CASE REPORT

Lipoid proteinosis

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ABSTRACT
Lipoid proteinosis is a rare disorder with autosomal recessive inheritance, characterized by progressive deposition of hyaline material in the skin, mucous membrane, and different organs of the body, resulting in a multitude of clinical manifestations. A 62-year-old male presented with hoarseness of voice since infancy, eyelid beading, and generalized acneiform scars on the facial skin and extremities, and yellowish papules on his tongue and buccal mucose. The patient was diagnosed clinically as a case of Lipoid proteinosis, which was confirmed by skin and mucosal biopsy. The objective of the present work is to describe this rare entity, with approximately 250 cases found in medical literature. This case report also illustrates that Lipoid proteinosis may show protean clinical features and yet may remain undiagnosed for many years. This report will hopefully spawn further studies that will lead to early diagnosis.
Key words: Acneiform scars, eyelid beading, hoarseness of voice, hyaline material, yellowish papules

INTRODUCTION

Lipoid proteinosis (LP) also known as Urbach – Weithe disease and Hyalinosis cutis et mucosae is a rare, autosomal, recessively inherited disorder, characterized by hoarseness from early infancy, together with various cutaneous manifestations, such as, acneiform scarring, waxy papules, eyelid beading (moniliform blepharosis), and so on, as well as, a non-cutaneous manifestation attributed to infiltration of hyaline-like material in the skin, larynx, and various organs.[1] This hyaline-like material is Periodic-Acid Schiff (PAS) positive and diastase resistant and is believed to be the result of the deposition of non-collagenous proteins and glycoprotein.[2] Although LP is most prevalent among descendents of German immigrants to South Africa, it is seen worldwide[3]. We herewith report this case for its rarity and very typical diagnostic features.

CASE REPORT

A 62-year-old man was referred to M. S. Ramaiah Dental College and Hospital, Bangalore, with oral and cutaneous lesions. He presented with hoarseness of voice since infancy followed by typical skin lesions at approximately four years of age. In the following years he developed oral and cutaneous lesions. He had no history of seizures, visual disturbances, photosensitivity, or respiratory obstruction, but presented with restricted tongue movement and speech impairment. The patient deferred indirect laryngoscopy and skull X- ray on several accounts.

Paternal sister was affected with similar skin lesions. None of the other family members were affected. There was no history of consanguinity.

Examination revealed an otherwise healthy individual with oral symptoms such as thickened lingual mucosa with nodular infiltration [Figure 1], xerostomia, and dysphagia. Enlarged tongue, with irregular pearly white infiltration [Figure 2], and protuberant, thickened, and scarred upper and lower lips were the other features noted. Dentition was normal for age.

Generalized acneiform scars of the face, beaded papules on the thickened margins of the eyelids [Figure 3], and multiple 2 – 3 mm, brownish warty papules on the dorsum of the hand [Figure 4] and feet were evident.

Systemic examination revealed no abnormalities. Routine investigations were normal.

Biopsies from skin (brownish warty papule on the dorsum of the hand) and oral mucosa (lower right labial mucosa) were taken.

Oral mucosal biopsied section, stained with H and E, revealed stratified squamous hyperplastic epithelium underlined with subepithelial hyalinized stroma, suggesting reduplication of basement membrane. Connective tissue showed increased vascular channels with perivascular hyalinization [Figure 5]. These deposits stained positive with Periodic-acid Schiff [Figure 6], thereby confirming our clinical diagnosis.

Histopathological examination of the skin biopsy showed a superficial dermis, with deposition of PAS positive material [Figure 7].

