

Blastic plasmacytoid dendritic neoplasm (BPDN) or BPDN-like lesion presenting after influenza vaccination and resolving with topical high potency steroid

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INTRODUCTION

Blastic plasmacytoid dendritic cell neoplasms (BPDN) are exceedingly rare T-cell neoplasms that carry a dismal prognosis. Today, the exact etiology of the disease is unclear, and to our knowledge, no cases of BPDN have been reported at the site of vaccination injection. Additionally, all currently described cases described have dismal prognosis, and, to our knowledge, there are no reports of such lesions responding to topical steroid treatment. Herein, we present an unusual case of BPDN occurring at an influenza vaccination site that subsequently resolved after high-potency topical steroid treatment.

CASE REPORT

A 71-year-old white man with no significant medical history presented with a 5.0-cm nontender, erythematous, and scaling plaque with an indurated border on the left upper arm. The lesion appeared at the site of an influenza vaccination that he received 7 days prior. The patient denied systemic symptoms and any such reaction with previous vaccinations. The initial clinical suspicion was that of an injection site hypersensitivity reaction. A punch biopsy was performed, and a topical high-potency steroid, diflorasone diacetate 0.05%, was prescribed.

The biopsy found an atypical dense lymphoid infiltrate in the papillary and reticular dermis. A grenz zone was present. The infiltrate shows prominent perivascular distribution (Fig 1). The individual

Abbreviations used:

BPDN: Blastic plasmacytoid dendritic cell neoplasm
HSCT: Hematopoietic stem cell transplantation

lymphocytes had hyperchromatic nuclei with irregular nuclear contour and nucleoli (Fig 2). Crush artefact was present at the periphery of the biopsy section.

Immunohistochemical profiling found the lesion to be diffusely CD4⁺ and CD56⁺ (Fig 3). Most of the lesional cells were also CD123⁺ and TdT⁺ (Fig 3). Repeat CD123 staining found more intense and diffuse positivity. Admixed were rare CD79⁺ B cells. Tests for myeloperoxidase, CD34, MUM1, PAX5, CD3, CD10, CD21, kappa, and lambda were negative. Epstein Barr virus in situ hybridization results were also negative. In addition to these markers, an outside hospital found that our lesion was TCL1⁺ and CD117⁻ and muramidase negative. After histologic and immunoprofiling of CD4⁺, CD56⁺, TCL1, and CD123⁺, a diagnosis of BPDN was rendered. Differential diagnosis included extramedullary myeloid sarcoma and an acute leukemia with ambiguous lineage. Absence of myeloperoxidase excluded myeloid sarcoma, and absence of CD34, myeloperoxidase, CD117, and muramidase ruled out acute leukemia. This diagnosis was confirmed by a senior hematopathologist and at major cancer center. At the 2-week follow up, the patient reported that the entire lesion had

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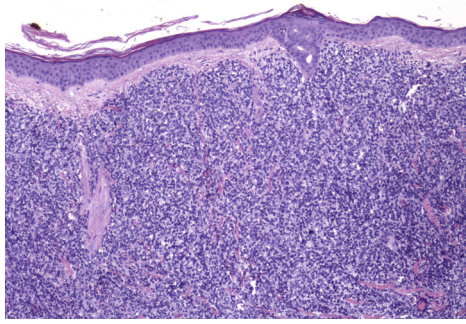


Fig 1. Dense atypical lymphohistiocytic infiltrate occupying the dermis with a Grenz zone. (Original magnification: $\times 100$.)

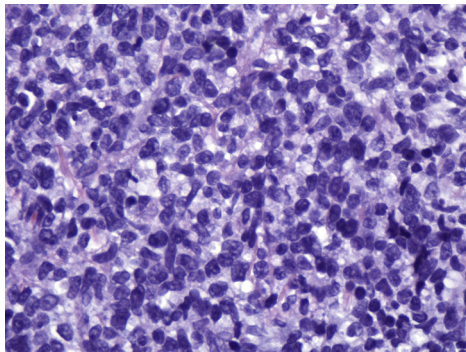


Fig 2. On higher magnification, atypical lymphocytes show hyperchromatic nuclei with irregular nuclear contour and nucleoli. (Original magnification: $\times 400$.)

resolved with topical steroid treatment. Despite the lack of clinical evidence of disease, radiation therapy was delivered at the site. At the time of this report, bone marrow and blood involvement were not found and leukemia was excluded, but watchful follow-up is necessary.

