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Case Report

Lipoid Proteinosis: A Case Report

Urbach & Wiethe Disease

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ABSTRACT

Lipoid proteinosis (LP) is a rare autosomal recessive disease 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. Skin and mucous changes develope, and the disease follows a slowly progressive course.

In this case report, a 49 year-old man presented with a longstanding hoarseness since childhood, dysphagia and asymptomatic skin lesions. Esophageal biopsy showed the deposition of homogenous eosinophilic hyaline-like material compatible with LP.

Keywords : Lipoid proteinosis of Urbach and Wiethe; Hoarseness; Skin

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INTRODUCTION

Lipoid proteinosis (LP) or Urbach–Wiethe's disease is a rare autosomal recessive disorder characterized by deposition of hyaline in the skin, mucosa, upper respiratory tract and internal viscera(1). Classic manifestations include skin scarring and plaques, beaded eyelid papules and laryngeal infiltration that causes hoarseness, which is usually the first symptom during early childhood(2).Other clinical features that include abnormal dentition, seizures, airway obstruction, and corneal opacities are also reported(3).

Histological findings include a capacious deposition of hyaline material around the capillaries, sweat coils, and in the thickened papillary dermis, which periodic acid-schiff (PAS) positive.

The etiology of LP is currently unknown but the prognosis is often good. Recent molecular genetic studies demonstrate mutations in the extracellular matrix protein 1 (ECM 1) gene that is located on chromosome 1q21(4). Currently, no curative treatment is available for this disease.

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CASE REPORT

A 49 year-old man from Semnan came to our outpatient clinic with complaints of longstanding hoarseness, loss of gustation, dysphagia, multiple asymptomatic skin lesions and progressive oral mucus membrane changes. The patient had hoarseness since early childhood.

There was no history of headaches, epilepsy or visual

disturbances, and his intelligence was normal. His parents were nonconsanguineous and there was no history of other affected family members.

On physical examination, multiple papules and plaques were present on the dorsum of his hands, both elbows and knees. Most papules were skin colored and developed over areas, which had been exposed to minor trauma (Fig. 1). Macroglossia, reddish ulcers and yellowish plaque on the tongue and soft palate, was noted (Fig. 2). In addition, the frenulum of the tongue was thickened with reduced movement, but dentition was normal. No other abnormalities were seen.

Routine laboratory tests included complete blood count, liver and kidney function tests, serum lipid profile, serum porphyrin level and urine, which were all within normal limits. The patient underwent esophagogastroscopy, which showed infiltration of the upper third of the esophagus, a medium-sized sliding hiatal hernia, normal stomach and duodenum, with no signs of gastroesophageal reflux, and prominent thickening and infiltration of the cricopharyngeous and vocal cords (Fig. 3).

Light microscopic examination of the esophageal biopsy showed non-keratinized stratified squamous epithelium. Lamina propria revealed deposition of homogenous eosinophilic hyaline-like material. In addition, a thick hyaline matrix surrounded the blood vessels. In total, these clinical and laboratory data were consistent with LP. Skin lesion biopsies were PAS^{+} and notable for pink amorphous hyaline material at the upper zone of the papillary dermis, surrounding the blood vessels, eccrine glands and at the dermo-epidermal junction (Figs. 4,5).

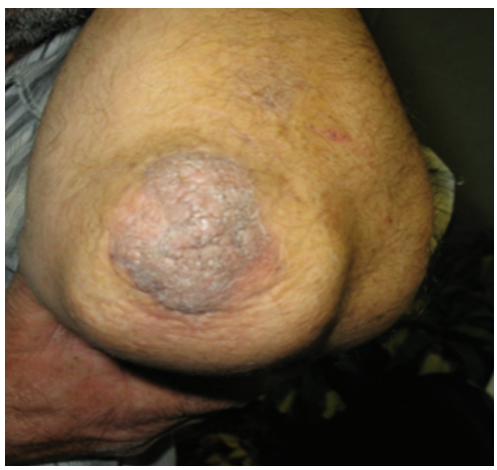

Fig. 1: Skin manifestation of LP as seen by verrucous plaque on the elbow.

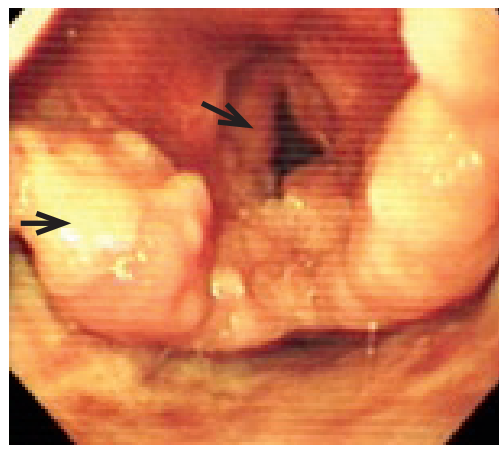

Fig. 3: Larynx with swelling arythenoid (black arrow) and cricopharyngeus (white arrow) due to submucosal infiltration.

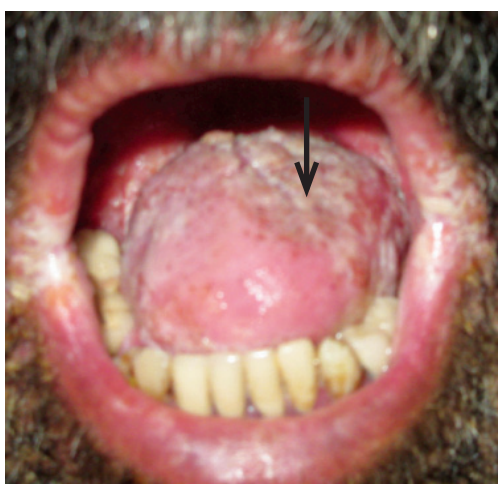

Fig. 2: Yellowish plaque (thick arrow) and reddish ulcers (thin arrow) on the ventral surface of the tongue.

