CRCP Case Reports in Clinical Practice

Case Report

Journal Homepage: http://crcp.tums.ac.ir

Primary Malignant Melanoma of the Esophagus: A Case Report

Mohsen Esfandbod[1], Freshteh Ensani[2], Bahareh Shateri Amiri[3*]

1. Department of Hematology and Oncology, Imam Khomeini Hospital Complex, Tehran University of Medical Sciences, Tehran, Iran.
2. Department of Pathology, Cancer Institute, Imam Khomeini Hospital Complex, Tehran University of Medical Sciences, Tehran, Iran.
3. Department of Internal Medicine, Imam Khomeini Hospital Complex, Tehran University of Medical Sciences, Tehran, Iran.

Use your device to scan and read the article online

Citation Esfandbod M, Ensani F, Shateri Amiri B. Primary Malignant Melanoma of the Esophagus: A Case Report. Case Reports in Clinical Practice. 2021; 6(5):218-222.

Running Title Malignant Melanoma

ABSTRACT

Primary Malignant Melanoma of the Esophagus (PMME) is an aggressive tumor with a median survival of about 13 months. Surgical extirpation is the only treatment for PMME. The most common clinical presentation is the onset of progressive dysphagia. Endoscopy presents a polypoid lesion occasionally in the middle and lower third of the esophagus. Definitive diagnoses are based on pathology and immunohistochemical examination with positive results for S-100, Human Melanoma Black (HMB)-45, and Melanoma-specific Antigen (Melan-A) proteins. We presented a 46-year-old man complaining of dysphagia and melena from the past two months. Gasteroesophagoscopy demonstrated a large polypoid in the lower third of the esophagus extending to the cardia. Histopathology of the biopsy specimen from the esophagus revealed positive staining for S-100, Human Melanoma Black (HMB)-45, and Melanoma-specific Antigen (Melan A) proteins that were all compatible with malignant melanoma of the esophagus. The patient underwent surgery followed by radiotherapy and Immunotherapy. The postoperative period was uneventful. No metastasis and recurrence was observed after more than 6 months of initial treatment. PMME is a rare but highly aggressive tumor. The diagnosis of PMME should be made by clinical symptoms, auxiliary examination, pathological examination, and immunohistochemistry markers. The problem of exact diagnosis at the early stages of the disease and effective treatment is still a challenge.

Article info:
Received: 18 Sep 2021
Revised: 03 Oct 2021
Accepted: 28 Oct 2021

Keywords:
Malignant melanoma; Esophageal neoplasm; Immunotherapy

* **Corresponding Author:**
Bahareh Shateri Amiri, MD.
Address: *Department of Internal Medicine, Imam Khomeini Hospital Complex, Tehran University of Medical Sciences, Tehran, Iran.*
E-mail: *shateri.bahareh@yahoo.com*

Introduction

Primary Malignant Melanoma of the Esophagus (PMME) is an extremely rare and aggressive neoplasm, comprising 0.1%-0.5% of all primary esophageal malignancies [1]. The mean survival duration from diagnosis is about 13 months, and the 5-year survival rate equals 4.2% [1]. It most often affects patients between the 6th and 7th decades of life. There is a 2.02:1 male predominance [1]. Baur reported the first case of PMME in 1906 [2].

Only ~300 cases have been reported in the literature [3]. PMME is a disease of unknown etiology, and the natural course of the illness remains undetermined [3]. Based on this theory that esophageal melanocytosis may be a precursor to PMME. In esophagitis and hyperplastic esophageal lesion, abundant and abnormal melanocytes may be precursor lesions of PMME [4].

The symptoms of PMME are not unique compared to other esophageal neoplasms [3]. The most common symptoms are dysphagia and retrosternal pain. Hematemesis and melena are observed infrequently [3]. Although Surgical excision is the standard treatment for PMME, treatment is not standardized due to its low frequency, leading to a highly aggressive course of this malignancy [3].

Esophagoscopy presents PMME as one or more polypoid lesions, usually pigmented and located in the middle and lower third of the esophagus [3]. Definite diagnosis is by pathology and immunohistochemical examination with positive results for S-100, Human Melanoma Black (HMB)-45, and Melanoma-specific Antigen (Melan A) proteins [3]. Recently, Endoscopic Ultrasonography (EUS) has been used to recognize the depth of tumor invasion and the lymph node status in patients and reveal this type of neoplasm as a hypoechoic mass or mixed echogenicity compared with the surrounding healthy tissue [3].

This case report presents a 47-year-old male with PMME diagnosed by endoscopy along with immunohistochemistry, i.e., positive for S-100 protein HMB-45 and Melan A. The patient underwent subtotal gastroesophagoscopy. He was treated with radiotherapy and ipilimumab as targeted therapy. He is still alive for more than 6 months without further chemotherapy, radiotherapy, and immunomodulatory therapy.

