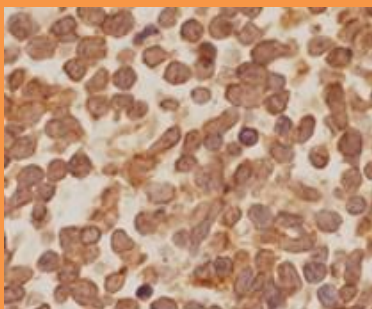
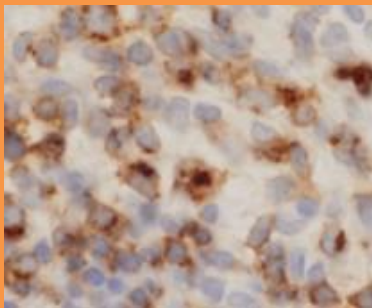
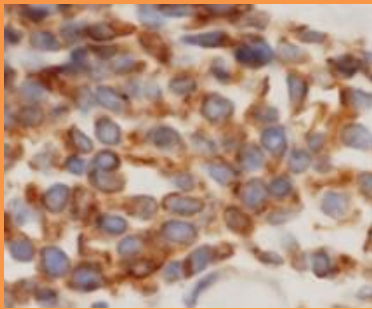


# Case Presentation 5

## PRIMARY CUTANEOUS BLASTIC PLASMACYTOID DENDRITIC CELL NEOPLASM



*This educational series for physicians is presented by the Weill Cornell Comprehensive Dermatopathology Service*

### Case author: Cynthia M. Magro, MD

#### ■ Clinical History

The patient was a 51 year old male who presented with a 1.5 year history of a progressive nodular and plaque-like eruption manifesting an exclusively truncal distribution. Clinical exam revealed multiple back lesions. There was no lymphadenopathy, splenomegaly and or hepatomegaly. The largest which measured 9x5 cm was the initial lesion and was followed by other over the ensuing months (figure 1). The application of topic steroids followed by a 10 day course of Doxycycline did not result in any improvement. He denied fever, chills, and weight loss. His past medical history was unremarkable. His work up to date does not disclose any evidence of extracutaneous dissemination.

#### ■ Light Microscope Findings

A biopsy was performed.

There was an extensive pan dermal infiltrate of monotonous appearing cells that had a lymphoblastic-like appearance (figure 2,3). The cells were in the 7 to 9 micron size range, showing round to oval nuclei with a finely dispersed chromatin (figure 4). Nucleoli were not conspicuous. Scattered mitoses were identified. Epidermotropism was not identified. There was a paucity of other inflammatory cell elements.

#### ■ Phenotypic Profile

The cells were extensively positive for CD4, CD56 (figure 5), CD123 (figure 6), HLADR and TCL1 oncogene (figure 7). Significant staining was not observed for lysozyme, CD11c, myeloperoxidase, CD3, CD20, MxA and CD2.

#### ■ Molecular Studies

A germline configuration was observed both in regards to evidence of T cell receptor and heavy chain immunoglobulin gene rearrangement.

#### ■ Discussion

The clinical presentation and biopsy findings in this case were diagnostic of so called blastic plasmacytoid dendritic cell neoplasm. The positivity of this neoplasm for CD56 lead hematopathologists to initially consider this neoplasm under the rubric of CD56+ Natural killer cell lymphomas. Its uniqueness lied in the positivity of this apparent NK lymphoma/leukemia for CD4. Most NK neoplasms are without positivity for CD4 and CD8 or rarely although rarely these tumors can be CD8 positive. This tumor fell under the designation of blastic NK like T- cell lymphoma. In the revised World Health Organization-European Organization for Research and Treatment of Cancer (WHO-EORTC) classification, blastic NK-cell lymphoma was considered a clinically aggressive T cell neoplasm; skin involvement typically occurred concurrently with leukemic dissemination. A blastic cytomorphology and expression of CD56 were held to be evidence of an NK-precursor cell origin. The designation of this neoplasm as CD4+CD56+ hematodermic neoplasm was by Kato and co-workers in 2001 although it was not until 2002 when a new cell of origin was proposed for this aggressive neoplasm, namely one of plasmacytoid dendritic cell origin for this neoplasm was proposed. Consequently the term blastic NK like T cell lymphoma was first supplanted by the term CD4+CD56+ hematodermic neoplasm and now more recently blastic plasmacytoid dendritic cell tumor. In those neoplasms categorized as true NK lymphomas, there is a frequent association with Epstein Barr virus (EBV), especially in Asian patients with nasopharyngeal involvement; EBV has not been pathogenetically implicated in CD4+CD56+ hematodermic neoplasms. At further variance with the classic NK lymphomas/leukemias, is the agranular nature of the tumor, with the absence of granzyme B and TIA cytotoxic protein expression. Most patients die within 12 months of initial presentation. Elderly patients are characteristically affected and as well, there is a male predominance. Disseminated disease is common involving peripheral blood and lymph nodes and bone marrow. The prognosis is grim with most patients succumbing to disease within 12 months of presentation.

While the dominant literature addressing CD4+CD56+ malignancies is in the context of CD4+CD56+ hematodermic neoplasm/blastic plasmacytoid dendritic cell neoplasm, there are other hematological malignancies that may express this particular phenotypic profile including MF, ALCL and leukemia cutis. It should be emphasized that the expression of other pan T cell markers however does not

*Continued*

exclude a diagnosis of CD4+CD56+ hematodermic neoplasm. In particular while CD4+CD56+ hematodermic neoplasms are typically CD2 and CD7 negative, CD7 and focal CD2 positivity can be seen in this neoplasm. The classic immunohistochemical stains for identifying plasmacytoid dendritic cells are BDCA-2, CD123, and TCL1. CD123 represents the alpha chain of the interleukin-3 receptor. This 60-70 kDa transmembrane protein binds to IL-3 with low affinity by itself, and when associated with CD131 (common  $\beta$  chain) binds IL-3 with high affinity.

