Generalized eruptive papular lesions

Hassab El-Naby H, MD, El-Khalawany M, MD

Department of Dermatology, Al-Azhar University, Cairo, Egypt

CLINICAL FINDINGS

A 31-year-old male presented with asymptomatic slowly increasing generalized skin lesions of 5 years duration. The condition started on the trunk, then rapidly progressed to involve almost whole body except face, palms and soles. Although the lesions showed gradual subsidence with residual pigmentation, new lesions continued to appear. There were no symptoms indicating systemic affection and there was no family history of similar lesions. Cutaneous examination showed bilaterally symmetrical, skin-colored to brown papules distributed on the trunk and extremities (Fig. 1). The lesions were mostly discrete, non-confluent and measured about 3-7mm (Fig. 2). General examination was irrelevant and routine investigations showed no significant abnormalities.

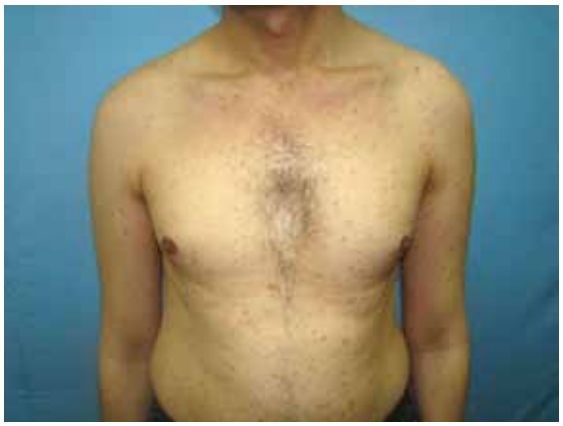

Fig. 1 Generalized papular eruption on the trunk and extremities composed of nonconfluent darkly pigmented papules.

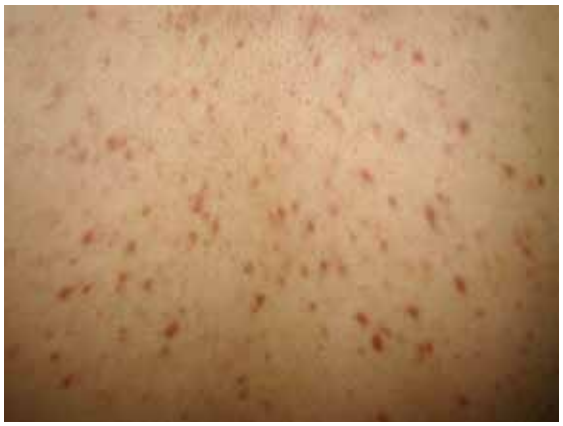

Fig. 2 The lesions are mostly formed of brown papules, measuring about 3-7mm.

What is your clinical differential diagnosis?

Eruptive syringoma, papular sarcoidosis, eruptive histiocystomas, disseminated xanthoma, juvenile xanthogranuloma, Langerhans cell histiocytosis and generalized mastocytosis,

PATHOLOGICAL FINDINGS

A skin biopsy from a representative lesion showed perivascular and interstitial inflammatory infiltrate, distributed mainly in the upper dermis (Fig. 3) and formed mainly of histiocytes intermixed with other inflammatory cells, mainly lymphocytes. The majority of histiocytes showed granular cytoplasm while few cells showed foamy cytoplasm (Fig. 4). The epidermis showed increased basal pigmentation with normal thickness. Immunohistochemical staining showed predominance of CD 68 +ve cells (Fig. 5).

Correspondence: *Dr. Hassab El-Naby H, Department of Dermatology, Al-Azhar University, Cairo, Egypt*

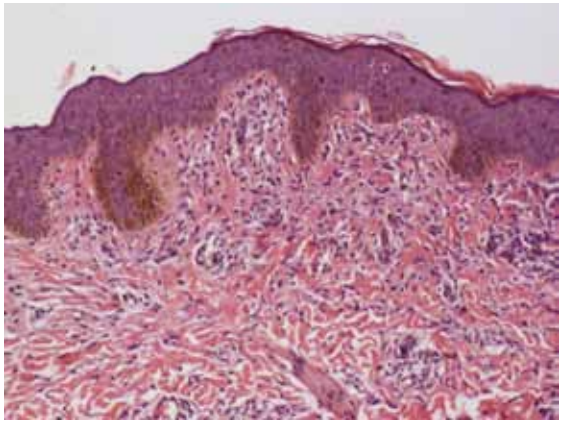

Fig. 3 Histologic examination showed perivascular and interstitial infiltrate composed mainly of histiocytic cells. The epidermis showed increased basal pigmentation (H&E x100).

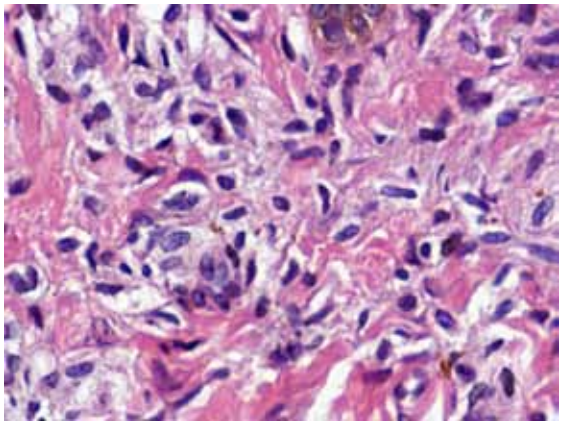

Fig. 4 The main infiltrate is composed of histiocytes with granular cytoplasm and few foamy cells (H&E x400).