Case Presentation

A 47-year-old otherwise healthy man presented with two months history of dysphagia and melena. The physical examination results were unremarkable, suggesting no pigmented lesions at the skin, eyes, rectum, or other locations. Gastroesophagoscopy and biopsy were performed, as per below:

Esophagus: Upper third and the middle third were regular. A large pedunculated polypoid lesion with a long pedicle in the distal third at 32 cm of incisor was detected.

Stomach: A suspicious subepithelial lesion with overlying ulceration and abnormal-looking mucosa was detected in the cardia.

Duodenum: The bulb and second part of the duodenum was normal (Figure 1).

CT scan of the abdomen and chest with contrast enhancement demonstrated a 17×18 mm hypodense mass lesion in the distal part of the esophagus with luminal narrowing.

A 44×69 hypodense mass lesion with the regular border was observed in the lesser curvature of the stomach. Chest CT revealed no metastasis to the lymph nodes, mediastinum, or the lungs. Further examinations also ruled out distant metastasis.

Endoscopic Ultrasound (EUS) was performed and indicated a large ulcerated semi pedunculated mass 35 cm from the mouth in the lower third of the esophagus extending up to the cardia and a large central ulcerated mass in the cardia and fundus.

Microscopic examination results:

Esophageal mucosa had been invaded by a neoplastic tissue composed of sheets of loosely cohesive large cells with oval nuclei bearing nucleoli (Figures 2A, B, C).

Immunohistochemistry (IHC) study indicated that the tumor cells were positive for HMB-45, S100 protein, and Melan A (Figures 2D, E, F). Immunostaining for Pan-Ck, P63&Ck5/6 were negative. The final diagnosis of primary malignant melanoma of the esophagus was made.

PET CT indicated hypermetabolism in the distal third of the esophagus and cardia (SUV 11.7) without any evidence of other hypermetabolic lesions suggestive of dis-

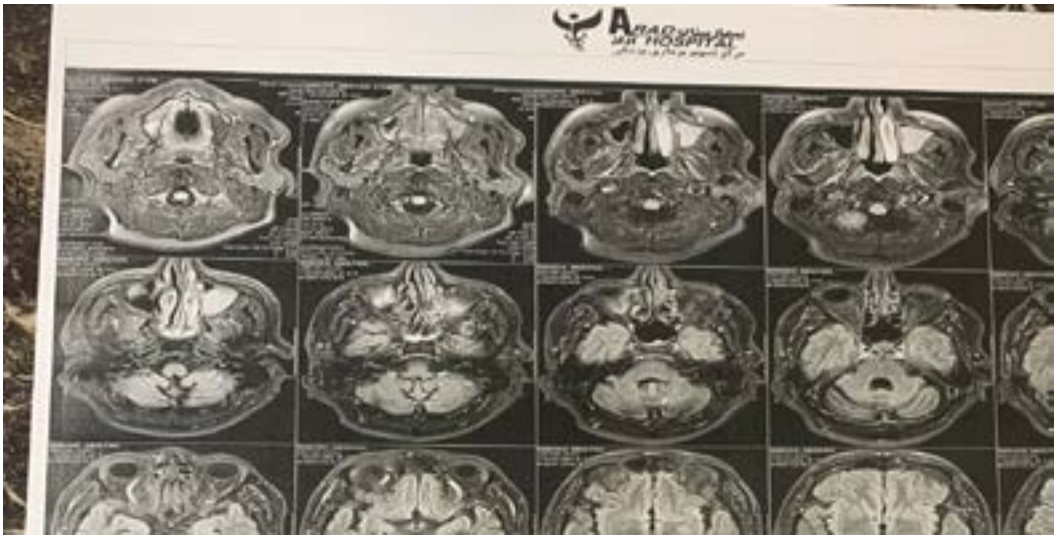

Figure 1. Gastroesophagoscopic view of a primary polypoid tumor of the esophagus at presentation

