JUVENILE XANTHOGRANULOMA

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Juvenile Xanthogranuloma is a benign disseminated xanthomatous and granulomatous condition of the skin, mucus-membrane and eyes occuring in very young children and clearing spontaneously.

The first case of Juvenile Xanthogranuloma (JXG) was reported by Adamson in 1905. He presented a child with yellowish papular lesion on body and mucus membrane in the first few weeks of life. He termed the lesion as Congenital Xanthoma Multiplex. In 1912 McDonagh reviewed five cases of this entity and coined the term "Naevoxanthoendothelioma". In 1954 the term Xanthogranuloma was introduced by Helwig and Hackney and they described histopathological picture more accurately. The following is the case report of a child with Juvenile Xanthogranuloma.

A 5 months old male child was brought to Skin Department with multiple papular lesions of few weeks duration. The first lesion was seen on back at the age of 3 months which subsided by itself in 3–4 weeks. Later on similar lesions developed on back, front of chest, arms and legs. The papules were oval, 0.2 to 1.5 cm diameter, yellowish in colour and were quite firm on palpation. They were non-itchy and were distributed discretely over back, neck, trunk and extremities. They persisted for 4–6 weeks and then subsided by themselves leaving dark pigmented atrophic area. Skin elsewhere was normal. Systemic examination did not show any enlargement of liver or spleen. Heart and lungs were normal. Mucus membrane and eyes did not show any abnormality.

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Laboratory Investigation:

Serum cholesterol 131 mg %. Radiological examination of skull, chest and long bones did not show abnormality.

Skin Biopsy:

Section showed hyperkeratosis with acanthosis. Rete pegs showed elongation at places. Dermis showed diffuse collection of histiocytes with many capillaries. Histiocytic cells showed pale, vacuolated cytoplasm with dark staining nucleus. Foam cells and Touton giant cells were not seen. However the histology is consistent with early naevoxanthoendothelioma.

Discussion:

Juvenile Xanthogranuloma usually occurs early in life. Cases in adolescence have also been recorded. Nomland in review of 42 cases taken from literature found that 66% had an onset before 6 months of age. There is no sex predilection. The onset is abrupt. The typical lesion is firm red-yellow papule 1-10 mm in diameter. Colour changes gradually to light yellow. Lesion shows predilection for head, neck, trunk and extremities.

Systemic involvement in Juvenile Xanthogranuloma is also known. Involvement of iris causes diffuse thicken-

ing with muddy discoloration or localised nodules. Cilliary body may be involved. Blindness may occur. Involvement of lungs, pericardium and testicles is also recorded. Plasma cholesterol and lipids are within normal limits. There is no familial tendency.

Histopathology :

Main features consist of poorly demarcated dermal infiltrate consisting of histiocytes, giant cells and various other inflammatory cells. The elevated epidermis may show flattened rete-ridges. Scattered Tuton giant cells are of a considerable diagnostic value as is the presence of lipid which is sudanophilic and also stains with (oil-red-o).

Lever mentions early lesion of Juvenile Xanthogranuloma in which there is uniform infiltration of histiocyte and absence of any lipid infiltration His observation was confirmed by Nodl. In his case the infiltration was composed almost exclusively of reticulo-histiocytic element.

Sudanophilic implants were absent and there were only a few giant cells. Montegomory confirms that one must accept an early histiocytic phase for Juvenile Xanthogranuloma.

The disorders which may have proliferation of reticuloendothelial or histiocytic elements which actively phagocyte fat/iron can be grouped as under :

(1) Histiocytosis X : This includes
   (a) Hand-Schuller-Christian diseases.
   (b) Letterer Siwe disease.
   (c) Eosinophilic granuloma.
(2) Xanthoma disseminatium.
(3) Histiocytoma.
(4) Reticulo histocytoma.
(5) Juvenile Xanthogranuloma.
(6) Plane xanthomatosis.

Histiocytosis X :

This includes three disorders i.e. Hand-Schuller-Christian disease, Letterer Siwe disease and Eosinophilic granuloma. They appear to be of different degrees of a similar reaction.

