CT findings associated with blastic plasmacytoid dendritic cell neoplasm: a case report

Daniel Jeong[1], Jung W Choi[1], Katherine Jeong[2] and Lubomir Sokol[3]

Abstract

Blastic plasmacytoid dendritic cell neoplasm (BPDCN) is a rare hematologic malignancy that is frequently misdiagnosed. We present a case of a 53-year-old man diagnosed with blastic plasmacytoid dendritic cell neoplasm with extensive computed tomography (CT) findings and provide an imaging focused review of this uncommon malignancy.

Introduction

A growing number of case reports have provided a better understanding of the presentation and diagnosis of blastic plasmacytoid dendritic cell neoplasm (BPDCN), a rare but rapidly progressive and deadly hematologic malignancy. However, few cases have explored the radiologic features which may be observed on imaging of this disease. We present the computed tomography (CT) findings associated with a case of BPDCN and provide an imaging-focused review of this uncommon malignancy. The goal of this article is to increase recognition of a rare but deadly disease and highlight the radiologic findings that may be seen during its workup and management.

Case report

A 53-year-old man presented to his physician following a blunt right knee injury. He subsequently developed a growing mass around the knee associated with pain and edema. He had no significant past medical history. Within 1 month, he noticed multiple, non-pruritic, erythematous skin lesions on the chest, trunk, and extremities. Lesions on the right knee and left thigh were biopsied and pathology revealed BPDCN. Malignant cells were strongly positive for CD4, CD43, CD56, CD123, and negative for EBER.

The patient underwent palliative radiation therapy but the lesions began to increase in size and number approximately 7–9 months following initial therapy. He presented to our tertiary cancer center at this time and underwent post-contrast CT imaging including the neck, thorax, abdomen, and pelvis. Unfortunately, pre-radiation therapy imaging was not available. Numerous superficial epidermal and subcutaneous lesions were demonstrated with ovoid morphology and isodensity to muscle (Fig. 1). The largest lesions were located in the anterior and lateral chest walls, with representative lesions measuring 6.1×2.6 cm in the midline anterior chest wall and a superficial 6.0×3.8 cm lesion on the left lateral thoracic wall. Many of the superficial cutaneous lesions demonstrated no evidence of underlying inflammation; however, some lesions involving the subcutaneous fat

[1]Department of Radiology, Moffitt Cancer Center, Tampa, Florida, USA
[2]Department of Internal Hospitalist Medicine, Moffitt Cancer Center, Tampa, Florida, USA
[3]Department of Malignant Hematology, Moffitt Cancer Center, Tampa, Florida, USA

Corresponding author:
Daniel Jeong, Department of Radiology, Moffitt Cancer Center, 12902 USF Magnolia Drive, Tampa, FL 33612, USA.
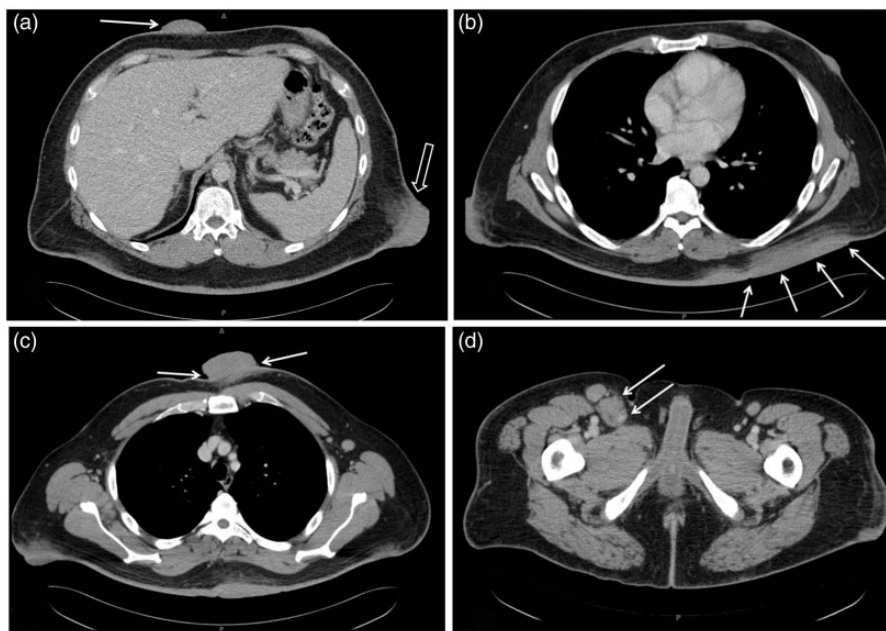Email: Daniel.jeong@moffitt.org

