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LETTER

Refining diagnosis is the prerequisite for the correct treatment: The cytodiagnostic utility of SOX10 in the diagnosis of metastatic melanoma

Dear Editor,

A 60-year-old male patient presented with a complaint of growing swelling in the left axilla for 3 weeks. The patient had no history of chronic disease or cancer. Physical examination showed no abnormal findings except for left axillary mass. Tumor markers including CEA, AFP, CA15.3, CA19.9, CA125, and PSA were within normal limits while high CRP (42 mg/l) and erythrocyte sedimentation rate (57 mm/h) were detected. Thorax Computed tomography (CT) and positron emission tomography (PET) scans revealed three nodular masses with a similar appearance in the right and left inferior lobes of the lungs and axilla, each with a diameter of 4 cm, indicating malignancy. Abdominal computed tomography showed no additional lesions. Cytomorphological assessment of fine-needle aspiration cytology (FNAC) obtained from the axillary mass showed a tumoral lesion composed of large, pleomorphic, and atypical cells with intensive brown pigmentation (Figure 1A-C). No lymphoid cells were detected. The presence of intensive brown pigmentation first suggested melanoma. However, soft tissue tumors with melanocytic differentiation and PEComa were included in the list of differential diagnoses. An immunocytochemical panel on the cell block obtained from a low amount of material was performed. Neoplastic cells showed diffuse nuclear positivity for SOX10 and cytoplasmic positivity for HMB-45 (with red chromogen) while they exhibited minimal staining for Melan-A and S-100 (Figure 1D-F). PanCK, SMA, Myo-d1, CD57, and chromogranin were negative. The lesion was diagnosed as metastatic malignant melanoma based on cytomorphological and immunocytochemical findings. Molecular testing showed no BRAF mutation. Since no lesions were observed in the detailed examination of the skin and other systems, we thought that the lungs could be the primary focus. However, fluorodeoxyglucose (FDG) uptake observed in the pulmonary lesions

