A Rare Case Report --Mimicking Lymphoma 18F-FDG PET/CT Findings of Blastic Plasmacytoid Dendritic Cell Tumor in a Young Female Patient

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AUTHORS' CONTRIBUTIONS
Hong ShaoMei was responsible for the collection of data and drafted the manuscript.
Xiao Gang contributed to the pathological diagnosis and the collection of relevant pathological data.
Ma LinFeng served as the PETCT reporting doctor for this case and was the corresponding author of this paper.
All authors read and approved the final manuscript.

DISCLOSURES
None.

CONSENT
Consent form obtained.

ABSTRACT

Blastic plasmacytoid dendritic cell neoplasm (BPDCN) is a rare hematologic malignancy originating from plasmacytoid dendritic cell precursors and is often misdiagnosed. Previous 18F-FDG PET/CT case reports have primarily involved middle-aged or elderly male patients. In this case, a 29-year-old female presented with misdiagnosed urticaria because of generalized rash and pruritus refractory to steroids. Back to hospital with recurrent enlarged and painful cervical lymph nodes after half a year. 18F-FDG PET/CT imaging revealed multiple small or slightly enlarged lymph nodes with FDG avidity throughout the body, as well as active bone marrow and active spleen, but no significant FDG uptake in the skin lesions. Imaging suggested a potential diagnosis of lymphoma. A cervical lymph node biopsy subsequently confirmed BPDCN.

CASE REPORT

CASE REPORT

The patient, a 29-year-old female, presented to our hospital with the chief complaints of “recurrent systemic rashes for 6 months and bilateral cervical lymphadenopathy for 2 months”. Six months prior, she developed generalized skin erythema and wheals without obvious triggers, accompanied by itching. The rashes subsided rapidly, leaving behind pigmentation, and there was no fever or other discomfort. She was admitted to the dermatology department. Physical examination revealed local flaky brown spots on the neck and trunk skin, covered with a few scales. Scattered red papules were observed on the chest, with some papules covered by dark red scabs that faded upon pressure. There were also scattered flaky edematous erythema on both upper limbs and thighs, with increased skin temperature. The left forearm was relatively swollen, and irregular light red wheals were found on the inner side of the left thigh, with slight tenderness in the limb rashes (Figure 1). Routine blood tests showed neutropenia, increased platelet count, lymphocyte ratio, and eosinophil ratio, as well as elevated immunoglobulin E (IgE). Coagulation function, rheumatic immunity, and infection indicators were unremarkable. The patient was diagnosed with “acute urticaria”. After steroid and anti-allergic treatment, symptoms improved slightly, but recurrent erythemas and papules persisted. Two months ago, she experienced recurrent bilateral cervical lymph node swelling and pain, accompanied by intermittent low-grade fever ranging from 37.5-38°C, without night sweats or weight loss. She was then admitted to the Hematology Department of our hospital six months later. Her past medical history was unremarkable. Physical examination showed local flaky brown spots on the neck and trunk skin, covered with a few scales. Scattered red papules were observed on the chest, and erythema was present on the trunk and limbs, but no wheals were seen. Multiple non-tender enlarged lymph

nodes were palpable in the bilateral submandibular and neck areas. Laboratory tests showed only a slight increase in the total white blood cell count.

To evaluate her overall condition, the patient underwent 18F-FDG PET/CT examination. The report revealed multiple enlarged lymph nodes in the bilateral parotid glands, levels I to V of both necks, the nape of the neck, bilateral axillae, hepatoduodenal ligaments, and bilateral inguinal regions. The bilateral tonsils and nasopharynx showed increased metabolism. The spleen was slightly enlarged with slightly increased metabolism, and there was diffuse and mildly elevated bone marrow metabolism in the axial bones and proximal limbs. Lymphoma was suggested (Figure 2-6). For further diagnosis and treatment, the patient underwent right posterior cervical lymphadenectomy. Postoperative pathology demonstrated partial disappearance of the lymph node structure, expansion of the paracortical area, and proliferation of medium-sized plasmacytoid cells with sparse cytoplasm. Immunohistochemistry showed tumor cells positive for TDT, CD123, and CD4, and negative for CD20, PAX5, CD2, CD3, CD7, CD15, CD30, CD33, CD56, MPO, CyclinD1, CXCL-13, and CK. In situ hybridization for EBER was negative. The lesions were consistent with BPDCN (Figures 7, 8).

DISCUSSION

Etiology & demographics

BPDCN is an exceedingly rare hematologic malignancy that originates from plasmacytoid dendritic cell precursor cells. According to available statistics, its incidence rate in the United States is approximately 4 per 10 million individuals [1, 2]. In China, only sporadic case reports have been documented, and specific incidence statistics are currently unavailable. The etiology of BPDCN remains unclear. To date, no definitive environmental or genetic risk factors for BPDCN have been identified. The median age at diagnosis ranges from 53 to 68 years, with a male-to-female ratio of 2-4:1 [3, 4]. Although BPDCN predominantly affects middle-aged and elderly individuals, cases have also been reported in other age groups [5].

