



A case of long-term survival of primary malignant melanoma of the esophagus after surgery and a review of the literature

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Abstract: We here reported a case of primary malignant melanoma of the esophagus (PMME) which was performed surgery 8 years ago. The patient is still alive now. PMME is a very rare disease with very dreadful prognosis. The only way to definitely diagnosis is pathology while clinical symptoms or image examinations are useful for clinical staging. Surgery is standard, and only treatment that can offer the opportunity for long-term survival.

Keywords: Primary malignant melanoma of the esophagus (PMME); metastasis; surgery; diagnosis

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Introduction

Primary malignant melanoma of the esophagus (PMME) is a very rare tumor occurs mostly in 60–70 years old male patients (1). PMME often presents as polypoid lesion in esophagus and the most common symptoms includes dysphagia, retrosternal or epigastric discomfort or pain or weight loss (1). With the development of technology of diagnosis, more and more PMME has been diagnosed in recent years. However, the prognosis of PMME is yet not encouraging due to the high potential of metastasis (1). Like most other malignant tumors, early diagnosis and treatment can significantly improve the prognosis of these patients (2). Image examination including upper gastrointestinal series and computed tomography (CT) are very useful for clinical staging. Positive expression of S100 protein, HMB45 and neuron-specific enolase from pathologic and immunohistochemical is helpful for definitive diagnosis of PMME (3). Eight years ago, we encountered a case of PMME in endoscopy and diagnosed it by pathology. We follow up the case until now and find that the patient is still alive.

Case presentation

A 75-year-old man came to our institute for an examination

in November 23, 2010 due to difficulty in swallowing for about one month. The symptom is getting worse when eating solid foods. Upper gastrointestinal endoscopy showed a dark brown mass (3 cm × 2 cm) in the esophagus 34–39 cm from the incisors. Microscopic examination revealed variously pigmented unusual cells were observed in the tumor. A circular filling defect in the lower esophagus was observed in upper gastrointestinal series (*Figure 1*). CT scan of the chest and upper abdomen revealed the esophagus wall was thicker than normal situation (*Figure 2*). PMME was suspected in this case and further examination was performed. The PET-CT examination did not find any proof of tumor metastasis and skin examination did not find any proof of melanoma. A subtotal esophagectomy was performed using the Sweet technique in December 1, 2010. Gross specimen showed a dark brown mass measuring 3 cm × 2 cm located in the lower part of esophagus. Postoperative pathological diagnosis was PMME and tumor invaded the submucosa of the esophagus, all the detectable lymph nodes (fifteen lymph nodes) are negative and the esophageal margin was free from tumors (*Figure 3*). The patient did not receive any further treatment due to his poor physical situation and early pathological stage. We have followed up the patient until now, the patient is still healthy currently,

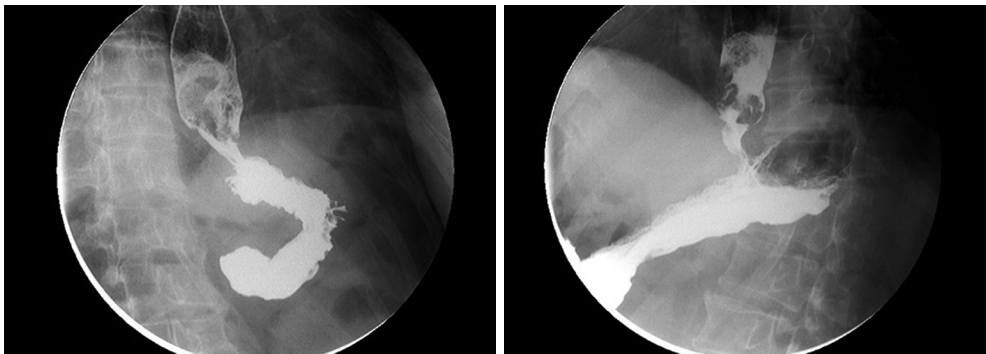


Figure 1 Upper gastrointestinal series showing a circular filling defect in the lower esophagus.