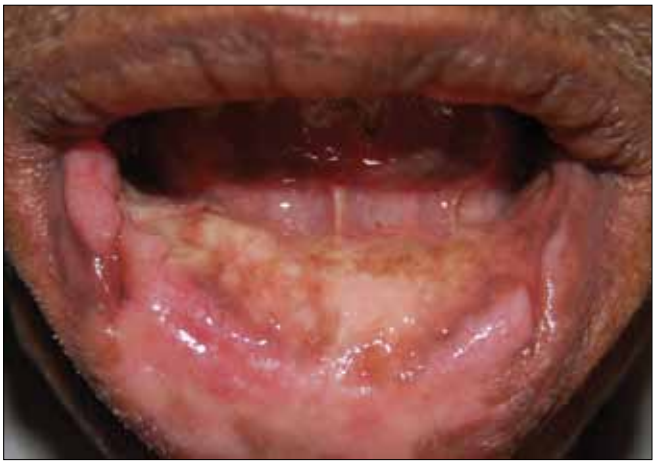

Figure 1: Thickened lingual mucosa with nodular infiltration

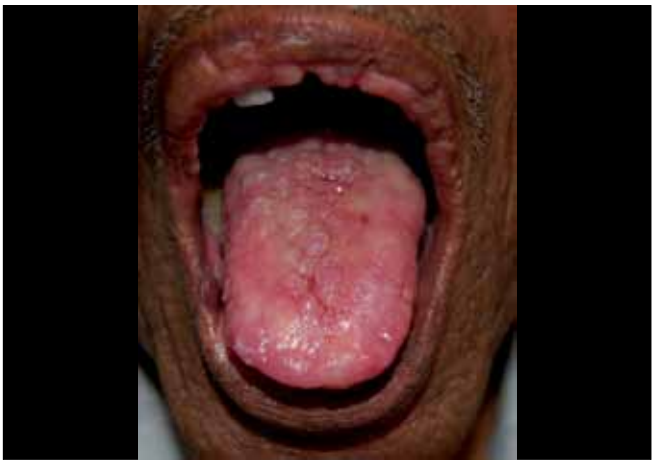

Figure 2: Enlarged tongue with irregular pearly white infiltration

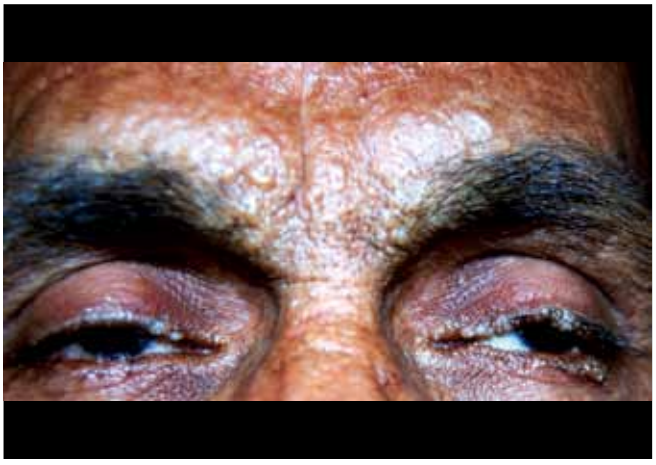

Figure 3: Beaded papules on the thickened margins of the eyelids

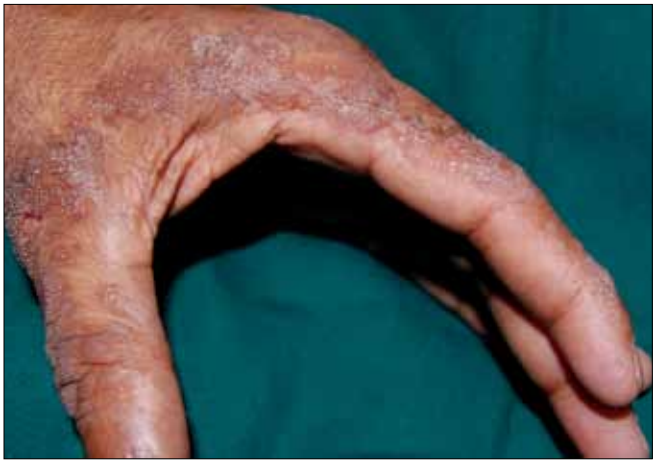

Figure 4: Multiple brownish warty papules on the dorsum of the hand

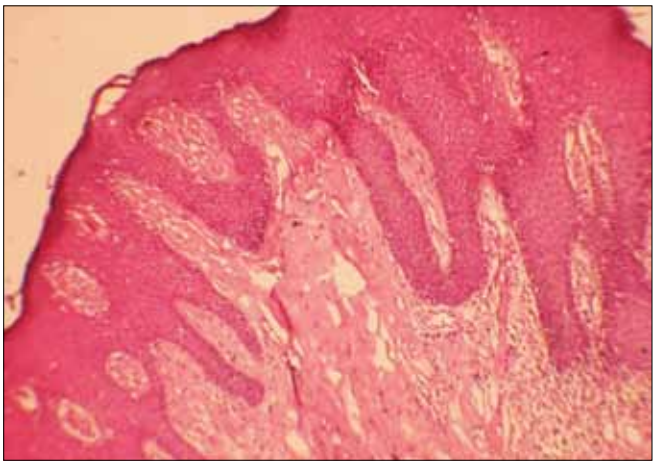

Figure 5: H and E stained section showing subepithelial and perivascular hyalinisation under 10×

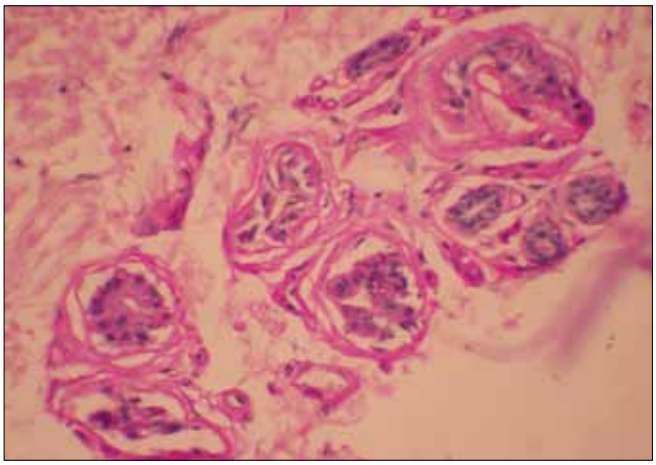

Figure 6: Oral tissue section stained with Periodic – Acid Schiff reagent shows PAS- positive material around vessels under 40×

DISCUSSION

Lipoid Proteinosis is a genetic disease and diagnosis can be established on the basis of characteristic clinical symptoms, confirmed by histopathology.