DISCUSSION

BPDN is a rare and aggressive hematologic disease, the etiology, incidence, clinical presentation, and treatment strategies of which are still being elucidated. Derived from precursors of plasmacytoid dendritic cells, BPDN is categorized under “acute myeloid leukemia and related precursor neoplasms” by the 2008 World Health Organization classification.^{1,2} Most patients are elderly men, with a male to female ratio of 2.2:1 to 3:1 and a median age of approximately 67 years.^{2,3} Pediatric cases have also been reported, and the clinical progression appears to be less aggressive with a more favorable prognosis.⁴ No racial or ethnic preferences have been found. The incidence of BPDN among cutaneous lymphomas is 1.4%.⁵

Patients most commonly present with cutaneous lesions, ranging from isolated or few purplish nodules, bruise-like macules, and disseminated macules and papules to lymphadenopathy.² Pulmonary and central nervous system symptoms may also occur. Cytopenia, splenomegaly, hepatomegaly, and other symptoms of leukemic dissemination signify disease progression. Fulminant leukemia indicates terminal illness. Regardless of the initial clinical presentation, prognosis is poor. Among patients presenting with primarily cutaneous symptoms, with or without lymph node, central nervous system, or bone marrow involvement, median overall survival was 12 months.² Among patients presenting with leukemic involvement, with or without cutaneous symptoms, median overall survival was 8.7 months.³

Patients receiving treatment in the early cutaneous phase of disease, with isolated or few lesions, may have more favorable outcome. Poor prognostic indicators include advanced age and clinical staging.^{2,3} Children with BPDN have improved median overall survival when given the same treatment as adults.⁴ Given the low incidence of the disease, no standard of care has been established for BPDN, and determinations of treatment efficacy rely on retrospective case or registry studies. Induction therapy includes focal radiotherapy, chemotherapy, and glucocorticosteroids to address cutaneous lesions. Late-stage disease treatments include cyclophosphamide, hydroxydaunomycin, vincristine, prednisone and hyperfractionated cyclophosphamide, vincristine, doxorubicin, dexamethasone alternating with methotrexate and cytarabine, but relapse occurs within months of remission on average.⁶ Patients that undergo hematopoietic stem cell transplantation (HSCT), often used to maximize consolidation of response or after relapse, show the greatest promise for long-term response, with better survival curves and overall survival rates than patients that only had conventional therapies. These determinations are primarily anecdotal from case studies, with small sample sizes and populations skewed toward younger males, so robust statistical evaluations are lacking.⁷⁻⁹ In one study of 47 patients with BPDN, overall survival in HSCT patients was significantly higher than that in non-HSCT patients (31.3 months vs 12.8 months).⁹

Misdiagnosis is common, leading to delayed treatment, as BPDN can be morphologically and clinically indistinguishable from leukemia cutis and acute myeloid leukemia. Immunophenotypic analysis, morphology, and clinical details are used for definitive diagnosis. As of now, there is no