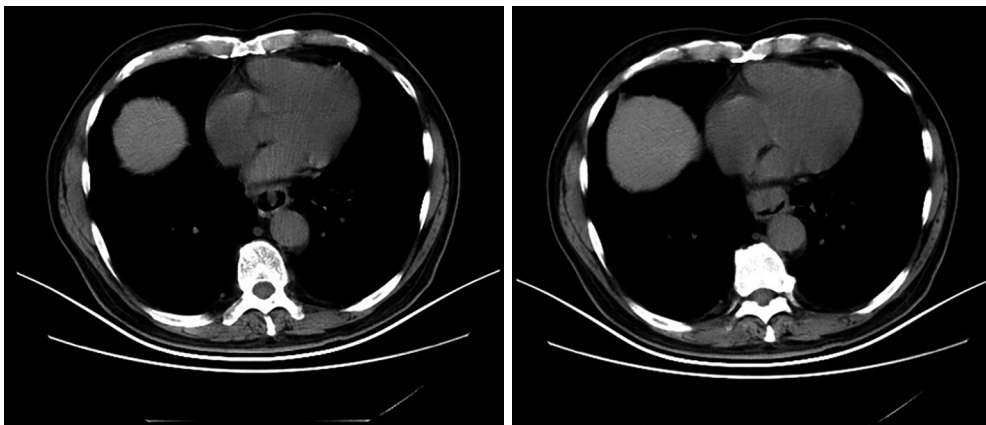


Figure 2 Plain computed tomography scan of the cervical region, chest and upper abdomen demonstrating the thickness of the middle esophagus wall.

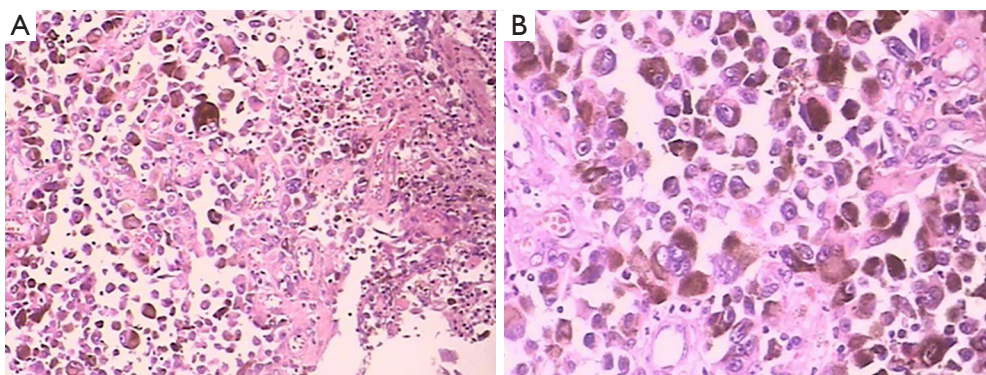


Figure 3 Pathological findings (hematoxylin/eosin staining) from the postoperative specimens. (A) One of the satellites ($\times 100$); (B) one of the satellites ($\times 200$).

Table 1 Characteristics of the long-term survival patients

Case No.	Author	Year	Age (year)	Sex	Stage ^a	Treatment	Survival
1	Khoury-Helou <i>et al.</i> (3)	2001	64	Female	T1bN0M0	Subtotal esophagectomy + radiochemotherapy	9 y
2	Kawada <i>et al.</i> (8)	2007	64	Female	T2N0M1a	Pre- and post-hormone chemotherapy + immunohormone therapy + subtotal esophagectomy	7 y
3	Gupta <i>et al.</i> (9)	2009	55	Male	T3N2M0	esophagectomy + postoperative adjuvant chemotherapy	69 m
4	Wang <i>et al.</i> (12)	2013	62	Male	0	Esophagectomy	94 m
5	Wang <i>et al.</i> (12)	2013	67	Male	IA	Esophagectomy	114 m
6	Suzuki <i>et al.</i> (13)	1980	NR	NR	NR	Surgery	10 y
7	Hamdy <i>et al.</i> (14)	1991	40	Female	T1bN+M0 ^b	Subtotal esophagectomy	12 y
8	De Mik <i>et al.</i> (15)	1992	75	Male	T1bN0M0	Esophageal resection	5 y
9	Suehs <i>et al.</i> (16)	1961	48	Female	T1bN0M0	Subtotal esophagectomy	6 y 6 m
10	Itami <i>et al.</i> (17)	2004	52	Female	T2N0M0	Neoadjuvant chemotherapy + adjuvant cisplatin + subtotal esophagectomy	11 y
11	Uetsuka <i>et al.</i> (18)	2004	45	Male	T1bN+M0 ^b	Pre- and post-hormone chemotherapy + immunohormone therapy + sub-total esophagectomy	7 y 4 m
12	Li <i>et al.</i> (19)	2007	46	Female	T2N0M0	Radiotherapy + esophagectomy	17 y
13	Sabat <i>et al.</i> (20)	2015	38	Male	T3N1M0	Esophagectomy	7 y

^a, according to the 7th edition of International Union Against Cancer (UICC) TNM staging system for esophageal cancers; ^b, metastatic lymph nodes were observed while the number of metastatic lymph nodes was not given in these articles. NR, not reported.

no tumor metastasis and recurrence signs have been seen.