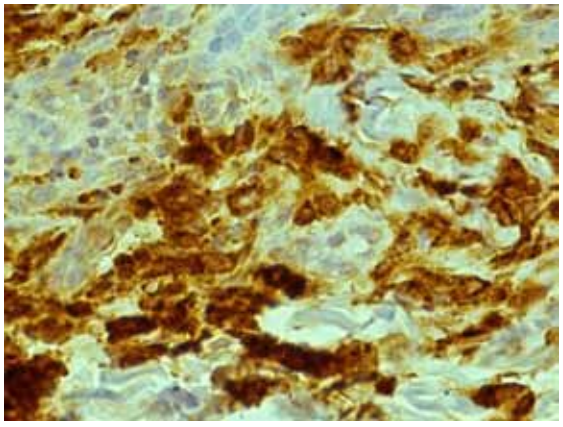

Fig. 5 Immunostaining showed predominance of CD 68+ve cells.

DIAGNOSIS

Generalized Eruptive Histiocystoma (GEH)

COMMENT

Histiocytosis is a group of proliferative disorders of the mononuclear phagocyte and immunoregulatory effector system composed of macrophages and dendritic cells. The macrophages constitute the phagocytic function and the dendritic cells, represented by Langerhans cells, indeterminate cells and the dermal dendrocytes, constitute the antigens presentation.[1-3]

GEH is a benign rare dermatologic disease that was firstly described by Winkelmann and Muller. It is more common in adults but may start at any age group. The disease is characterized clinically by asymptomatic erythematous or pigmented firm papules. The lesions are usually appear in crops with more involvement of the face, trunk and proximal parts of the extremities. The disease usually spares mucous membranes and is not reported to affect the visceral organs.[4-7]

The differential diagnosis among the non-Langerhan cell histiocytosis is based primarily on the duration and course of lesions, patient's age and presence or absence of associated systemic diseases. Recent medical literature has suggested that GEH may be considered as the initial spectrum for several histiocytoses, mainly for sharing clinical and immunophenotypical similarities. GEH is an early undifferentiated stage of various histiocytic disorders. It may precede the classical presentation of juvenile histiocytosis, disseminated xanthoma, progressive nodular histiocytosis and/or multicentric reticulohistiocytosis.[8-10]

Differential diagnosis of GEH includes, LCH and other forms of non LCH (xanthomata, benign cephalic histiocytosis, reticulohistiocytosis, juvenile xanthogranuloma and xanthoma disseminatum). LCH has a different immunohistochemical profile from GEH, staining positively with S100

The clinicopathological challenges of GEH.

Diagnosis	Clinical	Pathological
Eruptive syringoma	• More common in women • Usually occurs before or during puberty • Usually affects the eyelids • Usually skin colored	• Multiple ducts surrounded by fibrous stroma in the superficial dermis • The ducts are formed by two layers of epithelial cells and are filled with amorphous keratinous materials
Papular sarcoidosis	• Multisystemic disease with common pulmonary impairment • Described in all races, genders and age ranges • Nonspecific symptoms such as fever, malaise, fatigue in 1/3 of cases • Presented with erythematous-violet papules, some with central umbilication	• Nodular dermal granulomatous reaction • Well formed granulomas containing histiocytes with broad and vacuolated cytoplasm • Absence or minimal lymphocytes surrounding the tubercles • Negative Ziehl-Nielsen and PAS stains
Disseminated xanthoma	• Hundreds of discrete papules and nodules, which are red-brown to yellow in color • Chiefly involve the face and trunk, and occur in flexures and folds such as the axillae and groin • May involve the mucous membranes of the mouth, pharynx, larynx, conjunctiva, and cornea.	• Intradermal infiltrates of Touton-type giant cells, foam cells, and histiocytes • Scattered lymphocytes, neutrophils, and plasma cells • Immunohistochemical staining is negative for the CD1a and S-100 proteins but positive for CD68 • In early lesions, scalloped macrophages are dominant
Multiple juvenile xantho-granuloma	• Usually presented with asymptomatic, self-healing, red, yellow, or brown papules, nodules • Around 10% of cases manifest in adulthood. • Serum lipid profiles are usually normal • No definite sites of predilection • Lesions are usually asymptomatic.	• Early biopsy reveals a dense monomorphous histiocytic infiltrate in dermis. • Older lesions contain foam cells, Touton giant cells and foreign body giant cells • A mixed cellular infiltrate of neutrophils, lymphocytes, eosinophils and rarely mast cells
Diffuse cutaneous mastocytosis	• Present as a diffuse reddish-brown discoloration and have a peau d›orange appearance on the entire surface of the skin. • Bullae may be the initial symptom • May have a higher risk for systemic involvement and severe symptoms such as sudden death.	• Predominant perivascular and interstitial mast cell infiltrate (usually more than 20 mast cells per high power field). • Few eosinophils could be observed. • Cytoplasmic granules are stained metachromatically with Giemsa • Aberrant expression of CD25 and/or CD2

and CD1a. Histopathologically, the absence of multinucleated, touton giant and foamy cells excludes GEH from the non-LCH disorders. Benign cephalic histiocytosis is characterized clinically by the localization of the eruption to the head and neck and the appearance of the disease only in children. Multicentric reticulohistiocytosis is usually associated with arthritis and there are giant cells with ground-glass cytoplasm in the dermal infiltrate.[11-13]

The disease is self-limiting and does not produce systemic symptoms and usually there is no need for treatment. PUVA therapy and Oral isotretinoin may be effective in the treatment of some cases with less incidence of recurrence and relapse.[14,15]

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