Lipoid Proteinosis: A Case Report

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ABSTRACT

Lipoid proteinosis is a very rare genetic disorder with autosomal recessive inheritance characterized by the deposition of an amorphous hyaline material in the skin, mucosa and viscera. The classic manifestation is onset in infancy with a hoarse cry due to laryngeal infiltration. The infiltration progresses to skin and mucosa in a slowly progressive course.

We present here a 12 year old male child who was brought to the ENT department with complaints of hoarseness of voice, red, raised swelling over the tongue and yellow white papules over the oral cavity and oropharynx. The vocal cords and arytenoids were edematous on videolaryngoscopy. The patient also had beading of papules around the eyelids, scarring on the skin and verrucous plaques over knees and elbows. A biopsy was taken from tongue and skin and sent for histopathology and the report confirms as a case of lipoid proteinosis.

Key words: Lipoid Proteinosis, moniliform blepharosis, verrucous plaques

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INTRODUCTION

Lipoid proteinosis (Urbach & Wiethe Disease or Lipoglycoproteinosis or Hyalinosis cutis et mucosae) is a genetic disorder with autosomal recessive inheritance[1,2] characterized by the deposition of an amorphous hyaline material in the skin, mucosa and viscera.[3] Lipoid proteinosis is a rare disorder with fewer than 300 reported cases till date. The patient can report to an otolaryngologist with hoarseness of voice or oral lesions[4]. Alternatively, the patient can report to a dermatologist with beaded papules on the eyelid margins or verrucous plaques over elbows and knees. He can also report with other features like dysphagia, alopecia, airway obstruction, abnormal dentition and seizures. The disease is caused by mutations which cause loss of function at chromosome 1q21 (extracellular matrix protein 1).[5] On histopathological examination of the lesion one can find hyperkeratosis, acantholysis of epidermis, amorphous eosinophilic hyaline deposition at dermo-epidermal junction and adnexia, thickening of basement membrane, and concentric deposition around blood vessels. The material is periodic acid-Schiff (PAS) positive. Currently there is no effective cure for this disease. The life expectancy of the patient is normal as long as the side effects are properly addressed.

CASE REPORT

A 12 year old male child presented to the ENT outpatient department of Prathima Institute of Medical Sciences, Karimnagar with hoarseness of voice since childhood, raised mucosal erythematous lesion with yellow white papules on the tongue and oral cavity. Both his knees, elbows and buttocks showed multiple verrucous plaques. There were multiple small atrophic scars over the face (figure 1) and multiple hypopigmented well defined atrophic scars over the body. He also presented with beading of papules around the eyelid margins (figure 2). There was no history of headache, epilepsy or visual disturbances and his intelligence was normal. His parents were consanguineously married and there was a history of his elder brother affected similarly with hoarse voice and skin lesions who died at the age of 11years in an accident.

On physical examination multiple, hyperpigmented, verrucous plaques were present on both elbows and buttocks (figure 3, 4) Macroglossia, reddish ulcer on tongue (figure 5) and yellowish papules were there on the tongue and soft palate (figure 6). Frenulum of the tongue was thickened causing reduced movement and an inability to protrude (figure 7). Dentition was normal. Beading of papules around the eyelids was seen (figure 2). Also, there were

multiple hypopigmented well defined atrophic scars (figure 8) all over the body. Hair was normal over the scalp.

Routine laboratory tests included a complete blood picture, complete urine examination, liver function tests, thyroid function tests, X-ray chest and skull were normal. The clinical investigation included Videolaryngoscopy which showed diffuse thickening of the arytenoids, epiglottis and surrounding laryngeal mucosa (figure 9). The vocal cords were edematous and the mobility was normal.

A skin biopsy was done and it showed deposition of hyaline material up to half of dermis and amorphous eosinophilic material seen surrounding capillaries and sweat glands (figure 10). Biopsy was also taken from the tongue which shows Leucocytoclastic Vasculitis. The patient was put on Amlexanox oral cream local application which reduced the ulcer. The patient is not willing for microlaryngeal surgery as the hoarseness is improving from childhood gradually and presently is in follow up.

