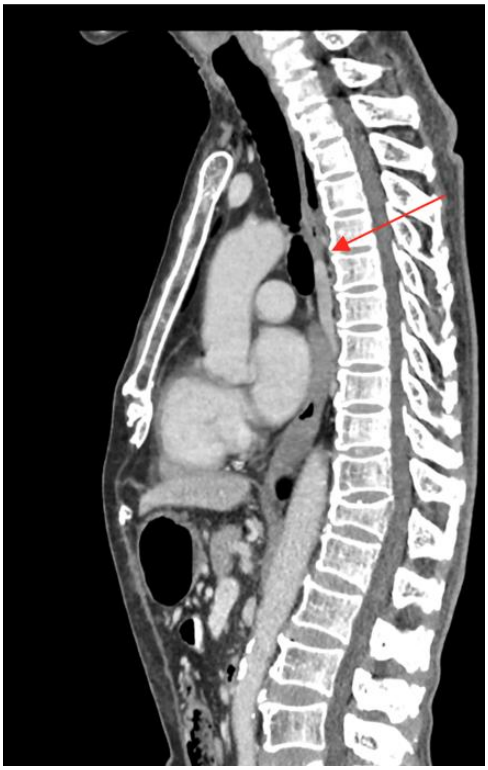

Figure 1 – Sagittal view of CT scan showing the tumor location at the mid-oesophagus (pre-operation)

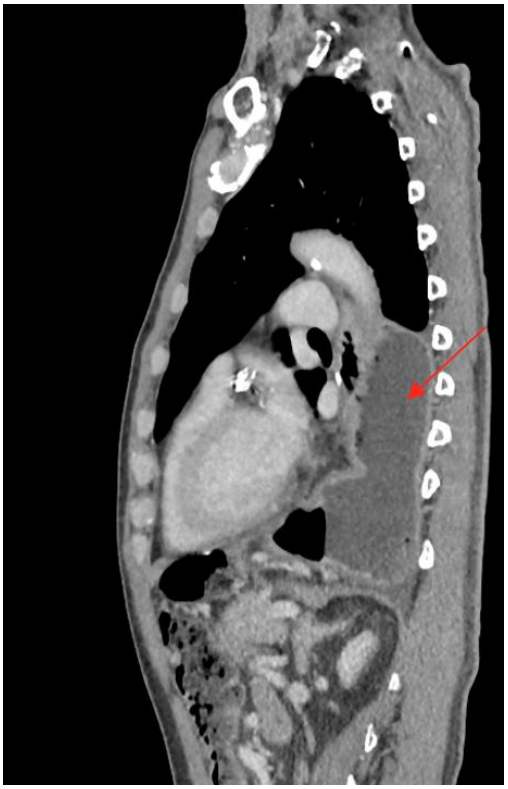

Figure 2 – Sagittal view of CT scan showing the gastric pull up, stomach noted to be within the thoracic cage (post-operation)

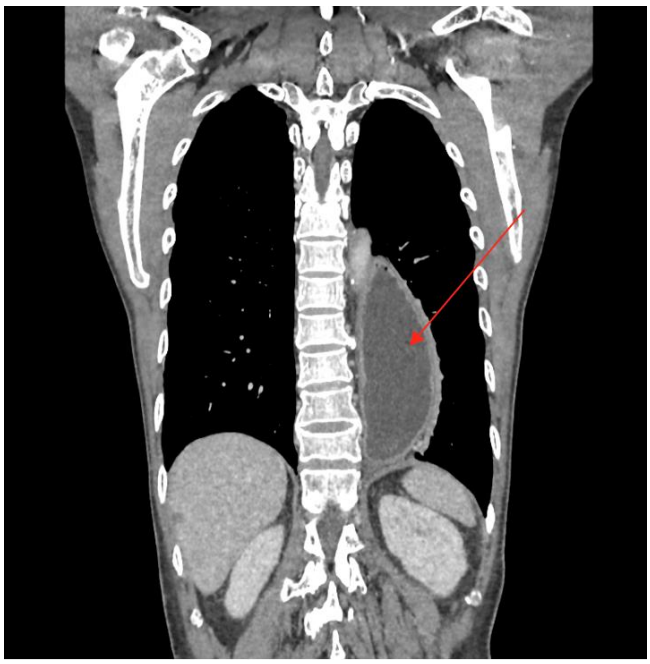

Figure 3 – Coronal view of CT scan showing the gastric pull up (post-operation)

DISCUSSION

Primary malignant melanoma most commonly originates from the skin; other less common extra cutaneous sites include squamous mucous membranes, uvea, retina, leptomeninges, genitourinary tract, digestive tract, biliary tract, and upper respiratory tract(4).

