

A Case of Cutaneous Blastic Plasmacytoid Dendritic Cell Neoplasm

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Blastic plasmacytoid dendritic cell neoplasm (BPDCN) is a rare lymphoma that has been recognized as an independent entity in the World Health Organization (WHO) 2008 classification for cutaneous lymphomas (1) and is thought to be derived from the precursors of plasmacytoid dendritic cells (pDC) (2). This neoplasm most commonly affects middle-aged or elderly patients with predominant skin or soft tissue involvement; thus dermatologists need to be familiar with its typical clinical features. We report here a case of a 36-year-old man with disseminated multiple violaceous maculopapules and nodules on the skin of his trunk and extremities. Histopathology and immunohistological staining confirmed the diagnosis of BPDCN.

CASE REPORT

A 36-year-old man presented with a 3-month history of disseminated, multiple, violaceous maculopapules and nodules on the skin of his trunk and extremities. Initially, the patient presented with dark-red macules and papules on the right upper arm. The lesions subsequently spread over the whole body, involving even the face. Treatment as "eczema" with topical corticosteroid was initiated. Despite topical treatment, no improvement was observed. The lesions became larger and purplish-red. The patient was in a good general condition, with no weight loss or general malaise.

Physical examination revealed disseminated multiple, solid, violaceous plaques and nodules on the skin of the trunk and on the upper and lower limbs as well as the face, which were most abundant on the trunk. The diameter of the well-defined lesions

was 1–4 cm, with a glossy surface (Fig. 1A and B). There was no evident enlargement of the lymph nodes or hepatosplenomegaly.

A blood test and a skin biopsy were performed to confirm the diagnosis. Laboratory tests revealed that complete blood count, blood chemistry and urine analysis were normal. Anti-HIV, tuberculin skin (purified protein derivative), rapid plasma reagin (RPR) and *Treponema pallidum* particle agglutination (TPPA) tests were negative. Furthermore, serology for Epstein-Barr virus showed no signs of an ongoing infection. The skin biopsy revealed a dermal diffuse infiltrate composed of medium-sized monomorphous blast cells with irregular nuclei. No epidermotropism, necrosis or angiocentric growth was found. The epidermis was not involved (Fig. 2a and b). Special staining with Giemsa staining revealed the presence of a small number of mast cells in the perivascular region. Immunohistological staining showed the tumour cells were positive for CD4, CD56, CD43 and terminal deoxynucleotidyl transferase (TdT), and negative for L26, CD3, CD5, CD68, CD99, myeloperoxidase (MPO), S100 and TIA-1 (Fig. 2c–d). In addition, the tumour cells were also positive for CD123, as tested at the Queen Elizabeth Hospital in Hong Kong. Staging procedures, including computed tomography scans, ultrasound of the peripheral lymph nodes, and a bone marrow aspiration, revealed no evidence for systemic spread of the disease.

Based on the typical clinical features, histopathology and immunohistological staining results, a diagnosis of early-stage BPDCN was made. Following diagnosis, the patient was transferred to the cancer centre of Sun Yat-Sen University. Considering the patient's age and the lack of systemic spread, treatment with prednisone 30 mg/day, was given for 5 days, and the lesions almost disappeared, showing partial remission. The patient then received radiotherapy and is currently waiting for bone marrow transplantation. No new lesions have appeared for almost 4 months since he first received the therapy.

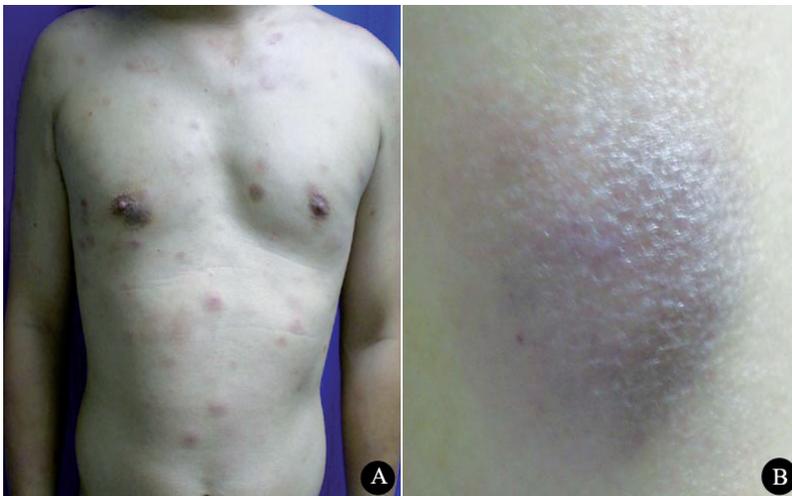


Fig. 1. (A and B) Clinical picture of blastic plasmacytoid dendritic cell neoplasm. Solid violaceous plaques and nodules on the skin of the trunk.