The exact pathogenesis of this disease is unknown, but has been postulated to be the result of a lack of extracellular matrix protein (ECM1), leading to defective protein binding. ECM1 normally binds to type 4 collagen, but the lack of this potentially regulatory or stabilizing protein–protein interaction

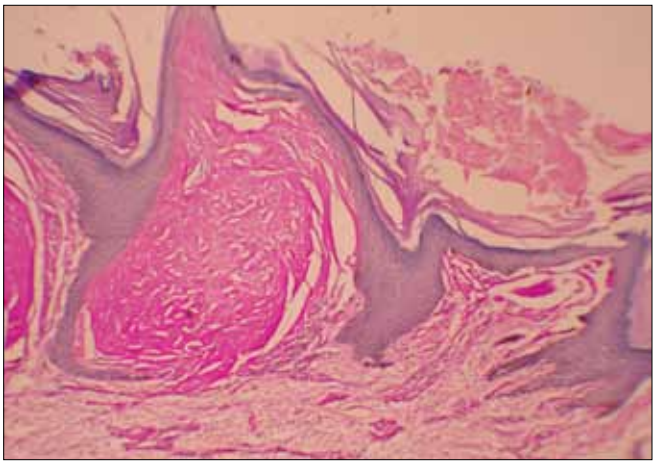

Figure 7: Periodic – Acid Schiff stained section of superficial dermis shows deposition of PAS positive material under 40×

in LP could then result in increased type 5 collagen expression and typical histopathological changes.[4] To date pathogenic mutations in gene encoding ECM 1 on chromosome 1q21 have been identified in LP.[5] The protean manifestations of LP are associated with extensive deposition of non-collagenous proteins and glycoproteins in the skin, larynx, and other organs.[6]

