

# Generalized Eruptive Histiocytosis Presenting with Warty Lesions on Face

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## ABSTRACT

Generalized eruptive histiocytosis is a benign proliferative disorder of non-Langerhans cells. It is a very rare disease. The disease presents with soft to firm fleshy papules on face, neck and upper trunk. Biopsy is often needed to make the diagnosis because of its rarity and diverse presentation. There is tendency for the disease to regress spontaneously without treatment. Treatment, if any needed, suffices to topical modalities.

We report here a case of generalized eruptive histiocytosis which presented with lesions of dual morphology. This is a very rare disease with diverse presentation being reported first ever in our country.

**Key words:** *Histiocytosis. Generalized eruptive histiocytosis. Non-langerhans cell histiocytosis. Histiocytoma.*

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## INTRODUCTION

The histiocytoses are a group of disorders involving proliferation and accumulation of cells derived either from Langerhans cells or from mononuclear macrophage system. They are, therefore, divided into two broad groups: Langerhans cells histiocytosis or histiocytosis X (Langerhans cell-derived) and non-Langerhans cells histiocytoses (derived from mononuclear-macrophage system).

Generalized eruptive histiocytosis (GEH) is a non-neoplastic proliferation of non-Langerhans cells. It is one of the several variants of non-Langerhans cell histiocytoses, which include xanthoma disseminatum, generalized eruptive histiocytosis, progressive nodular histiocytosis, xanthoma disseminatum and multicentric reticulohistiocytosis. This rare disorder has a benign self-healing course.<sup>1</sup> Literature search shows that upto January 2004, only 21-22 cases have been reported all over world.<sup>2-13</sup>

GEH is separated from other variants of its family by clinical and histopathological features.<sup>5</sup> Clinically, it presents as reddish-brown soft papules on face, trunk and proximal limbs. It runs a benign course showing tendency for spontaneous resolution with brown pigmentation.

We report a case of young adult in whom small, dome-shaped scattered, symmetrically distributed fleshy papules developed over chest and axillae. Similar papules but with warty appearance were found on face.

On histopathological examination, these proved to be non-Langerhans cell histiocytosis. A clinical diagnosis could not be reached emphasizing the importance of histological examination in rare disorders like this one.

## CASE REPORT

A young patient of 28 years of age presented at skin OPD with the complaints of multiple papules on face, neck, chest and both armpits. The lesions started to appear five months back. These appeared first on neck followed by face, chest and both axillae. Itching was the only symptom without diurnal variation. It varied in severity from time to time. There was no symptom pertaining to any other system. For these lesions, patient consulted a dermatologist who, considering it warts, advised and performed electric cauterization on some of the papules, which disappeared with residual pigmentation.

At the time of presentation, numerous papules about 60-70 in number were found distributed on face, neck, chest and both axillae (Photograph 1). Few similar lesions were also seen on abdomen and groins. Papules were small in size ranging from few mm to 1 cm in diameter. These were dome-shaped, soft to firm in consistency and bluish-red in colour; some being frankly brown (Photograph 2). Some of the lesions had already resolved spontaneously to leave pigmented patches. The lesions on face were more keratotic and brown in colour mimicking warts as compared to those on trunk (Photograph 3). No such lesions were seen in the oral and nasal cavity on examination. Few small papules were noted on the lower lid margin but none were found on palpebral or bulbar conjunctivae. Systemic examination of respiratory, cardiovascular, gastrointestinal and nervous system did not reveal any abnormality.

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Two papules, one from trunk and other from face were excised and submitted to laboratory with differentials of angiofibroma, neurofibroma and Kaposi sarcoma. At the same time, routine tests like complete blood counts, blood sugar, blood chemistry and urine analysis were also advised. There was no abnormality on these tests.

Histopathological examination revealed a single focus of proliferating small calibre vascular channels lined by endothelial cells (Figure 4). Large eosinophilic cells containing vesicular nuclei were seen in between the vascular channels. The vascular channels stained positively for CD<sub>31</sub> (Figure 5) and eosinophilic cells for CD<sub>68</sub> (Figure 6). Thus, the diagnosis of histiocytosis was established.

The lesions were frozen with liquid nitrogen and good response was seen. Patient noted regression of lesions within one week. Patient is under regular follow-up.



Figure 1: Erythematous fleshy



Figure 2: Erythematous fleshy



Figure 3: Close-up of lesions on

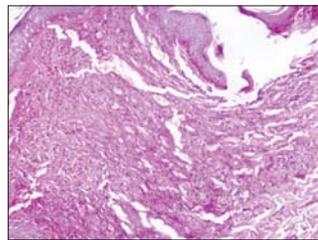


Figure 4: H and E section showing proliferation of histiocytes and occasional blood vessels.

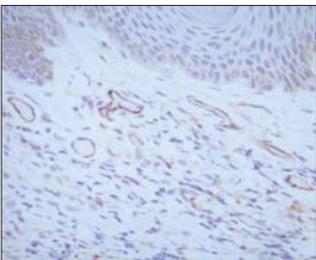


Figure 5: CD<sub>31</sub> staining the endothelial cells of blood vessels.