Clinical & imaging findings

Diagnosis of BPDCN relies on clinical presentation, histopathology, immunophenotyping, and medical imaging. Currently, ^{18}F-FDG PET/CT imaging findings in BPDCN lack specificity, and relevant reports are sparse. The PET/CT presentation in this case resembled lymphoma, yet differed from previously reported cases.

Cutaneous involvement is the initial symptom in 90% of patients, typically presenting as multiple bruise-like lesions, plaques, or nodules on the head, trunk, and limbs, and may be accompanied by erythema, purpura, and pigmentation [4,6,7]. The patient in this case presented with multiple wheals, papules, erythema, and brown spots scattered on the neck, trunk, and limbs, with pigmentation as the initial symptom. She was initially diagnosed with acute urticaria. After anti-allergy and hormone therapy, the wheals subsided, but the papules, erythema, and brown spots showed no significant improvement. Although a biopsy of the rash was not performed, BPDCN was still considered the primary cause of the patient's rash. The lack of obvious increased skin metabolism on PET/CT in this case may be related to the superficial nature of the skin lesions and minimal tumor infiltration.

Most BPDCN patients also exhibit extracutaneous manifestations, such as multiple superficial lymphadenopathy, low-grade fever, and fatigue [4,6,7]. This patient developed bilateral cervical lymphadenopathy and pain several months after the onset of cutaneous symptoms. The symptoms were recurrent and accompanied by low-grade fever, consistent with the clinical manifestations of BPDCN reported in the literature.

In immunohistochemistry, BPDCN is positive for CD123, CD4, and/or CD56, expresses at least one plasmacytoid dendritic cell (pDC) marker (TCF4, TCL1, CD303, or CD304), and does not express T-cell, B-cell, myeloid monocyte, or NK-cell markers; or if at least three pDC markers are expressed and all expected negative markers are absent, an immunophenotypic diagnosis can be made [8,9]. Immunohistochemistry of the cervical lymph node biopsy from this patient showed positive for TDT, CD123, and CD4, with no expression of T-cell markers (CD3, CD7, CD30), B-cell markers (CD20, CD30), myeloid monocyte markers (CD15, CD33, MPO), NK-cell markers (CD2), etc. The diagnosis of BPDCN was confirmed following a collaborative analysis and discussion between our hospital's pathology department and experts from Hong Kong.

BPDCN usually presents on PET-CT with slightly increased radioactive uptake in skin lesions, enlarged lymph nodes, involved bone marrow, and affected organs. The reported SUVmax range in the literature is 1.9-2.4 [10-13]. In addition to mildly increased metabolism in multiple enlarged lymph nodes, extensive bone marrow, tonsils, posterior nasopharyngeal wall, and right gluteus medius muscle, this patient also had a mildly enlarged and metabolically active spleen. The incidence of bone marrow infiltration in BPDCN is relatively high. We believe that the multifocal high metabolic changes observed in the bone marrow on PET-CT are likely caused by BPDCN infiltration. However, it is regrettable that the patient did not undergo bone marrow aspiration biopsy, and thus we are unable to definitively confirm the cause of the high metabolic activity in the bone marrow. The SUVmax range was 1.8-8.4, which was higher than that reported in the literature.

Treatment & prognosis

Treatment options for BPDCN include conventional chemotherapy, the biopharmaceutical agent tagraxofusp, and stem cell transplantation. BPDCN is an aggressive neoplasm of immature cells and generally carries a poor prognosis, with a median survival of 12 to 27 months. Longer survival is observed in pediatric cases [14].

Differential Diagnoses

The differential diagnosis of BPDCN needs to be distinguished from lymphoma, particularly. Additionally, systemic immune reactions caused by infection, autoimmune diseases, and adult-onset Still's disease (AOSD) also need to be distinguished from BPDCN. Lymphoma is characterized by multiple, symmetrically enlarged lymph nodes with high FDG uptake, typically involving the mediastinum, abdomen, and pelvis, and rarely presents with significant skin involvement. Systemic immune reactions caused by infections may show enlarged lymph nodes and hepatosplenomegaly with mild FDG uptake, and imaging findings are variable depending on the site of infection, commonly manifesting as pulmonary inflammation or pleural effusion. Autoimmune diseases generally exhibit non-specific findings on PET/CT, such as joint inflammation or pleural effusion, with increased FDG uptake in areas of inflammation but without clear tumor lesions. AOSD is non-specific on PET/CT, primarily characterized by enlarged lymph nodes and hepatosplenomegaly, and unlike BPDCN, it does not typically present with specific skin lesions or significant FDG-avid skin involvement. The diagnosis of BPDCN relies on histopathology and immunohistochemistry. Patients undergoing PET/CT whole-body imaging can not only assess the general condition but also guide tissue biopsies to aid diagnosis.

