Letter to the Editor

Primary pulmonary melanoma with brain metastasis: a case description and literature analysis

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Introduction

Melanoma, a highly malignant and aggressive tumor, is most commonly found in the skin but can also occur in the respiratory tract and oral cavity. Primary pulmonary melanoma is extremely rare, accounting for only 0.01% of all primary lung tumors (1). The prognosis is extremely poor, with most patients living for less than 18 months (2). The current primary pulmonary melanoma diagnosis should rule out metastatic melanoma from the skin or other organs and meet clinical and pathological criteria.

Clinical data

A 60-year-old man diagnosed with pulmonary malignant melanoma was admitted to our hospital in November 2021 for 8 days. He underwent a complete examination. A computed tomography scan of the chest revealed bilateral multiple nodules and masses in the lungs, suggesting pulmonary carcinoma and intrapulmonary metastasis, as shown in *Figure 1*. The right lung hilar lymph nodes were enlarged, and cranial magnetic resonance (MR) imaging revealed multiple occupancies in both cerebral hemispheres. On MR angiography, susceptibility weighted imaging revealed intra-focal combined hemorrhage, as shown in *Figure 2*. The N-acetyl aspartate peak of the larger lesion in the left parietal lobe was significantly decreased, while the Cho peak was significantly increased, according to MR spectroscopy. Pathological biopsy revealed a malignant tumor (both lungs) and the staining results were shown in the *Figure 3*. Immunohistochemistry demonstrated S-100(+), HMB-45(+), Melan-A(+), no evidence of melanoma in the patient's skin and mucosa, and no prior history of oncology or other brain diseases, and after consultation with a brain surgeon, brain lesions are considered malignant melanoma and metastases are likely. Treatment regimen comprised temozolomide, 350 mg PO d1–5; cisplatin, 40 mg ivgtt d1–3; and bevacizumab, 300 mg d1, d15. The patient was administered palonosetron hydrochloride to treat emetics. All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

Discussion

Primary pulmonary melanoma tumors are extremely rare; however, they are highly malignant, with a high recurrence rate and poor prognosis. A total of 76 patients have been reported in the literature worldwide, with a median age of 60 years (range, 51.25–68 years) and a male predominance (3). Endobronchial lesions are present in the tumors, causing cough, hemoptysis, and pulmonary atelectasis (4). However, its pathogenesis is still debated, with some researchers (5) suggesting that melanocytes migrate to the respiratory tract during embryogenesis, where they transform into cancer cells. Other researchers hypothesized

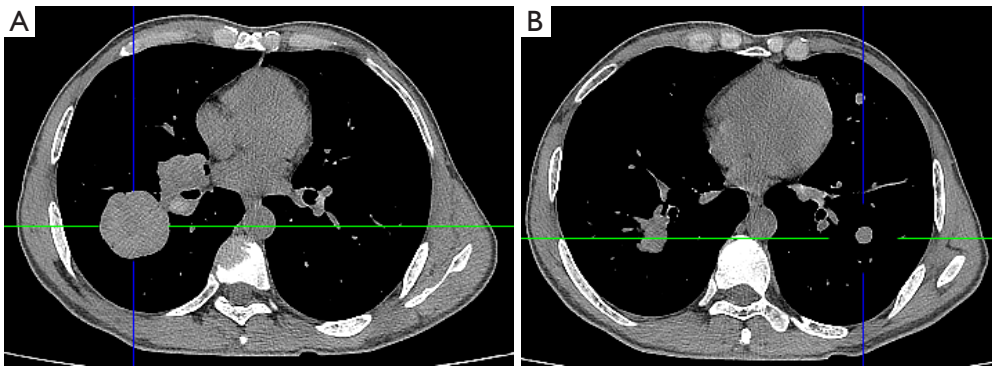

Figure 1 The image illustrates (A) the primary and (B) metastatic lesions in the lung.

