Journal of Pakistan Association of Dermatologists. 2014;**24 (1)**:89-92.

Case Report

Lipoid proteinosis in two Indian brothers - a case report from South Bengal

K Shome*, I Das, A Saha**, N Jain**, J Seth**, Rajesh****

* Department of Dermatology, Venereology and Leprology, Kolkata Medical College, Kolkata
** Department of Dermatology, Venereology and Leprology, Burdwan Medical College and Hospital, Burdwan, West Bengal, India

Abstract Lipoid proteinosis is a rare autosomal recessive disorder with variable phenotype, caused by defect in extracellular matrix protein-1 and is characterized by deposition of periodic acid-Schiff-positive, diastase resistant material in skin, mucous membrane and internal organs. There are only few reports regarding lipoid proteinosis in literature and in this part of the world. Here, we report a case of lipoid proteinosis in a 29-year-old male with positive family history and widespread distribution involving skin and internal organs. Histopathological finding was consistent with clinical diagnosis of lipoid proteinosis.

Key words
Lipoid proteinosis, hyalinosis cutis, calcification

Introduction

Lipoid proteinosis is a rare disease first described by Urbach and Wiethe in 1929.[1] It is autosomal recessive in inheritance and is due to mutation of the gene encoding extracellular matrix (ECM) protein-1. The clinical manifestations are variable and vary between different individuals. Manifestations range from hoarseness of voice, thickened frenulum of tongue, difficulty in protruding tongue, beaded eyelid papules, blistering in childhood followed by scarring with accentuation in sun-exposed areas, alopecia, to infiltrated warty papules over extensors. Central nervous system and ocular involvement are also a matter of concern. There is paucity of reports regarding lipoid proteinosis in this part of the world. We, therefore, here report a case of lipoid proteinosis with positive family history.

Address for correspondence
Dr. Joly Seth
Department of Dermatology, Venereology and Leprology,
Burdwan Medical College and Hospital,
Burdwan, West Bengal, India
Email- drjolyseth@gmail.com

Case report

A 29-year-old male presented with hoarseness of voice and multiple, asymptomatic, skin-colored lesions since childhood. There was history of recurrent spontaneous blisters chiefly over pressure points and extremities during childhood, which healed and left mildly depressed scars over knee, elbow and gluteal region. Later on, he developed multiple, asymptomatic, skin-colored papules over face, pubis, and acral portion of extremities since puberty which gradually increased in size. He was also unable to protrude tongue. As per patient, his younger brother was also suffering from the same problem. There was no history of consanguinity. On examination, there was sandpaper like feeling of lesional skin. The eyelid margins showed loss of eyelashes and typical beading with waxy papules (**Figure 1** and **2**). The tongue was large, thickened, infiltrated and showed teeth indentations at margin (**Figure 3**); palate was also diffusely infiltrated. The skin of the face including lips and the extremities had yellowish, waxy papules and nodules punctuated by pitted scars. Hyperkeratotic verrucous lesions were present over acral portion of extremities and

