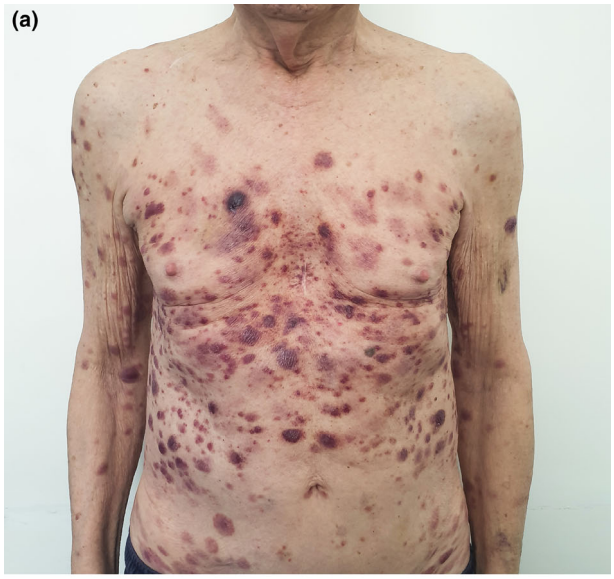
Acute leukemia as the initial presentation of blastic plasmacytoid dendritic cell neoplasm

Dear Editor,

A 90-year-old man presented with a 1-month history of fatigue and rapidly progressive, widespread skin lesions. Physical examination exhibited numerous erythematous to violaceous tumors and bruise-like patches scattered through his trunk and limbs (Fig. 1a,b). Enlarged bilateral axillary lymph nodes were noted.

Peripheral blood workup revealed mild macrocytic anemia (hemoglobin 11.3 g/dl, MCV 98 fl), normal white blood cell count (8490×10^9/l) with 27% circulating blasts, moderate thrombocytopenia (platelets 56×10^9/l), and elevated lactate dehydrogenase (424 U/l). Full body CT scan revealed enlarged cervical, axillary, thoracic, iliac, and inguinal lymph nodes, and no splenomegaly.

A skin biopsy revealed monomorphic dense dermal infiltrate extending into the subcutis of non-epidermotropic medium-sized cells with nuclei of irregular shape, finely dispersed chromatin, small or absent nucleoli, and increased mitotic figures (Fig. 2a,b). Axillary lymph node excisional biopsy revealed partial architecture effacement by diffuse infiltration of medium-sized cells with similar morphologic features. Bone marrow biopsy showed slight dyserythropoiesis and multifocal blast infiltration. Marrow aspirate revealed more than 10% dysgranulopoiesis and 9% blasts.



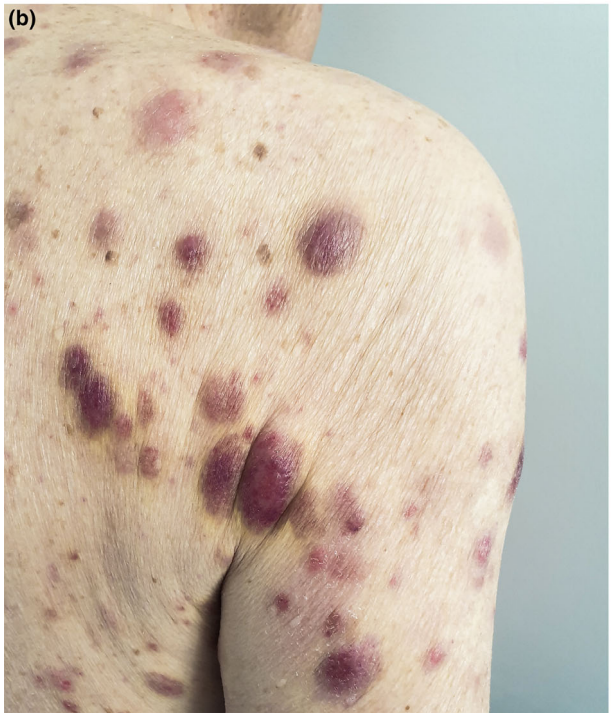


Figure 1 (a,b) Clinical images showing generalized erythematous to violaceous tumors and bruise-like patches

Flow cytometric and immunohistochemical studies were CD4, CD43, CD56, and CD123 positive in all tissue samples including peripheral blood (Fig. 3a,b). No expression of markers for T cells, B cells, NK cells, myeloid, and monocytic cells was observed. A diagnosis of blastic plasmacytoid dendritic cell neoplasm (BPDCN) was made.

