Misdiagnosis and treatment of a case of malignant melanoma found in an axillary mass: case report and review

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Abstract

Background

Malignant melanoma (MM) is a highly dangerous, potentially fatal tumor originating from melanocytes in the neural crest. It most often occurs in the skin, and regional lymph nodes (inguinal, axillary, cervical, and others) can metastasize at an early stage. Malignant tumors not involving the hematopoietic system initially appear as axillary masses, constituting a unique clinical manifestation. Moreover, MM in an axillary mass is difficult to diagnose preoperatively and is easily misidentified.

Case presentation:

Here, we report on a 62-year-old woman with MM occurring within an axillary mass; it was initially misdiagnosed as synovial sarcoma and fibrosarcoma. Under general anesthesia, the patient underwent radical surgery of a right axillary lymph node; she then received six cycles of chemotherapy. About 14 months later, the lesion recurred and metastasized to the chest wall and breast skin. After biopsy of the skin nodules on the chest wall as well as examination by immunohistochemistry (IHC) and gene detection, the lesion was confirmed to be a MM. Finally, after two cycles of targeted drug treatment, the lesions in the armpit, chest wall, and breast skin disappeared.

Conclusion

MM is an often lethal, highly malignant, easily misdiagnosed form of cancer that requires careful study, following its clinical course, and scrutinizing the findings from imaging, pathology, immunohistochemistry, and gene detection.

Background

Malignant melanoma (MM) has a high mortality rate and is prone to metastasize to lymph nodes and more distant sites. It has many mutations, which threaten patients’ physical and mental health as well as their quality of life (1, 2). Most patients with MM present with an odd-looking birthmark, nevus, or mole; the physical and imaging examinations then show that the regional lymph nodes are swollen. However, the initial finding of enlarged lymph nodes is later superseded when, after lymph node metastasis, the primary lesion of MM is found and the condition is confirmed (3–5). Here, we report on the misdiagnosis and treatment of a patient with an axillary mass, showing how challenging the diagnosis of MM can be and how it affects the clinical outcome. To our knowledge, no similar cases have been reported.

Case presentation
The patient was a 62-year-old Chinese woman who went to see a doctor on July 13, 2020, because she had had an axillary mass for 6 months. Her past medical history was unremarkable. Physical examination revealed that a mass of about 4 cm × 4 cm could be palpated on the deep surface of the right armpit. It was hard, had a distinct boundary, and could be pushed without tenderness. The surrounding lymph nodes were not swollen. After admission, the patient underwent complete relevant auxiliary examinations. Ultrasonography of the breast and lymph nodes in drainage areas as well as mammography showed that both mammary glands were Breast Imaging-Reporting and Data System for Ultrasound (US-BI-RADS) 1, and the right axillary lymph node was enlarged. A plain scan of the breast by magnetic resonance imaging along with enhanced angiography found an abnormal signal shadow in the right armpit suggesting a tumor, possibly neurogenic. Enlarged lymph nodes were also noted, suggesting the presence of infection. Further investigation was clearly required. Fine needle aspiration cytology (FNAC) showed that it was considered as small round cell malignant tumor. The right axillary mass was further examined by thick needle aspiration. The pathological biopsy results showed that small cell tumors, combined with the immunophenotype, considered mesenchymal tumors, tended to one-way synovial sarcoma.

The patient was told about the need for surgical treatment as well as the risk of refusing it; with her consent, surgery was then planned. Under general anesthesia, she underwent radical resection of the right axillary lymph node on August 5, 2020. Postoperative pathology combined with morphologic and immunohistochemical examination identified a malignant soft tissue tumor conforming to a poorly differentiated synovial sarcoma. Twenty-eight lymph nodes were detected and no tumor metastasis was found in any (0/28). Immunohistochemistry was as follows: HMB45 (-), Melan-A (-), S-100 scattered (+), Desmin (-), Bcatenin membrane (+), P53 wild type (+), P16 (-), CK (-), CD56 (-), Myogenin (-), CD10 (-), CyclinD1 (+), INI-1 (+), TLE1 (+), NKKX2.2 (-), BCL-2 (+), CD34 (-). After the pathologic specimen was re-examined under consultation, a spindle cell soft tissue sarcoma of the right armpit was identified and verified by SYT fusion gene test results, making this case consistent with fibrosarcoma. After the contraindication was eliminated, the patient received six cycles of AI (adriamycin plus ifosfamide) chemotherapy.

