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Letter to Editor

Lipoid proteinosis – An erratic disease with an archetypal presentation

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Sir,

Lipoid proteinosis (Urbach–Wiethe disease) is a rare autosomal recessive genodermatosis. Seibenmann had described the illness first in 1908. Urbach and Wiethe reported about the disease in detail in 1929.[1] The disease is characterized by hoarseness of voice since early childhood, skin and mucosal lesions.[2] We report a case of lipoid proteinosis with classical clinical features.

A 23-year-old man, born out of a non-consanguineous marriage, presented with a history of hoarseness of voice, multiple skin colored and hyperpigmented papules and vesicles which healed by scarring from the age of 1 year. His father revealed that his son had weak cry and hoarse voice since infancy. Similar complaints were absent among family members. Milestones were normal. There was no history of photosensitivity, dyspnea, dysphagia, seizures or neuropsychiatric disturbances.

On examination, facial skin was waxy in appearance with multiple, ill-defined atrophic scars of varying sizes [Figure 1]. Multiple, skin colored, linearly arranged, closely aggregated 1–2 mm sized papules were present over both eyelid margins. Ichthyotic scaling was present on legs. Multiple hyperpigmented papules with warty nature and waxy infiltrated yellowish plaques were distributed in axilla, trunk and both upper limbs. Multiple scars were present in a generalized manner mainly on trunk and around knee. Patchy scarring alopecia was noted over occiput. Macroglossia was present. Protrusion of tongue was restricted due to thick and short frenulum.

ENT examination revealed irregular growth in arytenoids region extending to posterior third of vocal cord [Figure 2]. Ophthalmological examination revealed nebular corneal opacity in the right eye. Other systems were normal.

With the classical features of weak cry, hoarse voice, papules and vesicles which healed with scarring since infancy and waxy papules along the eyelids, provisional diagnosis of lipoid proteinosis was considered. Congenital erythropoietic protoporphyria, Darier's disease and systemic amyloidosis were considered as differential diagnosis.

Hemogram, urine routine, renal and liver function tests, random blood sugar, thyroid function test, serum electrophoresis and computed tomography brain were within normal limits.

Skin biopsy from papule on trunk unveiled a tissue lined by stratified squamous epithelium. Pale eosinophilic amorphous material was deposited throughout dermis [Figure 3]. Eosinophilic material showed strong staining with periodic acid–Schiff (PAS) stain [Figure 4]. Histopathology was diagnostic of lipoid proteinosis.

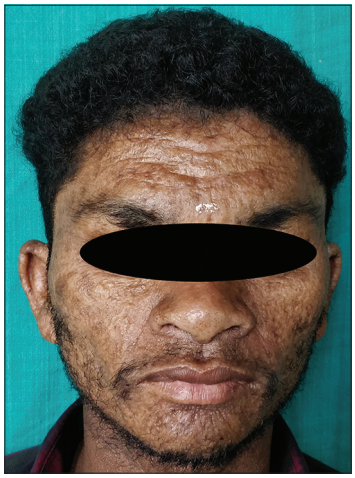

Figure 1: Waxy papules and atrophic scars on face.

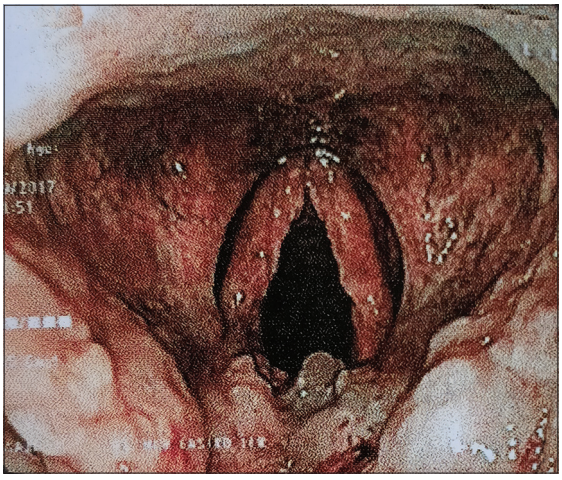

Figure 2: Irregular growth in arytenoid region.

Congo red staining followed by polarization microscopy did not reveal any fluorescence. Hence, systemic amyloidosis was ruled out. The absence of suprabasal clefts with acantholytic cells and dyskeratotic cells in histopathology ruled out the possibility of Darier's disease. The presence of oral lesions, laryngeal involvement manifested as hoarse voice, normal colored urine and absence of photosensitivity helped us to differentiate erythropoietic protoporphyria.