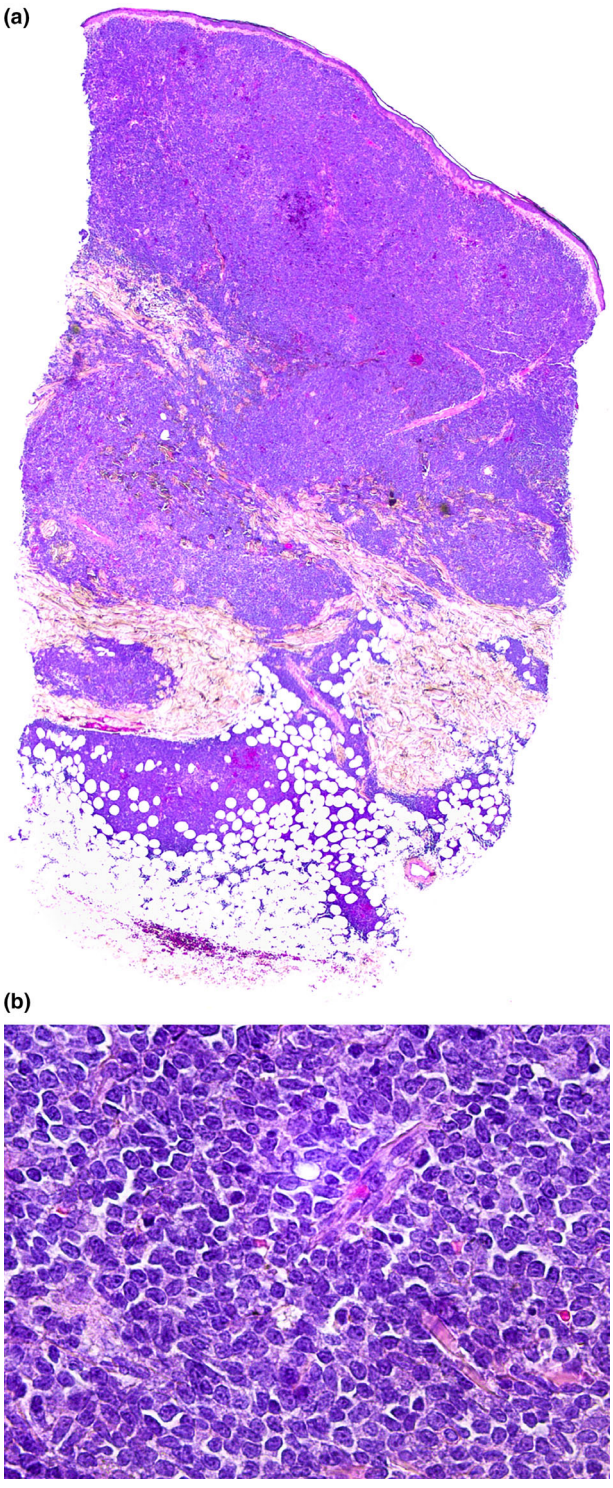


Figure 2 Histopathology features. (a) Dense dermal infiltrate extending into the subcutis but sparing the epidermis (H&E stain; ×5 magnification). (b) Detail of morphology of neoplastic cells characterized by a monotonous proliferation of medium-sized cells with round nuclei, finely dispersed chromatin, and small or absent nucleoli. (H&E stain; ×400 magnification)

