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Case Report

A Resected Case of Primary Malignant Melanoma of the Esophagus—Early Detection of Recurrence by FDG-PET/CT

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Primary malignant melanoma of the esophagus (PMME) is a rare, aggressive, therapy-resistant malignant tumor arising from esophageal mucosal melanocytes. It has been reported that fluorodeoxyglucose-positron emission tomography/computed tomography (FDG-PET/CT) has a clinical impact on PMME diagnosis; however, it remains unclear whether postoperative surveillance using FDG-PET/CT is useful for PMME patients. In this case study, FDG-PET/CT detected the recurrent tumors in their early stage after a curative resection of PMME. We report on a case of a 67-year-old Japanese male admitted to our hospital for the evaluation of polypoid tumors of the esophagogastric junction, which were diagnosed as PMME. He was treated with a curative resection by esophagectomy and 6 cycles of adjuvant chemotherapy of DAV (dacarbazine, nimustine, and vincristine). However, the PMME recurred 26 months after the surgery when surveillance FDG-PET/CT detected the recurrent tumors in their early stage. FDG-PET/CT may be useful to detect recurrence in the postoperative surveillance phase for PMME patients.

Key words: Esophagectomy – Melanoma – Adjuvant chemotherapy – 18F-FDG

Malignant melanoma is an aggressive, therapy-resistant malignant tumor that develops from melanocytes.[1] It is predominantly a disease of the skin, but, rarely, it can occur at other sites. When it arises from esophageal mucosal melanocytes, it is diagnosed as a primary malignant melanoma of the esophagus (PMME), a rare neoplasm representing 0.1% to 0.2% of all primary esophageal malignan-

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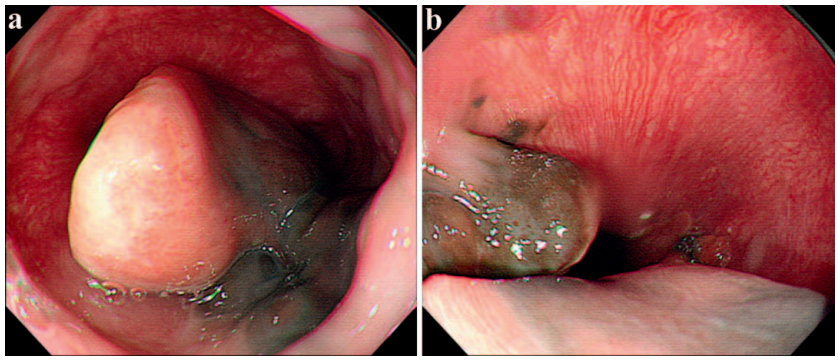

Fig. 1 Endoscopic examination demonstrated an intraluminal polypoid tumor measuring 2.5 cm in size (a) and its accessory tumor (b) distal to the primary tumor in the esophagogastric junction.

cies.[2,3] Although it has been well known that FDG-PET/CT has a clinical impact on PMME diagnosis,[2,4] there have been few reports to show the clinical impact of FDG-PET/CT on the early detection of recurrence in the postoperative surveillance phase.[5] Here, we report on a case of PMME treated with curative surgical resection and adjuvant chemotherapy; however, it recurred 26 months after the surgery when surveillance FDG-PET/CT detected the recurrent tumors in their early stage.

Case Report

A 67-year-old Japanese male was referred to our hospital for an evaluation of an esophageal tumor detected through an annual health check-up. His family history was not remarkable. No significant pigmented skin lesion or lymph node swelling was found on physical examination. The endoscopic examination showed gray intraluminal polypoid tumors of the esophagogastric junction including a primary tumor measuring 2.5 cm in size (Fig. 1a) with its accessory tumor located distal to the primary tumor (Fig. 1b). A gray pigmented mucosa in the midthoracic esophagus was also detected by the endoscopic examination. Pathologic examination of biopsies from the primary tumor and the pigmented mucosa revealed the diagnosis of a malignant melanoma. An upper gastrointestinal series showed a filling defect of about 3 cm in the esophagogastric junction (Fig. 2a). A positron emission tomography/computed tomography (PET-CT) scan showed fluorodeoxyglucose (FDG) uptake specifically in the esophagogastric junction tumors; however, no significant uptake was detected in regional lymph nodes or other organs (Fig. 2b). The disease was preoperatively diagnosed as PMME of clinical stage IB (T2N0M0) according to the 7th UICC-TNM classification.[6] He underwent subtotal esophagectomy *via* conventional thoracotomy with 2-field lymphadenectomy and gastric pull-up reconstruction. His postoperative course was uneventful except for delayed gastric emptying and he was discharged on postoperative day 22. The resected specimen was 17 cm in length, featuring 2 polypoid tumors of the esophagogastric junction, which were 2.2 cm and 1.8 cm in size, and a mucosal pigmentation measuring 1.0 cm in the midthoracic esophagus (Fig. 3). Microscopic examination of the primary tumor revealed infiltration into the submucosal layer (Fig. 4a). The