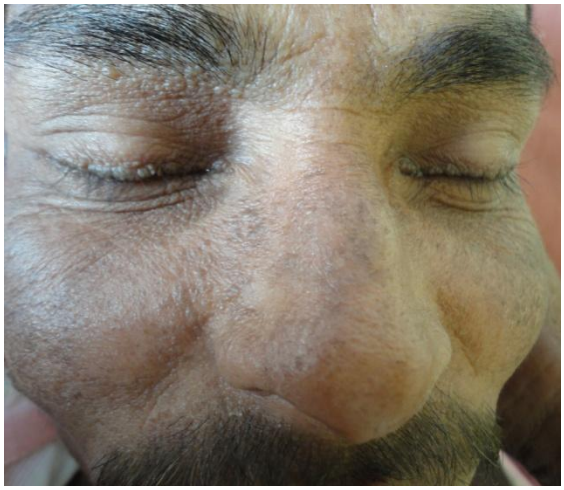

Figure 1

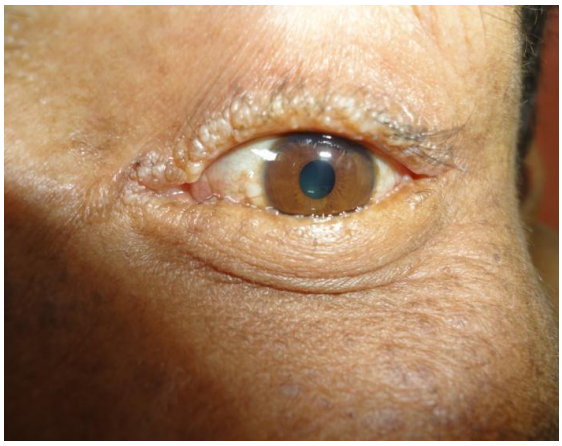

Figure 2 Symmetric, flesh coloured, beaded papules at eyelid margins (moniliform blepharosis).

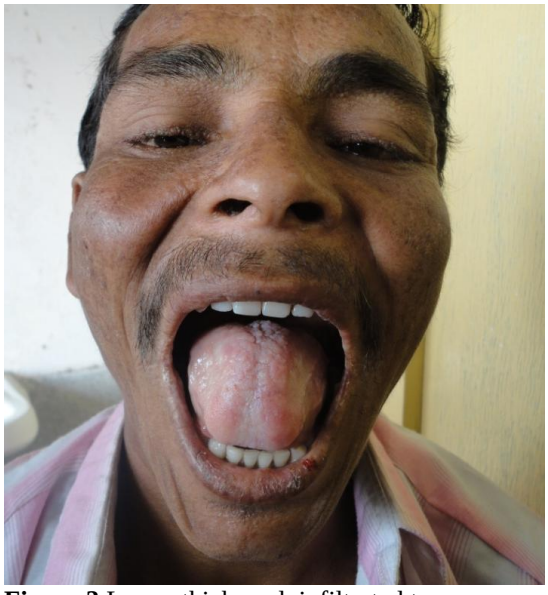

Figure 3 Large, thickened, infiltrated tongue.

buttock. Hair and nails revealed no abnormality.

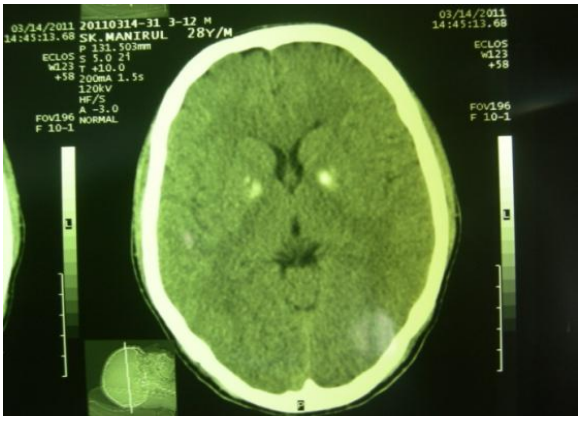

Figure 4 CT Scan of brain showing bilateral bean shaped calcification in the temporal lobes.

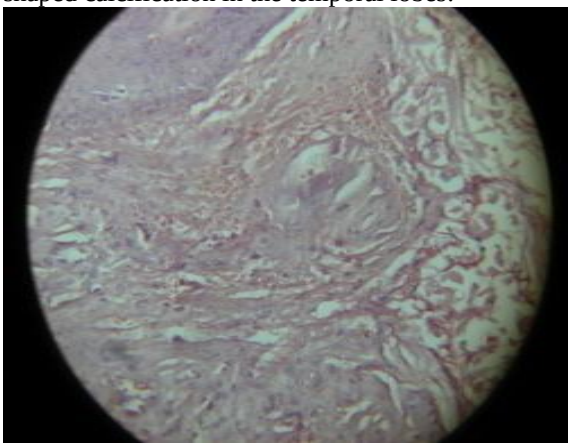

Figure 5 H & E showing deposition of amorphous, eosinophilic material in the dermis, around the blood vessels and adnexal structures.