CONCLUSION

BPDCN is an extremely rare hematological malignant tumor, and its diagnosis ultimately relies on pathological and immunohistochemical results. This case differs from those reported in the literature. Firstly, the patient in this case is a young woman. This disease tends to occur in middle-aged and elderly men, with fewer reports of cases in young women. Secondly, we propose that skin lesions may not show metabolic uptake on PET-CT imaging. However, given the lack of skin pathology in this case, this hypothesis requires further investigation to be validated. Furthermore, in this case's PET/CT, in addition to lymph node, increased metabolism was also observed in the bone marrow□spleen, nasopharynx, and tonsils, suggesting possible involvement of these organs. The SUVmax values in this case were higher than those reported in the literature.

TEACHING POINT

1. BPDCN predominantly occurs in middle-aged and elderly men; however, it is not restricted to this demographic and can also present in other age groups, including young women.

2. Cutaneous manifestations frequently represent the initial and mainly symptomatology of BPDCN; however, these lesions may not exhibit metabolic uptake on PET-CT imaging.

QUESTIONS

Question 1: In which age group do Blastic plasmacytoid dendritic cell neoplasm tumors tends to occur?

1. Newborns.
2. Children.
3. Young people.
4. Middle-aged and elderly men. (applies)
5. Older women.

Explanation: Unlike lymphoma, Blastic plasmacytoid dendritic cell neoplasm is more common in m Middle-aged and elderly men. [The median age at diagnosis ranges from 53 to 68 years, with a male-to-female ratio of 2-4:1.]

Question 2: Where is the first common clinical organ of BPDN disease?

1. Skin. (applies)
2. Lymph nodes.
3. Liver.
4. Spleen.
5. Bone marrow.

Explanation: The initial symptom in 90% of patients is involvement of skin, including multiple bruise-like lesions, plaques, or nodules on the head, trunk, and limbs, and may be accompanied by erythema, purpura, and pigmentation. [Cutaneous lesions are the most frequent initial symptom of BPDCN].

Question 3: What are its immunohistochemical characteristics of BPDCN?

1. CD3, CD4, CD8.
2. TCF4, TCL1, CD303, or CD304.(applies)
3. CD19, CD20,CD22.
4. CD15, CD33, MPO.
5. CD2, CD16, CD56.

Explanation: Blastic plasmacytoid dendritic cell neoplasm originates from a malignancy of dendritic cells, which expresses plasmacytoid dendritic cell marker including TCF4, TCL1, CD303, and CD304). B-cell markers are CD19, CD20, CD22, and T-cell markers include CD19, CD20,CD22. Myeloid monocyte markers are CD15, CD33, MPO), as well as CD2, CD16, CD56 of NK-cell markers.. [Immunohistochemistry of the cervical lymph node biopsy from this patient showed positive for TDT, CD123, and CD4, with no expression of T-cell markers (CD3, CD7, CD30), B-cell markers (CD20, CD30), myeloid monocyte markers (CD15, CD33, MPO), NK-cell markers (CD2), etc.]

Question 4: Which of the following is not a common manifestation of reported BPDN on PET/CT imaging?

1. Multiple active lymph nodes throughout the body.
2. Liver and spleen metabolism slightly enlarged.
3. Always intense activities in lymphadenopathies and extranodal organs. (applies)
4. Bone mass, nasopharynx and tonsils may be involved.
5. Difficult to identify skin lesions.

Explanation: BPDCN typically have skin lesions, enlarged lymph nodes, bone marrow involvement, and affected organs with slightly increased radioactive uptake on PET/CT. Except the skin lesions are often unremarkable FDG uptake, the other lesions always mildly or moderately metabolic. [The reported SUVmax range in the literature is 1.9-2.4]

Question 5: Which disease should be differentiated from the manifestations of BPDN on PET/CT?

1. Lymphoma.(applies)
2.Virus infection.(applies)
3.SLE.(applies)
4. Adult-onset Still's disease (AOSD).(applies)
5.Lymphatic tuberculosis.(applies)

Explanation: Lymphoma, tuberculosis infection, viral infection, connective tissue disease, etc. can all cause skin lesions, accompanied by involvement of systemic lymph nodes, liver, spleen, bone marrow, etc. Lymphoma is mainly tumor infiltration, while infection and connective tissue disease may cause activated mononuclear cell - macrophages that have increased FDG uptake, which requires differential diagnosis from BPDN. [the differential diagnosis of BPDCN needs to be distinguished from lymphoma, particularly. Additionally, systemic immune reactions caused by infection, autoimmune diseases, and adult-onset Still's disease (AOSD) also need to be distinguished from BPDCN.]

