Case Series

Lipoid Proteinosis: A case series and brief review of literature from India

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Abstract

Lipoid proteinosis is a very rare progressive autosomal recessive disorder characterized by deposition of hyaline material in the skin, upper respiratory tract, and internal organs. Patients present with a history of repeated blistering, skin scarring, beaded eyelid papules, waxy papules over the body, and laryngeal and tongue infiltration leading to hoarseness of voice. This disorder is caused by mutations in the extracellular protein 1 gene present on chromosome 1q21. We report four cases of lipoid proteinosis, who presented to our outpatient department with above mentioned features.

Keywords: Lipoid proteinosis; moniliform blepharosis; pock scars; Urbach-Wiethe disease.

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Introduction

Hyalinosis cutis et mucosae also known as Lipoid Proteinosis or Urbach-Wiethe disease is a rare autosomal recessive Geno-dermatosis which is characterised by the abnormal deposition of an amorphous hyaline material in various tissue, predominantly the dermis and mucosa of upper respiratory tract.[1] Less than 500 cases are available in literature, from both live patients as well as cadavers, with only about 51 cases from India.[2] Herein, we present 4 cases of Lipoid Proteinosis in Indian patients that presented to us with variable clinical manifestations.

Case Reports

Case Report 1

A 16-year-old male was brought to the Dermatology OPD with complaints of progressive thickening of the entire skin for one year of life and development of blisters after trauma. There was a history of difficulty in swallowing, hoarseness of voice and diffuse loss of hair. Family history was positive with his younger sister exhibiting similar complains that were progressive in the same fashion.

Cutaneous examination revealed the presence of multiple, yellowish, non-pruritic, infiltrated waxy papules involving the entire body with interspersed areas of non-tender hemorrhagic crusting [Figure-1A,1B] and pox-like scarring [Figure-2A,2B], especially on the trunk. Hyperpigmented, verrucous plaques were present over bilateral elbows. There was a characteristic presence of beaded papules over the bilateral upper eyelid margins which were skin-colored, closely aggregated and approximately 1-2mm in size. Examination of the oral cavity revealed the presence of macroglossia with lateral crenation caused by dental impressions and fissured oral commissures. A whitish waxy plaque was present over the left buccal mucosa.

Histopathological examination revealed the presence of acanthotic epidermis with the deposition of eosinophilic, amorphous hyaline material in the papillary dermis and perivascular areas. On clinicopathological correlation, a diagnosis of lipoid proteinosis was considered. The parents were counselled regarding the course and progression of the disease, and genetic testing was advised. However, the patient was lost to follow up.

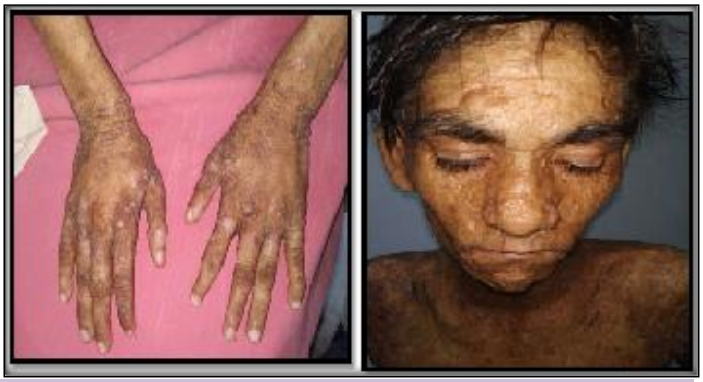

Figure 1: A- yellowish, non-pruritic, infiltrated waxy papules. B - yellowish, non-pruritic, infiltrated waxy papules