About a year after the end of chemotherapy, on March 17, 2022, the patient visited our hospital with the recurrence of an axillary mass with chest wall and breast skin metastasis (Fig. 1A). FNAC of the right chest wall mass suggests a small round cell malignancy with obvious nucleolus (Fig. 1B). The mass in the right chest wall was excised under local infiltration anesthesia. Histopathologic analysis was performed by two skilled pathologists, and postoperative pathology identified a malignant soft tissue tumor. Gene detection and immunohistochemistry were consistent with MM metastasis. Figure 2 shows hematoxylin and eosin (H&E) staining and IHC staining of tissues from the mass in the chest wall. The infiltrating growth of tumor cells is mainly round cells. The cells are obviously heterotypic, have abundant eosinophilic cytoplasm, and are easy to see nucleolus and mitosis. IHC staining results were as follows: SOX10 (+), S-100 (+), HMB-45 (+), Ki-67 (+, 70%), CD34 (-), CD99 (-), TLE1 (-), EMA (-), Vim (+), p53 (+, 1%), CK (-), Desmin (-), MelanA (+), SOX10 (+). With the consent of the patient, we performed Braf gene mutation detection on the tissue from the chest wall, verifying a type of Braf gene mutation (Fig. 3). Based
on the patient's gene test results, oncologists suggested that double-target combination therapy (dallafenil combined with trimetinib) should be carried out according to the guidelines, including or excluding chemotherapy. After two courses of targeted therapy, the MM metastasis disappeared. We plan to evaluate the long-term therapeutic and side effects over time.

Discussion and conclusions

The structure of the armpit is complex (6). There are many patients with axillary masses and the disease types are diverse. Such masses can be divided into primary and secondary types according to their cause, and they can be further divided into benign and malignant types (7–9). Malignant tumors originating from multiple systems of the body—such as breast cancer, lymphoma, gastric cancer, pancreatic cancer, lung cancer, and MM—can all metastasize to the armpit. In the case of axillary lymph node metastases, the most common primary focus is breast cancer, MM, and lung cancer. Liu et al. reported that only two of their seven patients with MM were diagnosed as having MM before surgery; the other five patients were misdiagnosed before surgery (10). Postoperative pathologic and immunohistochemistry examinations confirmed that the latter had metastatic MM. The case reported in this paper was admitted because she had an axillary mass, but it was misdiagnosed as sarcoma. After surgery, the patient was treated with chemotherapy appropriate for fibrosarcoma. Once her lesion had recurred, pathologic biopsy and gene detection confirmed that it was MM. To prevent the misdiagnosis of MM, a high index of suspicion is necessary.

In our case, the diagnosis of MM was so challenging that it misled both clinicians and pathologists and led to a delay in diagnosis. The primary aim in treating a patient with an axillary mass is to determine the nature of the mass. In this process, attention should be paid to the patient's medical history, and physical examination and ultrasonic examination of the axillary mass should be performed to determine its location, size, blood supply, and relationship to adjacent tissues. In this paper, we report on a patient who underwent ultrasound to determine the size of the tumor and pathologic examination to determine its nature. Fine-needle aspiration cytology led to the finding of a small malignant round-cell tumor. This procedure is highly useful in arriving at a diagnosis, and patients who undergo this procedure experience less pain than would be involved in tumor resection and biopsy; it also reduces the chance of irritating the tumor (11). In the case under discussion, no primary cutaneous MM was found after body examination. In fact, no primary focus is found in about 2–5% of patients with MM, which is called “MM without a primary focus” (12–14). The prognosis of MM without a primary focus is better than that of MM with a primary focus, which may be due to immune-induced complete regression of the primary tumor and better prevention or control of distant metastatic diseases (15). In addition, in some patients with MM without a primary focus, MM originates from nevus cells within lymph nodes and is not metastatic. Lymph node dissection not only removes the primary focus but also clears regional lymph nodes, which is beneficial to the prognosis (16).