Fig. 1. Axial contrast-enhanced CT images at different levels in the body. (a) A well encapsulated cutaneous mass in the anterior chest wall (arrow) with no underlying inflammation. A left lateral chest wall mass demonstrates underlying inflammation (open arrow). Underlying fat stranding extends to the level of the thoracic wall which is compatible with inflammation. No definite invasion of thoracic wall musculature is appreciated. (b) Plaque-like thickening of the left posterior thoracic wall (arrows). An intact fat plane separates the plaque-like thickening from the posterior thoracic wall. (c) Exophytic mass in the anterior chest wall with cutaneous and subcutaneous components. Mild subcutaneous inflammation is also noted without invasion of underlying musculature. (d) Enlarged right inguinal lymph node (arrows). A mildly enlarged left inguinal lymph node is also appreciated.

demonstrated surrounding inflammatory fat stranding. Plaque-like skin thickening was also seen in the patient's back on CT. Enlarged bilateral inguinal lymph nodes were seen. The lungs demonstrated no evidence of interstitial lung disease. The liver and spleen were normal in size and morphology, and no bony abnormalities were noted. A PET/CT was recommended, but the patient opted to try holistic therapy instead. His disease progressed and the patient subsequently transferred care to undergo a clinical trial at a different institution.

Discussion

Previously known as blastic natural-killer lymphoma, agranular CD4+ natural killer cell leukemia, and agranular $CD4^+CD56^+$ hematodermic neoplasm, BPDCN is now recognized as a distinct neoplastic entity among "acute myeloid leukemia (AML) and related precursor neoplasms" in the 2008 World Health Organization *Classification of Tumours of Haematopoietic and Lymphoid Tissue* (1–6). BPDCN represents approximately 0.7% of primary cutaneous hematological malignancies and 0.44% of all hematological malignancies (2,4). The disease typically presents during late adulthood with a mean age in the range of 60–70 years, and a 3:1 predominance in men as in our case

report (1,2,5,6). Clinically, patients present with asymptomatic cutaneous lesions and extracutaneous involvement of the bone marrow, peripheral blood, and lymph nodes (1,3,4). Skin lesions most commonly manifest as diffuse "bruise-like" macules, but can also present as nodular lesions, or disseminated nodules or plaques of variable sizes associated with erythema, hyperpigmentation, or ulceration (1,3,4). BPDCN typically involves the dermis, sparing the epidermis followed by extension into subcutaneous fat with aggressive and rapid systemic dissemination by lymphatic spread as the disease progresses (1). Splenomegaly, hepatomegaly, and involvement of soft tissue, lungs, and central nervous system may also develop (4). Pathologic evaluation of biopsied tissue is usually required for definitive diagnosis (4).

Immunohistochemistry and flow cytometry are paramount in the diagnosis of BPDCN and distinction from other hematologic neoplasms, with BPDCN cells typically expressing CD4, CD56, and CD123 as seen in our patient (1,6). T-cell leukemia/lymphoma 1 (TCL1) and CD43 may be expressed as well, while the cells are usually negative for typical lineage-specific markers specific to T cell, B cell, granulocyte, and monocytes (1). Co-expression of CD4, CD56, CD123, BDCA2, and/or BDCA4 and an absence of CD3, CD11, MPO, and CD79a have been proposed to be diagnostic

for BPDCN (4,7). The rarity of BPDCN, its initial bland presentation, and considerable overlap of immunohistochemical markers often lead to initial delayed or missed diagnosis (2,3,5).

