

Primary Malignant Melanoma of the Esophagus

Po-Wei Lin¹, Rheun-Chuan Lee^{1,2*}, Ming-Sheng Chern^{1,2,3}, Jen-Huey Chiang^{1,2}, Cheng-Yen Chang^{1,2}

¹Department of Radiology, Taipei Veterans General Hospital, ²Department of Radiology, National Yang-Ming University School of Medicine, and ³Eonway Health Maintenance Center, West Garden Hospital, Taipei, Taiwan, R.O.C.

Primary malignant melanoma of the esophagus is an uncommon but aggressive tumor with fatal prognosis. We present 2 male patients with a history of dysphagia for a period of time and describe the imaging features of esophagograms and chest computed tomography (CT) scan. Both were proved by endoscopic biopsy. One of them underwent surgical resection. Primary malignant melanomas of the esophagus should be included in the differential diagnosis of bulky and polypoid masses that expand the esophagus without causing obstruction on esophagograms and chest CT scan. [*J Chin Med Assoc* 2006;69(7):334–337]

Key Words: computed tomography, dysphagia, esophagogram, esophagus, melanoma

Introduction

Primary malignant melanoma of the esophagus is a rare but aggressive tumor that accounts for <1% of all esophageal neoplasms.¹ Worldwide, approximately only 250 cases have been published in the English literature to date,² however, individual case reports have been described in the radiology literature.^{3,4} We report 2 male patients with histopathologically confirmed primary malignant melanomas of the esophagus and describe the radiologic findings of barium esophagogram, coronal reformatted and curved multiplanar reformation computed tomography (CT).

Case Reports

Case 1

A 77-year-old male had been complaining of dysphagia for about 2 months. His family history was unremarkable. No significant pigmented skin lesion and lymph node swelling were found on physical examination. Routine blood and urine profiles were also unremarkable. Endoscopy showed a lobulated mass in the esophagus situated 26 cm from the incisors. CT scan

revealed a bulky, polypoid, intraluminal mass in the middle and lower third of the esophagus, 8 cm in diameter and extending for 16 cm (Figure 1), and several small nodules in both lower lungs suggesting metastases. There was no significant lymphadenopathy in the mediastinum or metastasis in the liver. Endoscopic biopsy was performed. Histologically, the tumor was composed of atypical melanocytes in oval-to-spindle shape and demonstrated great variation in size and shape. Melanin pigments were present. Immunohistochemistry was positive with antibodies against HMB-45, and negative with antibodies against cytokeratins. Based on histologic and immunohistochemical studies, the diagnosis of malignant melanoma was made. Four months later, follow-up CT showed multiple metastases in the liver and right adrenal gland as well as supraclavicular and mediastinal lymphadenopathy. The patient refused further treatment and was discharged.

Case 2

A 62-year-old man presented with a history of dysphagia for 1 month and lost approximately 2 kg in weight since the onset of illness. His past medical history, family history, routine blood and urine tests were

*Correspondence to: Dr Rheun-Chuan Lee, Department of Radiology, Taipei Veterans General Hospital, 201, Section 2, Shih-Pai Road, Taipei 112, Taiwan, R.O.C.
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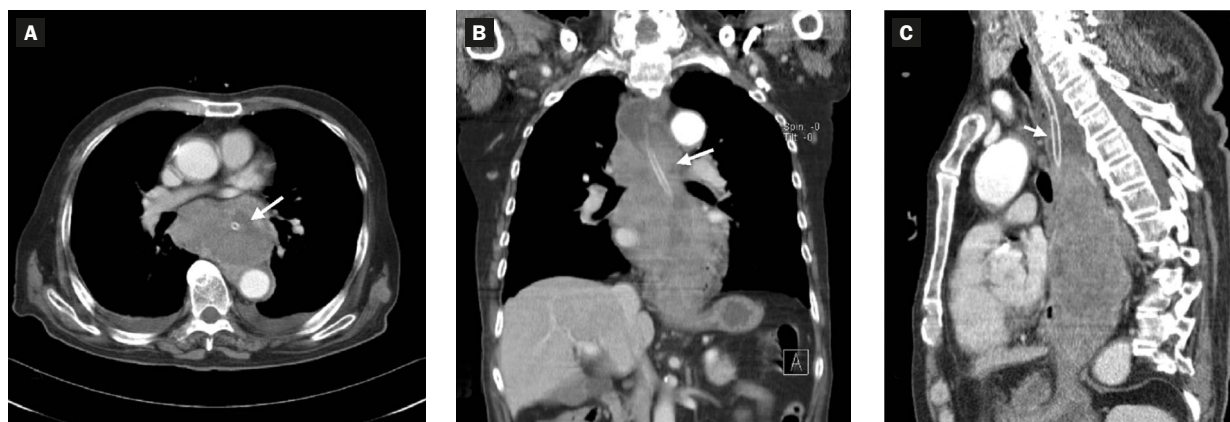


Figure 1. Primary malignant melanoma of the esophagus in a 77-year-old man with a nasogastric tube inserted (arrow): (A) axial, (B) coronal reformatted, and (C) curved multiplanar reformation contrast-enhanced computed tomography scans revealed a bulky, polypoid and intraluminal mass in the middle and lower third of the esophagus with compression of adjacent mediastinal structures.