The first clinical manifestation of LP is usually progressive hoarseness caused by diffuse deposition of hyaline material in the mucous membranes of the vocal cords. Hoarseness may develop either in infancy or during childhood, and this symptom was first noticed in our case. Our patient refused indirect laryngoscopy, which would actually confirm this finding. Various literatures also highlight similar features (Nanda *et al*., Rawal).[7,8] Therefore, the importance of LP should not be underestimated by otolaryngologists, and it should be included in the differential diagnosis of voice changes and hoarseness, in infancy and childhood.[9]

Skin lesions follow hoarseness, including waxy yellow papules with generalized skin thickening on the face, trunk, flexures, and extremities. Our patient developed these typical lesions at approximately age four. Acneiform scarring may occur predominantly on the face and trunk. Hyperkeratosis may appear in the region exposed to mechanical friction, such as, hands, elbows, knees, buttocks, and axillae, mimicking our case, and in favor of the findings noted by Rawal, Nagasaka *et al*.[8,10]

The classic and most easily recognizable sign is the beaded eyelid papules, as noted in our case. Similar findings were observed by Bozdag 2000 and Thapa D.M *et al.*, 2001.[11,12]

In clinical practice, LP is rarely a life threatening condition.[13] Infiltration of oral mucosa may lead to xerostomia and dysphagia. Other mucosal findings include thickening of the sublingual frenum and tongue limiting tongue movements, causing speech difficulties,[14] as noted in our case. The irregular pearly white infiltration on the tongue cited in our case is a less common finding.

Moreover diffuse infiltration of the pharynx and larynx may cause respiratory distress at times requiring tracheostomy.[14] Our patient presented with speech difficulty and xerostomia, but had no upper respiratory distress or dyspnea.

Extracutaneous features may include epilepsy, mental retardation, and other neuropsychiatric illnesses (Hamada *et al.*).[5,6] These findings were in contrast to our case.

As our patient deferred a skull x-ray, we could not rule out calcification of the temporal lobe or hioppocampi, usually appearing as bean-shaped opacities considered to be pathognomonic of the disease, as is hoarseness and eyelid beading.

No anomaly was detected on systemic examination, dentition was normal with age, and routine investigations were normal.

In relation to the histopathological study, there was extensive deposition of an amorphous eosinophilic substance around the capillaries, and papillary dermis, focal deposition can be found in the profound dermis. This hyaline substance is PAS positive (Touart).[2] The histopathological characteristics described for the present case are in agreement with the above-mentioned diagnostic criteria.

The differential diagnosis of this pathological entity should consider erythropoietic protoporphyria, the lesions of which are restricted to solar-exposed areas and there is involvement of the mucous membrane.[2,11,15]

Treatment is limited, reported approaches include oral steroids, Dimethyl sulfoxide, D-Penicillamine, intralesional heparin, and Etretinate. CO_2 laser surgery of vocal cords and beaded eyelid papules, and dermabrasion of skin result in cosmetic improvement. Except for the respiratory obstruction that occurs infrequently and rarely requires tracheostomy, life expectancy is usually normal. Specific and effective treatments are still not available.[3,14]

CONCLUSION

Hoarseness of voice since infancy, beaded papules along the margin of eyelids, firm and less mobile tongue, thickened protuberant lips, and thickened oral mucosa with yellowish tongue clinched the diagnosis of LP.

Scars on the face may poise differently in differentiating from erythropoietic porphyria. Absence of photosensitivity and presence of PAS-positive material on sun-protected areas and around vessels and superficial dermis helped to delineate this condition. This report will hopefully spawn further studies that will lead to early diagnosis.

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