Lipoid proteinosis is a rare disorder with autosomal recessive inheritance. It occurs due to mutation in the extracellular matrix protein 1 (ECM1) gene on chromosome 1q21.3.[3] This gene encodes a soluble protein that interacts with a variety of extracellular and structural proteins, contributing to the maintenance of skin integrity and homeostasis. It also plays a role in angiogenesis. A lack of functional ECM1 protein results in unstable extracellular matrix which may cause neighboring cells to overproduce proteins. Manifestations are due to the deposition of hyaline-like material in multiple organs such as skin, mucosa and brain.

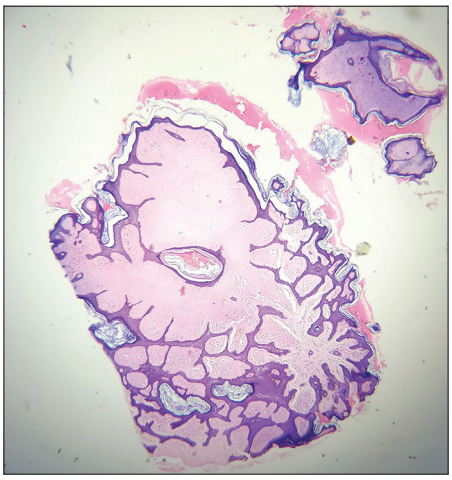

Figure 3: Eosinophilic amorphous infiltrate throughout dermis (H and E, ×40).

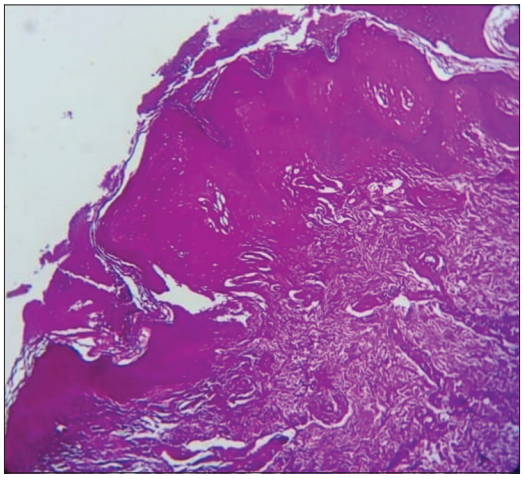

Figure 4: Eosinophilic infiltrate showed periodic acid–Schiff positivity (PAS stain, ×40).

The initial clinical manifestation is usually hoarseness of voice that presents at birth as a weak cry. Cutaneous lesions usually appear within the first 2 years of life. Skin lesions are vesiculobullous lesions and hemorrhagic crusts that heal with scarring and diffusely thickened facial skin with widespread yellow flat papules and plaques. Multiple acneiform and pox-like scars are described on face. Verrucous lesions are seen over extensor surfaces of elbows, knees and hands. Characteristic ocular involvement is beading of eyelid margins (moniliform blepharosis). Thickening of frenulum and tongue results in limited tongue movements due to the infiltration of oral mucosa.[4] Pharyngeal and laryngeal involvement leads to speech impairment and sometimes respiratory difficulties. There may be patchy alopecia and rarely visceral involvement. The disease usually progresses until early adult life but subsequently stabilizes.

Histopathology shows deposition of homogeneous, eosinophilic hyaline material at the level of basement

membrane and in the papillary dermis. These deposits are also seen around the basement membranes of blood vessels and appendages, eccrine sweat glands, in particular, in a concentric manner. They are PAS positive and diastase resistant.[5]

Extracutaneous involvement includes neurological manifestations in the form of psychosis, partial complex seizures, anger and panic attacks and progressive amnesia. A pathognomonic brain imaging finding in lipoid proteinosis is bilateral intracranial calcification in temporal lobes.[6]

There is no effective treatment. Dimethyl sulfoxide, D-penicillamine,[7] etretinate[8] and acitretin[9] have been tried with varying success. Retinoids were supposed to decrease the deposition of hyaline material in dermis by their inhibitory effect on collagen. Dermabrasion, chemical peeling, blepharoplasty and CO_2 laser therapy[10] may be helpful for the skin lesions.

Lipoid proteinosis has a benign course with a normal life expectancy.

In our case, the absence of family history suggests the possibility of a sporadic mutation. Eye and laryngeal involvement were noted in addition to skin involvement. Although we had a plan to start acitretin and do dermabrasion for his facial lesions after counseling, the patient was lost to follow up.

The case is put forward because knowledge regarding such rare diseases will aid the health professional in detecting the illness early in the course of the disease and in providing the appropriate treatment to improve the quality of life of the patient. In future, recombinant gene therapy targeting ECM1 gene may bring forth cure.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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