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CASE REPORT

Lipoid Proteinosis: A Case Report

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Abstract

Lipoid proteinosis (LP), also referred to as Urbach-Wiethe disease or hyalinosis cutis et mucosae, is a rare autosomal recessive storage disorder. It is characterized by the deposition of amorphous hyaline material in the mucous membranes, skin, brain, and internal organs. The symptoms of lipoid proteinosis are variable but typically begin with hoarseness in the newborn period. Skin-related symptoms usually appear during childhood and include acneiform scars, wart-like papules, and plaques. The clinical presentation of this condition varies between individuals, which can make diagnosis difficult and often requires a detailed dermatological examination.

Keywords: Acneiform scars; hoarseness of voice; hyaline material; temporal calcifications; yellowish papules.

Lipoid proteinosis (LP), also known as Urbach-Wiethe disease or Hyalinosis cutis et mucosae, is a rare autosomal recessive disorder. It is characterized by hoarseness from early infancy, along with various skin manifestations such as acneiform scarring, waxy papules, eyelid papules (moniliform blepharosis), and more. Additionally, non-cutaneous manifestations occur due to the infiltration of hyaline-like material in the skin, larynx, and multiple internal organs [1]. In various parts of the body, there is extracellular and perivascular deposition of hyaline material that stains positive with periodic acid-Schiff (PAS) [2]. LP is a genetic disease, and diagnosis can be established on the basis of characteristic clinical symptoms, confirmed by histopathology.

Case Report

A 28-year-old male patient presented to us with complaints of stiffening on the palms and soles, along with rashes on the oral mucosa and the body. The patient had experienced skin symptoms for a long time. In the following years, he developed oral and cutaneous lesions.

On dermatological examination, the patient had edema and infiltration on the lower lip, macroglossia, and nodular infiltration on the tongue (Fig. 1a–1b). Bilateral yellowish papules, measuring 2–3 mm in diameter, were observed in a linear distribution along the eyelid margin (Fig. 2b). On the face and scalp, acneiform scars were concentrated in the frontal and temporal regions (Fig. 2a–2c). Bilateral hyperpigmented verrucous plaques

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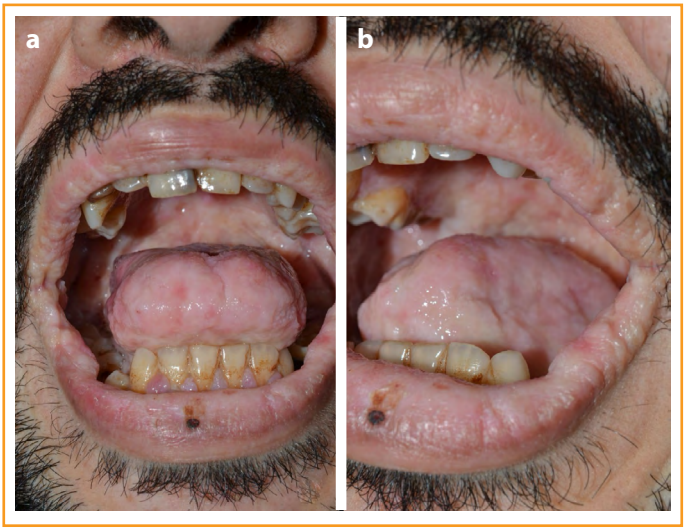

Figure 1. (a-b) Fissures at the oral commissures, macrolossia, ankyloglossia, and flattening of the tongue papillae.

and hyperkeratosis were present on the elbows (Fig. 3a–3b). On the lower extremities, xerotic-looking skin was observed bilaterally in the pretibial area, along with hyperpigmented papules and atrophic scars in the gluteal region (Fig. 3c).

The patient's medical history revealed that he had been diagnosed with epilepsy for two years, but he had discontinued his medication on his own. He had hoarseness of voice since infancy. The examination of other systems was normal. The patient's cousin on his mother's side also had similar complaints. Routine laboratory tests were within normal limits, and his ophthalmological, psychiatric, and neurological examinations were normal. No pathological findings were observed in the imaging studies.

Biopsies were taken with differential diagnoses of lipoid proteinosis, papular mucinosis, hydroa vacciniforme, systemic amyloidosis, and pseudoxanthoma elasticum.

