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Editorial

Indeterminate Cells Histiocytosis

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EDITORIAL NOTE

Dendritic cells comprise a large family of antigen-presenting cells whose cutaneous subset includes Langerhans cells, indeterminate cells, and dermal dendritic cells. These cells present antigens to lymphocytes, with whom they interact through specific surface receptors. The prototypical dendritic cell of the skin is the Langerhans cell [1]. Langerhans cells are derived from the bone marrow, are thought to locally renew in the skin, and express CD1a, S100, CD45, HLA-DR, and Langerin. A unique feature of Langerhans cells is the presence of Birbeck granules. Birbeck granules are recognized by the monoclonal antibody targeting Langerin (CD207), which acts as an endocytic receptor to translocate ligands from the cell surface into the Birbeck granule [1,2]. Indeterminate cells are morphologically and immunophenotypically similar to Langerhans cells. Various hypotheses regarding the origin of indeterminate cells have been published, but the most accepted theory is that indeterminate cells represent some variant of Langerhans cells with the lack of Birbeck granules and Langerin expression being reflective of Birbeck granules either not having developed yet in an immature precursor or having been lost after activation [2,3].

Indeterminate cell histiocytosis (ICH), also known as indeterminate dendritic cell tumor (IDCT), is a rare proliferative disorder with no age or sex predilection that predominantly involves the skin. ICH is histologically composed of a monomorphous infiltrate of mononuclear cells with reniform nuclei, scattered multinucleated cells, and lymphocytes. Some have questioned the classification of ICH, suggesting that it may simply be a variant of Langerhans Cell Histiocytosis (LCH) in which Birbeck granules cannot be demonstrated. However, ICH was recognized as a distinct entity in the 2016 update to the WHO Classification of Tumors of Hematopoietic and Lymphoid Tissue [3]. Patients with ICH often present with solitary or multiple cutaneous papules, nodules, or plaques. The clinical course is highly variable, ranging from spontaneous regression to rapid progression [4].

Systemic symptoms and extra-cutaneous manifestations are described but are rare and additional reported disease associations include acute myeloid leukemia and B-cell lymphoma [5,6]. Treatment is variably successful with reported therapies including narrowband ultraviolet B-light, low-dose methotrexate, and chemotherapy for aggressive, recalcitrant lesions [7].

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