

Otolaryngologic findings of five lipoid proteinosis cases

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Beş lipoid proteinozis olgusunun otolaringolojik bulguları

Lipoid proteinozis (Urbach-Wiethe hastalığı) ender görülen ve otosomal resesif geçiş gösteren herediter bir hastalıktır. Hiyalin madde-sinin dokularda birikmesi sonucu çok çeşitli semptomlar oluşabilir. Larinks ve cilt lezyonları sık görülür. Beş lipoid proteinozis olgusunun kulak burun boğaz bulguları incelendi ve literatür gözden geçirildi. Bizim serimizde larinks tutulumu bütün olgularda izlendi. Üç olguda oral bölgede, bir olguda dil kökünde hastalık saptandı.

Anahtar Sözcükler: Lipoid proteinozis, Urbach-Wiethe hastalığı, otolaringoloji

Abstract

Lipoid proteinosis (Urbach-Wiethe disease) is a rare autosomally recessive inherited disease, which presents with various symptoms due to deposits of hyaline material in tissues. Lesions of larynx and skin are frequent. Otolaryngologic findings of 5 cases of lipoid proteinosis were analyzed, and literature was reviewed. We observed involvement of larynx in all cases with skin lesions in our series. The disease was determined in oral cavities of 3 cases, and tongue base of a case.

Key Words: Lipoid proteinosis, Urbach-Wiethe disease, otolaryngology.

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Introduction

Lipoid proteinosis (Urbach-Wiethe disease) is an autosomally recessive genodermatosis characterized by widespread deposition of eosinophilic (periodic acid-Schiff (PAS)-positive) hyaline-like material in the skin, mucous membranes, and other internal organs.¹ The disorder has recently been shown to result from loss-of-function mutations in the extracellular matrix protein 1 gene (ECM1) on 1q21.² Clinical features are hoarseness starting in infancy and the formation of yellowish papules and plaques on the skin and mucous membranes of the nose, oral cavity, pharynx and larynx.³

The purpose of this study is to remind our colleagues about lipoid proteinosis in cases of chronic laryngitis with skin lesions.

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Case Report

We present otolaryngologic findings of 5 lipid proteinosis cases diagnosed in Gülhane Military Medical Academy between 1996 and 2003. All the patients were young males (20-23 years old) and privates of the army.

Diagnosis was made histologically by disruption / duplication of basement membrane and widespread deposition of typical periodic acid-Schiff (PAS)-positive material in the dermal capillaries and sweat glands.

Diffuse warty thickening of the skin along with beaded papules and pox-like acneiform scars were the common dermatologic lesions of all cases. All of them appeared with hoarseness caused by laryngeal lesions resembling Singer's nodule or chronic laryngitis (Figure 1). Three of 5 cases showed yellow-white infiltration on the tongue, buccal mucosa, and palate. In one case the tongue base was viewed with cauliflower-like appearance and diffuse nodular surface. All patients had a history of the disease since childhood.

T1 sagittal section of the MRI scan demonstrates iso-dense mass extending from the tongue base to the epiglottis (Figure 2). There was no biochemical abnormality except mild increase in pre-b band in protein electrophoresis. Table 1 presents the lesions of the lipid proteinosis which were seen in our cases.

Discussion

Lipoid proteinosis was identified by Sibenmann (1908) at first, but Urbach and Wiethe reported their series including 9 patients at 1926 and the disease was named than as Urbach and Wiethe disease. It is also known "Lipoidosis cutis et mucosae".^{4,5}

Involvement of the upper aerodigestive tract is common in lipid proteinosis.^{6,7} All of our patients were hoarse and thickened, hyperemic edematous mucosa was seen in the larynx of all cases. Three of 5 cases showed yellow-white infiltration on the tongue, buccal mucosa and palate. Tongue base of a patient was



Figure 1. Vocal folds with irregular free edges and the surface (case number 3).



Figure 2. T1 sagittal section of the MRI scan demonstrates the isodense mass (filled arrow) extending from the tongue base to the epiglottis as seen during the endoscopic view (case number 3).

viewed with cauliflower-like appearance and diffuse nodular surface. He had articulation problem secondary to diminished tongue mobility. Diffuse warty thickening of the skin along with beaded papules and pox-like acneiform scars were the common dermatologic lesions of all cases. There was no other systemic manifestation except skin lesions in our patients.

Histologically lipoid proteinosis is characterized by extensive deposition of amorphous eosinophilic material around the capillaries, sweat glands, hair follicles and in the papillary dermis. The hyaline material is PAS

positive but diastase resistant.⁸ We made the diagnosis histopathologically in our cases.

Chan⁹ reported the role of extracellular matrix protein 1 (ECM1) in the etiopathogenesis of lipoid proteinosis. ECM1 is a protein which regulates endochondral bone formation, and stimulates proliferation of endothelial cells and induces angiogenesis. Loss-of-function mutations in the ECM1 gene were discovered to be the cause of the rare autosomal recessive genodermatosis, lipoid proteinosis. Moreover, other recent studies have identified circulating autoantibodies

Table 1. Lesions of lipid proteinosis in our patients.

Patients	Sex	Age	Skin lesion	Oral lesion	Tongue base lesion	Laryngitis
1	Male	23	+	-	-	+
2	Male	21	+	+	-	+
3	Male	20	+	+	+	+
4	Male	20	+	-	-	+
5	Male	22	+	+	-	+

against the ECM1 protein with lichen sclerosus, a common chronic inflammatory condition that shares some clinicopathological features with lipid proteinosis. ECM1 thus serves as a target antigen in both an inherited and an acquired skin disorder. Within the epidermis, ECM1 has a role in the control of keratinocyte differentiation. Within the dermis, ECM1 binds the major heparan sulphate proteoglycan, perlecan. In this way, ECM1 may act as "biological glue" in the dermis, helping to regulate basement membrane and interstitial collagen fibril macro-assembly and growth factor binding.⁹ Hamada et al¹⁰ declared that exons 6 and 7 are the most common sites of ECM1 mutations in lipid proteinosis.

There is no definitive treatment of the disease. Wong and Lin¹¹ noticed remarkable response of lipid proteinosis to dimethyl sulfoxide. Kaya et al proposed D-penicillamine as a promising agent for the treatment of lipid proteinosis.¹² We observed our patients during their military service duty. Since, none of them had respiratory distress we did not perform any treatment.

Conclusion

Involvement of larynx in lipid proteinosis seems as common as dermatologic findings, so colleagues should be aware of lipid proteinosis for the patients with chronic laryngitis and alterations of mucous membranes and skin.

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