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Case Report

Rapidly progressing blastic plasmacytoid dendritic cell neoplasm causing diffuse skin thickening: A case report with sequential computed tomography examinations

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ABSTRACT

Blastic plasmacytoid dendritic cell neoplasm is a rare aggressive myeloid malignancy thought to be derived from precursor plasmacytoid dendritic cells. Rapid progression and poor prognosis have been known. We herein present a case of BPDCN in a previously healthy man who presented with suddenly developed multiple deep purple skin rashes, with sequential computed tomography examinations. The follow-up computed tomography demonstrated that multiple skin nodules observed in the initial MRI fused, resulting in a thickening of the entire skin, with some surface erosions and crusting. Blastic plasmacytoid dendritic cell neoplasm should be considered in the differentials in patients with a sudden onset and rapidly progressing skin rash or thickening.

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Introduction

Blastic plasmacytoid dendritic cell neoplasm (BPDCN) is a rare aggressive myeloid malignancy classified under World Health Organization (WHO) 2016 guidelines in its own category [1]. It mainly affects patients over 60 years old, and skin is the most frequently involved organ with frequent involvement of the bone marrow, lymph nodes, and peripheral blood [2]. Rapid

progression to the terminal leukemic phase is common, resulting in a short mean survival of 12–16 months [3]. To our knowledge, there have been at least 11 reports with CT findings [4–14], including 4 ¹⁸F- fluorodeoxyglucose positron emission tomography / CT (¹⁸F-FDG PET/CT) reports, associated with BPDCN; however, knowledge of chronological changes on sequential CT examinations have been limited [13,14]. We herein report a case of a patient with rapidly progressing BPDCN with a sequential evaluation on CT.

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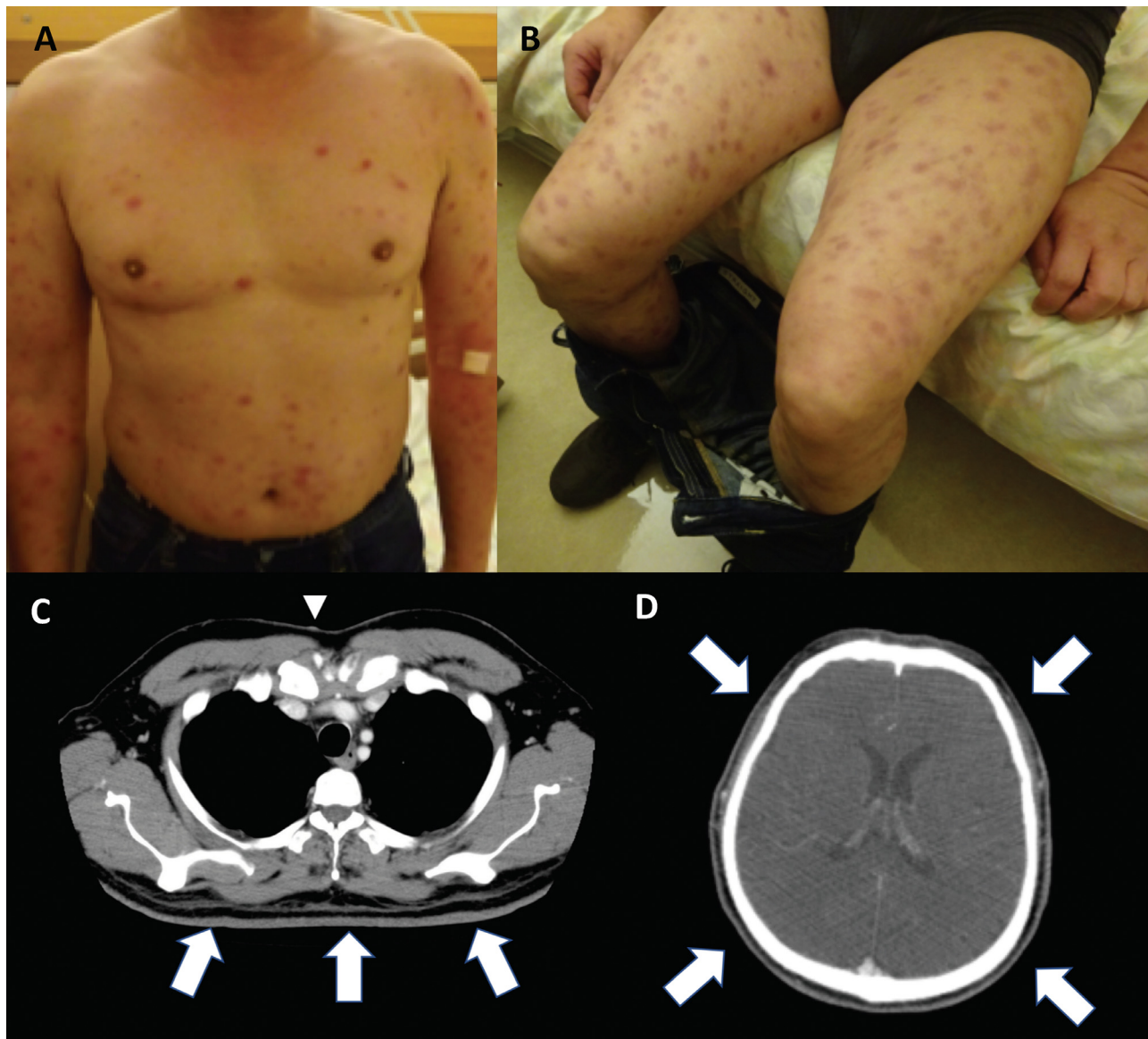


