Primary Thymic Malignant Melanoma

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ABSTRACT
A 72-year-old woman underwent complete video-assisted thoracic surgery for removal of a smooth, progressively contrasted, homogeneous 20-mm nodular anterior mediastinal tumor. The tumor was completely resected. The pathological diagnosis was malignant melanoma (MM), which was positive for HMB-45 and S-100. Postoperative positron emission tomography revealed no other lesions throughout the whole body. The tumor was therefore diagnosed as primary malignant melanoma of the thymus. The patient’s postoperative course was good, and she developed no recurrence. This tumor is reportedly highly malignant and prone to recurrence; hence, careful follow-up is necessary for this case.
Malignant melanoma (MM) has been found to occur in the oral cavity, pharynx, esophagus, anus, and vaginal mucosa.\textsuperscript{1} MM in the mediastinum is extremely rare. Herein, we report a patient with MM originating from the thymus.

A 72-year-old woman underwent left nephrectomy for treatment of kidney cancer in 2007. She was then followed up on an outpatient basis. The patient was asymptomatic at the time of her first visit to our department, and the results of clinical and routine laboratory tests were within normal limits. The patient had a history of hypertension and had undergone thyroid surgery, lung cancer surgery, and atrial fibrillation ablation.

A lateral chest radiograph showed a well-defined mass of 20 mm in the anterior mediastinum. Chest computed tomography (CT) showed a strongly contrasted and homogeneous interior (Figure 1A). On magnetic resonance imaging, the mediastinal tumor had a smooth surface and well-defined borders; T1-weighted imaging showed a low signal, and while T2-weighted imaging showed a faint high signal that was nonspecific (Figure 1B). Thymoma was suspected on the basis of the imaging findings.

Thymothymectomy was performed by complete video-assisted thoracic surgery for diagnosis and treatment. A small window was made in the fourth, sixth, and seventh intercostal spaces along the midaxillary line and right hypochondrium. The procedure was performed with artificial pneumothorax by carbon dioxide insufflation. The tumor was found in a ventral location, close to the midline. There was no evident invasion of the surrounding tissue.

Hematoxylin and eosin staining showed scattered macrophages phagocytosing melanin. There was no clear capsule formation, but the borders of the tumor were well
defined. The lesion was resected with negative margins. Immunohistochemical staining was positive for HMB-45 and S-100 (Figure 2C, 2D). The immunohistochemical staining excluded thymoma, poorly differentiated carcinoma. The tumor was completely resected pathologically. No other lesions were detected by whole-body postoperative positron emission tomography (PET) or brain magnetic resonance imaging (MRI). The skin of the whole body was closely examined, but there were no abnormal findings. The tumor was thus determined by a dermatologist to be MM originating from the thymus. The patient was alive and free of recurrence at the time of writing (7 months postoperatively).

COMMENT

Primary MM of the mediastinum is rare, with 12 cases documented. We performed a literature review of these cases. The median age was 57 (11–73) years, and 67% were women. The median tumor size was 50 (20–150) mm; the tumor in our patient was the smallest. The prognosis for patients with primary mediastinal MM remains unknown. In a review of these cases, the median overall survival (OS) was reported to be 14 (5–54) months. However, recurrence was observed in 33% of patients; the median time to recurrence was 13 (5–31) months, indicating the highly malignant potential of the disease. Case studies have suggested that most patients developed uncontrolled systemic metastases in the short term. This indicates that a combination of appropriate drugs and surgical treatment can improve the health status of patients but cannot significantly increase survival. Intrapulmonary metastasis was the most frequent site of metastasis.
Chemotherapy, radiotherapy, and lymphadenectomy are used to treat recurrent lesions in these reports.

PET is a valuable imaging modality for evaluating various primary mediastinal masses and distant metastases. In the present case, we suspected thymoma on imaging and did not perform a PET scan preoperatively. The preoperative PET scan of the tumor in the case of Taniguchi et al. revealed an abnormal maximum standardized uptake value of 6.7. Postoperative PET as well as a brain MRI scan in the present case showed no evidence of distant metastasis. As for the skin results, a dermatologist was consulted to confirm that there were no findings. The patient had no history of mole removal. The mucosal surface of the oral cavity, anus, and vagina was examined as much as possible and no abnormalities were identified. We consider it more likely that the tumor in the present case was a primary melanoma of the thymus.

Immune checkpoint inhibitors are lately used drugs for most cases of advanced melanoma, and combination therapy with BRAF inhibitors and MEK inhibitors is also used for patients with specific mutations (V600E/K) in BRAF (one of the molecules responsible for the mitogen-activated protein kinase pathway in cancer cells). Activating KIT mutations are rare and imatinib is the drug of choice for second-line or subsequent systemic therapy. MEK inhibitors have increased response rates in patients with metastatic melanoma harboring NRAS mutations. Postoperative specimens of the present case did not have BRAF\textsuperscript{V600E} activating mutations. Expression of programmed cell death ligand 1 (PD-L1) should not be utilized to exclude patients from anti-programmed cell death 1 (PD-1) monotherapy, but it may help decide between anti-PD-1 monotherapy and ipilimumab/nivolumab combination therapy. In this case, PD-L1 expression was 1% to 10%. Therefore such immunotherapy would be applied when
recurrence has occurred. Our surveillance plan includes observations that will be made at 3-month intervals for 2 years and then at 6-month intervals for 3 to 5 years, and CT scans are performed once every 6-12 months according to lung cancer. After that, annual observations should be made according to clinical indications. The OS and recurrence interval in our review showed recurrence early after surgery. Therefore, we suggest that patients should be followed up more frequently than patients with lung cancer.

In this case, multiple disciplinary tumor boards were held by the Department of Dermatology, Department of Respiratory Medicine, and Department of Oncology after surgery. The tumor in the present case was completely resected, and there was little evidence of the need for postoperative adjuvant chemotherapy. It was decided to follow up on a treatment plan after surgery, and thus this board was beneficial. Because of the high grade of the tumor and the frequent recurrence, close follow-up is required.

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REFERENCES


FIGURE LEGENDS

Figure 1. A, Chest computed tomography showed a nodule in the anterior segment. Contrast-enhanced computed tomography showed no evidence of distant metastasis throughout the whole body. B, The tumor showed a slightly high signal on plain T2-weighted magnetic resonance imaging and had not invaded the surrounding tissue.

Figure 2. A, The tumor was elastic, soft, and grayish-white in the cross section of the macroscopic image. B, Hematoxylin and eosin staining showed macrophages that had phagocytosed melanin (small arrow). C, D, Immunohistochemical staining was positive for HMB-45 and S-100, consistent with malignant melanoma.
Declaration of interests

☒ The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

☐ The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: