

A rare case report -Lipoid proteinosis with laryngeal and oral manifestations

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Abstract

Introduction: Lipoid proteinosis is a rare autosomal recessive disorder, characterized histologically by infiltration of periodic acid Schiff-positive hyaline material into the skin, upper aerodigestive tract, and internal organs. Classical clinical features include skin scarring, beaded eyelid papules, and laryngeal infiltration leading to hoarseness. Usually, the hoarse voice is present at birth or in early infancy, as the first manifestation. In more severe cases, diffuse infiltration of the pharynx and larynx might cause respiratory distress, at times requiring tracheostomy. This paper reports a classical case of lipoid proteinosis with laryngeal and oral manifestations.

Keywords: Larynx, Skin, Lipoid proteinosis (LP)

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INTRODUCTION

Lipoid proteinosis (LP) is a rare autosomal recessive disorder first described in 1929; fewer than 300 cases have been reported in the literature to date. The clinical manifestations of LP may vary considerably between affected individuals. The disease may have multiple system involvement, the skin and mucosal membranes of the upper aerodigestive tract are primarily affected. Onset is usually in early infancy, and characterized by a weak cry and hoarse voice due to laryngeal infiltration. In more severe cases, this infiltration may lead to respiratory obstruction. Diffuse skin infiltration and thickening occurs gradually, resulting in papules and chicken pox-like scars. Infiltrates in the tongue and its frenulum limit tongue movements and cause speech difficulties.

Calcifications in the temporal lobes or hippocampus have been reported, sometimes in association with neurological, psychiatric and neuropsychological sequelae. Histologically LP is characterized by intercellular deposits of periodic acid Schiff (PAS)-positive hyaline material in the skin, mucous membranes, and internal organs. Loss-of-function mutations in the gene encoding extracellular matrix protein 1 (*ECM1*) on chromosome 1q21 have been identified in LP; fewer than 20 variants have been reported, most of which occur in single families. Two distinct isoforms of different lengths have been described for *ECM1* depending on the presence of two alternatively spliced exons (exons 5a and 7) and both are expressed in the skin and upper respiratory tract, although ECM1a has a wider pattern of expression. The function of the protein ECM1 is still unclear, although an important role in skin physiology and homeostasis has been hypothesized.

CASE REPORT

11 years old boy, born to parents with third degree consanguineous marriage presented to dermatology outpatient department of Gokuldas Tejpal hospital with progressive skin and mucous membrane changes since early childhood. At the age of two years he started to develop multiple papules, vesicles and crusted eruptions on the face and extremities at the site of trauma which

progressively turned to waxy, thickened, yellowish plaques and nodules. The patient also had history of hoarseness since early infancy so referred to our Otorhinolaryngology department for detail clinical workup in view of hoarseness. patient had no history of seizures, behavioral changes and learning difficulties. patients elder sister also had similar illness since her early childhood but no medical advice was taken due to economical constraint. In our Otorhinolaryngology department the patient underwent indirect laryngoscopy

which showed thickening of vocal cords and hyaline deposits in the larynx, oral cavity and oropharynx. Tongue was firm and with impaired mobility. Light microscopy examination of laryngeal biopsy tissue showed massive deposits of periodic acid Schiff(PAS) positive and diastase negative homogeneous, eosinophilic, hyaline like material in the lamina propria without inflammation. Diagnosis was confirmed by skin biopsy and polymerase chain amplification by dermatologist.