Fig.1 – Multiple deep purple skin rashes are observed all over the body (A,B). Axial contrast enhanced CT shows multiple skin nodules (arrowhead) and skin thickening (arrow) of the body (C, D).

Case report

A 56-year-old previously healthy man presented with a skin rash that started suddenly. There are many deep purple skin rashes. (Fig. 1). Blood tests showed no abnormal findings except for high soluble interleukin-2 receptor levels (672 U/ml). His past medical history and family history were unremarkable. CT showed multiple skin nodules extending into the subcutaneous tissue were observed (Fig. 1). Lymphadenopathy or involvement of other organs was not found. A skin biopsy from the right upper arm was performed, and the histopathological exam found a monoclonal proliferation of the tumor cells. Immunohistochemical tests are positive for CD4, CD56 and CD68, and negative for CD3 and CD20. Markers specific for BPDCN are negative for CD123, but positive for

CD303. These led to the diagnosis of BPDCN (Fig. 2). The patient received chemotherapy with hyper-fractionated cyclophosphamide, vincristine, doxorubicin, dexamethasone alternating with high-dose cytarabine and methotrexate regimen for 4 courses, which improved the skin lesions. The scheduled bone marrow transplant was decided not to be performed due to the patient's refusal, and the patient was placed on observation. 5 months later (7 months since onset), the patient presented with generalized pain, insufficient oral intake, and decreased renal function with an estimated glomerular filtration rate of 10.6 ml/min/1.73m², and was readmitted to the hospital. Multiple enlarged skin nodules fused to each other, resulting in a thickening of the entire skin, with some surface erosions and crusting (Fig. 3). Histopathological examination again confirmed BPDCN. Given the patient's poor general condition, palliative treatment was performed. Unfortunately, the