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FIGURES

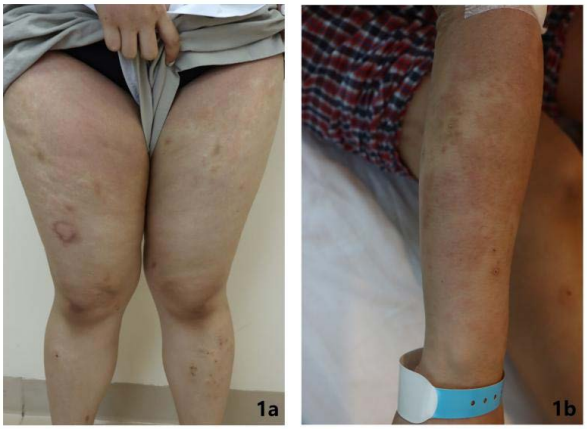

Figure 1: A 29-year-old female with BPDCN presented with scattered flaky edematous erythema, irregular light red wheals, and small flaky brown spots on both lower limbs. Papules were scattered on both sides of the lower legs, with some surfaces covered by dark red scabs (Figure 1a). Large areas of pigmentation and brown spots were observed on the left forearm, along with several scattered dark red papules (Figure 1b).

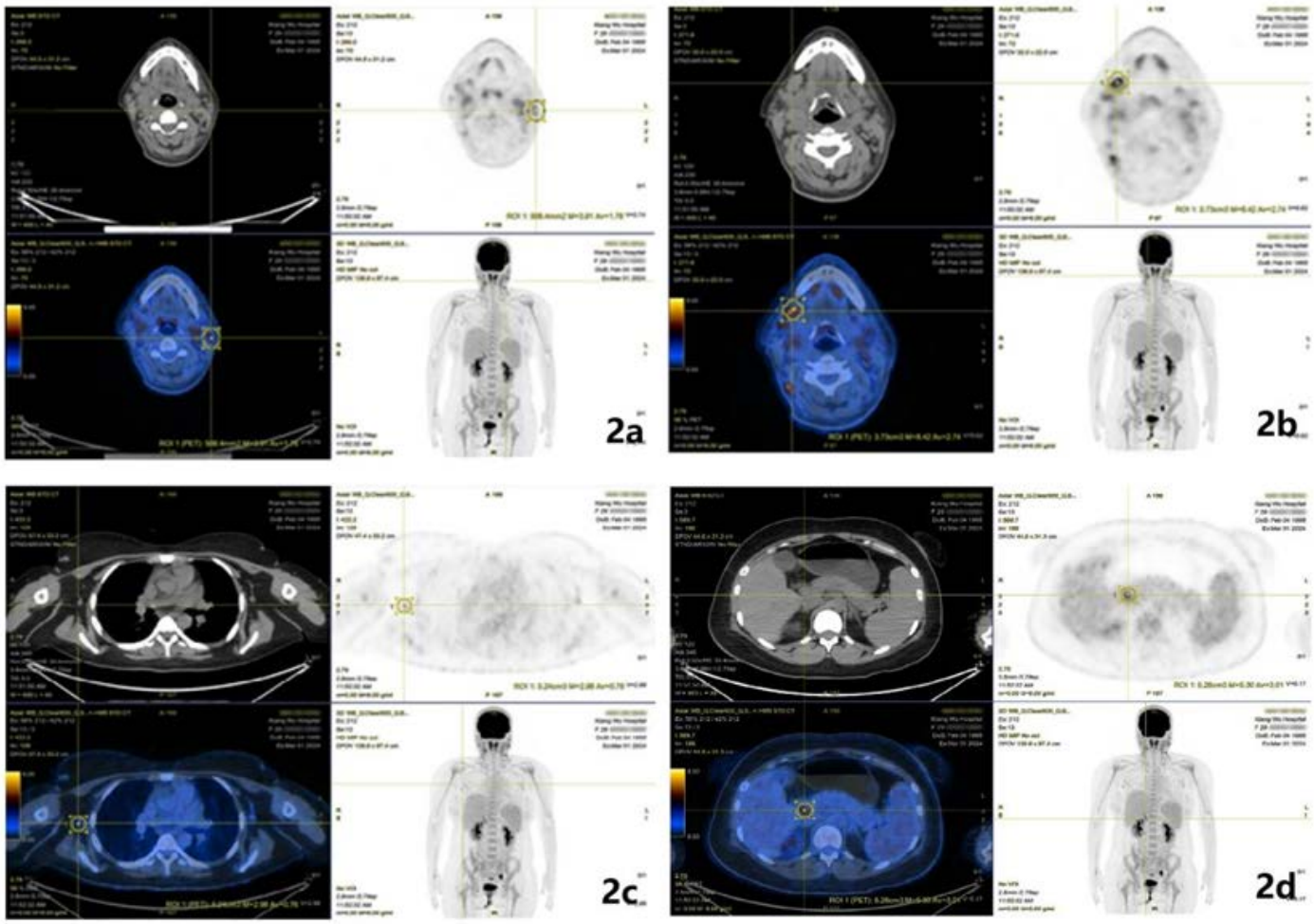

Figure 2: A 29-year-old woman with BPDCN underwent an 18F-FDG PET/CT examination, which revealed multiple active lymph nodes throughout the body with an SUVmax ranging from 1.8 to 8.4.