HMB45, Melan-A, and S100 are the main immunohistochemical markers in the clinicopathologic diagnosis of MM (17). However, in the present case of an axillary mass, the first and second biopsies
were negative for immunohistochemistry, which does not support MM. Interestingly, S100, HMB-45, Melan-A, and SOX10 were diffusely positive in the immunohistochemistry of the biopsy of the chest wall metastasis. This shows that MM is a malignant tumor with strong heterogeneity. Further analysis found that the B-RAF V600E mutant type gene mutations were detected in the armpit and chest wall biopsies, which also supports MM. This shows that although MM comprises strong heterogeneity and large differences in the expression of tumor cell protein, mutation of the Braf gene is consistent. This case also demonstrates the role of gene detection in the diagnosis of MM, especially in the diagnosis of MM with amelanotic and atypical morphology. Fortunately for patients with MM, scientists have developed BRAF inhibitors for melanoma: dallafenib and trametinib (18–20). The combination therapy of dallafenib and trametinib is an innovative combination with a dual target, providing comprehensive inhibition of signal pathways. Dallafenib is a selective inhibitor of BRAF kinase activity; Trametinib is a reversible, highly selective allosteric inhibitor of MEK1 and MEK2 kinase activities (21). Their combination can inhibit both BRAF and MEK targets simultaneously, thus achieving the effect of $1 + 1 > 2$. More importantly, these two targeted drugs were approved for marketing by the U.S. Food and Drug Administration in 2011 and for marketing by China in 2019. According to the guidelines, this patient received targeted treatment with dallafenib and trametinib, and the mass subsided after two cycles. To date, there has been no recurrence or metastasis of the tumor.

**Conclusions**

MM is a relatively common form of disease that is easily misdiagnosed, especially in the case of amelanotic MM. It should be diagnosed carefully, and the clinical course, imaging, pathology, immunohistochemistry, and gene detection findings should be considered. Specifically, in this case, owing to the heterogeneity of MM, the pathologic morphology and immunohistochemical expression of the first two biopsies were atypical; therefore, gene detection played an important role in the diagnosis and treatment of this patient. Timely and accurate diagnosis of melanoma is essential to achieve appropriate treatment and maximize patients’ prognoses.

**Abbreviations**

MM
Malignant melanoma
AI
Adriamycin plus ifosfamide
H&E
Hematoxylin and eosin
IHC
immunohistochemistry
FNAC
Fine needle aspiration cytology.
Declarations

Authors’ contributions

YW and CL are mainly responsible for the writing of the paper. CL and SW designed this study. YL and JW collected the information and images. SW reviewed the manuscript. All authors read and approved the final version and agreed to its publication. All authors reviewed the manuscript.

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Availability of data and materials

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Ethics approval and consent to participate

The patients gave written informed consent for the publication of any potentially identifiable images or data included in this article.

Consent for publication

Written informed consent was obtained from the patient for publication of the case.

Conflict of Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

References


**Figures**

**Figure 1**

(A) The patient visited our hospital with the recurrence of an axillary mass with chest wall and breast skin metastasis. (B) Cytomorphologic characteristics of the patient.
Figure 2

Histopathologic characteristics and IHC staining. (A) The HE staining of chest wall mass tissues (the microscope magnifying×200). (B) Immunohistochemical staining [HMB45(+)]. (C) Immunohistochemical staining [Melan-A(+)]. (D) Immunohistochemical staining [S100(+)]. (E) Immunohistochemical staining [SOX10(+)]. (F) Immunohistochemical staining [Ki-67(+)].
Figure 3

Results of BRAF gene mutation.