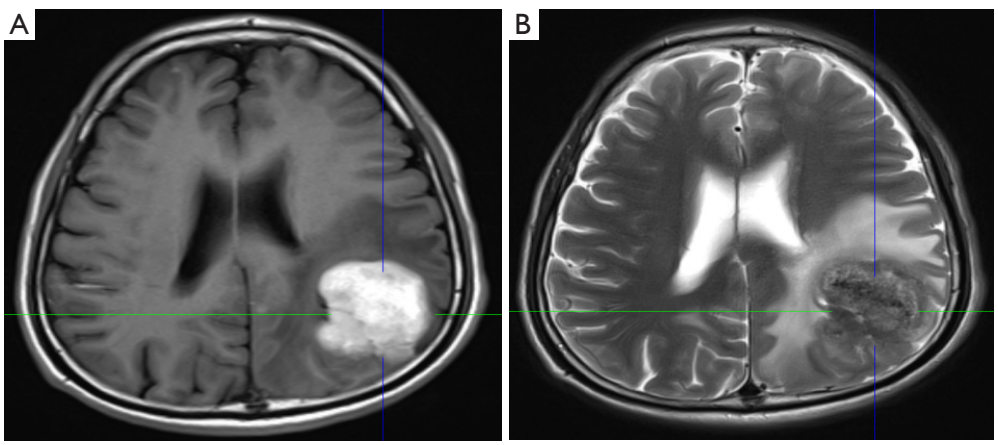

Figure 2 The image shows an intracranial metastatic lesion. (A) T1 signal enhancement, high signal shadow in the left occipital lobe, metastatic tumor considered, extensive peritumoral edema zone. (B) Bilateral cerebral hemispheres with multiple space occupying and intrafusal bleeding.

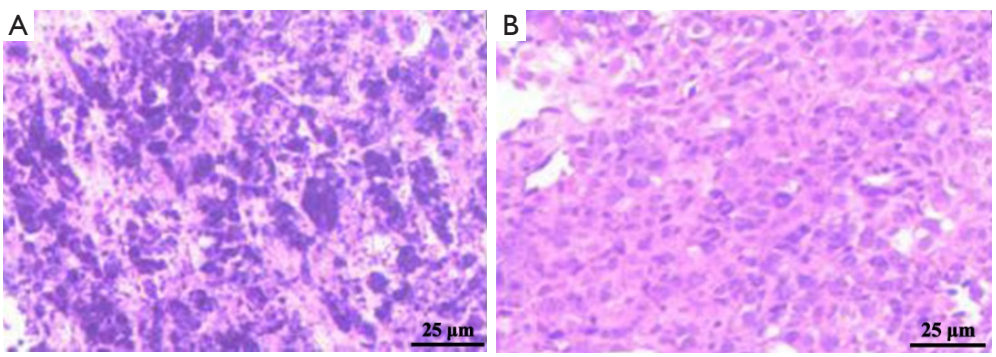

Figure 3 The histological slides demonstrate the pathological and immunohistochemical staining results: CK5/6(–), P40(–), CK7(+), Napsin-A(–), TTF-1(–), CD56(–), Syn(–), CgA(–), S-100(+), HMB-45(+), Melan-A(+), Ki-67 (index: 70%). (A,B) The tumor cells grew infiltratively and were arranged in a solid lamellar structure. Cell atypia was obvious. Tumor cells had abundant cytoplasm, eosinophilic acid, irregular nuclei, unclear cell boundaries, obvious nucleoli, and easy to see nuclear division. TTF-1, thyroid transcription factor 1; CgA, chromogranin A; HMB-45, melanoma marker (human) monoclonal antibody.

that melanocytes are derived from melanoblasts, which have the same origin as other melanoblasts found in the trachea, esophagus, and pharynx.