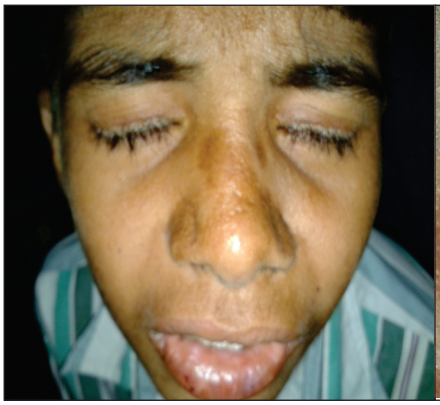
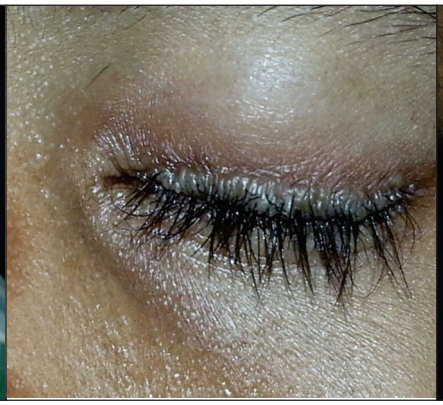


Figure - 1



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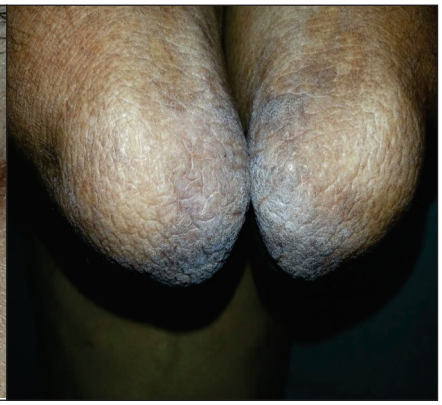

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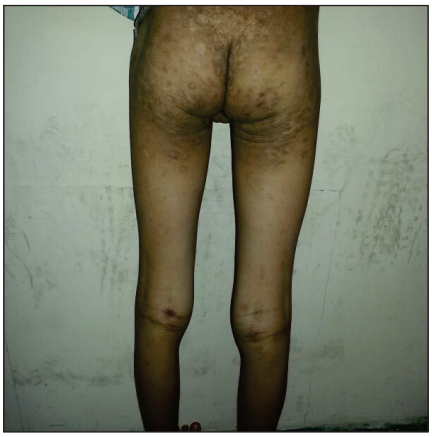

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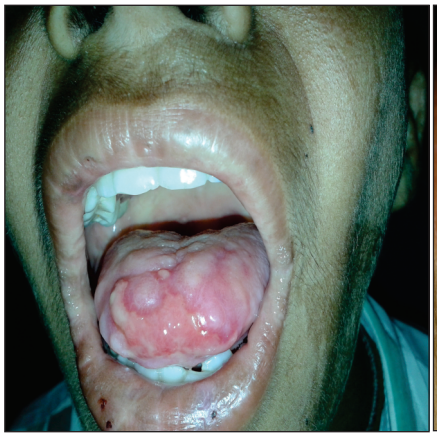

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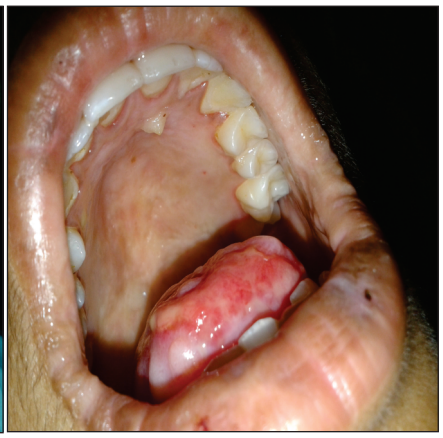

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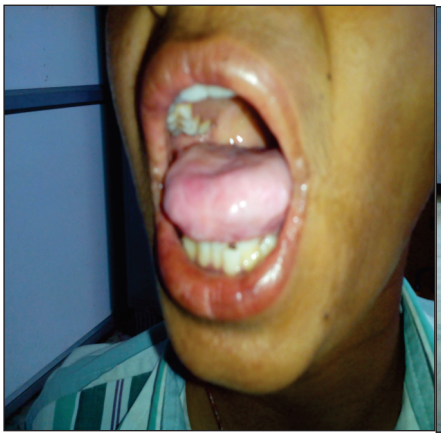

