CASE REPORT

Abstract
Lipoid proteinosis (LP) is a rare progressive autosomal recessive disorder caused by mutations in the extracellular matrix protein 1 gene present on chromosome 1q21. It is characterized by infiltration of hyaline material into the skin, mucosae, and internal organs. Patients present with a classical history of repeated blistering, skin scarring, beaded eyelid papules, waxy papules over the body, and laryngeal and tongue infiltration leading to hoarseness of voice and restricted tongue movement. A variety of ocular manifestations have been described in association with LP. We report a case of a 10-year-old female child with typical features suggestive of LP associated with unilateral esotropia. The case is reported here for its rarity and uncommon association with esotropia hitherto not documented. Dermoscopic findings of the case are also discussed.

Key Words: Dermoscopy, esotropia, hoarseness, lipoid proteinosis, moniliform blepharosis, Urbach-Wiethe disease

Introduction
Lipoid proteinosis (LP) also known as hyalinosis cutis et mucosae and Urbach-Wiethe disease, was first described as a distinct entity in 1929. It is a rare autosomal recessive genodermatosis characterized by infiltration of hyaline material in the skin, oral cavity, larynx, and internal organs. Although seen worldwide, it is most commonly prevalent among those of German ancestry in the Northern Cape province in South Africa. LP can present with variable phenotypic features involving multiple systems, but the skin and mucous membranes of the aerodigestive systems are primarily affected.[1] Hoarseness of voice from vocal cord infiltration is usually the earliest finding which starts at birth or in infancy. Mucocutaneous manifestations include spontaneous or trauma-induced acniform or pock-like scars, warty and waxy papules, nodules, plaques, moniliform blepharosis, yellow-white submucosal infiltrates in the oral cavity, and restricted tongue movement. The most common ocular finding is yellowish papules over the eyelid margins.[2,3]

Diagnosis is confirmed by histopathology which shows deposition of periodic-acid–Schiff (PAS) positive hyaline material in the dermis, at the dermo-epidermal junction, perivascularly and along adnexal epithelium.[3] Computed tomography (CT) of the brain may reveal bilateral medial temporal lobe calcifications, especially within the amygdala.[1]

A wide range of ocular manifestations have been reported in LP. Herein, we report a case of LP associated with esotropia. The present case documents this new association along with the dermoscopic features of LP.

Case Report
A 10-year-old female child presented to the outpatient clinic with chief complaints of skin lesions, hoarseness of voice, and inward deviation of the right eye. The parents gave history of hoarseness of voice since 1 year of age and spontaneous blistering and erosions followed by the development of atrophic scars over the face, trunk, and extremities since 6 months of age. There was also history of thickening of the skin over the neck, elbows, and knees. The patient had inward deviation of the right eye for the last 6 years, but...
there was no history of double vision. She did not have any history of photosensitivity, headache, convulsions, and neuropsychiatric symptoms. She was born of a nonconsanguineous marriage. There was no history of similar complaints in the family.

On examination, the patient was a healthy girl with normal mental development. Cutaneous examination revealed shiny and waxy facial skin with multiple acneiform scars and subtle beading of the eyelid margins. The skin of the bilateral axillae was nodulated and thrown into multiple folds with an uneven surface. Warty plaques were present over elbows, knees, and nape of the neck [Figure 1a-c]. Multiple well-defined pock-like scars were present over the trunk and extremities. Scarring alopecia was noted over the occiput. Oral examination revealed multiple yellowish papules over the buccal mucosa. The tongue was firm with indentations and short and thickened frenulum leading to difficulty in protrusion [Figure 1d].

Biopsy from the nape of neck revealed deposition of eosinophilic hyaline material around capillaries and skin adnexa in the thickened papillary dermis with foci in the deeper dermis. The material was PAS positive and diastase resistant [Figure 2a-c]. Based on clinical evaluation and histopathology, diagnosis of LP was made. X-ray and CT of the skull did not reveal any abnormality. On ophthalmological consultation, the patient was found to have uniocular 30° esotropia of the right eye. Indirect laryngoscopy revealed thickening of vocal cords.

