Blastic plasmacytoid dendritic cell neoplasm mimicking dermatomyositis

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INTRODUCTION

Blastic plasmacytoid dendritic cell neoplasm (BPDCN) is an aggressive hematologic malignancy occurring in children and adults, although most commonly in ages 60 years or older,[1] with an incidence of 0.4 cases per 100,000 individuals.[2] Approximately 90% of patients have skin involvement, and 50% have skin-limited disease at presentation.[3] There is also a proclivity to involve the bone marrow, lymph nodes, and/or peripheral blood.[1] Skin lesions are often asymptomatic purple papules, patches, plaques, or tumors and can mimic other dermatologic conditions. We report a case of BPDCN with clinical features of dermatomyositis to encourage providers examining purpuric eruptions to keep a broad differential diagnosis.

Abbreviations used:

ALT:	alanine transaminase
AST:	aspartate transferase
BPDCN:	blastic plasmacytoid dendritic cell neoplasm
IHC:	immunohistochemical
PET:	positron emission tomography

CASE

A 61-year-old female presented with a 3-week history of asymptomatic violaceous patches over her upper eyelids. Outside pathology obtained via skin punch biopsy reportedly revealed a superficial and deep periadnexal lymphocytic infiltrate, which combined with her clinical presentation was suggestive of a connective tissue disease, specifically dermatomyositis.

Additional work-up was initiated given the concern for connective tissue disease and revealed severe anemia (hemoglobin <6.0 g/dL), for which she was hospitalized. Complete blood count also revealed thrombocytopenia (128 K/mcL) and an increase in circulating blasts (52%). White blood cell count, creatinine kinase (CPK), aldolase, lactate dehydrogenase (LDH), aspartate aminotransferase (AST), and alanine transaminase (ALT) were within normal limits. There was no evidence of gastrointestinal bleeding by upper endoscopy or colonoscopy. Physical exam was notable for generalized lymphadenopathy. A positron emission tomography (PET) scan was obtained, which revealed diffuse lymphadenopathy suspicious for widespread malignancy. A subsequent bone marrow biopsy showed greater than 90% involvement of a diffuse infiltrate of intermediate-sized blasts with irregular contours and scant amounts of cytoplasm. Immunoperoxidase studies revealed a CD4(+), CD56(+), CD123(+), TCL-1(+), TdT(+) neoplastic process diagnostic of BPDCN.

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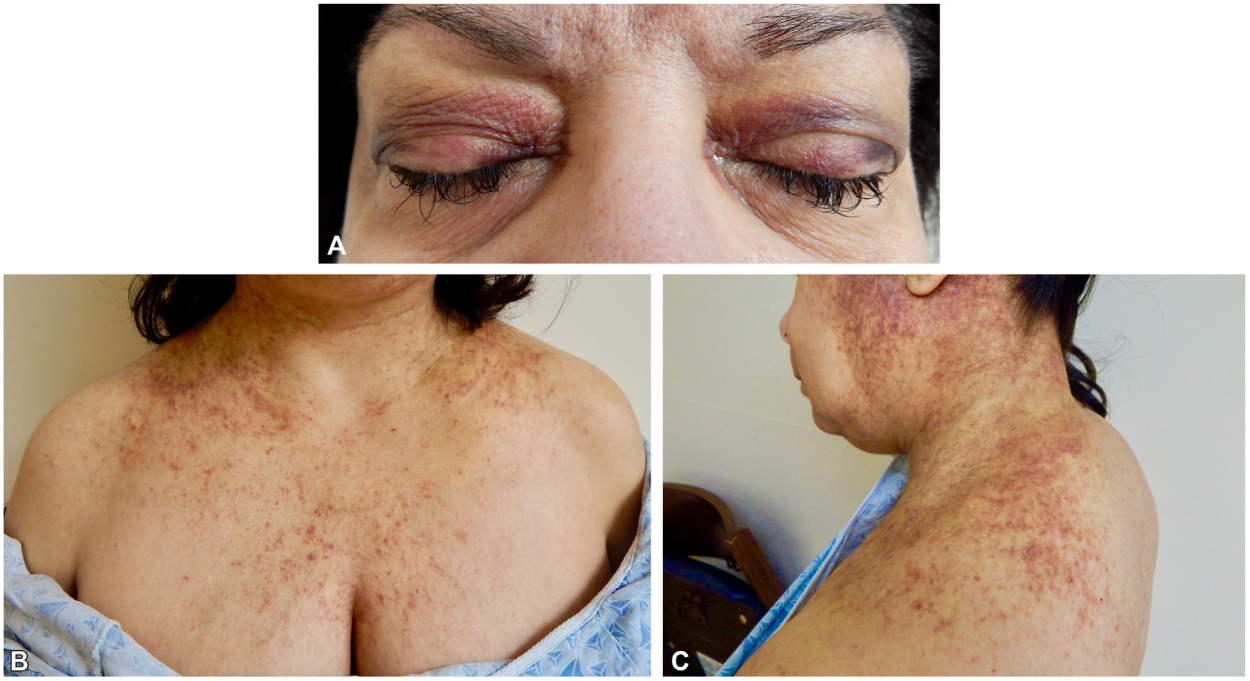

