



## Blastic plasmacytoid dendritic cell neoplasm with unusual lymphoid features and macrovacuoles

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Dear Editor,

Blastic plasmacytoid dendritic cell neoplasm (BPDCN) is a rare hematolymphoid malignancy derived from precursors of plasmacytoid dendritic cells. The skin, bone marrow, and lymph nodes are usually involved. The diagnosis often requires multiple diagnostic modalities, including histomorphology, immunohistochemistry, and/or flow cytometry. Tumor cell cytomorphology, which could be diagnostically helpful, has been infrequently emphasized in the literature. Characteristically, BPDCN cells are medium-sized cells with round to oval nuclei, fine chromatin, prominent nucleoli, and scant pale basophilic cytoplasm [1, 2]. Cytoplasmic pseudopodia, cytoplasmic tail, or “ping-pong paddle-like” configuration are terms that have been used to describe BPDCN cells [3–5]. Tumors cells have also been described to contain cytoplasmic microvacuoles, probably caused by glycogen deposits, with a peculiar arrangement along the cytoplasmic outline likened to a “pearl necklace.” Immunoblastoid cytomorphology has also been described in up to 35% of cases in a recent study [6]. Nevertheless, to the best of our knowledge, BPDCN cases in which the neoplastic cells exhibit prominent macrovacuoles have not been reported in the literature to date.

We hereby describe an intriguing BPDCN case with unusual cytoplasmic macrovacuoles and prominent lymphoid morphology. A 62-year-old woman presented with fatigue and dyspnea, and she was found to have leukocytosis and multiple maculopapular skin lesions (Fig. 1). Bone marrow evaluation demonstrated an extensive (>90%) infiltrate of neoplastic cells (Fig. 2a, b). The majority of neoplastic cells

had moderate amounts of lightly basophilic agranular cytoplasm containing distinctive clear macrovacuoles (Fig. 2c). The nuclear morphology was irregular, with somewhat clumped chromatin pattern and occasional intranuclear vacuoles identical to those in the cytoplasm. The macrovacuoles ranged from 2.83 to 7.99  $\mu\text{m}$  in diameter (median = 6.13  $\mu\text{m}$ ) and were negative for glycogen by Periodic Acid-Schiff (PAS) stain. By immunohistochemistry, the neoplastic cells co-expressed TCF4 and CD123 (Fig. 2d), and they were positive for TCL-1 and BCL2. By multiparameter flow cytometry immunophenotyping, the neoplastic cells expressed CD4, CD38, CD45, CD56, CD117, CD123, TDT, and HLA-DR and were negative for lineage-specific markers (CD3, CD19, CD64, and myeloperoxidase). Next-generation sequencing analysis demonstrated *NRAS* (p.G13D) mutation. Conventional cytogenetic analysis demonstrated a complex karyotype with myelodysplasia-related aberrations:



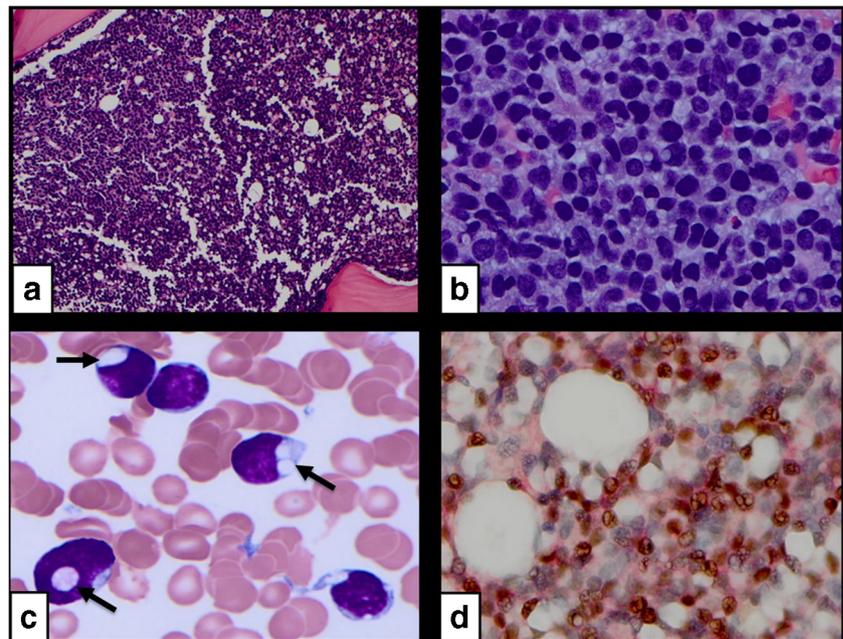
Fig. 1 Representative skin lesions

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Fig. 2 Bone marrow findings



44~45,XX,del(5)(q33q35),del(6)(q13q23),der(7;9)(q10;q10),-13[cp12]/46,XX[8].

This BPDCN case had an unusual and distinct cytomorphology resembling that of a lymphoid neoplasm, with PAS-negative macrovacuoles. Recognition of this unusual appearance is important for appropriate diagnostic evaluation. Differential diagnostic considerations based on the morphology identified in this case include high-grade lymphoid malignancies and certain carcinomas. Burkitt lymphoma cells commonly have cytoplasmic macrovacuoles, particularly when evaluated on touch-preparations or aspiration cytology material. High-grade B cell lymphoma and B lymphoblastic leukemia/lymphoma have also been reported to contain vacuoles. Rarely, lobular carcinoma of the breast and gastric signet ring cell carcinoma may have similar cytoplasmic vacuoles. Appropriate immunophenotyping studies would be helpful in distinguishing among these differential diagnostic considerations. In conclusion, pathologists and hematologists should be aware that rare BPDCN cases may have prominent lymphoid-like morphology with macrovacuoles.

### Compliance with ethical standards

**Conflict of interest** The authors declare that they have no conflict of interest.

**Research involving human participants and/or animals** This article does not contain any studies with human participants or animals performed by any of the authors.

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