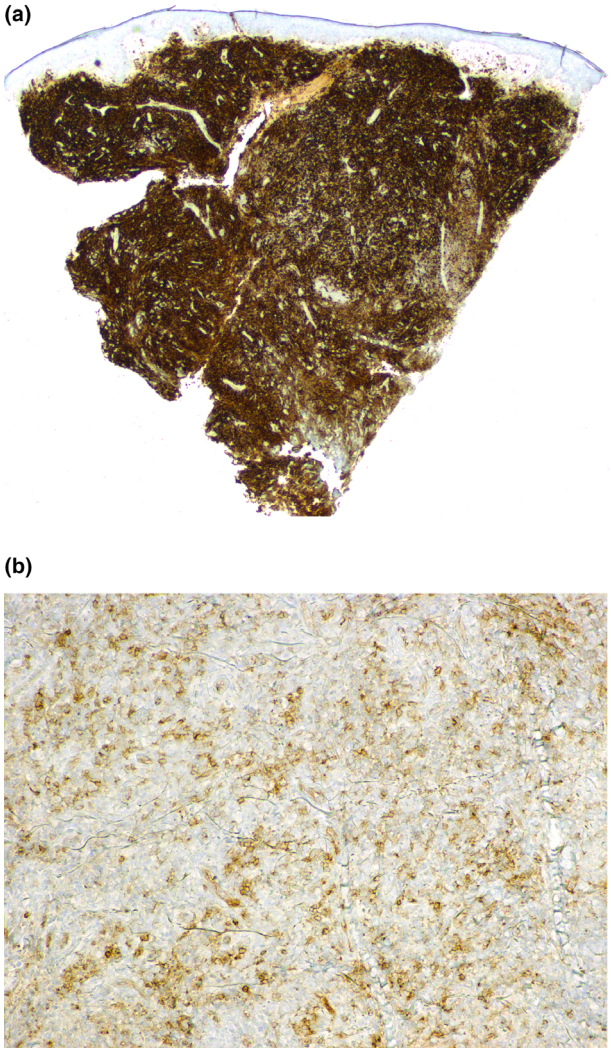


Figure 3 Immunohistochemical studies. (a,b) Positive staining of neoplastic cells for CD56 (CD56, ×25 magnification) and CD123 (CD123, ×100 magnification)

Azacitidine treatment was recommended because of the age of the patient and high toxicity of conventional BPDCN treatment. However, the patient died of pneumonia before starting chemotherapy.

BPDCN is a rare hematological malignancy derived from the precursors of myeloid-derived resting plasmacytoid dendritic cells.[1] Evolving nomenclatures have been used to describe this entity throughout the years since its first description in 1995, reflecting its complex pathophysiology. However, after the discovery of the cell of origin and better insights on the disease's biology, the last and still standing classification was defined in the 2008 World Health Organization classification of tumors of the hematopoietic and lymphoid tissues.[2]

BPDCN mostly affects elderly patients and is characterized by predominant cutaneous involvement with concomitant or ensuing spread to the bone marrow, lymph nodes, and peripheral blood. Skin lesions are usually the first symptom of BPDCN leading patients to seek medical advice, and without therapy, they rapidly disseminate. Patients typically present with asymptomatic, solitary, or multiple violaceus nodules and tumors and bruise-like macules and patches.[3]

A diagnosis of BPDCN is established by histopathologic assessment of the involved tissue coupled with germane immunophenotypic markers including CD4, CD56, and CD123 in the absence of lineage-specific markers of lymphoid, natural killer (NK), or myelomonocytic cells.[4]

The clinical course of BPDCN is aggressive, with a reported median overall survival of 24 months.[1] No standardized therapeutic approach has been established yet, and the optimal therapy remains to be defined. Intensive induction chemotherapy with regimens used for acute lymphoblastic leukemia followed by allogeneic hematopoietic stem cell transplantation is the only potentially curative treatment option.[5] However, elderly patients with low performance status and/or significant comorbidities are not eligible for these regimens and are usually treated with palliative intent with low-dose chemotherapy or best supportive care.[1]

This report portrays an exceedingly rare malignancy with an atypical full-blown presentation with disseminated skin lesions, acute leukemia, and extensive medullary and lymph node disease. Based on the growing understanding of the biological landscape of the disease, new treatment options are available and in development, and their use may challenge this malignancy's historical dismal prognosis.

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References

1 Pagano L, Valentini CG, Grammatico S, *et al*. Blastic plasmacytoid dendritic cell neoplasm: diagnostic criteria and therapeutical approaches. *Br J Haematol* 2016; **174**: 188–202.
2 Facchetti F, Petrella T, Pileri SA. Blastic plasmacytoid dendritic cell neoplasm. In: Swerdlow SH, Campo E, Harris NL, *et al*., *WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues*. Revised, 4th edn. Lyon: IARC Press. 2017.
3 Julia F, Petrella T, Beylot-Barry M, *et al*. Blastic plasmacytoid dendritic cell neoplasm: clinical features in 90 patients. *Br J Dermatol* 2013; **169**: 579–586.
4 Cota C, Vale E, Viana I, *et al*. Cutaneous manifestations of blastic plasmacytoid dendritic cell neoplasm-morphologic and phenotypic variability in a series of 33 patients. *Am J Surg Pathol* 2010; **34**: 75–87.
5 Falcone U, Sibai H, Deotare U. A critical review of treatment modalities for blastic plasmacytoid dendritic cell neoplasm. *Crit Rev Oncol Hematol* 2016; **107**: 156–162.