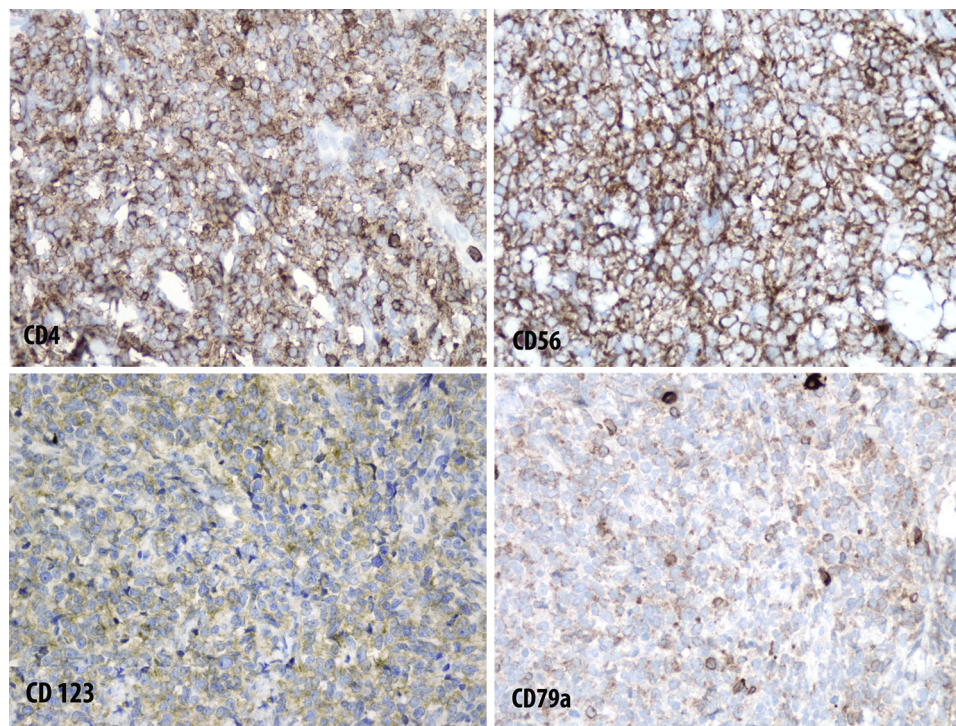


Fig 3. The infiltrate is diffusely and strongly positive for CD4 and CD56, diffusely positive for CD123, and only focally positive CD79a. (Original magnification: $\times 200$.)

consistent immunophenotypic algorithm for pathologic diagnosis of BPDN. The most characteristic markers for BPDN are CD4, CD56, CD123, CD303, and TCL1. In one retrospective study, diagnosis by immunophenotype was considered definite when patients coexpressed at least 4 of these main markers.¹⁰ In our case, positivity in 4 of these 5 main markers, along with exclusion of myloid sarcoma and acute leukemia of ambiguous origin from negative markers as described above, allowed for diagnostic completeness.

The etiology and pathogenesis of BPDN remains largely unknown. Studies into normal physiologic counterparts to malignant BPDN cells yielded plasmacytoid dendritic cells and plasmacytoid dendritic–like cells as candidates.^{11,12} A review of molecular data found that abnormalities in chromosomes 5, 9, 12, 13, and 15 are nonuniformly involved in pathogenesis, suggesting a diversity of genetic mutations that can dysregulate oncogenic pathways in BPDN.⁶ Epstein-Barr virus is not associated with BPDN.¹

A review of literature found that BPDN can manifest with a variety of cutaneous phenotypes. Julia and et al² observed a pattern of few lesions in early disease, progressing to cutaneous dissemination in late disease. The lesions ranged in type and color, described as nodes, patches, plaques, and

tumors, of brown or violaceous appearance.² Given the variety of its cutaneous manifestations and low incidence, BPDN can be mistaken for eczema or lupus erythematosus, leading to delay in appropriate treatment.^{13,14}

In the English-language literature, there are no reports, to our knowledge, of BPDN occurring at the vaccination site. In addition, BPDN also carries a poor prognosis, and the regression of our patient's lesion with topical high potency steroid makes our case novel and intriguing. The diagnosis of this lesion is dependent on histologic and immunologic evaluation. To date, there is no specific molecular test to confirm a diagnosis of BPDN. Therefore, based on the current standards, a diagnosis of BPDN was made on our biopsy. However, the atypical presentation and behavior of our case raises the question if our lesion was indeed a distinct presentation of BPDN that carries a good prognosis or was a BPDN-like reaction to the vaccination. At the time of this report, the benign clinical course of this case is highly uncharacteristic of BPDN. Regardless, given the possibility of true BPDN and the prognosis it carries, any such lesion with characteristic histology and immunophenotype should be met with extreme suspicion, and treatment measures appropriate to BPDN should be considered.

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