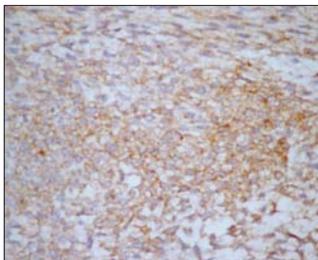


Figure 6: CD<sub>68</sub> staining diffusely histiocytes.

## DISCUSSION

While going through literature, we found that this case was slightly different from those already reported, in terms of clinical features. Most authors describe the features of lesions of generalized eruptive histiocytosis (GEH) as: soft, fleshy, reddish-brown, dome-shaped

papules ranging from few to several hundreds in number; situated symmetrically on trunk and proximal extremities with progressive development and ultimate healing with pigmented scars.<sup>1-11</sup> This patient had lesions of similar morphology on trunk and axillae; but the lesions on face were more keratotic and warty. These appeared to be viral warts on first sight. The reason for this appearance on face could not be inferred. It is believed that this is due to exposure of facial skin to comparatively more daily wear and tear and environmental insults like UV radiation. The lesions on trunk with spontaneous healing and cyclical recurrences in crops and fleshy nature were suggestive of lesions of angiomatous/fibrous origin. The cause for dual presentation of the disease could not be understood.

Generalized eruptive histiocytosis is a benign neoplastic disorder of histiocytes of monocyte-macrophage lineage. The disease was first described by Winkelmann and Müller in 1963 in three healthy patients.<sup>1</sup> Non-Langerhans cell histiocytoses are classified according to type of cells in dermal infiltrate. These may be either mononuclear e.g. vacuolated, spindle-shaped, xanthomatous and /or multinucleate e.g. touton, ground glass appearance, Langerhans or foreign body type, thus any clinical type of histiocytosis does not necessarily contain single type of cell. There is often a mixture of different cell types; with one cell type predominating. This predominant cell type helps differentiate various types of histiocytoses. For example, juvenile xanthogranuloma are vacuolated, spindle-shaped xanthomatous cells are found as predominant, while in adult xanthogranuloma, the predominant cell is scalloped oncocyctic cells. Mostly, vacuolated histiocytes are seen in mononuclear variants of histiocytoses such as early benign cephalic histiocytosis, and generalized eruptive histiocytoma. Vacuolated lipemic histiocytes predominate in papular xanthoma and rarely in xanthoma disseminatum, whereas spindle-shaped histiocytes outnumber in spindle cell xanthogranuloma and progressive nodular histiocytosis. The scalloped histiocytes are found in most cases of xanthoma disseminatum, and finally oncocyctic histiocytes are evident in reticulohistiocytoma and multicentric histiocytosis.<sup>14</sup>

In the present case, the lesions were bluish-red in colour, soft to firm in consistency and dome-shaped, thus, leading to consideration of diseases of angiomatous origin in differential diagnosis; angioma, angiofibroma, angiokeratoma and Kaposi sarcoma. Diagnosis of histiocytosis was not considered as it is a very rare entity in our country (not reported in literature). Some of the lesions also gave molluscum contagiosum-like look. In contrast, the lesions on face were more keratotic, less fleshy mimicking warts. The location of lesions in this case was typical e.g. trunk and proximal extremities. None of the factor triggering the lesions was

evident in the present case. Some of the lesions has already undergone spontaneous resolution to leave back pigmented scars as is reported variously in literature.<sup>2</sup> Tamiya<sup>15</sup> *et al.* reports resolution of their case following exanthema subitum. The cause for spontaneous resolution is guessed to be apoptosis. According to patient, the lesions first appeared in the last winter and some of them regressed spontaneously in summer. New lesions began to appear this winter, this confirmed the seasonal variation of disease activity as reported by Misery.<sup>5</sup>

Histologically, the cells in this case had eosinophilic cytoplasm with vesicular nuclei and stained positively for CD68. Further staining was not carried out with markers like mouse monoclonal antibodies anti-CD<sub>1a</sub>, CD<sub>3</sub>, CD<sub>4</sub>, CD<sub>8</sub>, CD<sub>14</sub>, CD<sub>22</sub>, CD<sub>25</sub>, CD<sub>30</sub>, CD<sub>36</sub>, CD<sub>40</sub>, CD<sub>45</sub>, CD<sub>56</sub>, CD<sub>57</sub>, Mac<sub>387</sub>, Ki<sub>67</sub> and  $\beta$ -2 microglobulin as shown by Cline.<sup>14</sup> due to non-availability of these in the local set-up. The disease is reported to be associated with other medical conditions e.g. rheumatic fever, acute monocytic leukemia.<sup>16</sup> This patient had no such association at all.

Various treatment suggested include thalidomide,<sup>17</sup> methotrexate, antimalarials<sup>18,19</sup> and PUVA.<sup>20</sup>

Rarity of disorder and the paucity of confirmatory investigations like further immunohistochemical staining and electron microscopy and full body scanning for detection of systemic involvement in this case is a limiting factor.

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