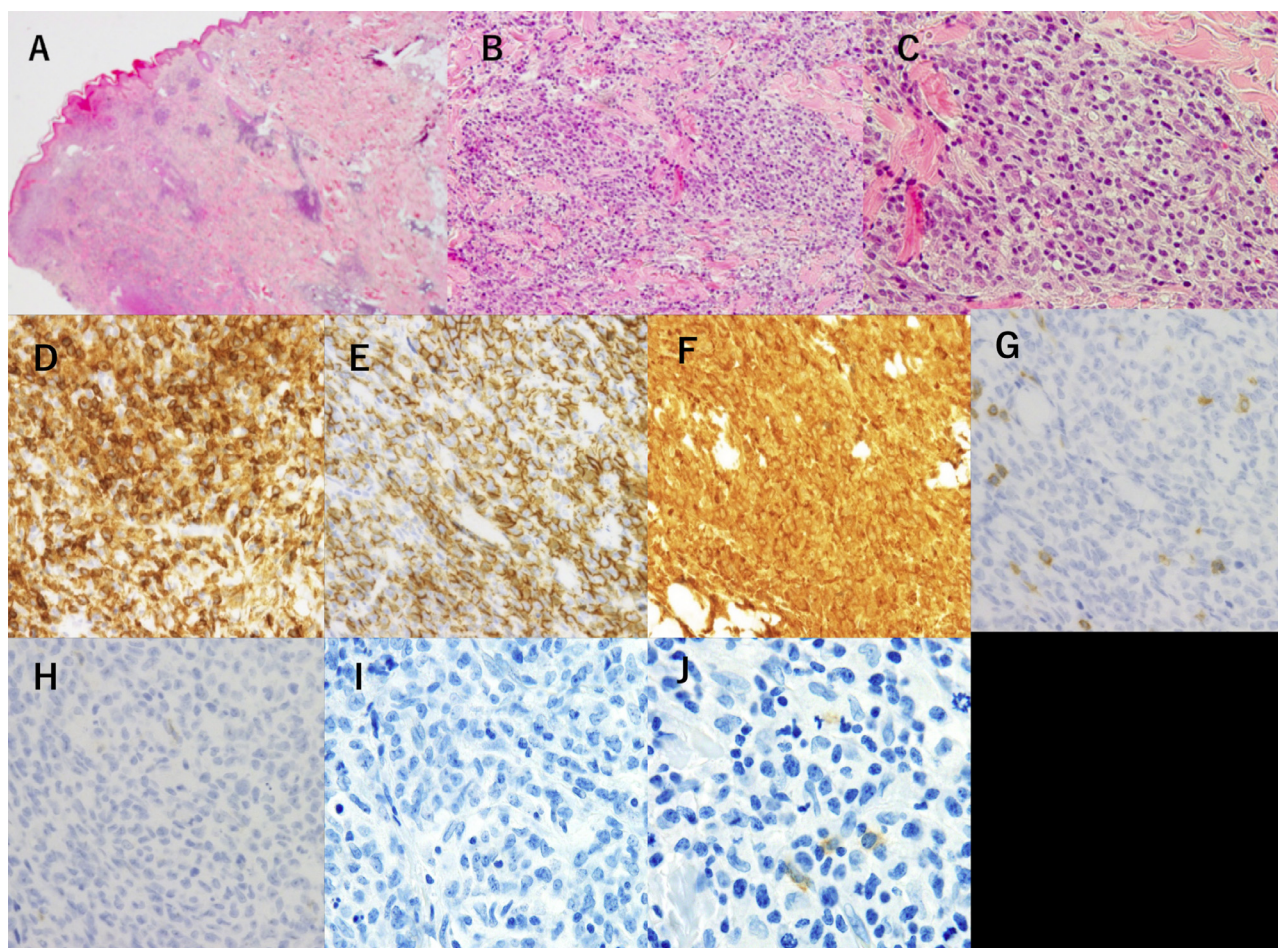


Fig. 2 – Pathological specimen from the initial skin biopsy. Tumor cells with a high N/C ratio are seen in the stroma from the dermis to the subcutaneous adipose tissue. Tumor invasion into the epidermis is not evident (A-C). Immunohistochemical tests are positive for CD4 (D), CD56 (E) and CD68 (F), and negative for CD3 (G) and CD20(H). Markers specific for BPDCN are negative for CD123 (I), but positive for CD303 (J).

patient died ten days after readmission due to worsening disease and progressive decline in renal function.

