Metastatic balloon cell melanoma—a rare differential in the diagnosis of clear cell tumors: Report of two cases

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ABSTRACT
Two patients aged 65 and 66 years old presented with an enlarged inguinal lymph node. Clinically and radiographically, the inguinal mass was considered to be metastatic; however, first patient had no history of primary neoplasm. A fine-needle aspiration (FNA) cytologic examination of inguinal lymph node in both the cases showed numerous discohesive, pleomorphic tumor cells with abundant, vacuolated cytoplasm and eccentrically placed round to ovoid nucleus with inconspicuous nucleoli and frequent intranuclear cytoplasmic pseudoinclusions. Pigment was not identified in the FNA of both the cases. Histopathological examination of the inguinal lymph node biopsy confirmed the diagnosis. These features, along with strong immunohistochemical positivity for HMB-45, suggested the diagnosis of metastatic balloon cell melanoma.

Key words: Malignant melanoma, balloon cell melanoma, metastasis

INTRODUCTION
A potential pitfall in the histological assessment of malignant melanoma is the inability to recognize unusual melanoma variants. Lymph node metastasis of balloon cell melanoma (BCM) has the potential to mimic other metastatic clear cell tumors. We encountered two such diagnostic challenges in the inguinal lymph node metastasis of a 65 and a 66 year old female.

CASE REPORTS
Case 1
A 65 year old female laborer presented to the surgical OPD with multiple enlarged lymph nodes in the left inguinal region. The patient gave history of undergoing surgery for the excision of a mass on the medial surface of the left foot 1 year before. She had lost all the records regarding the surgery and final histopathological diagnosis of the tumor. She had not taken any treatment after the surgery. Systemic examination of the patient was normal. Routine and radiological investigation of the patient also did not reveal any abnormality. Fine-needle aspiration (FNA) of the left inguinal lymph node was done.

Case 2
A 66 year old female presented to surgical OPD with enlarged right inguinal lymph node. The patient gave history of undergoing right great toe amputation 1 year before and has been diagnosed as malignant melanoma. The patient did not take treatment after that. Systemic examination of the patient was within normal limits. CT scan revealed enlarged right iliac lymph nodes. FNA of right inguinal lymph node was done.

Cytological examination revealed similar features in both the cases. Smear were cellular, comprising sheets of discohesive tumor cells with abundant foamy cytoplasm, indistinct cytoplasmic borders, eccentrically placed round to the ovoid nucleus with bland nuclear chromatin and occasional intranuclear cytoplasmic inclusions [Figure 1]. Bi- and trinucleate tumor cells were also present. No pigment was identified.

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Keeping in view the previous history of surgery for malignant melanoma in the second case, cytological diagnosis of metastatic BCM was rendered. In the absence of clinical history in the first case, a descriptive diagnosis was given and the differential diagnosis of metastatic granular cell tumor, oncocytoma, and histiocytic disorder were considered.

Histopathological examination of inguinal lymph node biopsy in both the cases revealed diffuse replacement of the lymph node parenchyma by sheets of large round to polygonal cells with abundant vacuolated cytoplasm and distinct cell borders. These tumor cells were showing pleomorphic, vesicular nucleus with inconspicuous nucleolus and frequent intranuclear cytoplasmic pseudoinclusions [Figure 2]. Occasional cells with multiple vacuoles in the cytoplasm scalloping the nucleus, remarkably resembling the lipoblasts, were also seen. Pigment was not identified in the first case. Based on these features, along with strong immunohistochemical positivity for HMB-45, the diagnosis of metastatic BCM in the left inguinal lymph node was rendered in the first case.

The second case showed scanty melanin pigment in some foci. Thus, the cytological diagnosis of metastatic BCM was confirmed.

**DISCUSSION**

The pathologic diagnosis of melanoma metastases can be achieved by fine-needle biopsy (FNB) or open biopsy. FNB has the advantages of rapidity, safety, noninvasiveness, and reduced morbidity compared with open biopsy.

The use of FNB for the detection of metastatic melanoma allows early diagnosis and treatment, which may prolong disease-free survival in a subset of patients. However, definitive and accurate FNB diagnosis is challenging owing to the varied morphologic appearances of melanoma in cytologic preparations.

Balloon cell malignant melanoma (BCMM) is the rarest histological type of primary melanoma and is composed of large, polyhedral, foamy cells with abundant cytoplasmic vacuoles. When BCMM metastasizes, it may present as a tumor consisting predominantly or entirely of foamy cells, also known as BCM cells, which may appear cytologically bland. Its benign morphologic appearance presents a challenge for accurate clinicopathologic diagnosis. In BCM, balloon cells are usually sparse in the primary melanoma, but have a potential of constituting the entire metastasis. Due to these reasons, the metastatic lesion was frequently misinterpreted. In the case by Gardner, the lymph node metastasis was initially diagnosed as clear cell sarcoma. Ranchold reported a case in which the diagnosis of round cell liposarcoma was made on lymph node metastasis.

Akslen reported a case in which metastatic tumor mimicked clear cell renal carcinoma. These cases illustrate the importance of clinical correlation in reaching a diagnosis of BCMM. Other main reasons why BCMM can be mistaken for a benign clear cell neoplasm is its bland cytology and general lack of melanin in BCM, in contrast to balloon cell nevus cells. In several case reports, the BMC contained no melanin pigment and stained negatively for Fontanella-Masson. This characteristic is further exacerbated by the fact that when BCM metastasizes, the metastases are often composed entirely of balloon cells with no residual spindle-shaped or epithelioid component.

The characteristic cytomorphological features of metastatic BCM were described by Baehner et al. in their case report. Fine-needle aspiration biopsy (FNAB) and cytologic examination of the cervical lymphnode in their case showed numerous discohesive, variably sized, malignant cells with abundant, vacuolated cytoplasm and pleomorphic...
nuclei with irregular nuclear contours, macronucleoli, and frequent intranuclear cytoplasmic pseudoinclusions. Pigment was not identified. These features, along with strong immunohistochemical positivity for S-100, HMB-45, and Melan-A, suggested the diagnosis of metastatic BCM.

In the absence of prior clinical and pathological history, numerous differential diagnoses were posed in this lesion composed exclusively of foamy to clear balloon cells, including renal cell carcinoma, adrenal tumors, malignant granular cell tumor, clear cell sarcoma, alveolar soft part sarcoma, perivascular epithelioid cell tumors (PECOMAS), liposarcoma, xanthomatous lesions, sebaceous lesions, hibernoma, and clear cell hidradenoma. Immunohistochemistry and electron microscopy are of great help in this regard. Balloon cells show positively for S-100 protein, HMB-45, Melan-A, and NK/1-C3. MART-1 has also been found to be a useful marker for the detection of metastatic melanomas in the lymph nodes. Melan-A is found to be a more important marker in the diagnosis of BCM than the classic melanoma antibody HMB-45. Ultrastructurally, balloon cells are characterized by the presence of numerous cytoplasmic vacuoles and abnormal melanosomes which confirm their melanocytic origin. The cytoplasmic vacuoles represent the grossly dilated melanosomes.

In conclusion, balloon cells are usually sparse or absent in primary melanomas. However metastatic deposits from these tumors are often composed entirely of balloon cells with no residual spindle-shaped or epithelioid component. While the characteristic cytological and histopathological features are supportive, immunohistochemistry is diagnostic. In addition, clinical history is most critical in the diagnosis of BCMM. A possibility of BCMM should be considered in the differential diagnosis of metastatic clear cell tumors.

REFERENCES


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