

Cutaneous Blastic Plasmacytoid Dendritic Cell Neoplasm Associated with Anaemia and Thrombocytopenia

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Sir,

Blastic plasmacytoid dendritic cell (BPDC) neoplasm was known formerly as blastic natural killer (NK)-cell lymphoma, agranular CD4⁺ NK cell leukaemia, blastic NK leukaemia/lymphoma and agranular CD4⁺CD56⁺ haematodermic neoplasm/tumour. It is a clinically aggressive systemic neoplasm commonly involving the skin, which often has a fatal course. This tumour is derived from precursors of plasmacytoid dendritic cells, with a high incidence of cutaneous and bone marrow involvement and leukaemic dissemination. BPDC neoplasm is a rare type of neoplasm, with no known racial or ethnic predilection. Patients are mostly elderly, although this neoplasm can occur at any age, including in young children. It has a male/female ratio of 3.3:1 (1).

The aetiology of BPDC neoplasm is currently unknown, but its relation to myelodysplasia may indicate a similar pathogenesis. At presentation, in most cases, the neoplasm is confined to the skin, and leukemic spread after a variable period of time is the usual course. Clinically, patients usually present with asymptomatic solitary or multiple cutaneous nodules or plaques. Sometimes lesions have a bruise-like violaceous aspect (2).

Immunophenotypically, the neoplastic cells are positive for CD4, CD43, CD45RA and CD56. They also express the plasmacytoid dendritic cell-associated antigens CD123, BDCA-2/CD303, *TCL-1*, *CLA* and the interferon- α dependent molecule *MxA* (1).

CASE REPORT

A 77-year-old man was admitted to the Department of Internal Medicine for treatment of heart failure symptoms and diagnostic procedures for anaemia and cutaneous tumour lesions. Prior to admission, the patient was hospitalized in the Department of Dermatology due to skin lesions in the form of multiple nodules and plaques localized on the upper and lower limbs as well as abdominal integuments. The skin lesions developed 5 weeks prior to admission. The first violaceous papules and nodules were located on the skin of the shins and arms, and then spread to the abdomen and thorax (Fig. 1).

A medical history revealed type 2 diabetes and arterial hypertension, which had been treated for 10 years. Moreover, the patient had a 5-year history of cardiac failure, diabetic nephropathy, initial stage of renal failure and chronic obstructive pulmonary disease.

Physical examination on admission revealed disseminated multiple solid violaceous plaques and nodules on the skin of abdominal integuments as well as on the upper and lower limbs, which were most abundant on the forearms. The diameter of



Fig. 1. Multiple skin nodules and tumours on the forearm.

the lesions was 2–3 cm and their surface was glossy. Blisters developed spontaneously on the surface of single nodules and ruptured. During hospitalization for 3 weeks the lesions spread over the whole of his body, involving even the face. Marked oedema developed on the shins. Physical examinations did not reveal any enlarged peripheral lymph nodes.

On admission the patient was afebrile. Numerous crepitations were heard at the pulmonary base over the lung fields. His abdomen was soft and non-tender, with no palpable organomegaly.

During hospitalization, the microcytic anaemia worsened and inflammatory parameters increased. Within 2 weeks haemoglobin concentration decreased from 9.4 to 8.2 g/dl. The serum iron level was normal, whereas that of ferritin was elevated to 650 ng/ml (normal 30–450). The patient was transfused with two units of erythrocyte mass. White blood cell count was 13.50 K/ μ l, C-reactive protein 17 mg/l (normal 0–10). The erythrocyte sedimentation rate was 17 mm/h. Moreover, thrombocytopenia (33 K/ μ l) appeared after 2 weeks of hospitalization, the glomerular filtration rate decreased from 31 ml/min/1.73 m² to 12 ml/min/1.73 m², urea increased (from 166 to 273 mg/dl). Liver function parameters were normal. The serum glucose level increased considerably after steroid treatment.

The levels of neoplastic markers (carcino antigen 19-9, carcino-embryonic antigen, and alpha-fetoprotein) were normal, while β_2 -microglobulin was markedly increased: 18.50 mg/l (normal 0.7–3.0). IgA was normal, whereas IgG and IgM were elevated: 18.35 g/l (normal 7–16) and 2.55 (normal 0.40–2.30), respectively. Moreover, serum concentrations of calcium, alkaline phosphatase and prostatic specific antigen were within the reference values. Lactate dehydrogenase was high: 1055 U/l (normal 200–450). Thoracic spine X-ray showed degenerative changes within the thoracic and lumbar spine. Chest X-ray revealed thickened stromal markings in the lower lung fields; a slight patchy shadow was observed in the middle field of the right lung. Skull and pelvis X-ray findings were normal. Abdominal ultrasound findings revealed hepato-, spleno- and prostatomegaly. Lower thoracic computerized tomography (CT) scan showed small amounts of fluid in both pleural cavities, whereas abdominal CT scan did not reveal pathological changes. Electrocardiography was normal.

Barium contrast studies of the oesophagus, stomach and duodenum were performed, but revealed no lesions. Colonoscopy did not show any pathology of the rectum and large intestine.

The biopsy was performed from lesional skin. Histopathological examination revealed diffuse non-epidermotropic monomorphous infiltrate of medium-sized blastic cells with irregular nuclei (Fig. 2a).