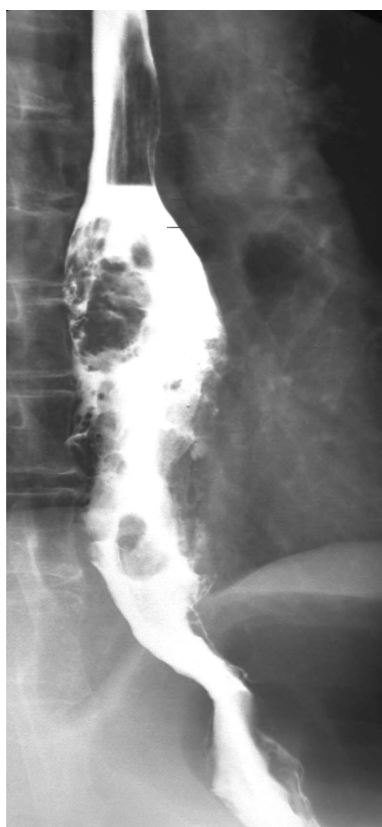


Figure 2. Double-contrast esophagogram in a 62-year-old man with primary malignant melanoma of the esophagus showed a long, polypoid mass expanding the distal esophagus without causing obstruction.

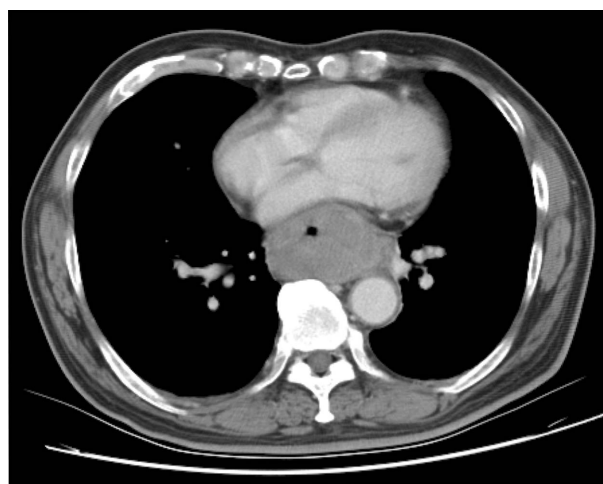


Figure 3. Contrast-enhanced computed tomography scan in a 62-year-old man with primary malignant melanoma of the esophagus demonstrated an eccentric polypoid intraluminal mass in the lower third of the esophagus.

unremarkable. There were no suspicious pigmented lesions of the skin or eyes on physical examination. Endoscopic examination disclosed an ulcerated lobulated mass in the esophagus extending 30–43 cm

from the incisors. Double-contrast esophagogram showed a long, polypoid mass expanding the distal esophagus without causing obstruction (Figure 2). CT scan confirmed an eccentric polypoid intraluminal mass (Figure 3) and enlarged lymph nodes in the mediastinum; there was no significant metastasis in the visceral organs. The endoscopic biopsy specimen identified the lesion as malignant melanoma. The patient underwent a transthoracic esophagectomy with cervical esophagogastric anastomosis. The histologic finding demonstrated the tumor to be composed of round to spindle cells with abundant melanin pigments. Cellular pleomorphism, prominent

nucleoli, and numerous mitotic figures were encountered. The tumor cells were positive for HMB-45 and negative for cytokeratins by immunohistochemical analysis. Two months later, follow-up CT revealed masses in the right adrenal gland and lower pole of the right kidney. Right radical nephrectomy was performed and metastases were proved. The post-operative course was uneventful and this patient is doing well.