Systemic examination revealed mild hepatomegaly. Mental functions were within normal limit.

Hematological and ophthalmologic examinations were within normal limit. Direct laryngoscopy showed thickened epiglottis. Computed tomography scans showed bilateral bean shaped calcification within temporal lobe (**Figure 4**). Histopathological examination of skin lesion showed deposition of periodic acid-Schiff positive, diastase-resistant amorphous eosinophilic material in dermis around blood vessels and adnexal structures (**Figure 5**).

Discussion

Lipoid proteinosis (LP) was first described by Urbach and Weithe in 1929,[1] also called Urbach-Weithe disease or hyalinosis cutis et

mucosa. It is an autosomal recessive disorder,[2,3] characterised by persistent papules on skin and mucous membrane.[4,5]

Most of the cases have been reported from South Africa and Central Europe.[6] However, a few cases have been reported from India, too.[7-9] It is characterised by deposition of eosinophilic hyaline like material in skin and viscera, leading to protean clinical manifestations. It has no sexual predilection.[3]

The exact pathogenesis of this disease is unknown. Recently, loss of functional mutation in gene encoding extracellular matrix protein 1 (ECM1) on band 1q21 has been identified as a cause of lipoid proteinosis. The most common location being at exon 6 and exon 7. Mutation of exon 6 causes severe clinical features while of exon 7 causes milder clinical features.[10,11] One of the main functions of ECM1 in dermis is to act as a form of "biological glue" maintaining dermal homeostasis, including regulation of basement membrane and interstitial collagen fibril macro-assembly, as well as, a growth factor binding.

The first clinical sign of lipoid proteinosis is hoarseness of voice caused by infiltration of vocal cords.[2,4,5] It can become prominent in early years of life and can progress to complete aphonia.[10] Mucosa of lips, tongue, and pharynx develop firm and yellow white infiltrates. Tongue is enlarged and becomes firm on palpation. Inability to protrude tongue is a useful diagnostic sign.

By contrast skin lesions usually develop within first year of life or develop later. In overlapping stages it can present as vesicles, pustules, bullae and hemorrhagic crusted eruption on face and extremities predominantly in sites exposed to trauma and heal with chicken pox-like scarring. Hyperkeratosis may appear in areas exposed to repeated friction, such as hands, elbows, knees, buttocks and axilla.

The eye lesions, pathognomonic for disease, are found in two third of cases. The lesions appear as a small flesh coloured papules along the margin of upper and lower eyelid,[1,2] also known as 'moniliform blepharosis'.[12]

Scalp involvement can lead to hair loss but it is not a significant finding.

In clinical practice, LP is rarely a life threatening condition.[13] However, diffuse infiltration of pharynx and larynx may cause respiratory distress, at times requiring tracheostomy. Hyaline deposits are seen in the conjunctiva, cornea, trabeculum, and retina.[14] Corneal opacities or secondary glaucoma, due to infiltration in the trabeculum, may appear later. LP is supposed to be a generalised disorder with deposits of hyaline material practically in every organ.

The central nervous system can also be involved. Bilateral intracerebral calcifications are frequently found in the LP and these are sometimes responsible for behavioural disturbances and epilepsy.[15-17]

Histologically it is characterised by deposition of eosinophilic mass which is periodic acid-Schiff (PAS) positive, but diastase resistant. It is deposited at the level of basement membrane, papillary dermis, around blood vessels and adnexal epithelia, specially sweat coils. Accumulations of type IV and V collagen occur around the blood vessels and appendages; type I and III collagen is reduced.[18, 19]

The hyaline deposits in the biopsies examined consist of a carbohydrate-protein complex containing hyaluronic acid and probably chondroitin-sulphate, plus large amounts of lipids.[20]

Radiological hallmark is the presence of bean to comma shaped intracranial calcifications in the temporal lobes in amygdala which is more evident in patients with prolonged affliction with LP.