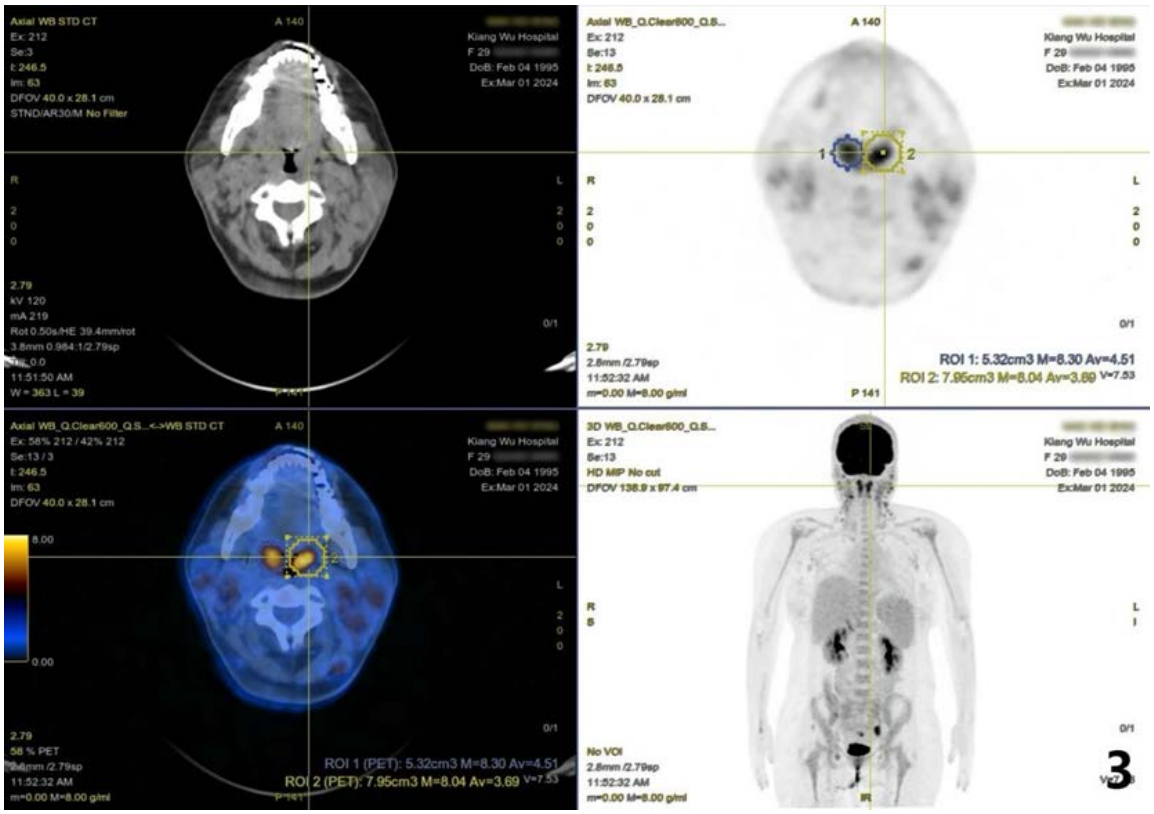

Figure 3: A 29-year-old woman with BPDCN underwent an 18F-FDG PET/CT examination. Bilateral tonsillar enlargement with increased metabolism was observed, with SUVmax values of 8.3 on the right and 8.0 on the left.