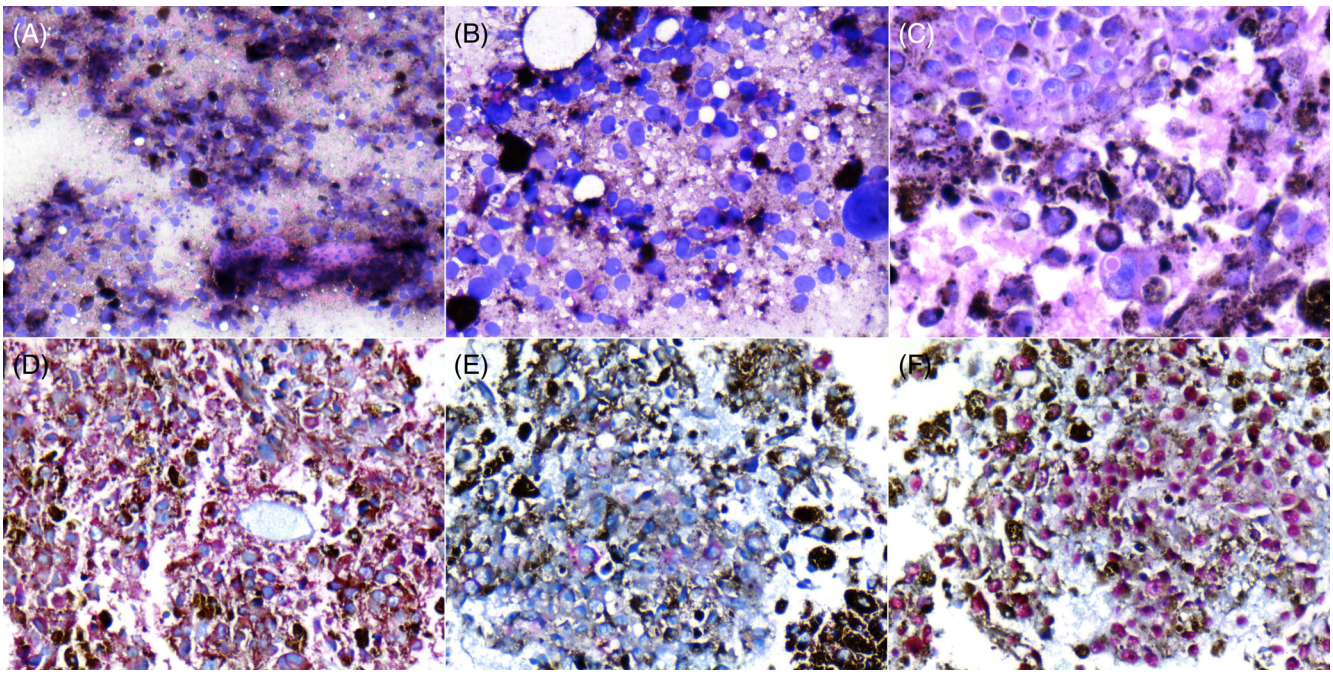

FIGURE 1 A,B, Cytomorphological examination of the metastatic melanoma demonstrated large, pleomorphic, atypical tumor cells with brown pigments (Papanicolaou, ×100; Papanicolaou, ×200); C, loosely cohesive, atypical epithelioid cells with multinucleation, prominent nucleoli and intranuclear inclusion (cell block; H&E stain, ×200); D, cytoplasmic HMB-45 staining in cell block (×200); E, focal weak positivity with Melan-A (×200); and F, diffuse nuclear positivity for SOX10 (×200)

on the PET imaging was reported to primarily support a metastatic process. Unfortunately, the patient rejected lung biopsy and a diagnosis of metastatic melanoma with the unknown primary was made. The TNM stage was assigned as Stage-4 melanoma based on the eighth Edition of the American Joint Committee on Cancer (AJCC) criteria.[1] The patient was referred to a specialized oncology center where targeted immunotherapy (Nivolumab, 240 mg intravenous, q2Weeks) was started. The patient received a total of four cycles of therapy without notable infusion reactions and adverse events. The first radiological assessment of response to the treatment was planned when a total of eight cycles were completed.

Melanoma is known to have a strong tendency to metastasize to any part of the body. It is usually not easy to made a diagnosis based only on cytological characteristics in metastatic melanoma, since melanoma can exhibit a wide variety of cytological features, imitating different types of epithelial, mesenchymal, and lymphoid malignancies. Metastatic tumors may have different cytological characteristics than primary ones.[2] Therefore, an accurate diagnosis of metastatic melanoma can be a real challenge. HMB-45, Melan-A, S-100, cytoplasmic markers for melanocytes, are frequently used immunocytochemical markers in cytology practice. However, their sensitivity has been demonstrated to be suboptimal, and their expression rates may be lower in metastatic lesions.[3,4] SOX10, a nuclear marker, is considered more reliable than cytoplasmic and membranous markers. Nevertheless, as it may also show positivity in breast carcinoma and spindle cell neoplasms, it should not be used as a sole determinant of melanocytic origin.[5,6] SOX10/keratin cocktail staining on FNAC cell blocks has been recommended as the initial method for the differential diagnosis of melanoma, sarcoma, and carcinoma in poorly differentiated epithelioid neoplasms.[7]

To sum up, we believe that SOX10 may be a useful marker in the setting of small cell block samples obtained from metastatic masses with unknown primary. Direct smears may also be an alternative for immunostaining in samples where no cell blocks can be made.

Informed consent was received from the participant.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHOR CONTRIBUTIONS

Asuman Kilitçi, Ömer Faruk Elmas: Literature searching, designing and writing the manuscript. Ömer Faruk Elmas, Abdullah Demirbaş, Mehmet Gamsızkan, Mustafa Atasoy: Substantial contributions to conception and design, interpretation of data. Ömer Faruk Elmas, Abdullah Demirbaş, Ümit Türsen, Torello Lotti: Editing, revising and final approval of the manuscript.

DATA AVAILABILITY STATEMENT

The data associated with the paper are not publicly available but are available from the corresponding author on reasonable request.

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