Figure 1: Patient with lipoid proteinosis



Figure 2: Thickening of vocal cord and hyaline deposits in the larynx

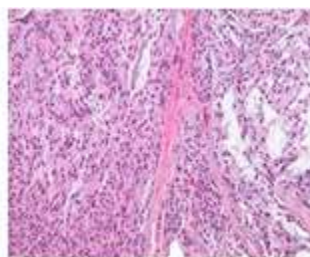


Figure 3: Histopathology slide suggestive of hyaline deposits in the larynx

DISCUSSION

Although in the dermatology literature several reports of LP With the typical dermatologic features have appeared, 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 This hoarseness may be present at birth, as a weak cry, or develop later, within the first few years of life. The development of a hoarse voice was noticed earlier in our patient. Therefore, the importance of LP should not be underestimated by otorhinolaryngologists and it should be included in the differential diagnosis of voice changes and hoarseness, in infancy and childhood. The skin of children with LP is highly susceptible to damage, being reflected in the appearance of chicken pox-like scars and yellowish papules. These lesions involve primarily the face and extremities and rarely appear elsewhere. Subsequently, infiltration of the skin may present as groups of warty plaques on the axillae and elbows. Beaded papules on the eyelid margins (moniliform blepharosis) are a characteristic finding in about two-thirds of patients. Our patient presented typical skin lesions, which appeared at approximately two years of

age. In clinical practice, LP is rarely a life-threatening condition. Infiltration of the oral mucosa may lead to xerostomia and dysphagia. Other mucosal findings include thickening of the sublingual frenulum and tongue, limiting tongue movements and causing speech difficulties. Moreover, diffuse infiltration of the pharynx and larynx may cause respiratory distress, at times requiring tracheostomy. Our patient presented speech impairment but no upper airway obstruction or dyspnoea. Hyaline deposits have been described in the conjunctiva, cornea, trabeculum, and retina. Corneal opacities or secondary glaucoma, due to infiltration in the trabeculum, may appear later. Deposition of hyaline material in the small bowel may lead to intestinal bleeding. Extracutaneous and extramucosal features may include neurological signs and symptoms, such as epilepsy, memory loss, and schizophrenic behavior, sometimes in association with intracranial calcification in the temporal lobes or hippocampus, easily detected by brain computed tomography. Histologically, LP is characterized by disruption/duplication of the basement membrane and deposition of hyaline material at the level of the basement membrane (resulting in its thickening at the dermo-

epidermal junction), papillary dermis, surrounding capillaries, and around adnexal epithelia, especially sweat coils. The hyaline material is eosinophilic, periodic acid Schiff (PAS) positive, and diastase resistant, indicating the presence of glycoproteins. Accumulations of type IV and V collagen occur around the blood vessels and appendages; type I and III collagen is reduced. In Our patient histopathological examination of a laryngeal biopsy specimen showed massive deposits of eosinophilic, periodic acid Schiff (PAS) positive, and diastase resistant material in the lamina propria corroborating the clinical diagnosis of LP. Skin biopsy and polymerase chain amplification confirmed the diagnosis. Recent cell biology studies have provided new data that helps our understanding of the function of ECM1 and that partially explain the disease phenotype in LP. ECM1 has been reported to regulate endochondral bone formation, to stimulate proliferation of blood vessel endothelial cells, to promote angiogenesis, and to be involved in the control of epidermal differentiation. However, clues to its physiological function in the dermis are now emerging. It has been demonstrated that ECM1 is a secreted glycoprotein that binds to perlecan, the major heparan sulphate proteoglycan of the basement membrane, as well as to growth factors and fibrillar proteins. Thus, ECM1 may act as a "biological glue" in the dermis, helping to regulate basement membrane and interstitial collagen fibril macro-assembly and growth factor binding. Therefore, loss of ECM1, within the dermis may have profound effects on dermal homeostasis, leading to the clinical features of skin infiltration and scarring. Meanwhile, lack of ECM1 within the epidermis may alter the normal pattern of keratinocyte maturation and differentiation and give rise to the clinical features of warty hyperkeratosis. The prognosis of LP patients is generally good despite the progressive nature of the disease until early adulthood. However, there is currently no effective therapy. Laser microlaryngoscopy, dissection of the vocal cords and excision of deposits may be performed to preserve or improve the voice. Respiratory obstruction is infrequent and rarely requires tracheostomy. Dermabrasion and chemical skin peeling can be performed in some cases. Approaches reported in the literature include oral steroids, dimethyl sulphoxide, intralesional heparin, and etretinate. Irrespective of evolution of the disease and use of symptomatic treatment, it is important that parents of affected children be counseled concerning the risks of having other affected offspring.

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