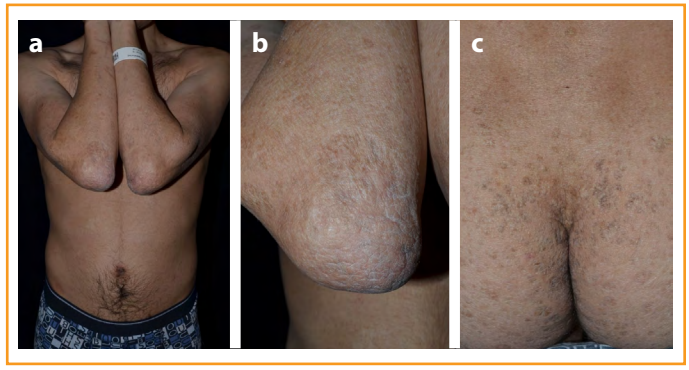

Figure 3. Bilateral hyperpigmented hyperkeratotic areas on the elbows **(a, b)**. Hyperpigmented atrophic lesions in the gluteal region **(c)**.

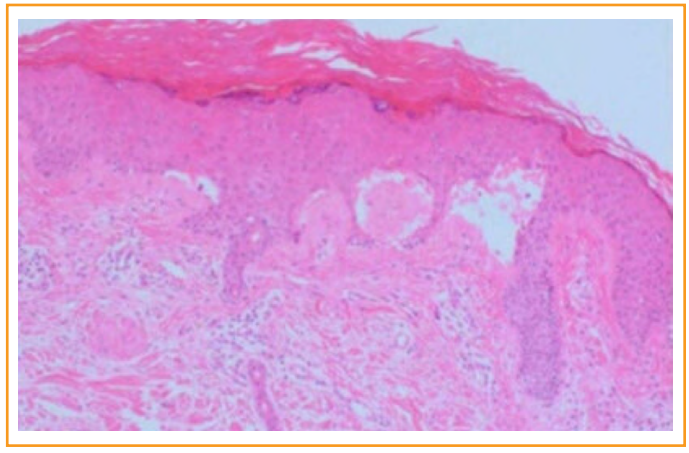

Figure 4. Histopathological examination showing amorphous eosinophilic material in the papillary dermis, staining positive for PAS. Image from Gambichler et al. [16], licensed under CC BY 4.0.

Histopathological examination of the skin biopsy showed hyperkeratosis and acanthosis in the epidermis, with the deposition of amorphous eosinophilic hyaline material in the upper dermis. Based on the clinical findings and histopathological examinations, the patient was diagnosed with lipoid proteinosis.

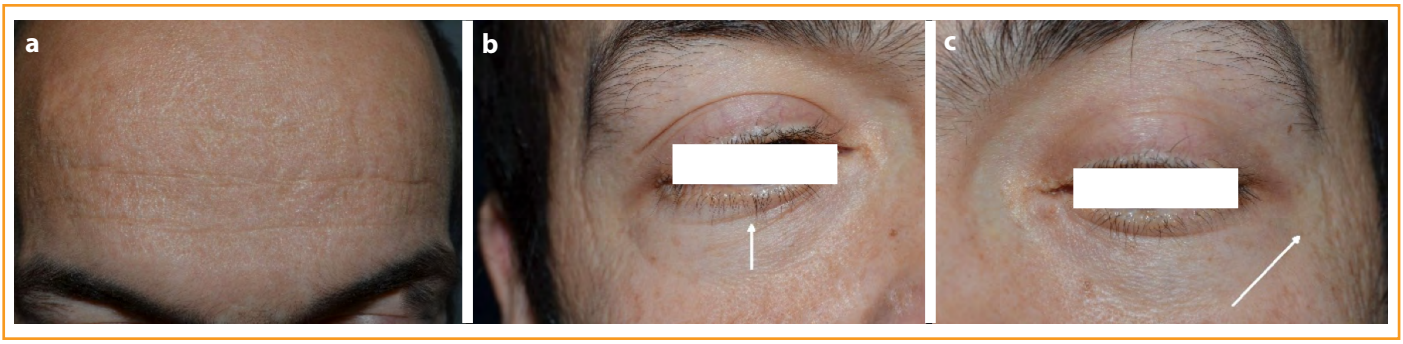

Figure 2. Acneiform scars concentrated in the frontal and temporal regions **(a)** Yellowish, translucent papules measuring 1-2 mm, showing a linear distribution along the eyelash line. **(b)** Acneiform scars concentrated in the frontal and temporal regions **(c)**.