Discussion

BPDCN is a rare, clinically aggressive hematologic malignancy thought to be derived from precursor plasmacytoid dendritic cells (pDCs). BPDCN occurs in patients older than 60, and male predominance has been known (incidence of 0.05 in males vs 0.02 in females per 100,000 population) [15]. 10–20% of the patients have previous or concurrent hematologic diseases including myelodysplastic syndrome, chronic myelomonocytic leukemia [16]. Clinically, skin is involved in basically every case, followed by the bone marrow, peripheral blood, and lymph nodes [2]. Skin lesions are often a deep purple color, and patients often develop multiple lesions. Rapid and aggressive progression to the terminal leukemic phase is common. The skin rash can be developed suddenly and spread rapidly, as seen in the present case. The diagnosis of BPDCN is

based on the identification of clonal cells derived from pDCs. BPDCN is immunophenotypically characterized by the expression of pDCs-specific markers, particularly CD123 and/or CD303 [17].

CT has been mainly used to assess the extent and depth of the skin lesions, as well as the metastases in patients with BPDCN [4–14]. CT shows round and ovoid homogeneous cutaneous mass with soft tissue density with or without subcutaneous invasion as seen in the present case. Although there has been at least eleven reports of BPDCN with CT findings, knowledge of chronological changes of CT findings has been limited. To our knowledge, only two case reports demonstrated the sequential CTs, both of which showed the chronological changes of the involved spleen [13,14], we first report the time course of skin lesions of BPDCN with sequential CT examinations [7]. CT demonstrated that multiple skin nodules fused to each other, resulting in a thickening of the entire skin, with some surface erosions and crusting in this case. Given that the patient was not receiving chemotherapy after the first discharge, changes from the initial CT to the follow-up CT seemed to be the natural history of BPDCN, which has been largely unknown. Other