No gold standard diagnostic criteria exist for the diagnosis of primary pulmonary melanoma. The recommended clinicopathologic diagnostic criteria (6) are as follows: (I) isolated lung tumor; (II) confirmation of melanoma using immunohistochemistry or electron microscopy; (III) no previous history of excision or electrocauterization of skin, mucosal, or ocular lesions; (IV) central lung lesion; (V) no obvious tumor anywhere else during diagnosis. Attention should be paid to the differential diagnosis of malignant tumors such as squamous lung cancer and metastatic pulmonary melanoma. It should be noted that the differential diagnosis of pulmonary melanoma and lung squamous cell carcinoma lacks specific clinical manifestations and imaging manifestations, so the diagnosis is primarily based on pathological biopsy, S-100, HMB-45, and Melan-A positive for pulmonary melanoma is highly diagnostic. S-100, HMB-45, and Melan-A are all positive in primary pulmonary melanoma; HMB-45 and Melan-A are usually negative in lung squamous cell carcinoma, which is a good point of differentiation. Therefore, immunohistochemistry is critical. The pathological and immunohistochemical findings confirmed the primary pulmonary melanoma with brain metastasis after excluding the primary lesions of skin and mucosa.

For primary pulmonary melanoma, the available treatment alternatives are surgery, chemotherapy, radiotherapy, immunotherapy, and targeted therapy. Moreover, for resectable lesions, surgery is the treatment of choice, with lobectomy or wedge resection of the lung being the common surgical alternative (7). In this case, the patient had intrapulmonary metastases and brain metastases at the time of consultation, so surgery was not considered, and the patient's family refused to administer radiation therapy to the brain metastases. BRAF mutations were found after genetic testing, and the patient was finally given chemotherapy combined with targeted therapy. In terms of the treatment plan, we chose temozolomide, cisplatin, and bevacizumab because temozolomide can penetrate the blood-brain barrier, has high bioavailability, and has a relatively satisfactory effect on the treatment of intracranial metastatic melanoma (8-10). Up to now, the patient has completed 2 cycles of treatment; however, due to the metastasis and poor physical fitness of the patient, no satisfactory effect has been obtained at present, but we will continue to follow up with the patient.

Summarizing the literature (1,3,4,7,11-15) on lung melanin in recent years, we found that: (I) Pulmonary melanoma has no specific clinical manifestations, but it is frequently characterized by coughing, hemoptysis, dull chest pain, and other symptoms. (II) It is more likely to occur in the lower lobe of the left lung, the metastasis rate of mediastinal lymph nodes is lower than that of lung cancer, and the mutation rate of BRAF is low, but the prognosis is poor, and the median survival is 24.3 months. (III) There are no clear diagnostic criteria, and it is necessary to diagnose through clinical manifestations, imaging, and pathology. Clinical diagnostic criteria: solitary lung tumor; confirmation of melanoma using immunohistochemistry or electron microscopy; no previous history of excision or electrocautery of skin, mucous membrane, or ocular lesions; central lung lesions; at the time of diagnosis, there are no visible tumors in other parts of the body. Diagnostic criteria for pathology: histological structural changes, such as nests, glandular bodies, trabeculae, papillae, vortexes, pseudoscales, or glomerular-shaped cell arrangement; cytological changes, typically manifested as large, large, medium-sized, small, spindle, ring-like, rhabdomyotic, plasmacytoid or balloon-like cells; varying degrees of interstitial changes, such as fibrogenesis, myxoid degeneration, and inflammatory cell infiltration. Imaging is non-specific. (IV) Surgery, including lobectomy or total pneumonectomy and mediastinal lymph node dissection, remains the primary treatment option. In addition to surgery, immunotherapy with anti-PD-1 (Nivolumab and Pembrolizumab) and anti-CTL-4 (Ipilimumab) antibodies is currently the most popular therapy, but large clinical trials to confirm its efficacy in pulmonary melanoma are lacking.

In short, in diagnosing and treating pulmonary melanoma, we must be careful and rigorous to avoid misdiagnosis and mistreatment.

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Footnote

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://qims.amegroups.com/article/view/10.21037/qims-22-1032/coif). 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 this study followed the ethical standards of the institutional and/or national research committee(s) and the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient to publish this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

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