Due to the rarity of this disease, there are no large case series to evaluate the therapeutic options. Only few good results have been reported with oral dimethyl sulphoxide (DMSO), D-penicillamine, etretinate and acitretin. Carbon dioxide laser surgery has been proposed in the treatment of affected vocal cords and eyelid papules.

References

1. Navarro C, Fachal C, Rodríguez C *et al*. Lipoid proteinosis. A biochemical and ultrastructural investigation of two new cases. *Br J Dermatol.* 1999;**141**:326-31.
2. Sarkany RPE, Breathnach SM, Seymour CA. Metabolic and nutritional disorders. In: Burns T, Breathnach S ,Cox N, Griffiths CH. *Rook's Textbook of Dermatology, Vol. 3, 7th edn*. Oxford: Blackwell Science; 2004. P.56-57.
3. Rosenthal AR, Duke JR. Lipoid proteinosis: case report of direct lineal transmission. *Am J Ophthalmol* 1967;**64**:1120-5.
4. Dyer JA. Lipoid proteinosis. In: Wolff K, Goldsmith LA, Katz SI *et al*., editors. *Fitzpatrick's Dermatology in General Medicine, Vol. 2, 7th edn*. New York: McGraw-Hill; 2008. P.1288-92.
5. Bozdağ KE, Gül Y, Karaman A. Lipoid proteinosis. *Int J Dermatol.* 2000;**39**:203-4.
6. Grosfild JCM, Spaas J, vande Staak WJBM, Stadhouders AM. Hyalinosis cutis et mucosae. *Dermatologia.* 1965;**130**:239-66.
7. Bansal NK, Mathur GK. Lipoid proteinosis. *Indian J Dermatol Venereol Leprol.* 1982;**48**:209-12.
8. Bagale RT. Lipoid proteinosis. *Indian J Dermatol Venereol Leprol.* 1982;**48**:295-97.
9. Kumar AS, Seetharam KA, Singh MK, Vasvani N. Lipoid proteinosis. *Indian J Dermatol Venereol Leprol*. 1986;**52**:95-8.
10. Hamada T, McLean WH, Ramsay M *et al*. Lipoid proteinosis maps to 1q21 and is caused by mutations in the extracellular matrix protein 1 gene (ECM1). *Hum Mol Genet*. 2002;**11**:833-40.
11. Hamada T, Wessagowit V, South AP *et al*. Extracellular matrix protein 1 gene (ECM1) mutations in lipoid proteinosis and genotype-phenotype correlation. *J Invest Dermatol*. 2003;**120**:345-50.
12. Staut CCV, Naidich TP. Urbach-Weithe disease (lipoid proteinosis). *Pediatr Neurosurg*. 1998;**28**:212-4.
13. Hamada T. Lipoid proteinosis. *Clin Exp Dermatol*. 2002;**27**:624-9.
14. François J, Bacskulin J. Manifestations oculaires du syndrome d'Urbach Wiethe. *Opthalmologica*. 1968;**155**:433-8.
15. Farolan MJ, Ronan SG, Solomon LM, Loeff DS. Lipoid proteinosis: case report. *Pediatr Dermatol*. 1992;**9**:264-7.
16. Singh G, Misra D. Lipoid proteinosis. *Int J Dermatol*. 1988;**27**:344-5.
17. Cinaz P, Gúvenir T, Gólúnsen G. Lipoid proteinosis: Urbach-Wiethe disease. *Acta Paediatr*. 1993;**82**:892-3.
18. Arnold HL, Odom RB, James WD, editors. *Andrews' Diseases of the Skin, 8th edn.* Philadelphia: WB Saunders; 1990.
19. Muda AO, Paradisi M, Angelo C *et al*. Lipoid proteinosis: clinical, histologic and ultrastructural investigations. *Cutis.* 1995;**56**:220-4.
20. Harper JI, Filipe MI, Staughton RCD. Lipoid proteinosis: Variations in histochemical characteristics. *Clin Exp Dermatol.* 1983;**8**:135-41.