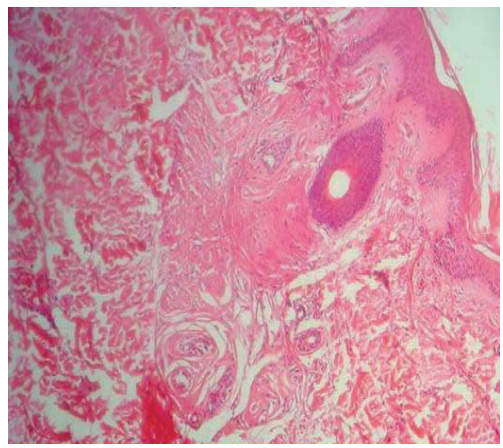

Fig. 4: Deposition of hyaline material in the dermo–epidermal junction of the skin.

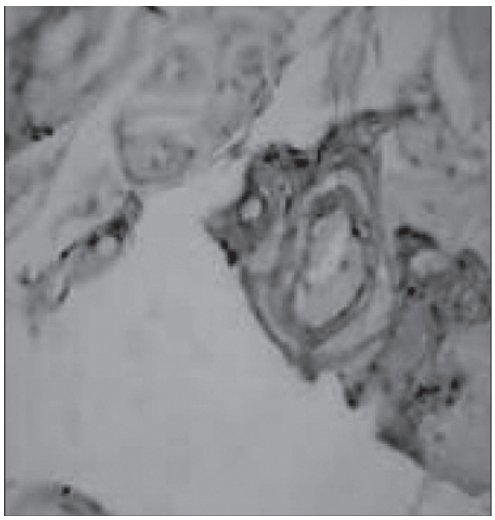

Fig. 5: **PAS positive material deposited around the blood vessels. (40x)**

DISCUSSION

LP was first described in 1929 by Urbach, a dermatologist, and Wiethe, an otolaryngologist(5). is a rare autosomal recessive disorder characterized by deposition of an amorphous hyaline material in the skin, mucosa and other viscera.

Loss of functional mutations in the ECM 1 gene on chromosome 1q21 was introduced as the cause of LP(1). But the exact mechanistic correlation between genetic mutations and clinical manifestations of the disease remains unclear. To date, 41 distinct germline missense, nonsense, splice site, and small and large deletions and insertions have been demonstrated. Recently, two new mutations and one recurrent mutation were reported in two unrelated patients of German and Arab-Israeli race (6).

More than 300 cases have been reported worldwide. The most common presentation of LP is progressive hoarseness which may be present at birth or early childhood due to diffuse infiltration of hyaline material in the mucous membrane of vocal cords(4). Development of hoarseness was the first symptom noticed in our patient. In a study, 22 Chinese patients with LP were evaluated. This study demonstrated that persistent hoarseness from early infancy with laryngeal involvement was the most common manifestation of LP and microlaryngosurgery improved the voice(7).

Skin manifestations at the early stage of the disease include vesicular or crusted acneiform eruptions on the face and the 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.

All sites of the oral cavity may be involved. Yellow–white, firm papules or plaques can be seen on the mucus membranes. Infiltration of the tongue and the ferenulum results in woody firmness and impaired mobility. Patients may not be able to protrude the tongue completely. Speech and gustation can also be impaired. Transient swelling and ulceration of the lips and tongue, in addition to hypoplasia or aplasia of the teeth, particularly premolars and lateral incisors, may be seen.

One of the complications of this disease is recurrent parotitis that results from stensen duct infiltration. Infiltration of the larynx, vocal cords and surrounding structures may cause hoarseness, dysphagia and respiratory distress. Hyaline material can also deposit in the conjunctiva, cornea, trabeculum and retina(9). Corneal opacity or secondary glaucoma due to infiltration in the trabeculum may present later(10).

Calcification of intracerebral para-sellar or hippocampal gyri may sometimes be associated with epilepsy, behavioral changes, learning difficulties(11). Notably, our patient did not have any visual or neurologic manifestations of the disease. Other rare presentations include patchy alopecia or diffuse hair loss, intestinal bleeding and dysphagia(12).

Histologic findings of early lesions are compatible with hyaline thickening of the papillary dermis capillaries. At later stages, hyperkeratosis, 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.

Erythropoetic protoporphyria is considered as a differential diagnosis. It may have similar skin involvements but without mucosal lesions(13).

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(14). In another study, improvement after administration of dimethyl sulfoxide (DMSO) at a dose of 60 mg/kg/day was reported(15). But a more recent report showed no benefit of DMSO in three patients from Turkey(16).

Other possible effective 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. In a report by Toosi and Ehsani, it has been postulated that acitretin in comparison with other agents is an effective drug to improve voice changes. We can assume that acitretin has more effect on laryngeal involvement rather than skin(17) According to this report, our patient was treated by acitretin (25 mg/BD) since two months prior. In the first follow-up visit, after one month, the patient reported partial improvement in hoarseness and dysphagia but there was no significant change in skin plaques.

Our patient is a typical case of LP. Only few reports have mentioned esophageal involvement. The course of the disease and therapeutic options are still unclear. Since dysphagia, intestinal bleeding and loss of gustation are some of presenting symptoms of LP, gasteroenterologists should consider this disorder. Performing a systematic evaluation to find other clinical and histological signs is warranted, particularly if hoarseness is a coexisting symptom.

One of the other important issues is that, because hoarseness is one of the first and common manifestation of LP, physicians should consider this disease in the differential diagnosis of any voice changes and hoarseness that present during childhood.

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