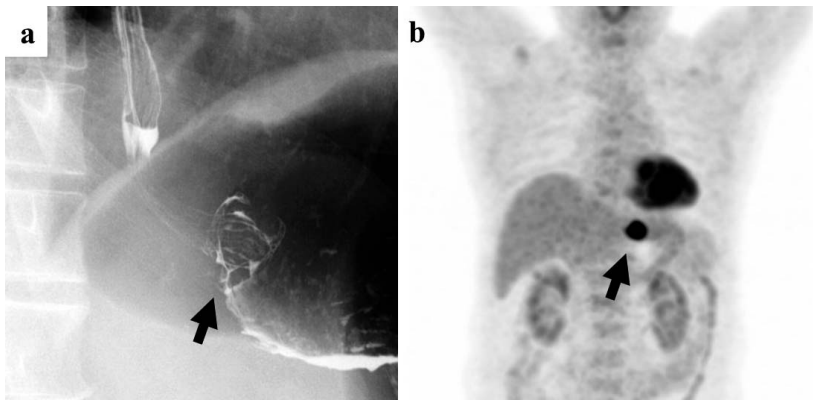

Fig. 2 (a) Upper gastrointestinal series showed a filling defect (arrow) of about 3 cm in the esophagogastric junction. (b) FDG/PET-CT showed FDG uptake (arrow) specifically in esophagogastric junction tumors.

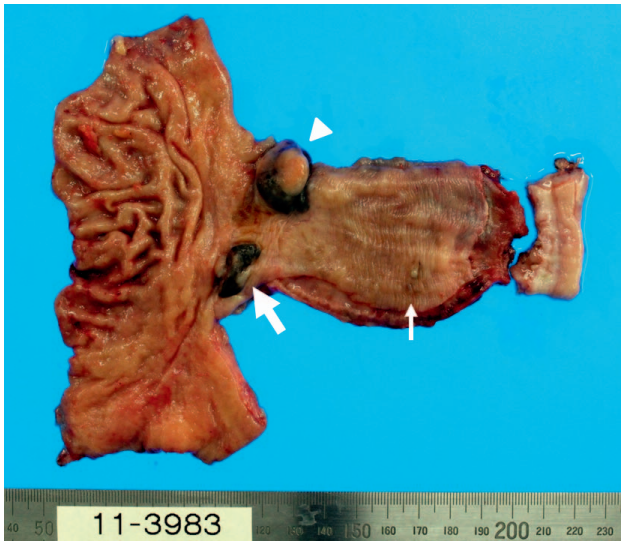

Fig. 3 Resected specimen revealed a primary tumor (arrow head) and its accessory tumor (thick arrow) in the esophagogastric junction, and a mucosal pigmentation (thin arrow) in the midthoracic esophagus.

tumor was composed of large cells with hyperchromic nuclei and cytosolic melanin granules (Fig. 4b). Immunohistochemistry showed the tumor cells were positive for Melan-A, S100, and HMB-45 (Fig. 4c). The accessory tumor invaded the submucosal layer of the esophagogastric junction. In the pigmented mucosa, tumor cells infiltrated the lamina propria mucosae (Fig. 4d). Since the tumor cells in these 2 satellite lesions showed the same characteristics as those of the primary tumor, they were diagnosed as intramural metastases. All surgical margins were negative for tumor cells from these lesions. Two out of 50 harvested lymph nodes were positive for tumor cell metastasis. They were located along the midthoracic esophagus and along the left gastric artery. The disease was finally diagnosed as PMME of pathologic stage IIB (T1bN1M0).[6] The patient received 6 cycles of DAV (dacarbazine, nimustine, and vincristine) in an adjuvant setting for 10 months after the surgery. However, surveillance FDG-PET/CT detected a metastatic lymph node along the gastric greater curvature and a recurrent tumor in the right lung 26 months after the surgery and FDG uptake was confirmed in these metastatic lesions (Fig. 5a and b). The gastric lymph node was biopsied and was pathologically diagnosed as a metastasis of PMME. The patient received chemotherapy with DAV initially after the recurrence, followed by immunotherapy with a human monoclonal antibody against programmed cell death ligand 1, and lastly underwent chemotherapy with paclitaxel plus carboplatin. However, none of these treatments resulted in tumor shrinkage, but instead was followed by an increasing number of abdominal lymph node metastases, and he died of progressive disease 37 months after the surgery.