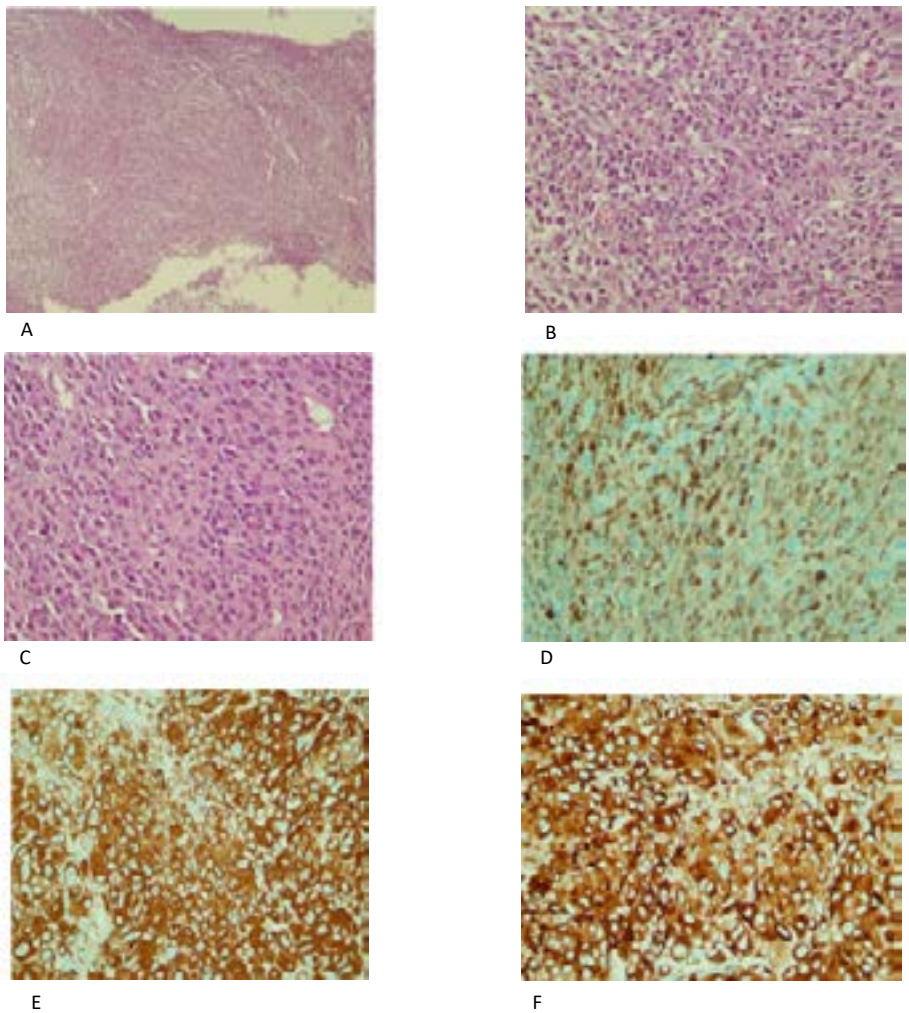

Figure 2. The bulb and second part

A: Primary malignant melanoma of esophagus stained with an H&E (×10); B, C: H&E (×40); D: S100; E: HMB-45; F: Melan A (×40).

tant metastases. Accordingly, a subtotal gastroesophagoscopy was performed. The patient received radiation therapy for the primary tumor at 45 Gy (gray) dose in 15 fractions over 3 weeks at 5 fractions per week.

Following surgery and adjuvant radiotherapy, the patient underwent treatment with three cycles of Immunotherapy. Ipilimumab was used as the Immunotherapy for 3 cycles, i.e., a monoclonal antibody that blocks the checkpoint of cytotoxic T-lymphocyte-associated protein 4 (180 mg per 3 weeks). Follow-up esophagogastroscopy examinations and CT scans revealed no signs of disease recurrence for >6 months. The latest clinical follow-up was 1 month ago, and the esophagogastroscopy examinations and CT scans showed no signs of disease recurrence.

Discussion

Although PMME prognosis is abysmal, the most important prognostic factor is the presence of nodal metastases [2]. Approximately 50% of patients with primary malignant melanoma of the esophagus have metastatic disease at presentation, most commonly to liver and mediastinum, followed by lung and brain, and long-term survival is uncommon [5]. Sabanathan et al., in 1989, reported a median survival of between 7 and 12 months in patients who underwent radical resection [5].

Chalkiadakis et al. reported, in a series of 110 patients, mean survival of 13 months [6]. Most cases manifest as progressive dysphagia [7]. The most common location (>90%) is in the middle and lower third of the esophagus [8]. The differential diagnosis consists of small round cell sarcoma, lymphoma, spindle cell sarcoma, carcinoma, gastrointestinal stromal tumor, or even epidermoid carcinoma, Kaposi's sarcoma, and leiomyosarcoma [2]. It is challenging to diagnose PMME esophageal tumors based on radiological criteria; histological approval is always crucial to diagnosing melanoma, especially in amelanotic cases [2]. Using antibodies against HMB-45 and S-100 protein in the immunohistochemical examination is essential to confirm the diagnosis [2]. Primary malignant melanoma of other organs must be excluded before the diagnosis is established [2].

