

Generalized eruptive histiocytosis: A case report

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The histiocytoses are a group of proliferative disorders of the monocyte-macrophage lineage that are neoplastic or reactive in nature. Based on immunophenotyping and electron microscopy, two main groups have been recognized namely 1) Langerhans cell histiocytosis (LCH) and 2) non- Langerhans cell histiocytosis (non-LCH). In this study, a fairly rare disease of the non-LCH group, generalized eruptive histiocytosis, has been reported.

Keywords: generalized eruptive histiocytosis, macrophage, neoplasm, non- Langerhans cell histiocytosis

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INTRODUCTION

The histiocytoses are a group of proliferative disorders of the monocyte-macrophage lineage, that are neoplastic or reactive in nature ¹. Based on immunophenotyping and electron microscopy, two main groups have been recognized namely 1) Langerhans cell histiocytosis (LCH) and 2) non- Langerhans cell histiocytosis (non-LCH) ²⁻⁴. Non-LCHs usually follows a benign course ⁵, indicating that a reactive pattern is more probable than a neoplastic process. This group of histiocytoses are further classified into various entities including benign cephalic histiocytosis (BCH), generalized eruptive histiocytosis (GEH), indeterminate cell histiocytosis (ICH), juvenile xanthogranuloma (JXG), xanthoma disseminatum (XD), reticulohistiocytosis, rosai-dorfman disease and necrobiotic xanthogranuloma ⁶. Apart from indeterminate cell histiocytosis, the others may

have similar immunophenotype ², which in most cases are easy to distinguish from each other, if one gives proper attention to the history and clinical presentations. For example, GEH and BCH may share some clinical features but involve different age groups; the former is two times more prevalent in adults and the later almost always begins within the first three years of life ⁶.

CASE REPORT

A 30-year-old woman presented with a 2-year history of non-pruritic rash, over different parts of her body. Multiple papules first appeared on the superior eyelids (Figure 1), subsequently spreading to the neck, anterior trunk, axillae, groins, and finally became generalized (Figure 2). Early lesions had a yellowish hue, but as the disease progressed, turned into darker red-brown lesions,



Figure 1. Multiple papules on the face



Figure 2. Multiple papules on the anterior trunk and groins

especially on the trunk. The mucous membranes were unaffected and these eruptions were not associated with itching or any other symptoms, except for their annoying appearance. There was no personal or family history of a similar condition, and on physical examination. The patient appeared to be healthy. Generalized eruptive histiocytosis, xanthoma disseminatum, mastocytosis and eruptive syringoma were used as the clinical differential diagnoses for this study. The biopsy specimen revealed an expanded upper dermis by monomorphic histiocytic infiltration and irregular fibrosis with scattered neutrophils, lymphocytes and multinucleated giant cells (Figures 3). The overlying epidermis showed mild acanthosis without involvement. Immunohistochemistry was recommended as a result of the high suspicion for histiocytosis and its results were compatible with the non-Langerhans cell histiocytoses i.e. CD1a and S100 negative, CD68 positive. Based on clinicopathological and immunohistochemical findings, a presumptive diagnosis of generalized eruptive histiocytosis (GEH) was assumed.

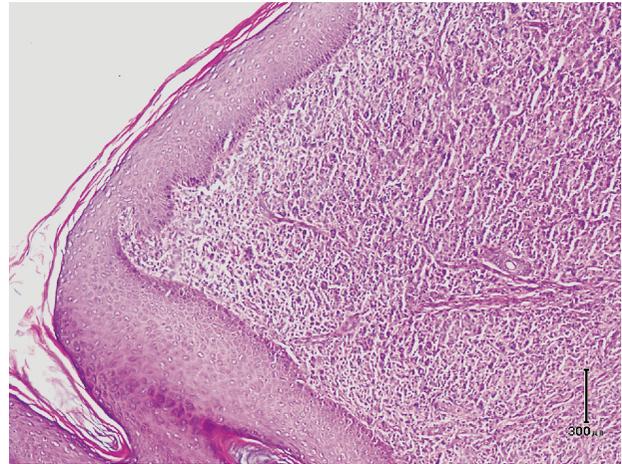


Figure 3. Histopathology view: monomorphic histiocytic infiltration and irregular fibrosis with scattered neutrophils, lymphocytes and multinucleated giant cells (H&E×40)

DISCUSSION

GEH is a proliferative disorder of non-Langerhans cell origin. First described by Winkelmann and Müller in 1963⁷, it is characterized by multiple discrete red-brown or flesh colored papules that develop in crops with a tendency for spontaneous resolution and recurrent episodes. Lesions usually appear on the face, trunk, and proximal extremities in a symmetrical distribution and are asymptomatic⁶, although it could have multiple differential diagnosis which is important to be considered⁸.

In the presented patient, lesions were distributed all over her body with only the mucous membranes, palms and soles spared. Consistent with earlier reports, clinical progression in this case was not typical for GEH, because the eyelids and face were the initial site of involvement rather than the trunk and extremities⁹, although this could not mitigate the diagnosis. The histological findings included dermal infiltration of histiocytes with few inflammatory cells. Although multinucleate giant cells were observed in this study, it was not considered as a clue against the diagnosis^{9,10}. Immunohistochemical findings showed features consistent with non-LCH, such as negative CD1a and S100, and positive CD68. Apart from one case of GEH associated with acute monocytic leukemia reported by Klemke et al.¹¹, no malignancies or internal involvement has been observed in GEH. Therefore, this study did not take on extensive paraclinical evaluation, since physical examination,

complete blood count, serum biochemistry, liver and kidney function tests were normal.

The differential diagnoses for this case mainly included other non-LCH. BCH tends to involve infants younger than 3 years and has a slightly different distribution pattern, although BCH, GEH and early non-xanthomatous JXG could not be differentiated based on histopathological features. ICH has distinct immunohistochemical features characterizing both LCH and non-LCH, i.e. being positive for CD1a, S100 and CD68. Histological examination revealed no foam cells or Touton giant cells; hence XD and JXG could be considered as less probable diagnoses². Furthermore, XD lesions tend to become confluent especially in the flexor areas. Papular xanthoma which may be a variant of other xanthogranulomatous conditions has similar clinical presentation but usually the mucous membranes are affected in adults and foamy histiocytes are present in the tissue^{1,2}.

Up to date, a total of approximately 43 cases of GEH have been reported in English literature. As a result of its rarity, no treatment has proven to be more effective than the other and most of the treatment modalities are based on case reports. For instance, Deng et al.¹² used a combination of hydroxychloroquine sulphate, thalidomide, and systemic corticosteroid. Although the treatment was said to be effective, it was not reassessed by other investigators in larger trials. Other treatments suggested for this entity include methotrexate and PUVA^{13,14}. Since the disorder is self-limited^{6,9,15}, a "wait and watch" approach and careful follow-up could be sufficient in many patients. Our patient had been severely compromised socially. Therefore, the PUVA therapy was adopted as first treatment because of its safety and feasibility. After fourteen sessions of phototherapy, as a result of no apparent improvement, the patient stopped the treatment. Lastly, because the lesions in this patient did not completely improve after two years, it could be the first presentation of other non-LCH like progressive nodular histiocytosis¹⁶ and follow-up is required.

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