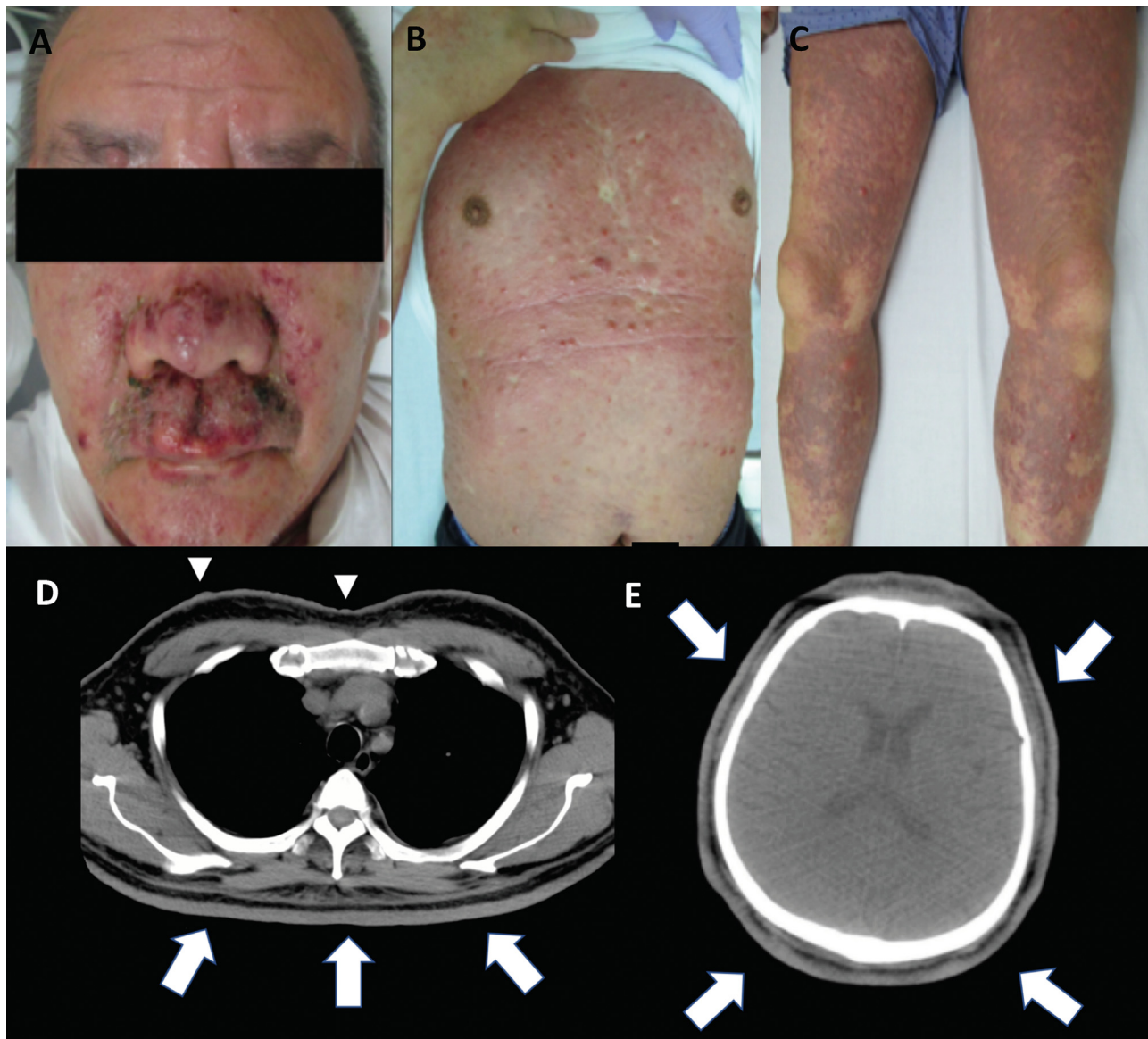


Fig. 3 – At the time of readmission (5 months later), multiple masses and skin sclerosis throughout the body has worsened, with some surface erosions and crusting (A-C). The multiple nodules are fused and the skin thickening becomes worse (D, E).

reported CT imaging findings of BPDCN include pulmonary ground-glass opacity with interlobular septal thickening, indicating diffuse alveolar hemorrhage, in a patient with BPDCN involving the lungs [5], and hepatosplenomegaly resulting in atraumatic splenic rupture [13].

Clinically, differential diagnoses of the skin lesions include insect bites, severe drug eruptions, malignant lymphoma (mycosis fungoides, Sezary syndrome, etc.), Kaposi's sarcoma, and BPDCN. Since it is often difficult to differentiate BPDCN by visual inspection alone, blood samples and skin biopsies should be taken, as well as detailed history taking.

Given the rarity, no standard of care has existed until tagraxofusp (a CD123-directed cytotoxin consisting of recombinant human interleukin-3 fused to a truncated diphthe-

ria toxin) was approved by the U.S. Food and Drug Administration (FDA) in 2018. Current treatment includes the use of tagraxofusp if available and feasible. If not, patients with good performance status would receive induction chemotherapy, typically with the regimen tailored to acute lymphocytic leukemia with intrathecal prophylaxis followed by stem cell transplantation at first remission. Older patients who are not fit for intense chemotherapy can be considered for lower intensity treatment, typically with a hypomethylating combination regimen. Surgical and radiation options have been tried in patients with limited skin disease with variable results [18]. In the present case, however, BPDCN progressed rapidly without stem cell transplantation at the patient's request.

Conclusion

We present a case of progressive BPDCN with sequential CT examinations. The follow-up CT demonstrated that multiple skin nodules fused, resulting in a thickening of the entire skin, with some surface erosions and crusting in this case. BPDCN should be considered in the differentials in patients with a sudden onset and rapidly progressing skin rash or thickening.

Patient consent

Informed consent to include the patient's information in the publication of this case report was obtained.

Declaration of Competing Interest

None.

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