Lipoid Proteinosis – Case Report

MASOOD A., AMAN S., KAZMI A.H.
Department of Dermatology Unit-I, KEMU / Mayo Hospital, Lahore
Address for Correspondence: *Dr. Anoosh Masood Chaudhry, 241-A, Ahmad Block, New Garden Town, Lahore Pakistan*
E-mail: atifkazmi80@yahoo.com

Lipoid proteinosis is an uncommon, autosomal recessive disorder characterized by infiltration of hyaline material into the skin, oral cavity, larynx and internal organs. The patients of this disease present with hoarseness of voice, beaded papules on eyelid margins, hyperkeratosis of skin and an inability to protrude the enlarged, thickened tongue. Many similar cases with additional features have been reported in foreign literature. We describe two cases of this disorder along with review of literature.

Key words: Lipoid proteinosis, hyaline material, macroglossia.

Lipoid proteinosis (hyalinosis cutis et mucosae) also known as "Urbach-Wiethe disease" is a rare, recessively inherited disorder characterized by hoarseness of voice, infiltration of hyaline material into the skin, oral cavity, larynx & internal organs and scarring of skin with mild injury[1,2]. Dental abnormalities, intracranial calcification and epilepsy are other associated features. More than 300 cases have been reported world-wide to date. Lipoid proteinosis (Lip) has been mapped to chromosome Iq21 and so far 26 different inherited mutations in ECM1 have been reported in this disease[3].

Case History

Two unrelated patients of ages 10 and 40 years, presented at the Department of Dermatology Unit-I, King Edward Medical University/ Mayo Hospital, Lahore Pakistan with complaints of generalized itching & pigmented lesions on neck, chest, abdomen, elbows and knees along with heaped up lesions on fingers & axillae since early childhood (Table 1). Both were born to a consanguineous couple, after an uneventful pregnancy and labour. They were normal at birth and their symptoms began at the ages of two & one year respectively, when they developed hoarseness of voice and generalized itching along with hyperpigmented, hyperkeratotic plaques on various parts of body. Gradually, other body parts were also involved including face, neck, back, axillae, elbows and dorsum of hands and feet. Their complexion gradually darkened and skin became dry and thick.

Table 1: *Clinical features noted in our patients.*

Cases	**I**	**II**
Hoarseness	++	+++
Inability to protrude the tongue	++	++
History of respiratory difficulty	-	+
Beaded eyelid papules	+++	+
Epilepsy	-	-
Blisters	-	-
Hair loss	-	-
Hyperkeratosis	++	+++
Skin infiltration	++	+++
Infiltration of mucosae	++	++
Scar formation	++	+++

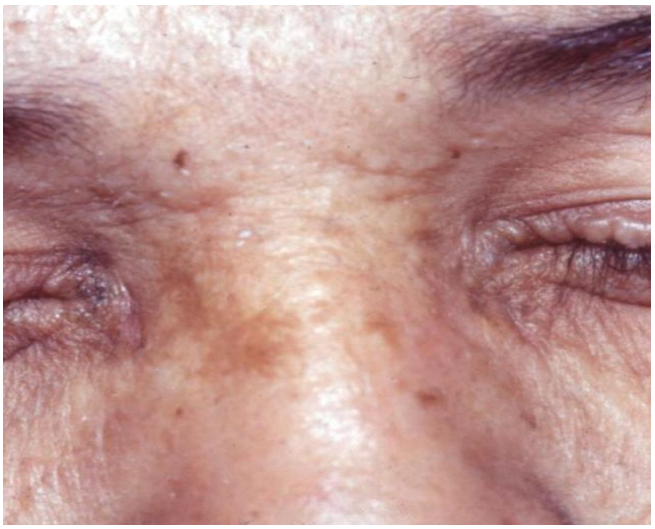

Fig. 1: *Yellow waxy cutaneous infiltration and beaded eyelid papules.*

Oral cavity was involved with yellowish white infiltrate. Both had thickened, enlarged tongue which they were unable to protrude beyond the margins of the lips. They also had history of increased scarring even on mild injury. There was no history of photosensitivity, facial edema, joint pain