Discussion

PMME is a rare esophageal neoplasm representing 0.1% to 0.2% of all primary esophageal malignancies.[2,3] From 1906, when Baur[7] reported the first case of PMME, until 2010, only 337 cases had been reported globally.[2] PMME is clinically confirmed when no other skin lesions are found. Its diagnostic criteria were defined in 1953,[8] and the characteristics of PMME have been well studied.[2,3] Here we discuss diagnostic tools and PMME characteristics that are unique to this case, including FDG-PET/CT, intramural metastasis, long survival, and chemotherapy.

FDG-PET/CT is an efficient and well-known diagnostic tool often used in the management of esophageal cancer patients.[9] Although it has been reported that FDG-PET/CT has a clinical impact on PMME diagnosis,[2,4] it remains unclear whether postoperative surveillance using FDG-PET/CT is useful for patients who undergo a curative resection of PMME. In clinical diagnosis of cutaneous melanoma, Jiménez-Requena *et al* reported that FDG-PET is not useful in the evaluation of regional metastases; however, it could be useful in the detection of distant metastases.[10] In our case, FDG-PET/CT failed to detect regional lymph node metastasis preoperatively, probably because it was microscopic. In contrast, the FDG-PET/CT postoperative surveillance detected the distant metastases at their early stage. Thus, FDG-PET/CT seems useful in the postoperative surveillance phase for PMME patients to detect recurrent tumors, which are large enough to be discovered. Recommending FDG-PET/CT as part of the surveillance protocol would enhance detection of early stage recurrence.

In our patient, satellite tumors were found on both the oral and anal side of the primary tumor preoperatively. Because microscopic examination had diagnosed the pigmented mucosa in the midthoracic esophagus as a malignant melanoma,