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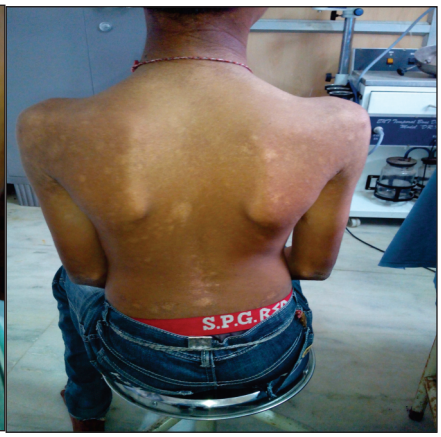

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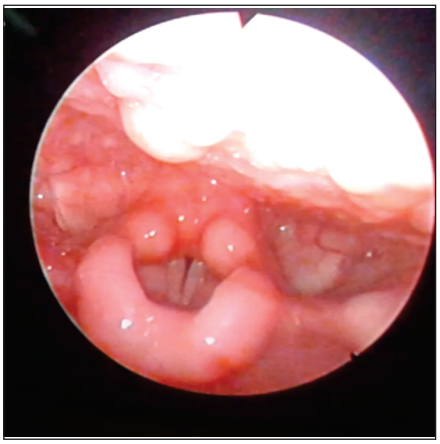

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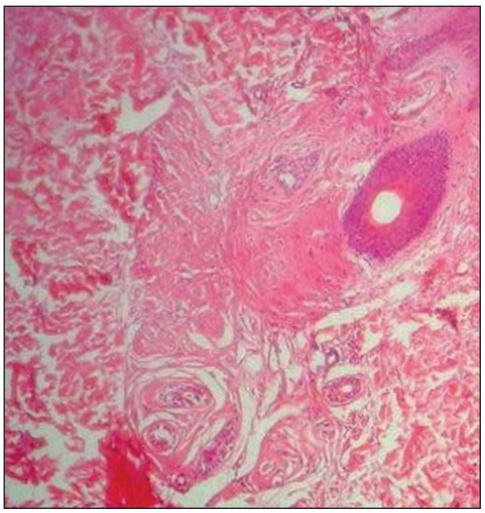

Figure - 10

Figure 1 : Healed atrophic scars on face
Figure 2 : Beaded papules on eyelid margin(Moniliform Blepherosis)
Figure 3 : Verrucous plaques on knees
Figure 4 : Verrucous plaques on buttocks
Figure 5 : Erythematous ulcer with yellow papules over the tongue
Figure 6 : Yellow papules over hard palate
Figure 7 : Macroglossia with inability to protrude tongue because of thickened frenulum
Figure 8 : Multiple hypopigmented well defined scars on the back
Figure 9 : Videolaryngoscopy picture showing thickened vocal cords, arytenoids, aryepiglottic folds, epiglottis and lymphoid follicles on posterior pharyngeal wall
Figure 10 : Deposition of hyaline material at dermo epidermal junction

DISCUSSION

Lipoid proteinosis, first described in 1929 by Urbach, a dermatologist, and Wiethe, an otolaryngologist is a very rare genodermatosis.[6] It is relatively common in Namaqualand area in South Africa which is likely contributed by founder effect.[1] It is inherited in an autosomal recessive pattern and is characterized by deposition of an amorphous hyaline material in the skin, mucosa and other viscera. Mutations in the ECM 1 gene on chromosome 1q21 resulting in dysfunctional extracellular matrix protein 1 was introduced as the cause of Lipoid proteinosis.[3] But the exact mechanistic correlation between genetic mutations and clinical manifestations of the disease remains unclear. Till now about 41 distinct germline, missense, nonsense, splice site, and small and large deletions and insertions have been demonstrated with also two new mutations being reported in two unrelated patients of German and Arab-Israeli race.[7]

The most common presentation of Lipoid proteinosis is progressive hoarseness which may be present at birth or early childhood due to diffuse infiltration of hyaline material in the mucous membrane of the vocal cords.[5] They have a thickened sublingual frenulum which prevents protrusion of tongue-thus the clinical clue "Listen to them talk and have them stick out their tongues."[1] Our patient came to the hospital with a hoarse voice and inability to protrude tongue. Also, this disorder has an autosomal recessive inheritance pattern, hence a detailed pedigree chart is indicated. Notably, our patient had an elder brother with similar features.

