GENERALISED ERUPTIVE HISTIOCYTOMA
(A case report)

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Summary

Winkelmann and Muller in 1963[1] described a new entity called Generalised Eruptive Histiocytoma (GEH). Generalised Eruptive Histiocytoma represents a widespread reactive hyperplasia of histiocytes derived from reticuloendothelial elements. The histiocyte is produced in response to certain chemical or pathological stimuli and is capable of phagocytosis. Phospholipids, colloidal particles, cholesterol in olive oil, saccharated iron and polysaccharides stimulate the formation of histiocytes from reticular cells. Purely histiocytic dermal masses occasionally occur unassociated with inflammatory cells, vascular or connective tissue changes as seen in GEH.

Review of Literature

Classification of histiocytic tumours of skin (Histiocytic-reticulosis).

I. Primary
   - (i) Benign
   - (ii) Malignant

II. Benign
   - (i) Generalised eruptive histiocytoma
   - (ii) Naevoxantho - endothelioma or xanthogranuloma
   - (iii) Xanthoma-disseminatum
   - (iv) Reticulohistiocytoma cutis
   - (v) Histiocytosis - X

ii. Malignant
   - (i) Histiomonocytic reticulosis
   - (ii) Histiomonocytic form of reticulum cell sarcoma

2. Secondary
   - (i) Histiocytoma (Dermatofibroma - Lenticulare)

Nodular histiocytoma in its classic form, as described by Worringer[2], is a solitary tumour of the skin. It has been described under various terms by different authors. Unna[3] described it originally as fibroma simplex; later to become widely known as "Dermatofibroma lenticulare"[4], Michelson[5] described it under the name, "Nodular Subepidermal Fibrosis". Worringer[2] labelled it "Histiocytoma" on the basis of his observation that in all the above conditions the diagnostic feature is a histiocyte and not fibroblast. Arnold and Tilden[6], gave the concept that the precursor of foam cell of xanthoma is the histiocyte and hence histiocytoma cutis is related to xanthomas and not to fibromas. Maximow and Bloom[7] also report that fibroblast is incapable of changing its structure and function under most stimuli whereas histiocyte is highly labile and becomes actively amoeboid and phagocytic under many types of inflammatory stimuli. Both Montgomery[8,9] and Senear and Caro regard histiocytoma as a separate entity though related to xanthomatosis. They regard histiocytoma as a xanthic form of tumour or a

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tumourous sort of xanthoma. Alerte[10] described histiocytoma under the name xanthofibroma with systemic lesions. Lewis and Sachs[11] used the term lipoidal histiocytoma in 1927. If systemic lesions are present in a case of histiocytoma the differentiation from xanthogranuloma is very important as reported by Stout[12], who has stressed that fibroxanthoma or xanthofibroma are small and located only on skin and subcutaneous tissue whereas xanthogranuloma are large and involve vital structures as well. The case of adult negro female reported by Robinson et al in 1963[13] as multiple lipoidal histiocytoma is considered xanthogranuloma by Montgomery. This again shows that differentiation between xanthogranuloma and multiple histiocytoma or fibroxanthoma is very important.

Winkelmann and Muller[1] first stressed about a different type of histiocytoma characterised by many, even thousands of histiocytic tumours that erupt as generalised papules over the body surface. The lesions are generalised, symmetrical, discrete, flesh coloured to bluish red papules with no tendency to grouping. Lesions develop in crops and often involute spontaneously.

The histological picture is that of a monomorphous infiltrate composed of a mass of reticular and histiocytic cells without fat, mucin, iron or changes in connective tissue or blood-vessels. This process is more closely related to first histiocytic stage of xanthogranuloma, histiocytosis-X or xanthoma-disseminatum than to the classic solitary histiocytoma (Dermatofibroma) and represents benign proliferation of reticular cells (reticulosis). These authors thought it is a distinct entity representing benign eruptive histiocytoma and labelled it as Generalised Eruptive Histiocytoma (G.E.H.). They had also referred to about 4 cases earlier described in literature, without proper classification. Solitary histiocytoma occurs in response to trauma and histiocyte accumulation is a secondary feature.

Diagnostic features of G.E.H. are :

1. Widespread, essentially symmetrical lesions occurring particularly on trunk and proximal part of extremities.
2. Distinct flesh coloured to bluish red papular lesions without grouping.
3. Progressive development of new lesions without history of trauma.
4. Spontaneous resolution of lesions leaving brown macules or complete disappearance.

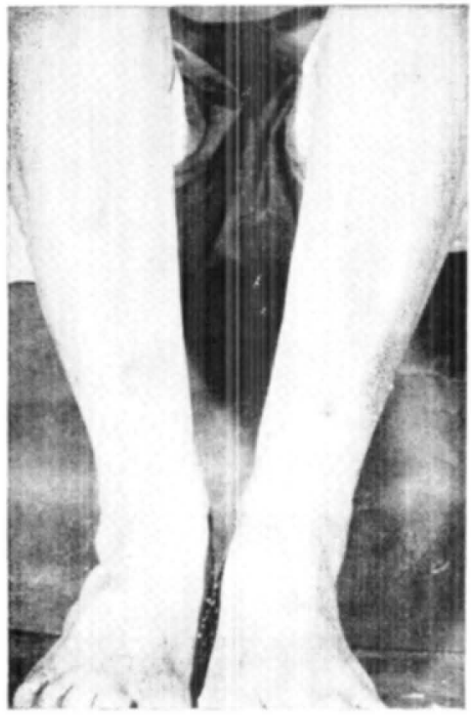

Fig 1 Showing multiple nodules of variable size.