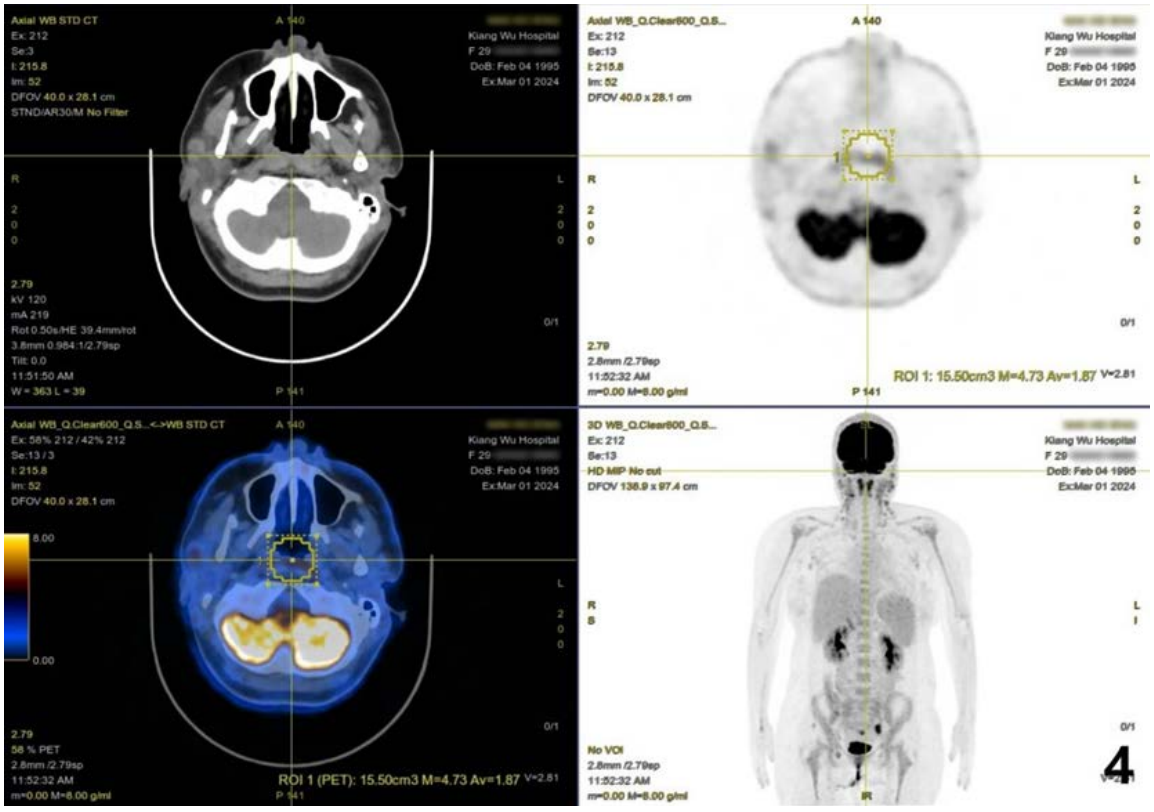

Figure 4: A 29-year-old woman with BPDCN underwent an 18F-FDG PET/CT examination. The posterior wall of the nasopharynx exhibited an SUVmax of approximately 4.7.

