Abstract

Indeterminate cell histiocytosis (ICH) is a rare, heterogeneous disorder that is characterized by immunophenotypic features of both Langerhans cell histiocytosis (LCH) and non-LCH. We describe a 12-month-old boy with a four-month history of asymptomatic, small, pink-tan papules on his face. Histopathologic evaluation showed a superficial, dermal infiltrate of histiocytes that was positive for S100, CD1a, CD68, and Factor XIIIa. To our knowledge, this represents the first report of the clinical presentation of benign cephalic histiocytosis with immunohistochemical findings of ICH. We review the classification of histiocytic disorders and the clinical and immunohistochemical features of both ICH and benign cephalic histiocytosis.

Case synopsis

History: A 12-month-old boy presented to the Pediatric Dermatology Clinic at the Skin and Cancer Unit with a four-month history of an asymptomatic, papular eruption on his face. The lesions first appeared on his cheeks and then spread to involve the periocular area and chin. Treatment with topical glucocorticoids and antibiotic preparations failed to produce any improvement. He was otherwise healthy, with normal growth and development.

Physical examination: On the cheeks, eyelids, temples, and chin were numerous, pink-to-pink-tan, monomorphic papules that were 1-to-3-mm in size.
Laboratory data: A complete blood count and metabolic panel were normal.

Histopathology: Within the superficial dermis, there are aggregates of cells that are characterized by enlarged, ovoid, vesicular nuclei with nuclear grooves and moderate amounts of pale cytoplasm. Scattered eosinophils are present. Immunostains show reactivity for CD1a, S-100, CD68, and factor XIIIa. There is no immunoreactivity for MAC-387.

Discussion

Diagnosis: Indeterminate cell histiocytosis that presented clinically as benign cephalic histiocytosis

Comment: The histiocytes are characterized by proliferation of cells that share a CD34-positive precursor in the bone marrow [1, 2]. These diseases have a broad spectrum of cutaneous and extracutaneous manifestations and are divided into two major categories: Langerhans cell histiocytosis (LCH) and non-Langerhans cell histiocytoses (non-LCH). In LCH, the Langerhans cells contain cytoplasmic Birbeck granules and have an immunophenotype positive for S100, CD1a, and Langerin (CD207). In contrast, non-LCH features cells express CD68 and other markers of the monocyte-macrophage lineage [3]. Non-LCH is a heterogeneous group that includes indeterminate cell histiocytosis (ICH), which is a controversial entity with variable clinical findings and immunophenotypic markers of both monocytes/macrophages (e.g. CD68, factor XIIIa) and Langerhans cells (S100, CD1a), but not Langerin or Birbeck granules [1].

Benign cephalic histiocytosis (BCH) is a self-limited form of cutaneous non-LCH that occurs in the first few years of life. It presents with multiple, small, pink-tan to red-brown papules on the face, especially the cheeks. The eruption may spread to involve the neck, upper trunk, arms, and occasionally other sites [4-7]. The median age of onset is seven months, with a slight predilection for boys (male:female ratio = ~1.5:1) [7]. Spontaneous resolution occurs over months to years and frequently leaves residual, hyperpigmented macules. Among the nearly 60 patients with BCH reported to date, only two individuals had extracutaneous findings (diabetes insipidus and type 1 diabetes mellitus) [7].

The morphology, distribution, age of onset, and evolution of our patient’s skin lesions were highly suggestive of BCH. Histopathologic evaluation showed a well-circumscribed, superficial, dermal infiltrate of histiocytes that also was consistent with this diagnosis; epidermotropism and reniform nuclei (features of LCH) were absent. However, immunohistochemical stains were positive for S100 and CD1a (both typically negative in BCH) as well as CD68 (positive in BCH) – the constellation of findings that characterizes ICH.

Considering that the immunohistochemical staining patterns of monocytes/macrophages and dendritic cells are inconsistent, some authors have suggested that most patients with ICH actually have a variant of another type of non-LCH, e.g. reticulohistiocytosis, reticulohistiocytoma, or juvenile xanthogranuloma [1]. With this reasoning, our patient would represent an example of BCH with the immunophenotype of ICH. There have been at least two prior reports of BCH with S100-positive histiocytes [6, 8]. To our knowledge, a clinical presentation of BCH associated with histiocytes positive for both S100 and CD1a previously has not been described.

Although ICH primarily affects adults, there have been reports of children with both solitary and generalized forms [1, 2, 9-13]. ICH typically presents as red-to-brown papules or nodules and favors the trunk and extremities [3]. The clinical course ranges from regression to persistence or progression. Disease is usually limited to the skin, but involvement of the eyes or bones and association with leukemia have been described [2, 14, 15]. Of note, narrowband ultraviolet B was successfully utilized to treat generalized LCH in a child [9].

References