Biopsies typically show a striking effacing nonepitheliotropic mononuclear cell infiltrate exhibiting variable angiocentricity. The cells have a lymphoid-like appearance and are of medium size (i.e. in the 9-micron size range). The chromatin is more finely dispersed than a mature lymphocyte. The cells demonstrate conspicuous nucleoli. In foci of angiocentric infiltration, red cell extravasation is observed.

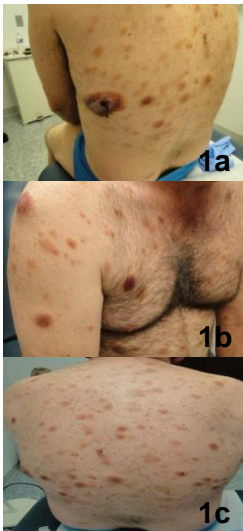
The infiltrate expresses CD4 CD56+ and CD123+. As well, there is positivity for cutaneous lymphocyte antigen. Other markers that may be positive include CD2, CD7, MxA, CD83, and TCL1. The cells do express granzyme and T-cell intracellular antigen (TIA). TCR clonality studies revealed a germ line configuration and/or a polyclonal T-cell population. Markers of myeloid differentiation including CD11c, lysozyme, myeloperoxidase, CD14, and CD68 are negative. A few cases of purported CD4 + CD56+ hematodermic neoplasm do not express CD4. The vast majority of cases reported in the literature however describe CD4 staining.

Although the clinical course in the vast majority of cases of blastic plasmacytoid dendritic cell neoplasm is poor, cases presenting in the skin without evidence of extracutaneous disease at the time of presentation may have a potentially indolent course and or at less the aggressive clinical course compared to the more classic presentation of blastoid plasmablastic dendritic cell neoplasm. The cases of primary cutaneous blastic plasmacytoid dendritic cell neoplasm affect a young age group compared to the more common multiorgan variant. Of the few reported cases in the literature, the patients have undergone polychemotherapy with a hyper CVAD regimen and obtained a remarkable clinical response with regression of skin lesions. Bekkenk et al suggested that patients less than 40 years of age, presentation with skin lesions, high TdT expression and an aggressive acute leukemia protocol treatment have a superior prognosis.

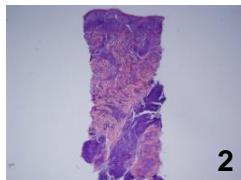
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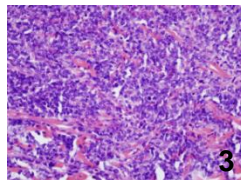
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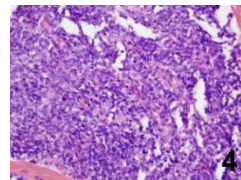
**Figure 1a, b, and c:** The patient has an extensive eruption on his back characterized by variably sized hyperpigmented plaques and nodules. The lesions are dark brown to violaceous in color and are surrounded by an ecchymotic halo.



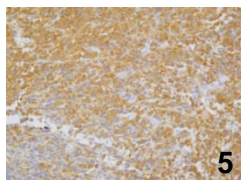
**Figure 2 :** There is an effacing pan dermal infiltrate of small to intermediate sized blastic lymphoid appearing cells.



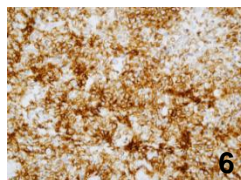
**Figure 3:** The infiltrate is largely nonepidermotropic.



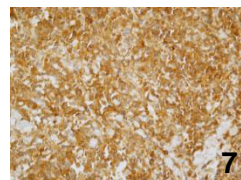
**Figure 4:** The cells have a finely dispersed chromatin with minimal cytoplasm. Despite the lymphoid-like appearance of the cells, the cell of origin of this neoplasm is a plasmacytoid dendritic cell.



**Figure 5:** The cells stain positively for CD56.



**Figure 6:** There is extensive immunoreactivity for CD123.



**Figure 7:** Marked staining is noted for TCL1 oncogene.

Under the direction of Dr. Cynthia M. Magro, the Weill Cornell Comprehensive Dermatopathology Service is a leading edge consultation service and CAP-accredited laboratory for dermatologists, plastic and general surgeons and other dermatopathologists. Dr. Magro is an internationally renowned dermatopathologist, educator and author. She is a Professor of Pathology and Laboratory Medicine at the Weill Cornell Medical College in Manhattan, and is board certified in anatomic pathology, dermatopathology and cytopathology. Dr. Magro is an expert in the diagnosis of complex inflammatory skin diseases. Her areas of expertise include cutaneous manifestations of auto-immune disease, systemic viral disease and vasculitis, atypical drug reactions, benign, atypical and overtly malignant lymphocytic infiltrates of the skin, and diagnostically difficult melanocytic proliferations. The award-winning author of *The Melanocytic Proliferation: A Comprehensive Textbook of Pigmented Lesions*, Dr. Magro has recently completed her second book, *The Cutaneous Lymphoid Proliferation, a comprehensive textbook on benign and malignant lymphocytic infiltrates*. She has co-authored over 250 peer reviewed papers and several textbook chapters. Dr. Magro frequently presents courses on inflammatory skin pathology and difficult melanocytic proliferations to the American Academy of Dermatology, the United States and Canadian Academy of Pathology, and the American Society of Clinical Pathology. Dr Magro has consistently been recognized in Who's Who in America®, Castle Connolly's renowned America's Top Doctors – New York Metro Area® edition and in the Super Doctors® list published in The New York Times Magazine.

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