Lipoid Proteinosis: Case Report and Review Literature

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ABSTRACT

Lipoid proteinosis is a rare autosomal recessive deposition disorder due to mutation in the extracellular matrix protein 1 gene. Until now, there were only 300 cases reported in literature. Moreover, case reports in Thailand are limited. This report demonstrated a case of lipoid proteinosis in a 14-year-old Thai girl, who presented with hoarseness of voice since infancy. Skin examination revealed multiple beaded skin-color papules along eyelid margins, hyperkeratotic papules on both elbows and thickening of her sublingual frenulum. Microscopic examination demonstrated deposition of hyaline material in her skin and mucous membrane. From literature review, some patients had complications from upper respiratory tract infiltration which led to early mortality. It is important to recognize this disease in a patient that presents with hoarseness for early diagnosis, treatment and prevention of complications.

Keywords: Lipoid proteinosis, hoarseness, moniliform blepharosis

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INTRODUCTION

Lipoid proteinosis (LP) is a rare autosomal recessive disorder caused by defect in extracellular matrix protein-1 (ECM 1). Hoarseness is the earliest and most frequent finding. Most patients had typical clinical findings which included hoarseness of voice and beaded papules at eyelid (moniliform blepharosis); and some had abnormality in brain calcification. In severe cases lipoid proteinosis can cause respiratory obstruction or seizure.

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CASE REPORT

A 14-year-old Thai girl presented with hoarseness of voice since infancy. She developed beaded papules over eyelid margins in the following years. She had no history of recurrent blister lesion, respiratory obstruction, speech impairment, visual disturbances or photosensitivity. She was found to be healthy and active since birth and never had a history of convulsion or any other neurologic symptoms. She was born of non-consanguineous parents. There was no family history of a similar condition.

Skin examination revealed multiple beaded skin-color papules along eyelid margins (Fig 1), hyperkeratotic papules on both elbows. She had thickening of her sublingual frenulum, hoarseness, low pitch and low intensity of

Fig 1. There are multiple beaded skin-color papules along eyelid margins (moniliformblepharosis).

voice. Indirect laryngoscope showed bilateral true vocal cord swelling and irregular surface. Laryngostroboscopy found many tiny masses at her posterior glottic and interarythenoid. (Fig 2) Neurological and ocular examinations were normal.

The diagnosis was confirmed by a biopsy, taken from a beaded papule at her left lower eyelid margins (Fig 3) and posterior glottic. Both tissues showed diffuse hyaline material deposited in her dermis. The hyaline material was Periodic acid Schiff (PAS) positive, diastase resistant and congo red negative. Computed tomographic scan of the brain was normal. She was treated with CO^2 laser for vocal cords lesion.

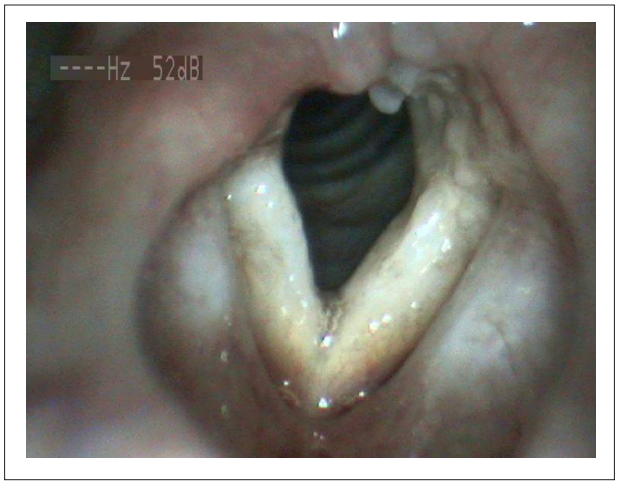

Fig 2. Laryngostroboscopy showed bilateral true vocal cord swelling, irregular surface and many tiny masses at posterior glottic and interarythenoid.

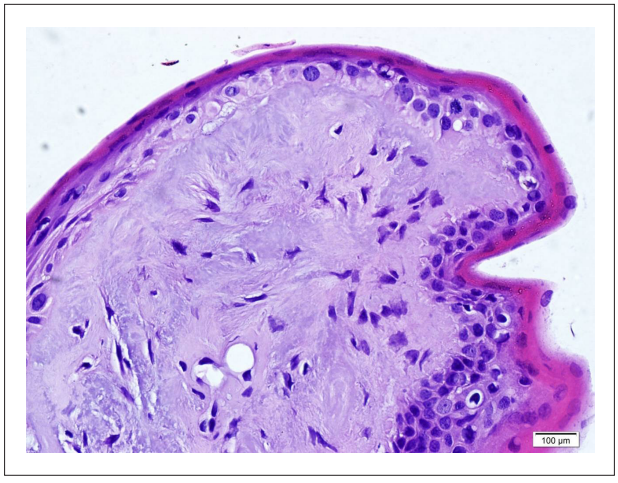

Fig 3. Skin biopsy from lower eyelid showed diffuse hyaline material deposited in dermis.