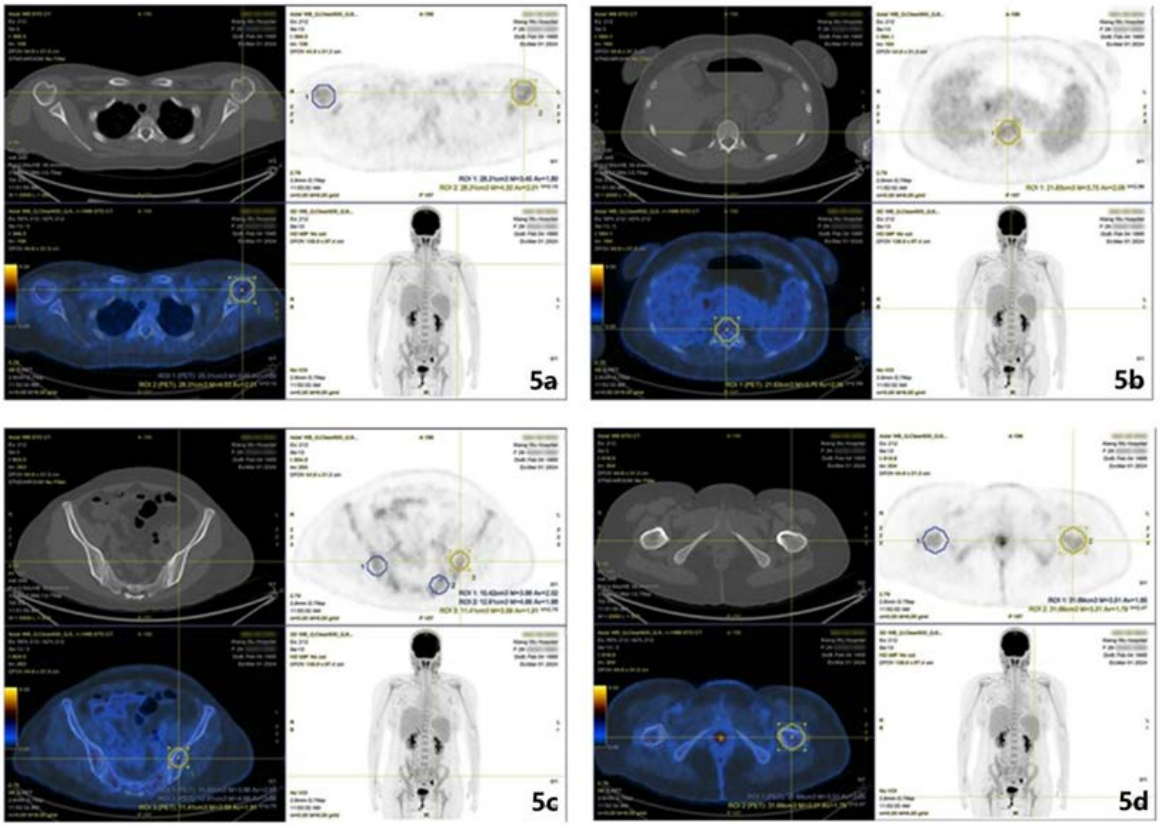

Figure 5: A 29-year-old woman with BPDCN underwent an 18F-FDG PET/CT examination. The bone marrow showed an SUVmax ranging from 3.3 to 4.6.

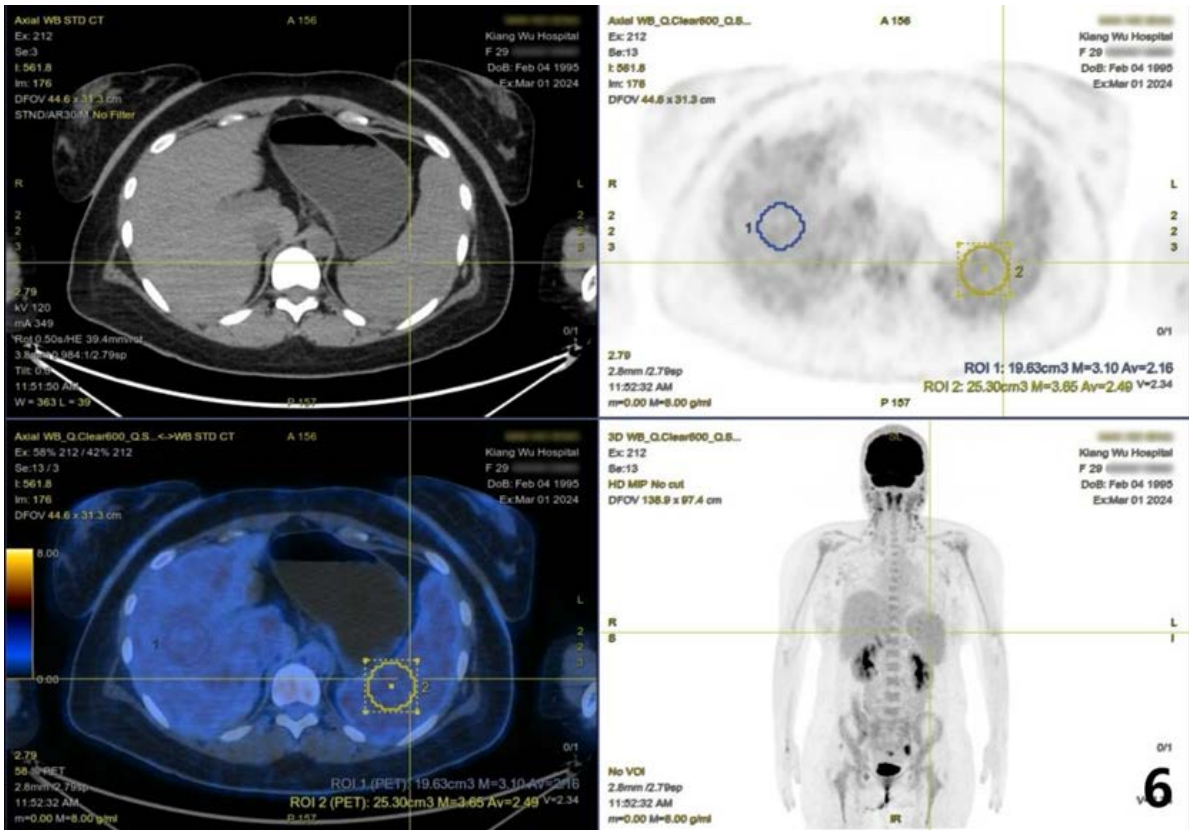

Figure 6: A 29-year-old woman with BPDCN underwent an 18F-FDG PET/CT examination. The spleen demonstrated an SUVmax of 3.7, which was slightly higher than the liver's SUVmax of 3.1.

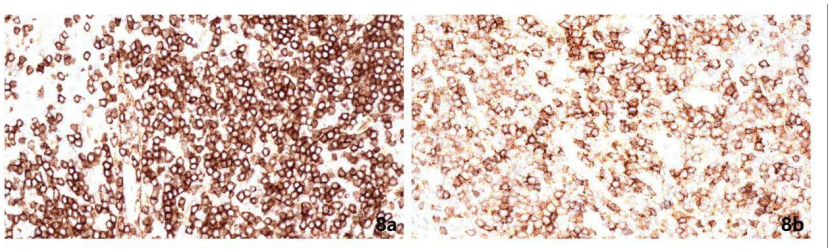

Figure 7: A 29-year-old female with BPDCN underwent a cervical lymph node biopsy. Hematoxylin and eosin (H&E) staining at low magnification (4×10) revealed partial loss of lymph node structure, enlargement of the paracortex, and proliferation of plasmacytoid cells (Figure 7a). H&E staining at high magnification (40×10) showed medium-sized plasmacytoid cells with sparse cytoplasm (Figure 7b).