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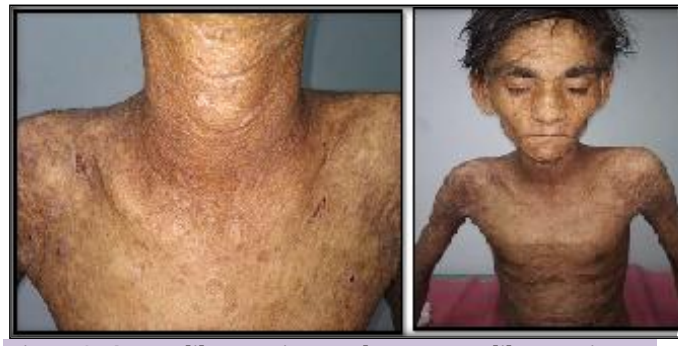
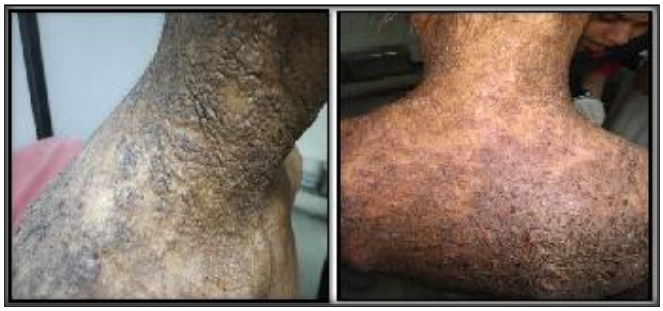


Figure 2: A- Pox like scarring on chest. B- Pox like scarring on chest



Case Report 2

The second case is of a 6-years old child, born of a non-consanguineous marriage who was brought by his parents with the complaint of development of lesions over elbows and knees following minor trauma since the age of 2 years that healed spontaneously with scarring. History of disfigurement of the face, progressive loss of hair and hoarseness of voice was also present. There was no history of photosensitivity, dyspnoea, dysphagia, headache. epilepsy, psychosis, schizophrenia, visual disturbances or other neuro-psychiatric disorders. No similar family history was present.

Cutaneous examination revealed the presence of diffuse alopecia, predominantly over the vertex and bilateral fronto-temporal regions. Multiple well-defined, oval to irregular atrophic varioliform scars were present over the face predominantly involving the forehead and central face with sparse involvement of the cheeks. Similar well-defined, larger varioliform scars were distributed bilaterally symmetrically over the elbows and knees with superficial ulcers, crusting and hyperpigmentation representing the varied stages of evolution of lesions. The trunk was relatively spared. Oral cavity revealed the diffuse infiltration of lips with involvement of the bilateral angles of mouth and small superficial ulceration with yellowish crusting. The tongue showed limited protrusion, diffuse infiltration giving it a “woody” consistency and dental impressions. Bilateral buccal mucosa revealed the presence of waxy, translucent plaques. However, characteristic beaded papules of the eyelids and waxy papules were not seen.

The differential diagnosis of lipoid proteinosis, hydroa vacciniforme and erythropoietic protoporphyria were initially considered. However, the parents refused further testing. So, the diagnosis was made clinically. The characteristic oral findings and photosensitivity ruled out the latter two. The course and prognosis were explained to the parents.

Genetic counselling and testing were advised, especially before planning second pregnancy since the family was incomplete. Thereafter, the patient did not present for follow-up.

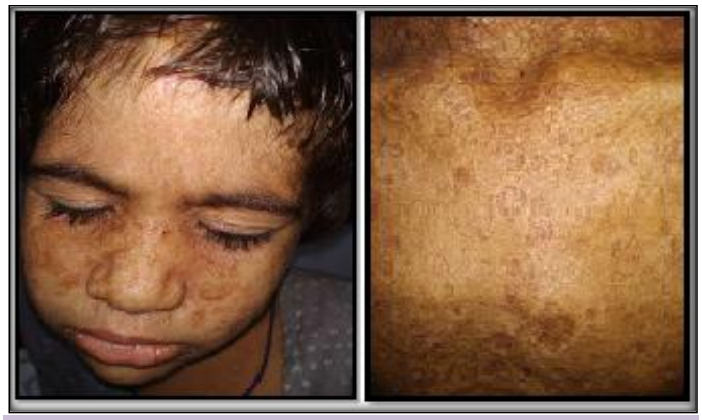
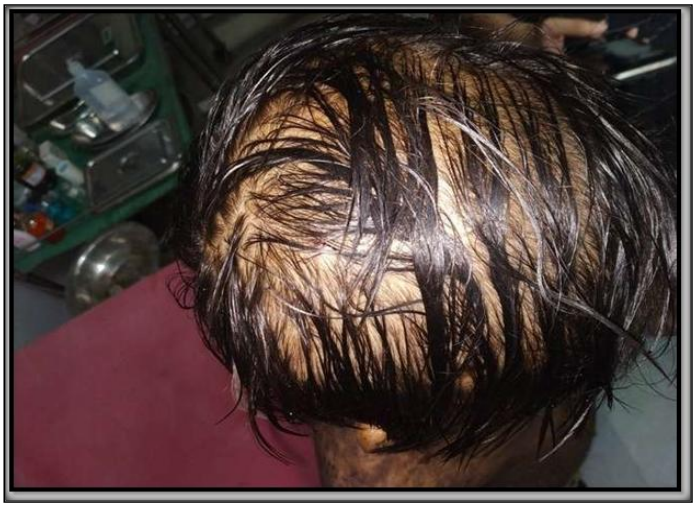