Skin manifestations at the early stage of the disease include vesicular or crusted acneiform eruptions on the face and extremities, which are self–limited and heal with scarring. At subsequent stages, deposition of hyaline matrix results in a diffuse, thick, waxy appearance of the face, eyelids, axillae and scrotum. Finally, verrucous plaques arise on skin sites vulnerable to trauma or friction (elbows, knees and knuckles).[8] Our patient presented with typical skin lesions on his elbows and knees. Beaded papules along the eyelid margin (moniliform blepharosis) is a classical clinical finding which is also seen in our patient. In Lipoid proteinosis all sites of the oral cavity may also be involved and yellow–white, firm papules or plaques can be seen on the mucus membranes. Infiltration of the tongue and frenulum results in woody firmness. Speech and gustation can also be impaired. Transient swelling and ulceration of the lips and tongue (which our patient had) may be there. Also, there can be dental abnormalities like hypoplasia or aplasia of the teeth, particularly premolars and lateral incisors. One of the complication of this disease is recurrent parotitis that results from stensen's duct infiltration. Infiltration of the larynx, vocal cords and surrounding structures may cause hoarseness, dysphagia and respiratory distress which may sometimes necessitate a tracheostomy.

Hyaline material can also deposit in the conjunctiva, cornea, trabeculum and retina. Corneal opacity or secondary glaucoma due to infiltration in trabeculum may present later.[9] Calcification of intracerebral para-sellar or hippocampal gyri may sometimes be associated with epilepsy, behavioral changes and learning difficulties.[10] Our patient did not have any visual or neurological manifestations of the disease. Other rare presentations include alopecia, significant pruritis, alterations in the ability to sweat, abnormal pain sensation and intestinal bleeding.

Microscopic findings of early lesions reveal deposition of amorphous eosinophilic material at the dermal-epidermal junction and perivascular areas. At later stages, irregular acanthosis and hyperkeratosis in the epidermis, extension of deposits around hair follicles, eccrine glands, and arrector pili muscles are seen. Hyaline material stains positively with PAS stain and is resistant to diastase. Concentric "onion skin" layer deposition around blood vessels are seen which also include type 3, type 4 collagen and laminin. The presence of lipid varies and is considered a secondary phenomenon due to its adherence to glycoproteins. CT scan of the brain may show bilateral anterior medial temporal lobe and amygdala calcifications. Erythropoetic protoporphyria which resembles this disorder may show similar skin involvement, but can be differentiated because of absence of mucosal lesions. [11]

The prognosis of Lipoid proteinosis is variable. The skin lesions may clear or worsen further by infiltration. Life expectancy may not be affected, but the quality of life may be hampered. Today, no effective treatment is available for this disease. In one case study, continuous treatment with D-penicillamine, a chelating agent, resulted in clinical and histological improvement[12] and in another study, administration of Dimethylsulfoxide (DMSO) improved the lesions.[13] Other possible therapies include topical and oral corticosteroids, etretinate, acitretin, carbon dioxide laser ablation, and dermablation as well as other surgical procedures, but they show variable response rates.

Our patient is a typical case of Lipoid proteinosis. He has the typical presentation of hoarse voice, beaded papules in eyelid margin, and verrucous skin lesions. He presented with an erythematous ulcer surrounded by yellow papules over the tongue which healed with amlexanox applications. He was discharged as the parents were not willing for microlaryngeal surgery and is being followed up. It is of importance that hoarseness is one of the first and common manifestations of Lipoid proteinosis and otolaryngologists should consider this disease in the differential diagnosis of any voice changes and hoarseness that present during childhood.

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