DISCUSSION

BPDCN is formerly known as blastic natural killer cell lymphoma (3) or CD4+/CD56+ haematodermic neoplasm (4). Cutaneous involvement is often the first manifestation of this disease, and the lesions have special features, presenting as solitary (5) or multifocal bruise-like nodules and plaques.

The aetiology of BPDCN is currently unknown. Unlike extranodal nasal type natural killer (NK)/T-cell lymphoma, no correlation with Epstein-Barr virus was evident (6). Wiesner et al. (7) analysed skin biopsy samples and found that losses of chromosomes 9, 12, 13 and 15 were detected most frequently. These results

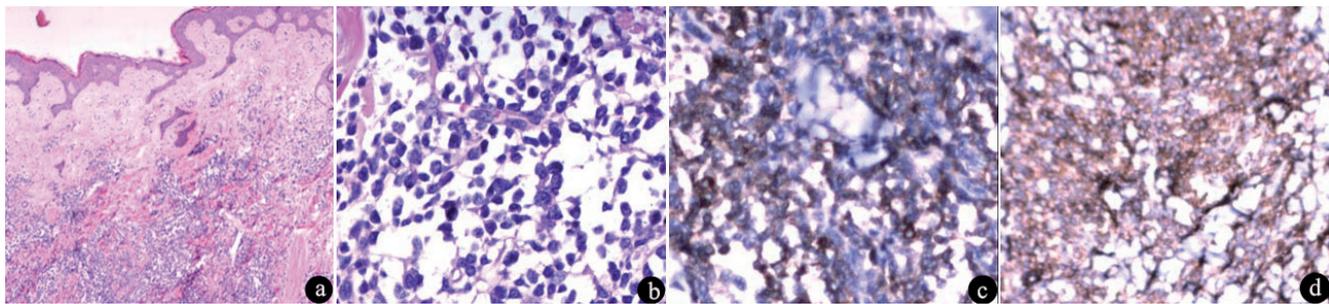


Fig. 2. (a) Diffuse non-epidermotropic infiltrate of dermis (haematoxylin and eosin (H&E) staining, original magnification $\times 40$). (b) Medium-sized monomorphic cells with irregular nuclei (H&E staining, original magnification $\times 200$). (c–d) Immunohistological staining results: positive for CD4 and CD56.

imply that alterations of the cell-cycle checkpoint controlling proteins p27 (KIP1), p16 (INK4a) and RB1 may exert a profound effect in malignant transformation in BPDCN. BPDCN always shows a rapid and fatal clinical course. The median survival time is 12–14 months, with no difference in patients presenting with or without concurrent extracutaneous involvement (4). Dalle et al. (8) showed that only 17% and 2% of patients reached 2 and 5 years of survival, respectively.

The histopathology of BPDCN shows a dense infiltration of monotonous medium-sized cells with finely dispersed chromatin and inconspicuous nucleoli. The infiltrate colonizes the dermis and subcutaneous and typically spares the epidermis, often with a Grenz zone. The tumour cells show no necrosis or angiocentric growth. Cutaneous appendages are generally erased by the tumour cell infiltration. The neoplastic cells are positive for CD4, CD56, CD43 and CD45RA. They also express the pDC-associated antigens CD123, BDCA-2, etc. But the common B-cell lineage, T-cell lineage and myelomonocytic cell lineage markers are negative with rare exceptions (1, 9). Although tumour cells of acute myeloid leukaemia with cutaneous involvement often express the CD4 and CD56 antigen on their membranes, CD123 and MPO can distinguish them easily. In addition, the absence of CD33 or MPO on immunohistochemical analysis can help to differentiate BPDCN from other myeloid tumours. The neoplasm described here was positive for CD4, CD56, CD43, CD123 and TDT, but negative for L26, CD3, CD5, CD99 and MPO, thus a diagnosis of BPDCN was made.

The response to chemotherapy, such as acute leukaemia regimens, usually results in complete remission; however, relapses occur rapidly. As reported previously, long-lasting remissions have been reported in only a few younger patients who received allogeneic stem cell transplantation (10, 11). Dalle et al. (8) showed that only aggressive initial therapy may improve the patients' prognosis and only bone marrow transplantation significantly improved the outcome.

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