Dermoscopy was done on three sites using Dermalite DL4 dermoscope in polarized contact mode. Following dermoscopic features were noted: (1) Left axilla: sulci and gyri with pale-white structureless areas [Figure 3a]; (2) Nape of neck: small-rounded pinkish-white structures arranged in multiple clumps giving a “pulpy or pulp-like” appearance [Figure 3b], and (3) Right eyelid: multiple pale white beads along the eyelid margin and distichiasis. The dermoscopic findings corresponded to deposition of hyaline material in the dermis. Beading of the eyelid margins which was subtle clinically appeared more distinctive on dermoscopy and distichiasis was also noted [Figure 3c].

**Discussion**

LP is a rare progressive autosomal recessive genodermatosis, first described by Siebenmann in 1908 and later established as a distinct clinical and histologic entity by Urbach and Wiethe in 1929.[1] It is caused by mutations in the gene encoding extracellular-matrix-protein 1 (ECM-1). ECM-1 is present both in the epidermis and as a secretory protein in the dermis. Reduced expression of this protein results in aberrant deposition of eosinophilic hyaline-like material in the skin and viscera, leading to protean clinical features.[3,4] Hoarseness of voice which may initially be noted as a weak cry is the earliest and most striking feature. Skin lesions are usually absent at birth and start as blisters and erosions in early childhood which heal with scarring. At this stage, LP may mimic epidermolysis bullosa or erythropoietic porphyria. As the disease progresses, more distinct cutaneous stigmata develop which may vary from yellow waxy papules and nodules, warty plaques over trauma-prone sites to generalized skin thickening and acneiform or pock-like scars. Neuropsychiatric illness is well recognized but variable feature of LP.[3]

Ocular manifestations in LP, although rare, can be diverse involving any part of the eye. The most common ocular lesions include beaded eyelid papules often termed as

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**Figure 1:** (a) Waxy, shiny facial skin and moniliform blepharosis. (b) Infiltrated, nodulated skin of left axilla with an uneven surface. (c) Hyperkeratotic plaque over the nape of neck. (d) Short and thick frenulum and waxy, infiltrated lips

**Figure 2:** (a) Photomicrograph showing elongated rete ridges and deposition of homogenous eosinophilic hyaline material in the dermis (H and E, ×10). (b) The eosinophilic material is seen surrounding the blood vessels and adnexa. (H and E, ×40). (c) Periodic-acid-Schiff positive magenta colored hyaline material (PAS, ×40)
“moniliform blepharosis.” It may be associated with madarosis, trichiasis, and sometimes distichiasis as was seen in our case. Less common ocular manifestations include glaucoma, cataract, lens subluxation or dislocation, uveitis, corneal ulceration, keratoconus, retinal complications, nasolacrimal duct obstruction, and transient blindness. Among the ocular features, our case had beaded eyelid papules, distichiasis, and esotropia. There has been no previous report of esotropia in a case of LP.

The dermoscopic findings in our case varied according to the site and type of lesion. Sulci and gyri and pale-white structureless areas predominated in the lesion over the axilla while clumps of small pinkish-white structures giving a “pulpy or pulp-like” appearance were seen in the hyperkeratotic plaque over the neck. Sulci and gyri have also been described in dermoscopy of nevus lipomatosus cutaneous superficialis, but the latter shows yellowish structureless areas and honeycomb-like pigment network which were not seen in our case. The dermoscopic findings from hyperkeratotic plaque over the nape of the neck had a unique “pulpy or pulp-like” appearance hitherto not reported. Although beading of the eyelid margins is considered a classical clinical finding, it is variable and often subtle as in our case. Dermoscopy can help in better recognition of eyelid beading and associated findings in such cases and act as an aid to early diagnosis.

LP usually runs a progressive course with worsening of cutaneous features and development of infiltrative lesions, having a major impact on the quality of life. Many treatments have been tried, but none is reported to have any sustained benefits. CO\textsubscript{2} laser ablation of the eyelid and vocal cord lesions may be beneficial in some patients. Cutaneous lesions can be treated by dermabrasion, chemical peeling, and resurfacing with fractional CO\textsubscript{2} laser. Oral dimethyl sulfoxide, steroids, d-penicillamine, retinoids, and intralesional heparin have been tried with variable results.

**Conclusion**

LP is a rare entity with an array of clinical presentations involving multiple systems with skin and mucosa being the most commonly affected. The early cutaneous lesions may often be elusive, and diagnosis may be missed. Dermoscopy can serve as a useful aid in such cases. As LP patients often have concomitant involvement of the aerodigestive and ocular system, a multidisciplinary approach is necessary for holistic management to improve the quality of life of these patients.

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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**Conflicts of interest**

There are no conflicts of interest.

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