Hand-Schuller-Christian disease :

Syndrome combines skin eruption and clinical triad consisting of defect in cranial bones, exophthalmous and diabetes insipidus Onset is between 2–6 years. Cutaneous changes are variable and occur in 30% of cases. Most characteristic lesion are erythematous patches, petechiae, papules and macules. Site is on scalp, face, trunk and buttocks. Other manifestations include ulceration of gums, pulmonary infiltration, enlargement of liver, spleen and lymph glands. Mortality rate is over 50% but spontaneous recovery can occur.

Letterer-Siwe disease :

Onset is between 3 months to 3 years. Skin eruption consists of discrete yellow brown scaly papules occuring in crops on scalp, neck, face and trunk, and tendency to haemorrhage. Systemic involvement causes loss of weight, fever, splenomegaly, heptomegaly, lymphadenopathy and anemia.

Eosinophilic granuloma :

This is the least severe variety with excellent prognosis. It occurs usually between the ages of 2 to 3 years. Characteristic lesion consists either of multiple or solitary lesion similar to that of Hand-Schuller Christian complex. Diabetes insipidous can occur if pituitary fossa is involved. Occasionally patchy dermatitis resembling Seborrhoeic dermatitis occurs on scalp.

Xanthoma disseminatum :

This is the rare histiocytic proliferative disorder characterised by wide spread cutaneous xanthoma frequently associated with diabetes insipidous. Cutaneous lesion consists of yellow, yellow-brown

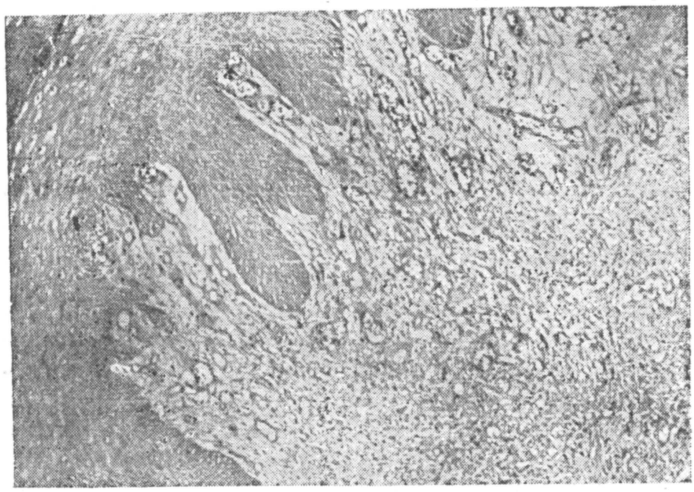


Fig. 1
Photomicrograph showing acanthosis with elongation of rete pegs. Dermis shows dense cellular collection with many capillaries.
(H & E x 100)

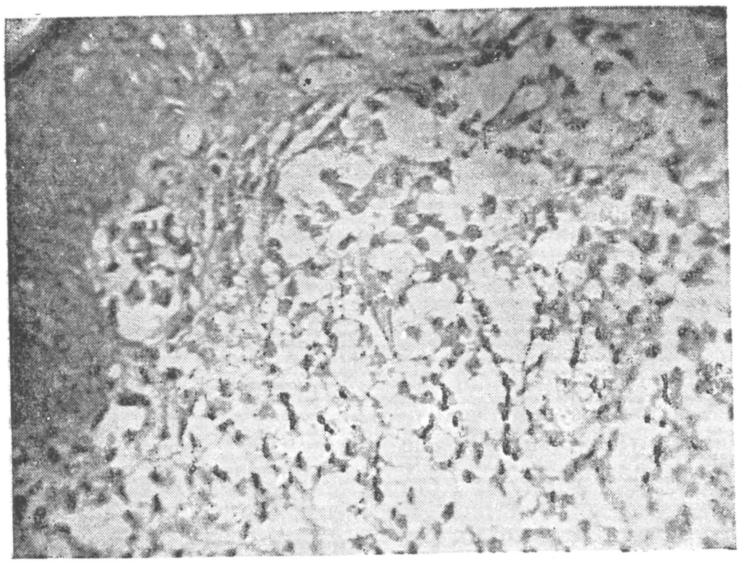
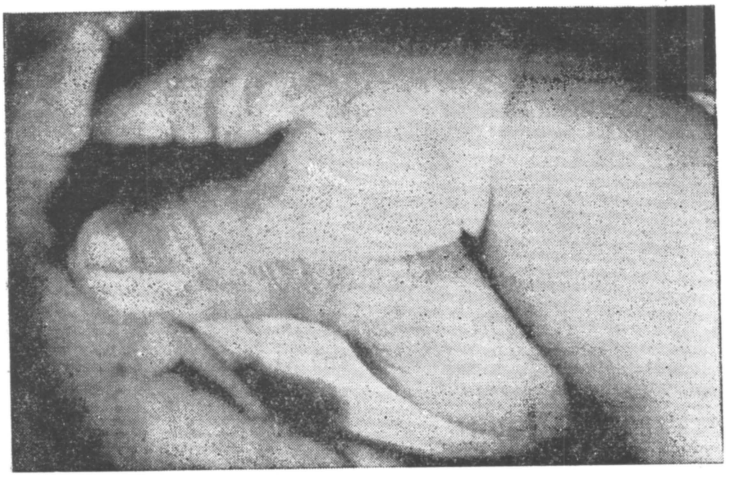