Primary melanoma of the gastrointestinal tract is exceedingly rare, whereby cutaneous melanoma is the most common malignancy to metastasize to the gastrointestinal tract. Primary malignant melanoma of the esophagus (PMME) is a rare disorder and has a reported prevalence of 0.1–0.5% of all esophageal malignancies. The overall prognosis is poor, however early detection of PMME allows better prognosis for patients. Like all cancers, if early detection can be done, the disease progress can be controlled by performing esophagectomy with or without chemoradiation, case to case basis(5).

PMME is most commonly located in the middle or distal third of the esophagus, in approximately in 90% of cases, probably because of the greater concentration of melanocytes in these regions. The diagnostic criteria for PMME require the presence of melanin granules within the tumor cells as well as melanocytes in the overlying epithelial layer and areas of junctional activity within squamous mucosa and the adjacent epithelium

Diagnostic criteria for PMME are defined by Allen and Spitz(6) as follows, (1) a typical histological pattern of melanoma, with melanin granules inside the tumor cells, and an (2) origin in an area of junctional activity in the squamous epithelium. Junctional activity is defined as some nests of melanocytes with varying degrees of atypia found at the mucosal-submucosal junction adjacent to the tumor mass. Immunohistochemical studies also offers accurate diagnosis of PMME, in which it reveals a positive antibody-specific cytoplasmic reactivity to HMB-45 and S-100 proteins, similar to our case discussed earlier. In the present case, melanocytosis and junctional activity were surrounding the main tumor, and positive results of HMB45, S-100 and Melan-A were revealed by immunohistochemical staining, which led to definitive diagnosis of PMME.

Treatment of PMME should be tailored based on each patient. The choice of intervention should be based on tumor size and location, presence of metastases, age, and co-morbidities of the patients(7). Kimura et al(8) on the other hand reported the first case of PMME treated by EMR and discussed the indications for EMR of superficial-type PMME. On the other hand, for patients with PMME at T1a, curative surgical resection could improve their overall prognosis. Although there is no absolute indication of adjuvant therapy for stage T1a and negative lymphoid metastatic cases because of low risk of metastasis and recurrence, as with regards to esophageal cancer, careful follow-up such as blood tests including tumor marker and contrasted enhanced imaging such as CT scan or PET scan is warranted. Table 1 below compares various study and the treatment approach in tackling PMME.

Table 1: Adapted from Japanese Classification of Esophageal Cancer, 11th edition.

Author	Year	Age	Sex	Location	Size (cm)	Depth[*a]	Treatment	Course[*b]
Kido [16]	2000	60	M	Lt	4.0 × 2.0	T1a	CR	33 months
Mikami [17]	2001	41	F	Mt	0.8 × 0.6	T1a	CR	31 months
Kimura [18]	2005	73	M	Lt	1.8 × 1.3	T1a-LPM	EMR	15 months
Suzuki [19]	2008	62	M	Mt	7.0 × 4.5	T1a-EP	CR	33 months
Suzuki [19]	2008	67	M	Lt	5.5 × 5.5	T1a-LPM	CR	53 months
Miyatani [11]	2009	64	F	Lt	0.5	T1a-LPM	EMR	20 months
Minami [20]	2010	72	M	Lt	unknown	T1a-EP	CR	25 months
Wang [14]	2013	62	M	Mt	7.0 × 4.5	T1a	CR	93.7 months
Yamamoto [21]	2015	75	M	Lt	1.5 × 1.0	T1a-MM	CR	83 months
Our case	2015	78	F	Lt	5.7 × 3.8	T1a-MM	CR	39 months

*[a]: According to the Japanese Classification of Esophageal Cancer, 11th Edition. Japan Esophageal Society Esophagus (2017). *[b]: All reported cases are still alive after the treatment, and none have had any symptoms of relapse or distant metastasis
Mt middle of the esophagus, *Lt* lower esophagus, *EMR* endoscopic mucosal resection, *CR* curative resection (subtotal esophagectomy and radical lymphadenectomy of the neck, mediastinum, and abdomen)

CONCLUSION

PMME is a rare and aggressive disease. A better survival rate can be achieved if the diagnosis is made early. However, its diagnosis is difficult and usually made late, in the advanced stages of the disease, providing a poor prognosis with low long-term survival rates even after appropriate treatment. The treatment as described earlier is based on case to case scenario. Radiotherapy and chemotherapy have not shown benefits in survival rates to date.

Other forms of therapy are being studied, but still no benefits in survival rates have been demonstrated. Due to rarity of the disease, studies with a high level of evidence are not feasible for implementation.

Conflict of interest

No conflict of interest was declared by the authors.

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