While the clinical features and pathology establish the diagnosis of BPDCN, it is important to recognize the radiologic features which can characterize the extent of disease involvement. The case we presented was particularly striking with respect to its impressive radiologic findings. The radiologic presentation most commonly involves well circumscribed cutaneous and subcutaneous masses. CT and PET/CT can detect the depth of visually evident lesions and provides a more accurate measurement of lesion thickness than clinical exam (8). On CT these lesions are round and ovoid with homogenous soft tissue density. Cutaneous lesions often demonstrate well defined margins with no significant surrounding fat stranding, while subcutaneous lesions can have associated inflammation. Plaque-like skin thickening can also be seen.

No previous research studies have investigated the post-radiotherapy appearance in BPDCN, however, available studies in other cutaneous lymphomas suggest response to radiotherapy is demonstrated by decreased lesion size and associated erythema on clinical exam and decreased lesion size and FDG avidity on imaging (9–11). Our case demonstrated several cutaneous and subcutaneous lesions with surrounding fat stranding, though these findings may be confounded by previous radiotherapy administration. When peritumoral inflammation on CT is solely related to radiotherapy, lesion size would be expected to decrease on subsequent follow-up imaging. However, with a clinical increase in disease burden, peritumoral fat stranding may be related to tumor-related inflammation in addition to post-therapy changes.

Necrosis can be detected within lesions as central decreased density on CT or central photopenia with increased peripheral metabolic activity on PET. Necrosis within a cutaneous lesion might not be evident on clinical examination, and added information by PET/CT may guide target lesion selection for biopsy. On magnetic resonance imaging, superficial BPDCN lesions have been reported isointense to muscle T1 signal, hyperintense to muscle proton density signal with homogeneous enhancement and fusiform morphology (5). Skin lesions and lymph node metastases have also been shown to be hypermetabolic on F18-FDG PET imaging; however, positive bone marrow involvement is not always evident on F18-FDG PET (5). Previous reports of SUV max in superficial lesions associated with BPDCN have been in the range of 2.4–3.5 (12,13).

More advanced forms of the disease can also include hepatosplenomegaly and lymphadenopathy, which may

be seen on imaging, and demonstrated by inguinal lymphadenopathy in our case. PET/CT offers accurate nodal staging and the PET component may detect lymph node disease even when pathologic size criteria may not be met. Pulmonary involvement has been described as interstitial opacities with a ground glass and reticular opacity predominance on CT with FDG avidity on PET, and pulmonary involvement has been reported without cutaneous lesions (14,15). Other cases have reported BPDCN without initial cutaneous findings, including a case of BPDCN presenting as a soft tissue mass in the ethmoid sinus, and a historical series of 27 patients with BPDCN lacking cutaneous involvement (6,16). When cutaneous lesions are absent, extracutaneous manifestations such as hepatosplenomegaly, pulmonary involvement, or lymphadenopathy may be the only signs of disease on imaging (14).

Similarities in the expression of myeloid antigens create a pathological differential diagnosis that includes myeloid sarcoma or acute myeloid leukemia (AML), T-cell lymphoblastic leukemia or lymphoma, NK-cell lymphoma, and some mature T-cell lymphomas (1,2,5). Skin lesions may be clinically mistaken for other dermatologic conditions such as eczema, myeloid leukemia cutis, or cutaneous lupus erythematosus (3).

The main radiologic differential diagnoses include metastatic disease, de novo infection, or inflammation. While similar imaging findings may be seen in other cutaneous lymphomas such as mycosis fungoides, CD56+ AML, or NK/T cell lymphomas, malignancies such as melanomas typically do not present with thickened cutaneous plaques or nodules (17). Moreover, the pattern of multiple well circumscribed nodules and plaques seen in BPDCN on radiologic imaging allows for differentiation of this entity from other non-malignant diagnoses. While most cutaneous and subcutaneous infections tend to have a contiguous distribution of lesions, BPDCN usually presents with well-defined lesions separated by normal fat.

Patients with BPDCN have poor outcome with a median survival of 12–14 months (1,3,14). Advanced stage and older age are indicators of poor prognosis (1). As no standardized therapeutic approach exists for this malignancy given its rarity, most patients have been treated with regimens similar to those used for acute myeloid leukemia, acute lymphoblastic leukemia, or aggressive non-Hodgkin's lymphoma (2,3). Patients usually respond to initial therapy but often relapse (1–6). Diagnostic imaging can play an important role in guiding palliative radiation therapy for patients with BPDCN who fail or are unable to tolerate conventional intensive medical therapy.