Discussion

Primary malignant melanoma most commonly originates from the skin; other less common extracutaneous locations include squamous mucous membranes, uvea, retina, leptomeninges, genitourinary tract, digestive tract, biliary tract, and upper respiratory tract.⁵ The vulva and urethra are the most common sites of origin of malignant melanomas in the genitourinary tract. Primary melanoma of the gastrointestinal tract is exceedingly rare, conversely, cutaneous melanoma is the most common malignancy to metastasize to the gastrointestinal tract. In 1 series, the small intestine (75%), large bowel (25%), and stomach (16%) were common sites for metastases; the small intestine was the most frequent site of metastatic melanoma because of its rich blood supply.⁶ Metastasis to the esophagus is extremely rare. It reportedly occurs in only 4% of patients who die of metastatic melanoma at autopsy.⁷ Classically, metastatic melanoma to the stomach and duodenum appears as a polypoid mass with or without central ulceration, the so-called "Bull's-eye" lesion.⁸

Primary malignant melanoma of the esophagus is a rare condition and has a reported prevalence of 0.1–0.5% of all esophageal malignancies.¹ It is generally considered that primary melanoma could not develop in the esophagus because of the lack of precursor cells, until De La Pava et al⁹ in 1963 demonstrated the presence of typical melanocytes in the esophageal mucosa in 4% of normal esophagi at autopsy. This finding clarified definitively that malignant melanoma can occur as a primary tumor from the esophageal mucosa. It is twice as common in males as in females, occurring prevalently in the 6th and 7th decades of life. This malignancy is most commonly located in the middle or distal third of the esophagus, approximately in 90% of cases, probably because of the greater concentration of melanocytes in these regions.^{2,10}

The diagnostic criteria for accepting a melanoma as arising from the esophagus were defined by Allen and Spitz,¹¹ and 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. The more accurate diagnosis is confirmed by immunohistochemical studies: primary malignant melanoma of the esophagus typically reveals a positive antibody-specific cytoplasmic reactivity to HMB-45 and S-100 proteins with a negative reaction for cytokeratin or CEA.¹⁰ Ruling out a metastatic lesion is important if melanoma is found in the esophagus. Consequently, the diagnosis of primary esophageal melanoma can be accepted only in patients with no history of melanoma and no evidence at physical examination of melanoma involving the skin, eye, anus, or vagina.

There is no significant risk factor of primary malignant melanoma of the esophagus. The most common symptoms are dysphagia, substernal or epigastric pain, hematemesis, and melena. Physical signs other than weight loss are uncommon. On endoscopy, these tumors usually appear as lobulated and darkly colored masses with intact mucosa or occasional ulceration.¹⁰ However, data obtained from specimens after endoscopic biopsy are limited for a definitive diagnosis and occasionally misdiagnosed as poorly differentiated carcinoma. The histopathologic diagnosis is usually confirmed after *en bloc* resection.¹²

Barium esophagography usually reveals a bulky, polypoid intraluminal mass focally expanding the esophagus. A considerable degree of obstruction is uncommon. CT of the thorax reveals a bulky esophageal mass compressing the adjacent mediastinal structures. Approximately 40.9% of patients are reported to have metastases at the time of diagnosis. The most commonly involved sites are the paraesophageal lymph nodes (10.8%), supraclavicular lymph nodes (7%), liver (7%), lungs (6%), celiac lymph nodes (4%), and bones (2.9%).¹³ CT might be useful in demonstrating mediastinal invasion, nodal enlargement, and distant metastatic disease. Magnetic resonance imaging shows high signal intensity masses in the esophagus on T1-weighted imaging due to paramagnetic scavenging by melanin, which helps preoperative diagnosis.

The differential diagnosis of primary esophageal melanoma includes spindle cell carcinoma, leiomyosarcoma, and Kaposi's sarcoma. A large lobulated intraluminal lesion that expands the lumen without causing obstruction is the characteristic findings of barium study for spindle cell carcinoma. The manifestation of leiomyosarcoma is a heterogeneous, large, and exophytic mass with central areas of necrosis on CT scan. Kaposi's sarcomas typically appear as multiple submucosal masses or polypoid lesions in the esophagus. These tumors are difficult to differentiate

from malignant melanoma on the basis of radiographic criteria.

The prognosis of primary malignant melanoma of the esophagus is dismal regardless of therapy in comparison with other common primary malignant tumors of the esophagus. The average overall survival is only 10–13 months, with the 5-year survival rate ranging from 0% to 4%.¹³ Metastases are present at the time of diagnosis in 40.9% of cases. Approximately 85% of patients progress to early death with disseminated disease. The most common sites involved at autopsy are the liver (39.3%), mediastinum (34.4%), lungs (24.6%), pleura (19.7%), supraclavicular lymph nodes (19.7%), peritoneum (14.8%), brain (13.1%), kidneys and adrenals (11.5%).¹³

The treatment preferred for primary malignant melanoma of the esophagus is surgical resection. A total or near-total esophagectomy is mandatory as the tumor spreads longitudinally. Currently, radiotherapy, chemotherapy, and immunotherapy have not proved beneficial. However, these alternative therapeutic modalities play a palliative role if surgery is not possible.^{2,10}

In conclusion, primary malignant melanomas of the esophagus are rare, aggressive tumors with fatal prognosis and should be considered in the differential diagnosis of bulky, polypoid masses that expand the esophagus on esophagograms and chest CT scan.

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