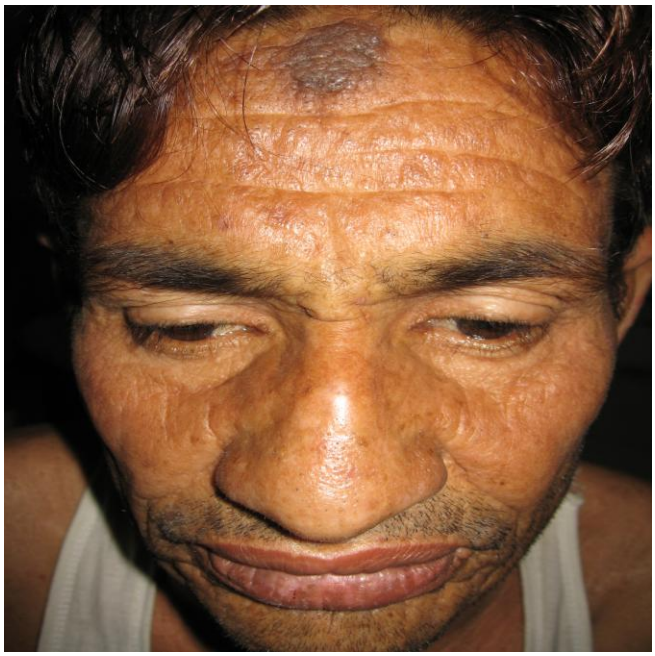

Fig. 2: *Cutaneous hyaline infiltration.*

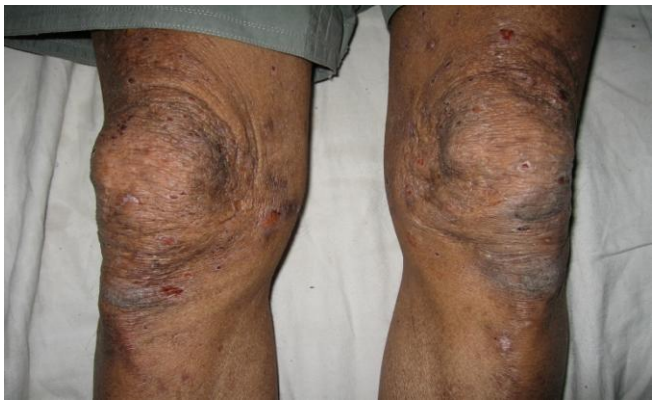

Fig. 3: *Excoriated hyperpigmented papular lesions.*

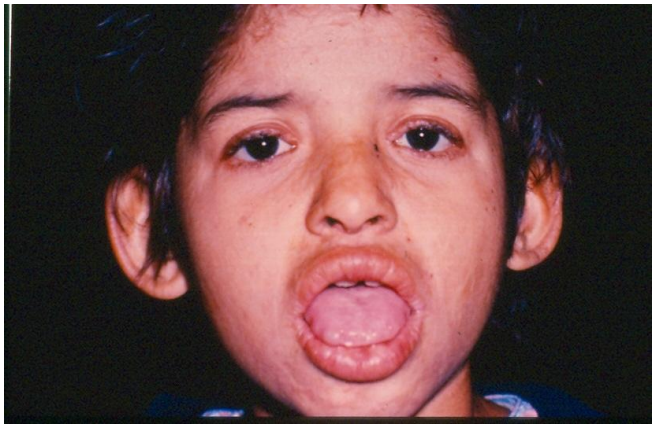

Fig. 4: *Mucosal infiltration & macroglossia.*

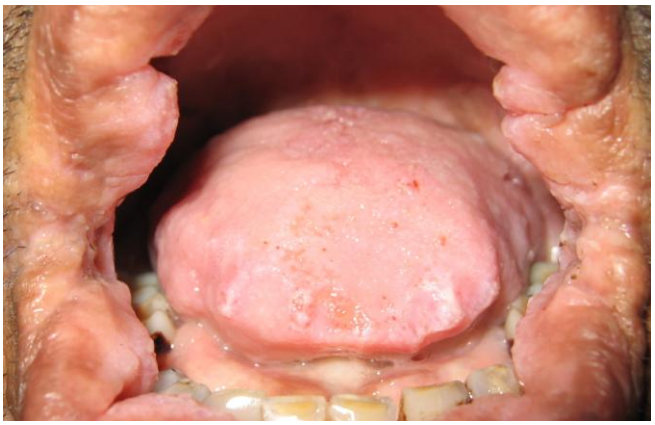

Fig. 5: *Enlarged tongue with yellowish mucosal infiltrates and ulceration.*

Table 2: *Investigations.*

Tests	Case I	Case II
Porphyrins (Blood, urine, stool)	--	--
Thyroid profile	--	--
Lipid profile	--	--
X-ray skull & CT scan	--	--
Ultrasonography	--	Tiny Calculi in gall bladder
Flexible laryngoscopy (Yellowish infiltrates over larynx and vocal cords)	+	+
Histopathology (Epidermal hyperkeratosis & irregular acanthosis + dermal hyaline deposition)	+	+

and seizures in both patients. Elder brother of one of the patients had similar complaints but to a lesser extent.