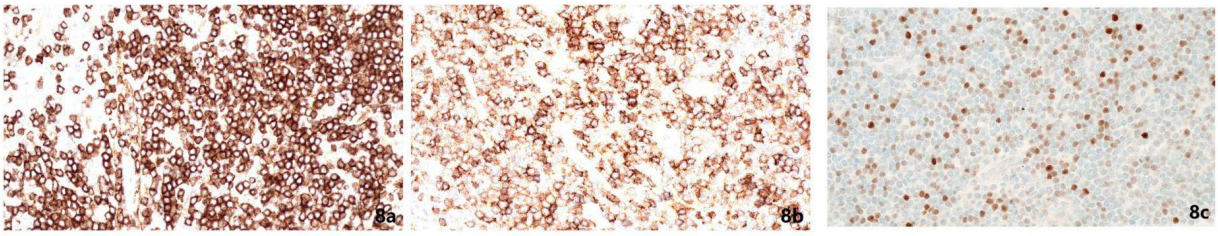

Figure 8: A 29-year-old female with BPDCN underwent a cervical lymph node biopsy. Immunohistochemistry revealed that the tumor cells were positive for CD123 in the cytoplasm (Figure 8a), CD4 in the cytoplasm (Figure 8b), and TdT in the nucleus (Figure 8c).

SUMMARY TABLES

etiology	Unclear
incidence	Approximately 4 per 10 million individuals in the United States
gender ratio	Male: Female= 2-4:1
age predilection	Middle-aged and elderly individuals
risk factors	Unclear
treatment	Conventional chemotherapy, the biopharmaceutical agent tagraxofusp, and stem cell transplantation.
prognosis	Median survival of 12 to 27 months
findings on imaging	Slightly increased radioactive uptake in skin lesions, enlarged lymph nodes, involved bone marrow, and affected organs. SUVmax range 1.8-8.4.

This table provides a concise summary of the key clinical and imaging features of Blastic Plasmacytoid Dendritic Cell Neoplasm (BPDCN). The etiology and risk factors remain unclear, with a higher incidence in middle-aged and elderly males. Treatment options include chemotherapy, targeted therapy with tagraxofusp, and stem cell transplantation, although prognosis remains poor with a median survival of 12 to 27 months. Imaging findings on PET/CT typically show mild to moderate FDG uptake in affected tissues.

DIFFERENTIAL TABLE

	PET/CT findings
BPDCN	FDG-avid skin/subcutaneous lesions with thickening; lymphadenopathy and hepatosplenomegaly with increased FDG uptake.
Lymphoma	Multiple, symmetrically enlarged lymph nodes with high FDG uptake; commonly involves mediastinal, abdominal, and pelvic lymph nodes with clear margins.
Systemic Immune Reactions (Infection-related)	Enlarged lymph nodes and hepatosplenomegaly with mild FDG uptake; variable findings depending on the site of infection (e.g., pulmonary inflammation, pleural effusion).
Autoimmune diseases	Non-specific findings; possible joint inflammation or pleural effusion; increased FDG uptake in areas of inflammation without clear tumor lesions.
Adult-onset Still's disease (AOSD)	Enlarged lymph nodes and hepatosplenomegaly without specific skin lesions or FDG-avid skin involvement.

PET/CT plays a crucial role in the diagnosis of BPDCN, particularly in evaluating FDG uptake in skin, lymph nodes, and visceral organs. BPDCN often shows high FDG uptake in skin lesions and multi-organ involvement. In contrast, lymphoma typically presents with symmetric lymphadenopathy and high FDG uptake. Systemic immune reactions and autoimmune diseases may also show increased FDG uptake but lack clear tumor lesions. AOSD is non-specific on PET/CT, mainly showing lymphadenopathy and hepatosplenomegaly.

KEYWORDS

Blasticplasmacytoid dendritic cell neoplasm; BPDCN; Acute urticari; Lymphadenopathy; Bone marrow; Spleen; 18F-FDG PET/CT

ABBREVIATIONS

BPDCN: BLASTIC PLASMACYTOID DENDRITIC CELL NEOPLASM

18F-FDG PET/CT: FLUORODEOXYGLUCOSE POSITRON EMISSION TOMOGRAPHY-COMPUTED TOMOGRAPHY

IGE: IMMUNOGLOBULIN E

PDC: PLASMACYTOID DENDRITIC CELL

AOSD: ADULT ONSET STILL'S DISEASE