In conclusion, our case report demonstrates the extensive nature of BPDCN cutaneous and subcutaneous lesions as seen on CT imaging. Although

immunohistochemical analysis is necessary for the final diagnosis, it is important to be aware of the appearance on radiologic studies and the role that radiology can play in the management of BPDCN. Recognition of this rare malignancy clinically and on imaging studies will expedite diagnosis and facilitate early treatment.

References

1. Shi Y, Wang E. Blastic plasmacytoid dendritic cell neoplasm: a clinicopathologic review. Arch Pathol Lab Med 2014;138:564–569.
2. Pagano L, Valentini CG, Pulsoni A, et al. Blastic plasmacytoid dendritic cell neoplasm with leukemic presentation: an Italian multicenter study. Haematologica 2013;98: 239–246.
3. Cui XB, Jin J, Pang XL, et al. A case of blastic plasmacytoid dendritic cell neoplasm with ecchymotic lesions on the whole body. Int J Clin Exp Pathol 2014;7:4391–4399.
4. Riaz W, Zhang L, Horna P, et al. Blastic plasmacytoid dendritic cell neoplasm: update on molecular biology, diagnosis, and therapy. Cancer Control 2014;21:279–289.
5. Nizza D, Simoneaux SF. Blastic plasmacytoid dendritic cell neoplasm presenting as a subcutaneous mass in an 8-year-old boy. Pediatr Radiol 2010;40:S40–S42.
6. Paluri R, Nabell L, Borak S, et al. Unique presentation of blastic plasmacytoid dendritic cell neoplasm: a single-center experience and literature review. Hematol Oncol 2015;33:206–211.
7. Menezes J, Acquadro F, Wiseman M, et al. Exome sequencing reveals novel and recurrent mutations with clinical impact in blastic plasmacytoid dendritic cell neoplasm. Leukemia 2014;28:823–829.
8. Kuo PH, McClennan BL, Carlson K, et al. FDG-PET/CT in the evaluation of cutaneous T-cell lymphoma. Mol Imaging Biol 2008;10:74–81.
9. Neelis KJ, Schimmel EC, Vermeer MH, et al. Low-dose palliative radiotherapy for cutaneous B- and T-cell lymphomas. Int J Radiat Oncol Biol Phys 2009;74:154–158.
10. Wilson LD. Radiation therapy and cutaneous lymphoma. Clin Lymphoma Myeloma Leuk 2010;10:S99–102.
11. Shapiro M, Yun M, Junkins-Hopkins JM, et al. Assessment of tumor burden and treatment response by 18F-fluorodeoxyglucose injection and positron emission tomography in patients with cutaneous T- and B-cell lymphomas. J Am Acad Dermatol 2002;47:623–628.
12. Ishibashi N, Maebayashi T, Aizawa T, et al. Radiation therapy for cutaneous blastic plasmacytoid dendritic cell neoplasm: a case report and review of the literature. Int J Clin Exp Med 2015;8:8204–8209.
13. Sugimoto KJ, Shimada A, Yamaguchi N, et al. Sustained complete remission of a limited-stage blastic plasmacytoid dendritic cell neoplasm followed by a simultaneous combination of low-dose DeVIC therapy and radiation therapy: a case report and review of the literature. Int J Clin Exp Pathol 2013;6:2603–2608.
14. Takiuchi Y, Maruoka H, Aoki K, et al. Leukemic manifestation of blastic plasmacytoid dendritic cell neoplasm lacking skin lesion: a borderline case between acute monocytic leukemia. J Clin Exp Hematop 2012;52: 107–111.
15. Endo K, Mihara K, Oiwa H, et al. Lung involvement at initial presentation in blastic plasmacytoid dendritic cell neoplasm lacking cutaneous lesion. Ann Hematol 2013; 92:269–270.
16. Rauh MJ, Rahman F, Good D, et al. Blastic plasmacytoid dendritic cell neoplasm with leukemic presentation, lacking cutaneous involvement: Case series and literature review. Leuk Res 2012;36:81–86.
17. Lee HJ, Im JG, Goo JM, et al. Peripheral T-cell lymphoma: spectrum of imaging findings with clinical and pathologic features. Radiographics 2003;23:7–26. (discussion 26–28).