Fig 1. Clinical presentation of blastic plasmacytoid dendritic cell neoplasm. **A,** Purple infiltrative thin plaques over the bilateral eyelids, mimicking a heliotrope rash. **B,** Erythematous-to-violaceous macules and patches over the anterior chest in a shawl distribution. **C,** Extensive reticular poikiloderma over the *left* cheek, neck, and upper back.

During the hospitalization, her rash became more extensive. The patient had purple infiltrative thin plaques over the bilateral eyelids (Fig 1, *A*), mimicking a heliotrope rash. Erythematous-to-violaceous macules and patches were appreciated over the forehead and scalp, pre- and postauricular areas, neck, anterior chest (Fig 1, *B*), and upper back in a shawl distribution. There was extensive reticular poikiloderma over the shoulders and lateral upper back (Fig 1, *C*).

Purple nodules were noted on the gingiva. No nailfold changes or proximal muscle weakness were appreciated. Skin punch biopsies were obtained from the right postauricular area (Fig 2) and upper back, which demonstrated a dense superficial and deep dermal perivascular and periadnexal inflammatory infiltrate predominantly composed of intermediate-sized immature mononuclear cells with scant cytoplasm, irregular angulated and folded nuclei, dispersed chromatin, and prominent nucleoli, with no involvement of the overlying epidermis. Immunohistochemistry revealed this infiltrate was diffusely positive for CD4, CD56, CD123, TCL-1, and TdT, consistent with a diagnosis of BPDCN.

Additionally, the cytomorphology and immunoprofile were identical to that observed in the bone marrow biopsy. No significant interface change or mucin was noted.

The patient received tagraxofusp, a CD123-directed cytotoxin approved for treatment of BPDCN,[5] with rapid, near complete remission of her cutaneous BPDCN. After 2 cycles, exam was notable only for faint brown macules and patches consistent postinflammatory hyperpigmentation (Fig 3).

Previous violaceous erythema resolved, and lesions were entirely flat at the time of interval assessment. The gingiva was without hemorrhage, and prior papules had flattened substantially.

Unfortunately, PET scan revealed nodal disease progression after her second cycle of treatment. She underwent chemotherapy and later matched donor allogeneic stem cell transplant. She experienced severe graft-versus-host-disease and died from complications.

DISCUSSION

We report a novel case of BPDCN clinically mimicking dermatomyositis. While dermatomyositis as a paraneoplastic phenomenon secondary to underlying BPDCN was considered, review of the outside pathology and repeat skin biopsy and immunohistochemical (IHC) findings were pathognomonic for the diagnosis of BPDCN. Additionally, the patient had no other symptoms or clinical features of dermatomyositis and her eruption