Fig. 2
Photomicrograph showing collection of histiocytes in the dermis. Cells show pale, vacuolated cytoplasm
(H & E x 400)



papules of 1–2 cm. size usually occur in flexures. Mucus membrane involved in 3% of cases and diabetes insipidous occur in 40% of cases. Plasma lipids are normal and prognosis is good.

Histiocytoma is too well known to merit any description. The histological picture is quite typical.

Reticulo histiocytoma is a systemic disorder of small xanthomatous giant cell granulomata in the skin, mucus membrane and synovial membranes. The lesions are firm, brown yellow papulonodules in the dermis and are found on the face, ears and buccal mucosa. Mono or polyarthritis may precede or follow most of the skin lesions. The histology is characterised by presence of mono and multinucleated giant cells.

Diffuse plane xanthomatosis is characterised by development of extensive plaques of xanthomatous infiltration. In 50% of cases association with multiple myeloma or leukaemia has been noted. The disease may manifest as xanthelesma on the eyelids and then followed by diffuse papular xanthomatosis symmetrically distributed on the trunk or limbs. The plasma lipids are normal.

Pathogenesis of Juvenile Xanthogranuloma:

Pathogenesis of Juvenile Xanthogranuloma has received much discussion and postulation. McDonagh's original concept was that the lesion represent a congenital proliferation of endothelial cells. This theory is not well supported to-day. Lamb and Lain felt that the condition represent a systemic proliferative process of the Hand-Schuller-Christian type, involving mainly the skin but capable of producing systemic lesion. Thannharger agrees with this postulation and he states that JXG is benign form of the Hand-Schuller-Christian complex generally confined to the skin and mucus membrane and normally showing spontaneous involution. Fleischmger feels that JXG represents a benign inflammatory granuloma some time accompanied by lipoid deposit. Helwig and Nomland also feel the condition is a separate entity from the systemic reticulo-endotheliosis. Most important is the fact that even with the internal lesion in JXG, the usual course is one of spontaneous remission in a comparatively short period of time. The short remission is decidely uncommon for the systemic reticuloendotheliosis. There has been no case of JXG merging into the systemic reticuloendotheliosis. Therefore pathogenesis of JXG represents a benign reactive process composed primarly of histiocytic cells usually showing xanthomatisation.

Generally course of JXG is self limited. Nomland stated that 1/3 of the cases cleared spontaneously in six months. Another 1/3 disappeared within 6–12 months The remaining 1/3 persists for more than one year. Either a flat atrophic scar or an area of altered pigmentation remains as the cutaneous lesion regresses.

Summary:

A case of Juvenile Xanthogranuloma has been described with review of its literature. The case discussed was in the early histiocytic phase and did not show any evidence of lipid infiltration.

Acknowledgement:

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TRUE or FALSE?

Chloroquin and Hydroxychloroquin have beneficial effect on Hepatic Porphyrias.

(Answer at Page No. 122)