In the absence of distant metastases or considerable lymph node involvement, surgical resection should be the first treatment choice [7]. Adjuvant therapy includes chemotherapy, radiotherapy, and immunomodulatory therapy, while curative treatment is not always possible [7]. Despite the radioresistant nature of PMME, it may have a palliative role if the patient seems to be inoperable [7]. Fogarty et al. reported a patient with metastatic malignant melanoma of the esophagus who received 36 Gy with a photon beam in six fractions given twice weekly and achieved excellent palliation of his dysphagia and CT after 4 months following completion of radiotherapy presented no residual mass [9]. Molecular analysis is a helpful target for targeted therapy in PMME [10]. Mutations in the BRAF and KIT genes in subgroups of melanoma have been reported [10]. Langer et al. detected a c-KIT gene mutation in 2 patients with PMME [11]. BRAF inhibitors may be helpful in the treatment of metastatic melanoma in patients with BRAF mutations [11]. However, in patients with PMME, its efficacy remains unproven [11].

Conclusion

PMME is a highly malignant tumor with a poor prognosis. Diagnosis in the early stages, timely operation therapy, and appropriate adjuvant chemotherapy and Immunotherapy may prolong overall survival. Diagnosis should be established with a combination of clinical imaging and histopathological findings, including immunohistochemical markers.

Ethical Considerations

Compliance with ethical guidelines

A written informed consent form was obtained from the patient to publish this case report and accompanying images. Principles of the Helsinki Convention were also observed.

Funding

This research did not receive any grant from funding agencies in the public, commercial, or non-profit sectors.

Conflict of interest

The authors declared no conflict of interest.

Authors' contributions

All authors equally contributed to preparing this article.

References

[1] Liu H, Yan Y, Jiang CM. Primary malignant melanoma of the esophagus with unusual endoscopic findings: A case report and literature review. Medicine. 2016; 95(17):e3479. [DOI:10.1097/MD.0000000000003479] [PMID] [PMCID]

[2] Navarro-Ballester A, De Lazaro-De Molina S, Gaona-Morales J. Primary malignant melanoma of the esophagus: A case report and review of the literature. The American Journal of Case Reports. 2015; 16:491-5. [DOI:10.12659/AJCR.894041] [PMID] [PMCID]

[3] Wang M, Chen J, Sun K, Zhuang Y, Xu F, Xu B, et al. Primary malignant melanoma of the esophagus treated by endoscopic submucosal dissection: A case report. Experimental and Therapeutic Medicine. 2016; 12(3):1319-22. [DOI:10.3892/etm.2016.3482] [PMID] [PMCID]

[4] Zheng J, Mo H, Ma S, Wang Z. Clinicopathological findings of primary esophageal malignant melanoma: Report of six cases and review of the literature. International Journal of Clinical and Experimental Pathology. 2014; 7(10):7230-5. [PMID] [PMCID]

[5] Sabanathan S, Eng J, Pradhan GN. Primary malignant melanoma of the esophagus. American Journal of Gastroenterology. 1989; 84(12):1475-81. https://web.p.ebscohost.com/abstract?direct=true&profile=ehost&scope%3d16141851

[6] Chalkiadakis G, Wihlm JM, Morand G, Weill-Bousson M, Witz JP. Primary malignant melanoma of the esophagus. The Annals of Thoracic Surgery. 1985; 39(5):472-75. [DOI:10.1016/S0003-4975(10)61963-7]

[7] Nonoshita T, Shioyama Y, Nomoto S, Ohga S, Ohnishi K, Atsumi K, et al. Effective palliative radiotherapy in primary malignant melanoma of the esophagus: A case report. Cases Journal. 2009; 2(1):1-4. [DOI:10.4076/1757-1626-2-6928] [PMID] [PMCID]

[8] Sanchez AA, Wu TT, Prieto VG, Rashid A, Hamilton SR, Wang H. Comparison of primary and metastatic malignant melanoma of the esophagus: A clinicopathologic review of 10 cases. Archives of Pathology & Laboratory Medicine. 2008; 132(10):1623-9. [DOI:10.5858/2008-132-1623-COPAMM] [PMID]

[9] Fogarty G, Tartaglia C, Peters L. Primary melanoma of the esophagus well palliated by radiotherapy. The British Journal of Radiology. 2004; 77(924):1050-2. [DOI:10.1259/bjr/26921127] [PMID]

[10] Cheung MC, Perez EA, Molina MA, Jin X, Gutierrez JC, Franceschi D, et al. Defining the role of surgery for primary gastrointestinal tract melanoma. Journal of Gastrointestinal Surgery. 2008; 12(4):731-8. [DOI:10.1007/s11605-007-0417-3] [PMID]

[11] Langer R, Becker K, Feith M, Friess H, Höfler H, Keller G. Genetic aberrations in primary esophageal melanomas: Molecular analysis of c-KIT, PDGFR, KRAS, NRAS and BRAF in a series of 10 cases. Modern Pathology. 2011; 24(4):495-501. [DOI:10.1038/modpathol.2010.220] [PMID]