Discussion

Lipoid proteinosis was described in 1929 by the dermatologist Urbach and the otolaryngologist Wiethe, who referred to it as "lipoidosis cutis et mucosae."[3] LP is a very rare autosomal recessive disorder, characterized by infiltration of hyaline material into the skin, oral cavity, larynx, and internal organs. LP affects males and females equally. As per the literature, it is more commonly observed in regions such as Sweden, South Africa, and Asia[4]. The pathogenesis of this disease is unknown. Recent molecular genetic studies have revealed that the disease's pathogenesis is associated with mutations that result in the loss of function of the extracellular matrix protein (ECM1) gene [5]. This gene encodes a glycoprotein that acts as a negative regulator in endochondral bone formation and affects angiogenesis [6]. Mutations in the ECM1 gene lead to disruptions in the glycolipid or sphingolipid degradation pathway, reduced synthesis of fibrous collagens, and excessive production of basal membrane collagens, resulting in the deposition of PAS-positive hyaline materials in the dermis and submucosa [7].

The first clinical manifestation is usually a weak, cry-like, or hoarse voice caused by diffuse deposition of hyaline material in the mucous membranes of the vocal cords. This condition generally persists throughout life and may progress to dysphonia or even aphonia [8].

Cutaneous lesions typically present in two successive stages. In the initial stage, trauma-related vesicles and hemorrhagic crusts are commonly seen on the skin of the face, extremities, and oral mucosa. These skin lesions may develop into "ice-pick"-shaped acneiform scars. In the second stage, skin changes are observed, which are thought to be related to an increase in the deposition of hyaline material. The skin becomes thickened, with a waxy appearance and yellowish discoloration. Papules, plaques, and nodules also appear in the axilla, scrotum, and face [9]. Yellowish papules arranged in a linear pattern along the eyelid margins, known as moniliform blepharosis, are a characteristic feature of lipoid proteinosis [9]. Verrucous lesions may appear on extensor surfaces, particularly the elbows, knees, and hands. Other skin manifestations include alopecia and palmoplantar hyperkeratosis. Additionally, dental abnormalities and parotitis may be observed [10].

Neurological findings are common. Epilepsy, mental retardation, and other neuropsychiatric illnesses may occur. The pathognomonic radiographic finding is the presence of bilateral intracranial temporal lobe horn-shaped calcifications [11,12]. Multiple yellowish nodules can be found throughout the esophagus, stomach, duodenum, and colon, and are usually asymptomatic [13].

In histopathological studies, there is hyperkeratosis and acanthosis in the epidermis, along with the deposition of amorphous eosinophilic hyaline material in the upper dermis, particularly around blood vessels and eccrine glands. Histochemical staining reveals that the material deposited in the dermis is PAS(+) (Fig. 4).

Lipoid proteinosis (LP) is a chronic disease that generally has a benign prognosis and does not impact the patient's lifespan. However, complications such as laryngeal obstruction or respiratory failure during infancy or adulthood, along with neurological complications, can present life-threatening risks. There is no effective treatment for the lesions; management is available for complications like secondary infections and epilepsy [14]. The management of patients with LP should be individualized based on the characteristics of the individual affected. A multidisciplinary approach is often necessary, involving specialists such as dermatologists, otolaryngologists, neurologists, psychiatrists, ophthalmologists, dentists, and genetic counselors [15].

In summary, lipoid proteinosis is a rare disease involving multiple systems. A history of hoarseness and weak crying since infancy, typical skin findings such as acneiform scars on the face and body, yellowish papules arranged in a linear pattern along the eyelid margins, a family history of lipoid proteinosis or consanguinity between the parents, a history of seizures, and the presence of typical calcifications in the temporal region on imaging should raise suspicion for lipoid proteinosis. Life expectancy is usually normal, and treatment is symptomatic. A multidisciplinary approach is recommended.

Ethics Committee Approval: This is a single case report, and therefore ethics committee approval was not required in accordance with institutional policies.

Informed Consent: The patient gives consent to the use of information about him in relation to the above topic for the purpose of display in a journal article or mature presentation or for the presentation of a thesis.

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