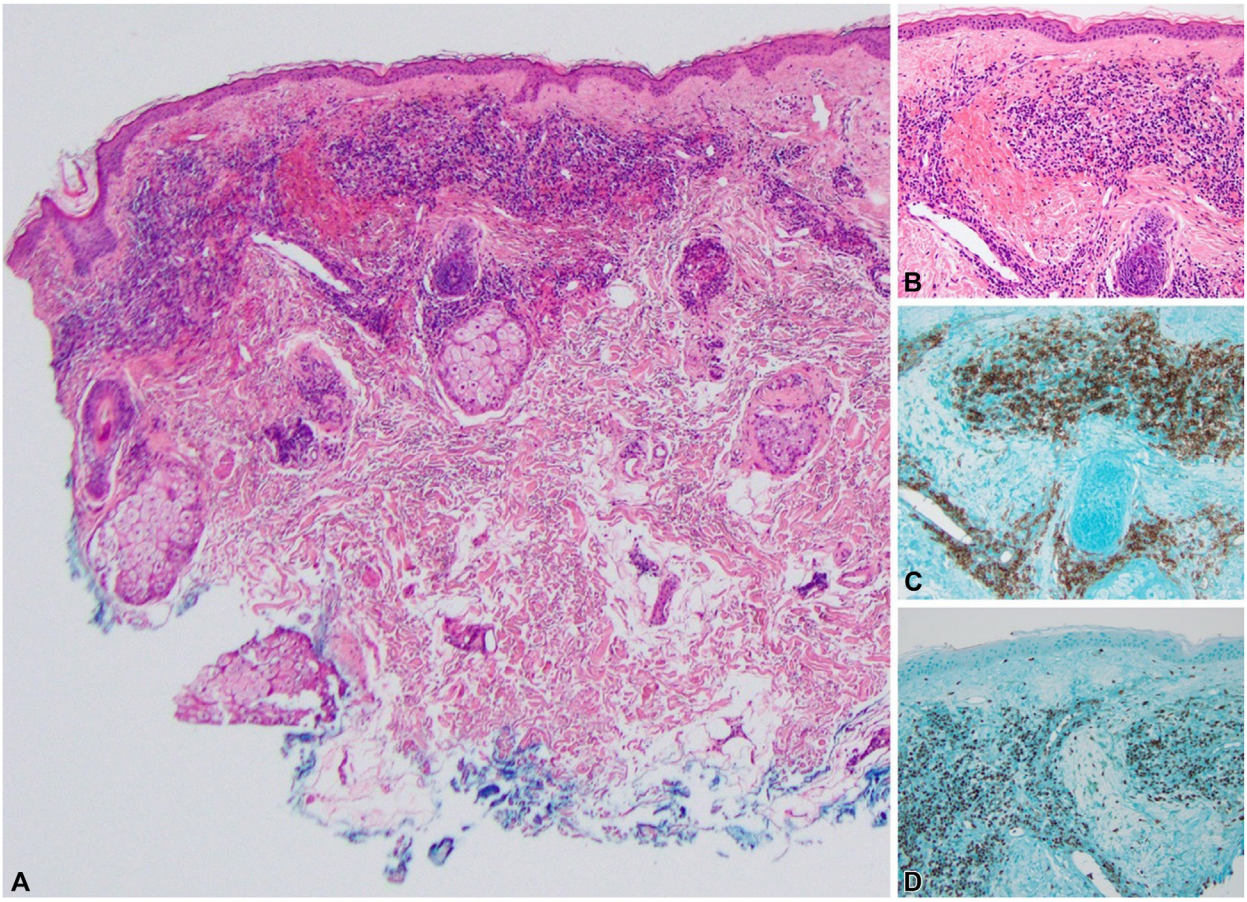

Fig 2. Representative images of a skin punch biopsy from the right postauricular area. Photomicrographs of H&E-stained tissue sections collected at (**A**) low (40× total magnification) and (**B**) high power (200× total magnification), demonstrate an infiltrate composed of immature mononuclear cells in a perivascular and periadnexal distribution that spares the epidermis with a well-defined Grenz zone. To further characterize the infiltrate, immunostains were performed, which revealed the cells were diffusely positive for CD123 (200×, **C**) and TCF4 (200×, **D**), the combination of which is extremely sensitive and specific for BPDCN.[4]

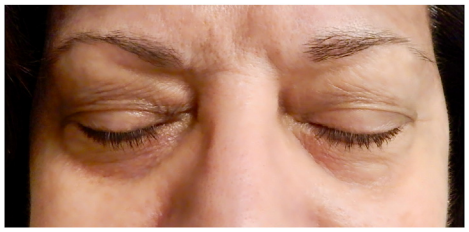

Fig 3. Faint brown patches on bilateral eyelids consistent with post-inflammatory hyperpigmentation, after 2 cycles of tagraxofusp.

regressed within days on targeted anti-CD123 therapy. BPDCN is a rare leukemia with striking skin predilection, with leukemia cutis affecting 90% of cases.[3] It typically presents with deep purple or violaceous plaques and tumors, with a predilection for the head, neck and upper trunk. Dermatologists should be familiar with this atypical clinical presentation of BPDCN to promote early diagnosis of this potentially rapidly progressive disease and prompt referral to medical oncology for multidisciplinary care.

Biopsy is required for diagnosis, and as seen in our patient, the initial biopsy may not immediately lead to the diagnosis. The immunohistochemical (IHC) profile is critical for distinguishing BPDCN from dermatologic and hematologic mimickers. Current guidelines recommend that for any tumor expressing CD4 but not CD11c, MPO, cytoplasmic CD3, or cytoplasmic CD79a, there should be evaluation for CD123 expression, whether there is CD56 expression or not.[6] Positivity of CD123 in addition to BDCA2 or TCL-1 favors a diagnosis of BPDCN. Dermatologists should share their clinical suspicion in patients presenting with deep purple

infiltrative disease with pathologists and have multidisciplinary discussions to assist in the diagnosis.

Conflicts of interest

The authors declare no conflicts of interest with respect to the research, authorship, and/or publication of this article. Nicole R. LeBoeuf is a consultant and has received honoraria from Bayer, Seattle Genetics, Sanofi, Silverback, and Synox Therapeutics outside the scope of the submitted work.

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