XANTHOMA DISSEMINATUM

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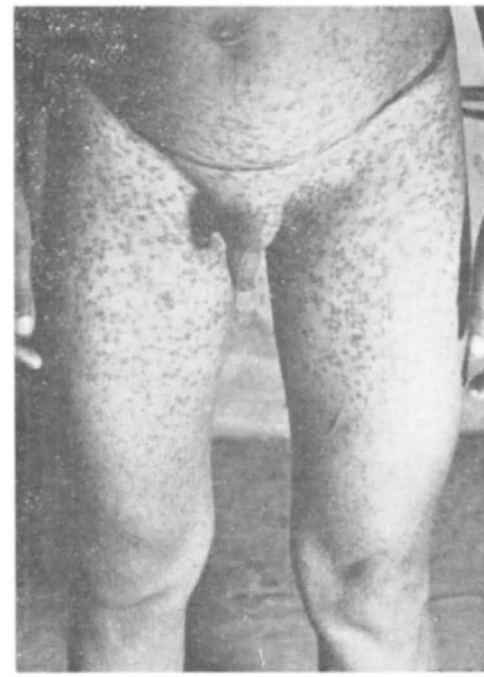
An 11-year-old male developed classical xanthomatous papules predominently over the face, neck, axillae, groins and genitalia. The patient had hoarseness of voice and associated diabetes insipidus which responded dramatically to clofibrate. Bony involvement was not apparent and plasma lipids were normal.

Key words : Xanthoma disseminatum, Diabetes insipidus.

Xanthoma disseminatum is a rare normolipemic, histiocytic proliferative disorder. Thannhauser and Magendantz[1] consider the first case of xanthoma disseminatum to be one reported by Virchow in 1871 entitled xanthoma multiplex. Since then, only about 30 cases have been reported.[2] To my knowledge, no case has yet been reported from India. Classically, the xanthomatous papules are predominently distributed over the major flexors. Mucous membranes of the mouth and upper respiratory tract may be involved in about one third of the patients.[3] Infiltrative lesions at the base of the skull may produce clinical diabetes insipidus in about 40% of the patients. Although xanthoma disseminatum has some features in common with histiocytosis X, this is regarded as a distinct entity.[3,4] Serum lipids are normal in this condition, and it is thought to be due to local tissue metabolic derangements causing primary proliferation of histiocytic elements with secondary accumulation of lipids in them.[4]

Case Report

An 11-year-old boy presented with multiple skin lesions of about 3-4 years' duration, and polyuria and polydypsia for about 5-6 months. The skin lesions were fleshy, firm, brownish, round to oval, discrete papules varying in size from 3-5 mm. These were located predominantly over the face, especially around the eyes, neck, antecubital and popliteal fossae, groins (Fig. 1), shaft of penis and scrotum. Some



papules were dome-shaped while others were flat. The lesions were not associated with itching or any other symptom. There was no ulceration or scaling. A few papular lesions were also seen over the buccal mucosa and soft palate. There were no obstructive symptoms such as dyspnoea or dysphagia but hoarseness of voice was conspicuous. There were no lesions on the cornea or conjunctiva. The vision was unimpaired. Liver and spleen were not palpable. There was no jaundice, lymphadenopathy,

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oedema or any bony lesion. Investigations such as haemoglobin, total leucocytic count, differential leucocytic count, erythrocyte sedimentation rate, liver function tests, plasma lipids, serum cholesterol level, fasting and post-prandial blood sugar levels were normal. Specific gravity of urine was 1002 and the 24-hour output was 3500-4000 ml. VDRL test was negative. X-ray skull did not reveal any abnormality. X-rays of chest, long bones, joints and pelvic girdle were normal. Histopathological examination of the lesion showed histiocytic proliferation in the dermis with occasional Touton-giant cells and a few inflammatory cells. There was no evidence of iron deposition. The epidermis showed mild hyperkeratosis without parakeratosis.

The patient was treated with four tablets (250 mg) of clofibrate a day. The polyuria and polydypsia responded very dramatically and within 10 days, the urine output was reduced to about 2000 ml/24 hours. The skin lesions did not improve, although some of the lesions did become flatter.

Comments

This disorder manifests with disseminated, xanthomatous papules occurring predominantly in young male children. The papules which are yellowish brown to brown are usually asymptomatic, distributed symmetrically, predominantly over the flexures. The papules are discrete initially, but may coalesce to form nodules or verrucose plaques with the passage of time. My patient had very typical papules distributed predominantly on the flexures, face and genitals.

The mucous membrane lesions are present in about one third of the cases in the mouth and upper respiratory tract. Lesions in the larynx may cause hoarseness and severe dyspnea, and may require tracheostomy.[3] Exceptionally, death may be caused by asphyxia. Xanthomatous masses may be present on the anal mucosa[6] and may cause partial obstruction of the anal orifice.[2] Ocular lesions may be present on the sclera and cornea[7] and may cause partial obotructive blindness.

Meningeal lesions in the form of infiltration at the base of the skull may produce clinical diabetes insipidus. This may occur in about 40% of the cases and is usually mild. This usually accompanies or follows the skin lesions but may be a presenting manifestation. My patient developed mild diabetes insipidus about 3 years after the appearance of skin lesions.

Although xanthoma disseminatum has some features in common with histiocytosis X (especially Hand-Schuller-Christian disease) this is regarded as a distinct clinical entity because of its predominent occurrence in adults, characteristic distribution, common involvement of mucous membranes, absence of bone lesions and exophthalmos, histopathological features and the course of the disease.[3,4,8] However, except for their distribution, the cutaneous lesions are similar in both diseases and both diseases are fairly commonly associated with diabetes insipidus. Furthermore, a case of xanthoma disseminatum with multiple osseous lesions has been described.[2] Rarely, both conditions may be present in the same patient. It is possible that xanthoma disseminatum represents only one point on the spectrum of related diseases, with nevoxantho-endothelioma and histiocytosis X at the opposite ends of this spectrum.[9]

Histopathology of the earliest lesion shows histiocytic proliferation, while xanthoma cells or Touton's giant cells may be absent. Iron granules may be present in the histiocytes. The case of Halprin and Lorincz[9] showed considerable accumulation of iron granules within the histiocytes and they proposed the new term xanthosidero-histiocytosis, which is now accepted to be a distinctive form of xanthoma disseminatum. The serum lipids are also normal in xanthoma disseminatum and therefore, this xanthoma probably results from local tissue metabolic derangements, and most likely it

represents a primary proliferation of histiocytic elements with secondary accumulation of lipids in them.[5]

The prognosis is generally good. After a few months to a few years, the skin lesions may regress spontaneously and diabetes insipidus may resolve. But it is unpredictable. Kalz et al[6] observed one patient at regular intervals for a period of ten years without any tendency for the lesions to clear. Severe involvement of the upper respiratory tract is the only serious hazard to the life of the patinet by causing dyspnoea or asphyxia.[3] The diabetes insipidous is usually mild and does not require any active treatment but may be severe enough to require treatment with vasopressin. Corticosteroids are usually of no use. It has been reported that continuous corticosteroid therapy will prevent recurrence of the lesions which have been removed surgically. It is best done by dermabrasion or by electrocoagulation, if the lesions are few.[6] Superficial radiotherapy reduces the size of the lesions but this is not practicable when the lesions are widespread.

The diabetes insipidus in this patient was controlled promptly with clofibrate. There were no side effects and the drug was tolerated well. Clofibrate is capable of stimulating ADH release from the neurohypophysis which results in prompt and sustained antidiuresis.

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