DISCUSSION

Lipoid proteinosis, also known as Urbach-Wiethe disease or hyalinosis cutis et mucosae, was first described by Urbach and Wiethe, in 1929.[1] LP is characterized by deposition of hyaline material in skin, mucous membranes, and internal organs.

About 300 cases of LP have been reported until now. LP is a rare autosomal recessive disorder. It is caused by mutations in gene encoding ECM 1 on chromosome 1q21.[2] Exons 6 and 7 are the most common sites for ECM1 mutations. Patients with exon 7 mutations may have a slightly milder phenotype. ECM-1 has been reported to inhibit bone mineralization, to be involved in the control of epidermal differentiation, and to stimulate angiogenesis.[3] ECM1 binds to the major heparin sulphate proteoglycan, perlecan in the dermis and loss of this protein binding may cause skin infiltration and scarring.[4]

LP is deposition of hyaline material in skin, mucous membranes and internal organs leading to various manifestations. The first clinical finding of LP is hoarseness caused by deposition of hyaline material in the vocal cords. Hoarseness may be present at birth, or appear within the first few years of life and may progress during the lifetime of a patient. Similarly, this present patient had hoarse voice as the first noticed symptom.

Onset of cutaneous lesions is variable from the first year until after 10 years of age.[5] Skin lesions have 2 stages. The first stage, presents with vesicles and hemorrhagic crusts, is predominant at the face and extremities, often occurs in association with trauma and resolves with pock-like or acneiform scars. Some patients have vesiculobullous lesions. At the second stage, skin becomes diffusely thickened and waxy, and yellow discoloration appears. Beaded papules on the eyelid margins are a characteristic finding in about two-thirds of patients. There are papules, plaques and nodules located on the face, axillae and the scrotum. Hyperkeratosis and verrucous lesions occur in any repeated area of trauma, such as extensor surfaces, especially the elbows, knees and hands. Alopecia with varicelliform scarring has been reported.[6] This present case had characteristic beaded papules on her eyelid margins and hyperkeratosis papules on both elbows.

Other mucosal findings include thickening of sublingual frenulum which leads to difficulty in protruding the tongue and causes speech difficulties, such as those found in this present patient. Hyaline material also deposits at pharynx, tongue, soft palate, tonsils, and lips. Infiltration of salivary glands can cause xerostomia, leading to poor oral hygiene. Sometimes the patients have respiratory distress due to laryngeal and pharyngeal involvement, and tracheostomy has been considered. The ocular findings present with focal degeneration of macula and drusen formation in Bruch's membrane. Open-angled glaucoma is caused by hyaline deposition in the trabecular meshwork. Hyaline deposits can also be found on the iris, meibomian glands or uvea and develop uveitis in LP.[7]

Corneal ulceration was present in this patient caused by trichiasis due to eyelid infiltration. Ocular examination of this patient revealed normal findings.

(Some text refers to LP in general and some to the present case, interspersed, so they have been separated by paragraph with appropriate adjustment of tense.)

Neurologic abnormalities include seizures, which are reported in about 25% of patients, mental retardation and behavioral change.[8] A pathognomonic radiologic finding is bilateral, bean or comma shaped intracranial calcifications in the temporal lobes or amygdala. Epilepsy may be related to these calcifications. Neurological examination and imaging were normal in this patient.

Histological examination has revealed the deposition of PAS positive and diastase resistant hyaline material around the walls of dermal vessels, appendages and papillary dermis, often perpendicular to the basement membrane. This hyaline material is negative for Congo red staining. This histological finding was also shown in this patient.

Early lesions may have been found in intraepidermal blister with nondyskeratotic acantholysis. Moreover, subepidermal blister could be presented in LP so LP may be one of the differential diagnoses of a cell-poor subepidermal blister.[9] Ultrastructural examination shows concentric, "onion-skin" layers of excess basement membrane around blood vessels which have type III, type IV collagen and laminin, and appearance of irregular reduplication lamina densa at dermoepidermal junction.[10]

Currently, there is no effective treatment for lipoid proteinosis. There are reports of oral steroids, dimethyl sulfoxide, d-penicillamine, intralesional heparin, and etretinate which have been used. Acitretin have been reported in one patient, with improvement only in hoarseness.[11] CO_2 laser surgery and dermabrasion for vocal cords, beaded eyelid papule and skin lesions result in cosmetic improvement. Life expectancy is usually normal except for respiratory complication.

This patient demonstrates the typical manifestations of LP with hoarseness since infancy and beaded papules at eyelid margins. Histopathology was consistent with LP. Close follow up was done for early detection of respiratory tract obstruction, or life threatening complication. Therefore it is important to

recognize this disease in the patient that presents with hoarseness for early diagnosis, treatment and prevention of complications.

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