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CASE IMAGE

Case of metastatic melanoma in bone marrow smear

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A 56-year-old female patient came into the emergency room for epistaxis and the appearance of hemorrhagic petechiae on the hips and abdomen. She had a clinical history of primary melanoma of the nasal mucosa, a rare subtype of melanoma (1% of all malignant melanomas),[1] characterized, compared with all malignant melanomas, by later onset (median age 70 vs. 55), worse five years survival (25% vs. 80%) and advanced stage at diagnosis, being asymptomatic in almost all cases.[2] She was treated with surgical resection, representing the primary treatment modality[2,] followed by radiotherapy and low-dose interferon. She then underwent a lobectomy for pulmonary metastatic localization two years later. At the time of presentation to our hospital, she underwent proton therapy, a form of external beam radiotherapy,[3] for sphenoidal sinuses recurrence.

Upon arrival, vital signs (blood pressure, heart and respiratory rate, and temperature) were normal. Blood tests showed anemia (hemoglobin 9.2 g/dL) and marked thrombocytopenia (platelet count 16×10^9/l); white blood cell count (5.64×10^9/l) and differential were normal, except for five circulating nucleated red blood cells per 100 WBC at peripheral blood smear. Additional laboratory tests showed increased serum lactate dehydrogenase (LDH: 1112 U/l), C-reactive protein (PCR: 7.2 mg/L), and D-Dimer (12451 ng/mL). Nutritional deficiencies (iron, vitamin B12, and folate), thrombotic thrombocytopenic purpura, autoimmune hemolytic anemia, infections, and hematologic malignancies were considered in the differential diagnosis.

Bone marrow aspirate smears showed reduced cellularity with an almost complete absence of the megakaryocyte lineage. Large atypical immature blast cells infiltrated all areas of the bone marrow smear. They were either cohesive in small clusters (Figure 1A) or non-cohesive, scattered throughout the slide (Figure 1B) and, particularly, within the smeared bone marrow particles and in the feathered edge of the smear. Nuclei occupied a large part of the cytoplasm (moderately high nucleo-cytoplasmic ratio) and had a predominant blastic aspect. Nuclear chromatin was smooth and finely homogeneous, with some prominent and even giant prominent nucleoli, well visible thanks to thick circular borders. The cytoplasm was relatively abundant, with many vacuoles of different sizes, disorderly dispersed, and even in supranuclear position. Cytoplasm staining was basophilic and sometimes could appear empty due to the fusion of vacuoles in large unstained lakes (Figure 1A, black arrows). Nuclear and cytoplasmic borders were sharp and regular in most cases. Besides vacuoles, two types of cytoplasmic inclusions were present. They allowed a morphological differentiation from Burkitt-type lymphoma, rhabdomyosarcoma, or metastatic carcinoma. Firstly, there were dark pigment bodies of melanin (confirmed by positive immunohistochemistry for Melan-A) (Figure 1C, black arrow). Secondly, giant vacuoles included cells in various states of degradation, showing hemophagocytosis and auto-hemophagocytosis by these tumor cells (Figure 1B,C, empty arrows).

Bone marrow core biopsy confirmed the involvement by metastatic melanoma and showed interstitial and macronodular infiltration by cells with pigmented cytoplasm cells (positive for Melan-A/Tyrosinase and negative for CD34, CD11, MPO, and S-100).

Bone marrow metastatic melanoma infiltration is considered infrequent and has been described in a relatively small number of patients.[4] The cell morphological features have been variably reported as large blasts of heterogeneous size, with immature heterogeneous

[Correction added on 28 April 2022, after first online publication: the order of the third and fourth authors was interchanged in the original published article and has been corrected in this version.]

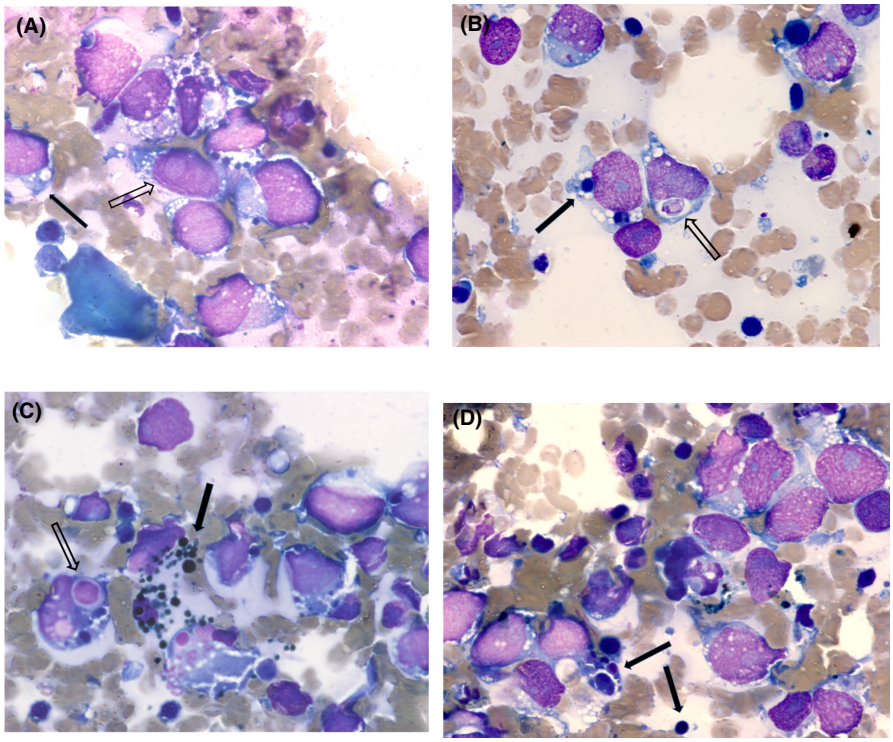

FIGURE 1 (May-Grünwald-Giemsa stain, original magnification x500). (A) Small cluster of large cells, with moderate size heterogeneity, ample basophilic cytoplasm full of heterogeneous size, apparently empty vacuoles, sometimes merging into larger clear lakes (black arrows). A giant blast with thin homogeneous chromatin displays a prominent, clear nucleolus with a well-designed round profile (empty arrow). Supranuclear vacuoles are also present. A few dark, blue–black spherules are present extracellularly. (B) Cells are isolated and scattered. The extensively vacuolated cytoplasm displayed two round black inclusions (melanin bodies, dark arrow). The other central cell on the right shows residual of phagocyted cell material in a large unstained cytoplasmic vacuole (empty arrow). (C) Hemophagocytosis (empty arrow), and intra- and extracellular melanotic bodies (black arrow) are prominent in this field. (D) Clusters of large blast cells with blue vacuolated cytoplasm and very immature nuclei, not very dissimilar from Burkitt lymphoma infiltrating bone marrow. A few extracellular dark spherules are scattered around (arrows)

nuclei and basophilic cytoplasm, which contains melanin pigment inclusions in typical cases. S-100 positivity was not observed in our case, while it is described as frequent in the literature. However, the positivity of Melan-A/tyrosinase and the clinical history confirmed the diagnosis.

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DATA AVAILABILITY STATEMENT

Data are available on request

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