On physical examination, yellowish dry skin, hyperpigmented papules & plaques over the trunk and extremities, more marked on extensors, were noted (Fig. 1 & 2). Facial poc-like scarring was also present. There were irregular hyperpigmented eczematous lesions on nape of the neck, back, scrotum, knees (Fig. 3), axillae, elbows and lateral margins of all fingers. Nails were found to be clubbed with yellowishdiscolouration in one patient. Examination of oral cavity revealed yellowish coloured infiltrates on inner aspect of lips, sides of the tongue, soft palate and pharynx with no other dental abnormality. Tongue was enlarged, thick and firm to touch in both cases (Fig. 4 & 5) Eye examination showed beaded papules (moniliforme blephrosis) on upper and lower eyelid margins (Fig-1). The cornea, iris and retina were normal. Systemic examination showed no abnormal finding.

Table 3: *Differential diagnosis.*

o Erythropoietic protoporphyria
o Amyloidosis
o Xanthomatosis
o Myxoedema
o Lichen myxoedematosus

On laboratory investigations (Table 2), the blood, urine and stool porphyrins were all within normal limits. X-ray skull and CT scan were normal and multiple tiny calculi in the gall bladder were noted on abdominal ultrasonography in one patient. Flexible laryngoscopy showed yellowish infiltration over larynx and vocal cords. Histopathology of skin in both cases revealed hyperkeratosis and irregular acanthosis of epidermis and extracellular hyaline deposition of dermis along with dilatation of the blood vessels.

Immunochemistry, immunoflourescense labeling, polymerase chain amplification and direct nucleotide sequencing of ECM1-gene could not be performed due to unavailability and limited resources.

Discussion

In our cases, hoarseness of voice in early childhood, beaded eyelid papules, hyperkeratosis, infiltration of skin & mucosae and inability to protrude the thickened enlarged tongue favoured the diagnosis of lipoid proteinosis. The condition has to be differentiated from some other clinical entities. Scars on the face may pose difficulty in differentiating it from erythropoietic protoporphyria (Table 3). Typical histology, absence of photosensitivity, presence of skin lesions on covered areas and normal blood, urine and stool porphyrin levels helped to delineate the condition[4]. In primary cutaneous amyloidosis, hyperpigmented, papulo-nodular eruptions occur, especially on the shins and upper limbs that may coalesce into thickened plaques. A skin biopsy with Congo red stain helps in making the diagnosis[5]. Xanthomatosis is deposition of lipids in the skin and elsewhere, caused by hyperlipidaemia. This can be caused by primary genetic defect or can be secondary to defective metabolism. Lipid profile shows high cholesterol levels. Skin biopsy establishes the diagnosis[6]. In myxoedema, hoarseness of voice, macroglossia, thickening of skin and chronic periorbital infiltration secondary to deposits of mucopolysaccharides frequently develop as a result of decreased thyroid hormone[7]. In our patients, thyroid function tests were normal. In adult life, differential diagnosis from lichen-myxoedematosus should be considered. Lichen-myxoedematosus is a disorder of unknown aetiology. Small, dome-shaped, flesh to cream coloured, firm, waxy, lichenoid papules, arranged in a linear manner particularly on the face (especially the glabella & behind the ears) and dorsum of hands, make a distinct clinical appearance.

The prognosis of Lip is generally good despite the progressive nature of the disease until early adulthood. Treatment is limited and consists of dissection of vocal cords, carbon dioxide laser surgery of thickened vocal cords and dermabrasion for skin lesions. Treatment with Dimethyl sulfoxide and etretinate / acitretin has had variable results.[8,9] The patients are under observation to prevent the risk of respiratory obstruction and early detection of neuropsychiatric abnormalities leading to fatal seizures and they are on oral etretinate therapy.

Conclusion

Lipoid proteinosis can be considered a well-known distinct clinical entity and there exists a possibility that this disease can lead to respiratory obstruction and fatal seizures but long term follow-up is required for early detection of these problems.

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