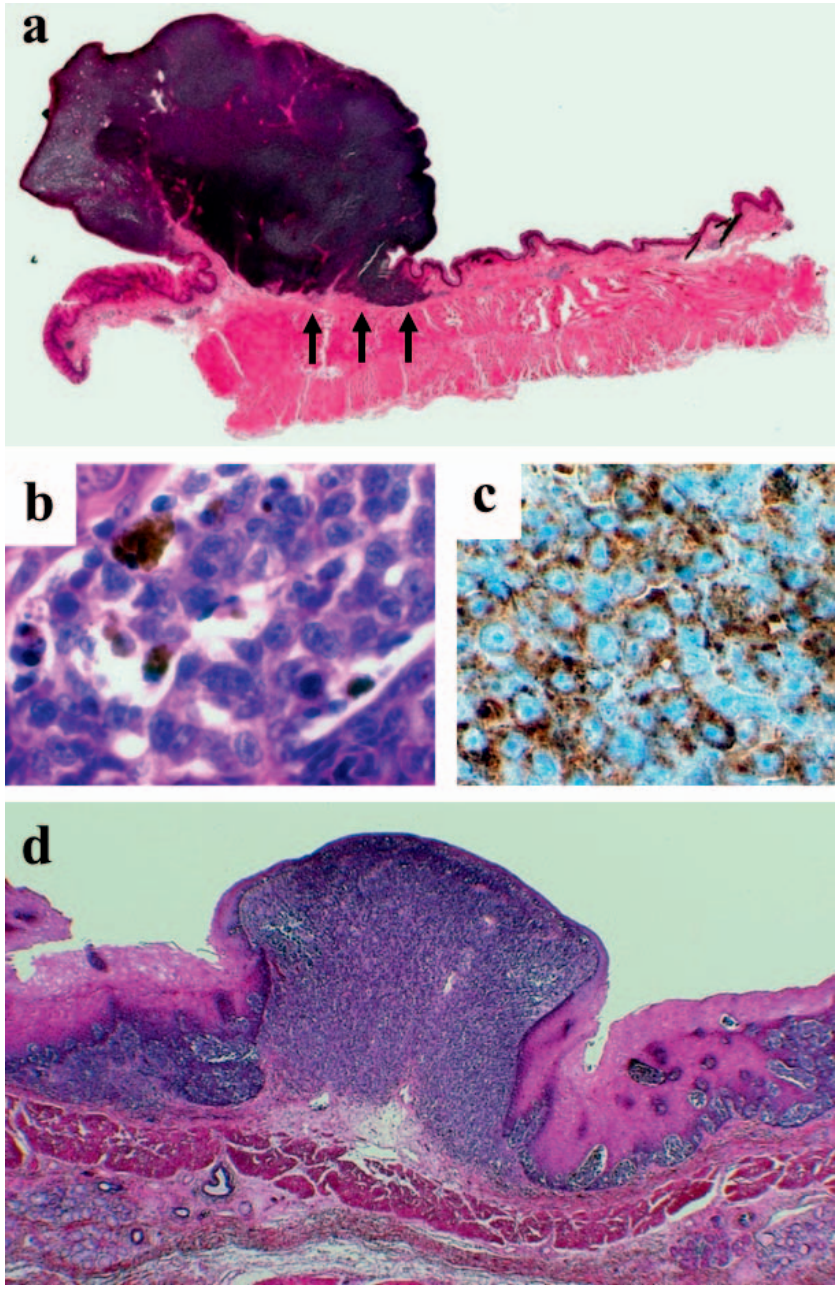

Fig. 4 (a) The primary tumor of esophagogastric junction invading the submucosal layer (arrows, hematoxylin & eosin stain, loupe). (b) The tumor cells contained hyperchromic nuclei and cytosolic melanin granules (hematoxylin & eosin stain, ×400). (c) The presence of melanin confirmed by immunostaining with HMB-45 (HMB-45 antibody, ×200). (d) The tumor cells in the pigmented mucosa invaded into the lamina propria mucosae (hematoxylin & eosin stain, ×20).

we chose subtotal esophagectomy to remove the PMME completely. Cutaneous melanoma frequently develops adjacent to skin metastases in the natural history of the disease.[11] Similarly, PMME has been known to be accompanied by intramural metastasis.[12,13] Because esophageal intramural metastases arose on both the oral and anal side of the primary tumor,[14] a careful examination of the whole esophagus by endoscopy was necessary to detect possible intramural metastases.

The patient survived 37 months after the surgery before he died of progressive disease in this case study. We conclude that our case showed a relatively long survival given that a comprehensive literature review has reported that only 9 out of 77 PMME patients were able to survive 36 months or more after surgery.[2] Surgical resection is the only poten-

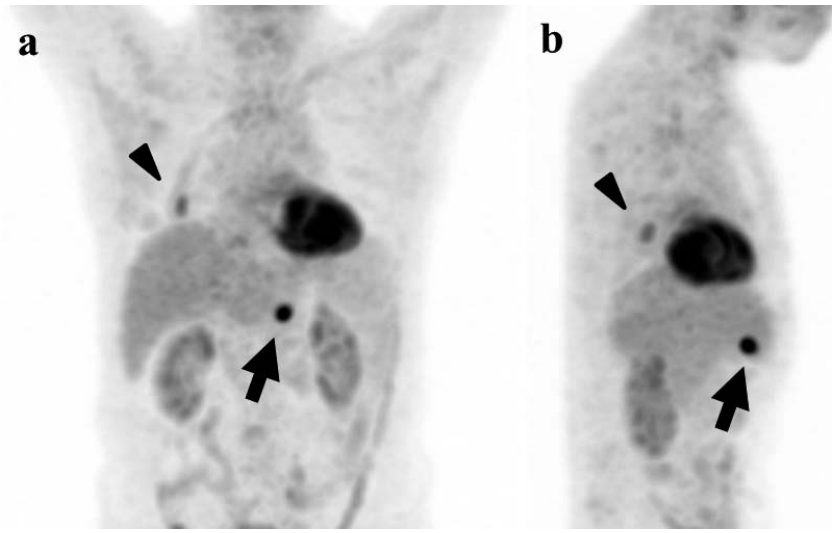

Fig. 5 FDG uptake was detected in metastatic lesions in the gastric lymph node (arrow) and lung (arrow head) in the anteroposterior (a) and the lateral (b) views of FDG/PET-CT images.

tially curative treatment that influences survival.[15] Surgically resected cases have reported a long survival after surgery, even if the disease involves regional lymph nodes as in our case.[2,16,17] A review also reported that 8 out of the 9 survivors had a T1-tumor when it was resected.[2] As our case had an asymptomatic T1-tumor and showed a long survival, there may be a relationship between an early detected T1-tumor and long survival, which is known as "lead time bias."[18]

The effectiveness of chemotherapy is controversial in PMME treatment.[2] Chemotherapy usually includes dacarbazine, nimustine, vincristine, and cisplatin.[2] Although the combination of these drugs with immunotherapies has been used based on the effectiveness against the cutaneous melanoma,[19] some case reports indicated that the drug combination contributed to PMME treatment.[20,21] Although the patient in our case received DAV for 10 months after the curative resection, it is unclear whether the adjuvant DAV prolonged patient survival. This is because DAV showed no significant effect on the metastatic PMME after it recurred. Recently, a new immunotherapy with a human monoclonal antibody against programmed cell death ligand 1, and chemotherapy with paclitaxel plus carboplatin have been used to treat metastatic cutaneous melanoma.[22,23] However, metastatic PMME in our case did not show any response to these treatments. Therefore, these treatments likely did not contribute to the long survival in our case.

In conclusion, FDG-PET/CT may be useful in the postoperative surveillance phase for PMME patients who underwent curative resection in order to detect recurrent tumors in their early stage.

Acknowledgments

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