The infiltrate occupied the dermis; the epidermis and the subcutaneous tissue were not involved. The immunophenotype examination showed the presence of the malignant neoplasm infiltration expressing CD45RA(+), CD56(+), CD4(+), CD43(+), CD20(-), CD3(-), CD30(-), MPO(-), TdT(-), CD-138(-), Ki67 90%.

The microscopic picture and immunohistochemical reactions corresponded to a diagnosis of BPDC neoplasm, formerly known as CD4+CD56+ blastic NK-cell lymphoma.

Moreover, the patient underwent trephine biopsy of bone marrow. The bone marrow filled 70% of the surface of marrow lacuna and included peri-trabecular infiltrations consisting of CD45RA(+), CD56(+), CD4(+), CD43(+), CD20(-), CD3(-), MPO(-), TdT(-), CD-138(-), cells constituting about 40% of marrow texture, which corresponded to blastic plasmacytoid dendritic cell neoplasm (Fig. 2b).

Treatment involved intensive insulin therapy and infusions of sodium chloride, compound electrolyte solution, prednisone and furosemide. Despite therapy, the features of heart failure and renal failure increased and the patient died 8 weeks after the onset of skin lesions due to pulmonary oedema resistant to pharmacological treatment, together with renal and respiratory failure. Chemotherapy was not instituted due to the patient's severe condition.

DISCUSSION

This case of BPDC neoplasm showed a rapid and fatal course. The patient presented with disseminated multiple skin nodules and bone marrow involvement. Regional lymph nodes were not enlarged, though peripheral lymphadenopathy in this type of neoplasm is common. The patient showed peripheral blood involvement with anaemia and thrombocytopenia. In approximately 10–20% of cases of this neoplasm myelomonocytic leukaemia or acute myeloid leukaemia can develop (1). However, neither was observed in the case described here. In our patient, the time between the onset of skin lesions to death was 8 weeks. The neoplasm developed aggressively. Histopathological and im-

munochemical findings revealed the presence of BPDC neoplasm. During hospitalization, skin lesions disseminated rapidly and some of them ruptured.

BPDC neoplasm, accounts for 0.7% of cutaneous lymphomas. Survival time is often short despite initial limited-stage disease and treatment with systemic chemotherapy (3). Agranular CD4+/CD56+ haematodermic neoplasm, first described by Adachi et al. (4) in 1994, is a distinct form of lymphoma with aggressive behaviour and marked predilection for cutaneous involvement. Since 1994, more than 100 cases of CD4+/CD56+ haematodermic neoplasm have been described (5). Because of CD56 positivity, natural killer cells were initially suggested as cells of origin in this tumour. In the WHO-EORTC classification, the term blastic NK-cell lymphoma was replaced by CD4+/CD56+ haematodermic neoplasm because of its derivation from precursors of plasmacytoid dendritic cells (5). Currently the term CD4+/CD56+ haematodermic neoplasm has been replaced by BPDC neoplasm. The disease has a distinct clinical presentation of primary skin lesions in 100% of patients, as papules, nodules, or bruise-like lesions, bone marrow involvement with or without leukaemic phase, and a fatal course (6). The skin lesions are localized at onset and become multiple and more generalized during the course of the disease. The median survival time has been 14 months, with no difference in patients presenting with or without concurrent extracutaneous involvement (7). The absence of CD33 or myeloperoxidase on immunohistochemical analysis can help to differentiate BPCD from other myeloid tumours. In addition, most cells are CD3-, CD2-, CD4+ and CD56+, and oncogenic transformation is not associated with Epstein-Barr virus (8).

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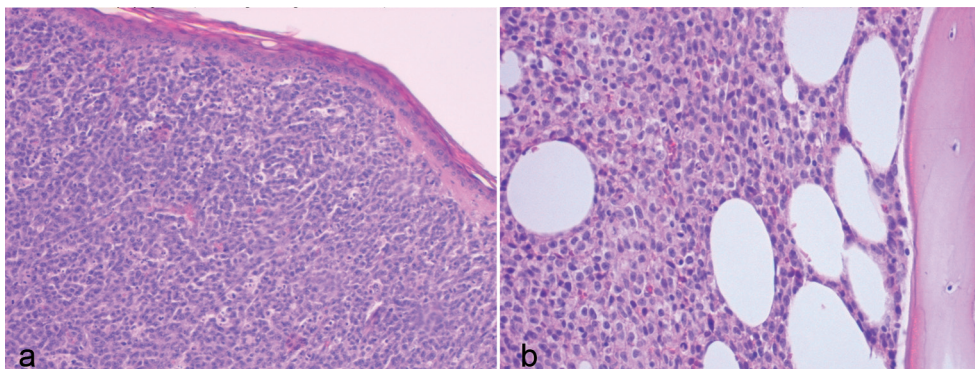


Fig. 2. (a) Diffuse non-epidermotropic infiltrate of dermis of medium-sized cells with finely dispersed chromatin and scanty cytoplasm (haematoxylin and eosin (H&E), original magnification $\times 200$). (b) Bone marrow involvement of blastic plasmacytoid dendritic cell neoplasm (H&E, original magnification $\times 200$).

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