Discussion

PMME is very rare tumor only representing 0.1% to 0.2% of all esophageal malignancies and 0.5% of noncutaneous melanomas are detected in esophagus. It occurs mostly in 60–70 years old male patients, only few younger patients have been reported (1).

Baur *et al.* reported the first case of PMME in 1906 (4). Garfinkle and Cahan confirmed the first diagnosis of PMME with histological evidence in 1952 (5). There were only 337 cases had been reported throughout the world by 2011 (6). PMME often presents as polypoid lesion and the most common symptoms includes dysphagia, retrosternal or epigastric discomfort or pain or weight loss (1). Most of PMME are distributed in the middle-lower part of the esophagus (7). With the development of technology of diagnosis, more and more PMME has been diagnosed in recent years. Examinations including

chest and upper abdominal CT, barium swallow, EUS and fluorodeoxyglucose positron-emission tomography (FDG-PET) are useful for clinical staging (8,9). FDG-PET is very sensitive in detecting lymph node metastases (2), so it is necessary to perform FDG-PET when lymph node metastases were suspected. Positive expression of S100 protein, HMB45 and neuron-specific enolase in pathologic and immunohistochemical examination is essential for pathologic diagnosis of PMME (10).

The prognosis of PMME is not encouraging due to its high potential of metastasis (11). The average survival period of PMME after diagnosis is about 10–14 months, with a 5-year survival rate of 4.2% (1). Wang *et al.* showed that none of patients with tumor later than stage Ib had survived longer than 5 years in their study (12). Only a few cases of survival time amount to 5 years after operation were reported (3,8,9,12-20). The characteristics of all included patients were listed in *Table 1*. All included patients underwent esophagectomy and several patients received adjuvant treatment, which includes chemotherapy, radiotherapy,

radiochemotherapy and immune hormone therapy. One patient was treated with radiochemotherapy 30 months after surgery due to metastasis to a supraclavicular lymph node was found (3). The patient had survived at least 9 years after operation, which suggested that radiochemotherapy might be an effective therapy when distant metastasis was found after surgery. Most patients with tumor later than stage Ib received adjuvant therapy. However, two patients with tumor later than stage Ib also obtained long-term survival without adjuvant therapy (14,20). So the effectiveness of adjuvant therapy for patient with tumor later than stage Ib may be still controversial.

The prognosis of melanoma has changed over past few years. Immunotherapy is becoming more and more promising in treating patients with advanced melanoma. Agents targeting the programmed death-1 (PD-1) receptor and its ligand (PD-L1) are hopeful treatment for advanced melanoma nowadays (21,22). Nivolumab is being developed to treat above disease and many other malignancies with promising results. Several trials have showed encouraging effect in advanced melanoma and non-small-cell lung cancer with a tolerable toxicity profile (23), which may provide a new approach to the treatment of PMME. Vaccines, cytokines (IL-2) have also been used for the clinical treatment of melanoma (24). Zheng *et al.* reported two patients underwent postoperative radiotherapy and chemotherapy and immunotherapy had longer disease-free survival than patient underwent postoperative radiotherapy and chemotherapy (25), which indicated immunotherapy may contribute to the better disease-free survival.

To sum up, PMME is a rare disease with dreadful prognosis. In this article, we presented a case of PMEE with long term survival after surgery. By review the previous cases of PMME with long-term survival, we found surgery is standard, and only treatment that can offer the opportunity for long-term survival. When distant metastasis occurs, radiochemotherapy might be an effective therapy to prolong survival. Immunotherapy is a promising therapy and may result in better disease-free survival.

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Footnote

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <http://dx.doi.org/10.21037/aoe.2019.03.03>). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in studies involving human participants were in accordance with the Declaration of Helsinki (as revised in 2013). Written informed consent was obtained from the patient for publication of this manuscript and any accompanying images.

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