5. A benign histological picture of mononuclear histiocytes.
6. Absence of any associated systemic or other problem.

Case History

A 40 year old female attended the skin department with 6 years' history of asymptomatic erythematous brownish papules and nodules which were gradually increasing in size. Lesions started as erythematous brownish papules on right leg and gradually spread to dorsum of right foot and then left foot, left leg, dorsum of right hand, both arms, chest, abdomen and back. Past history of menorhagia was present. On investigation, patient was found to be a diabetic. General and systemic examinations were normal.

Local Examination

Innumerable papules and nodules of varied sizes were present, maximally on upper extremities. Colour varied from reddish brown to dark brown. Nodules were non-tender, firm and could be moved freely over the underlying structures. The overlying skin was adherent except over some nodules, where the skin was free and wrinkled. Total number of lesions was 640 (Rt. forearm 190, left forearm 216. Rt. leg 46, Lt. leg 53, Rt. thigh 10, Lt. thigh 13, Front of chest 34, Back 34, Lt. arm 11, Rt. arm 33). Investigations revealed Hb. 9.6 gm.%, TLC 8,650/cmm., DLC P 71, L 28, M 0, E 1 ESR 39 mm. 1st hour westergren, FBS 150 mg.%, serum proteins total 5.2 gm.% with albumin 2.8 gm.%, globulin 2.4 gm.%, serum uric acid 3.8 mg.%, serum cholesterol 200 mg.%, urine contained 3% sugar. X-ray skull N.A.D., Histopathology was consistent with GEH.

Discussion

A probable diagnosis of GEH/Xanthogranuloma was made. G.E.H. was considered as the first probability because of the late onset at the age of 34 years, multiplicity of papules and nodules with their peculiar brown colour and symmetrical distribution, tendency for spontaneous involution, absence of grouping, and absence of systemic involvement. Histologically it is very difficult to differentiate between GEH and early stage of xanthogranuloma as both are characterised by large accumulation of histiocytes or macrophages without any lipid infiltration. Few lymphoid cells and eosinophils are present in Xanthogranuloma and the epidermis is atrophic. Histopathologically diagnosis of GEH[15] was made in this case on the basis of the monomorphic histiocytic infiltrate with a few foreign body giant cells, epidermal changes consisting of hyperkeratosis and acanthosis and complete absence of eosinophils and wreath shaped giant

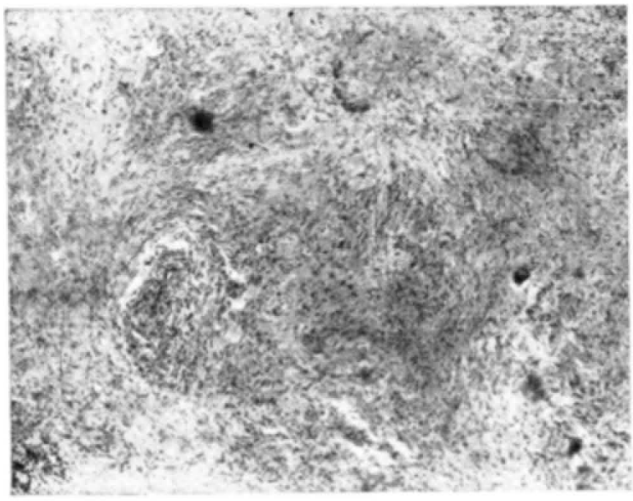

Fig. 2 Monomorphous histiocytic infiltrate with few foreign body giant cells.

cells. In addition the connective tissue and blood vessels were normal and no mucin or iron could be detected within the histiocytes though a rare histocyte contained fat. Lever (1975)[15] has mentioned that histiocytes in GEH contain few lysosomes and occasionally few lipid droplets under electron microscope.

GEH is considered to be a reactive hyperplasia of histiocytes. Juvenile Xanthogranuloma is also considered an independent entity as a reactive granuloma of unknown cause and is believed to be related to GEH which is closely related to conditions characterised by wide spread reactive hyperplasia of histiocytes e.g. Juvenile Xanthogranuloma, histiocytosis-X and Xanthoma-disseminatum. All the other related conditions like reticulohistiocytosis, Xanthoma tuberosum, granuloma annulare and necrobiosis - lipoidica were ruled out clinically and histologically. Main differential diagnosis was between GEH and early histiocytic stage of Juvenile Xanthogranuloma. The latter usually appears at young age and systemic involvement is common. Few odd points in our patient are the presence of more lesions on limbs as compared to trunk and associated diabetes. Diabetes is seen in some diseases characterised by histiocytic hyperplasia and slight overlapping of clinical features of one disease and another are already reported. Winkelmann and Muller[1] also reported one patient with GEH who had skull lesions resembling histiocytosis-X.

In the foreseeable future, when we come to know about their histogenesis, we might be able to ascertain a common factor responsible for hyperplasia of histiocytes in these different diseases. Muller et al[14] have done histochemical studies to reveal the absence of lipids iron and mucin in histiocytes of GEH.

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