Figure 3: A & 2- Pox like scarring on chest and face



Case Report 3

The third case is of an 8-years old male child, born of a non-consanguineous marriage who presented with the complaint of progressive thickening of elbows and formation of depressions over the skin of face since early childhood. Recently there had been formation of small beads over the eyelids. Patient has hoarseness of voice. There was no history of convulsions, headache, memory impairment, cognitive decline, other neurological or psychiatric disorders. No similar complaints were present in the family.

On cutaneous examination, there was presence of characteristic beaded papules of bilateral upper eyelids. Waxy infiltration of the skin of face and presence of atrophic scarring over the face with relative sparing of lateral cheeks and nasal ala was seen. There was hyperkeratosis of bilateral elbows and multiple atrophic shiny scars over the trunk. Oral mucosa and Genital mucosa were relatively uninvolved.

The diagnosis was made by histopathological examination

which revealed the deposition of eosinophilic, amorphous hyaline material in the superficial dermis and perivascular areas. The parents were counselled regarding the course of the disease. The patient is currently on follow-up. While there were speech abnormalities, there was no respiratory distress or difficulty in swallowing.

Case Report 4

The fourth case is of a 19-years old male, born of a non-consanguineous marriage who presented with the complaint of formation of depressions over the skin of face since early childhood. Recently there had been formation of small beads over the eyelids. Patient has hoarseness of voice. There was no history of convulsions, headache, memory impairment, cognitive decline, other neurological or psychiatric disorders. Similar complaints were present in the younger brother in family.

Patient complained of pain over B/L cheeks which was diagnosed as recurrent parotitis. On cutaneous examination, there was presence of characteristic beaded papules of bilateral upper eyelids. Waxy infiltration of the skin of face and presence of atrophic scarring over the face, buttocks, B/L lower limb (B/L thighs, B/L calf muscles), lower back, upper back, B/L elbows, neck with relative sparing of lateral cheeks and nasal ala was seen. There was hyperkeratosis of bilateral elbows and multiple atrophic shiny scars over the trunk. Oral & Genital mucosa was relatively uninvolved.

The diagnosis was made clinically as patient refused further investigation. The course and prognosis were explained to the parents.

Genetic counselling and testing were advised, especially before planning next pregnancy since the family was incomplete. Thereafter, the patient did not present for follow-up.

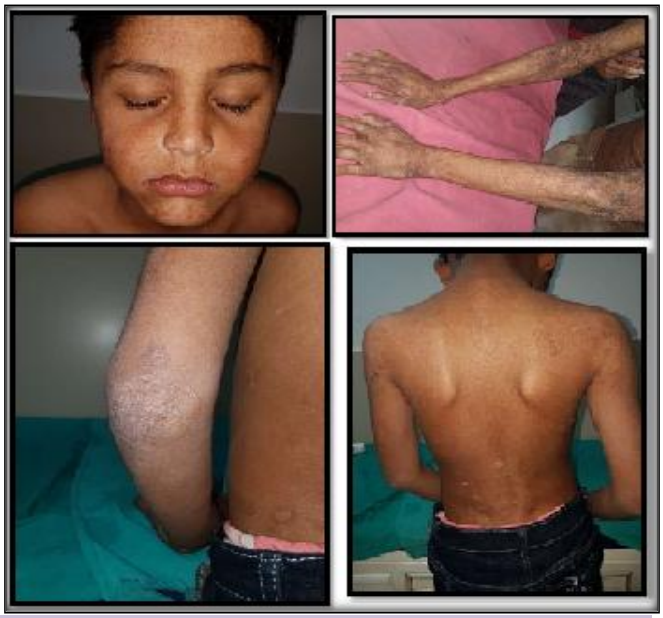


Figure 4: A- Atrophic Scarring over face. B & 3C- Varioliform scars over B/L elbows upper limb. 3D- Atrophic Scarring over back

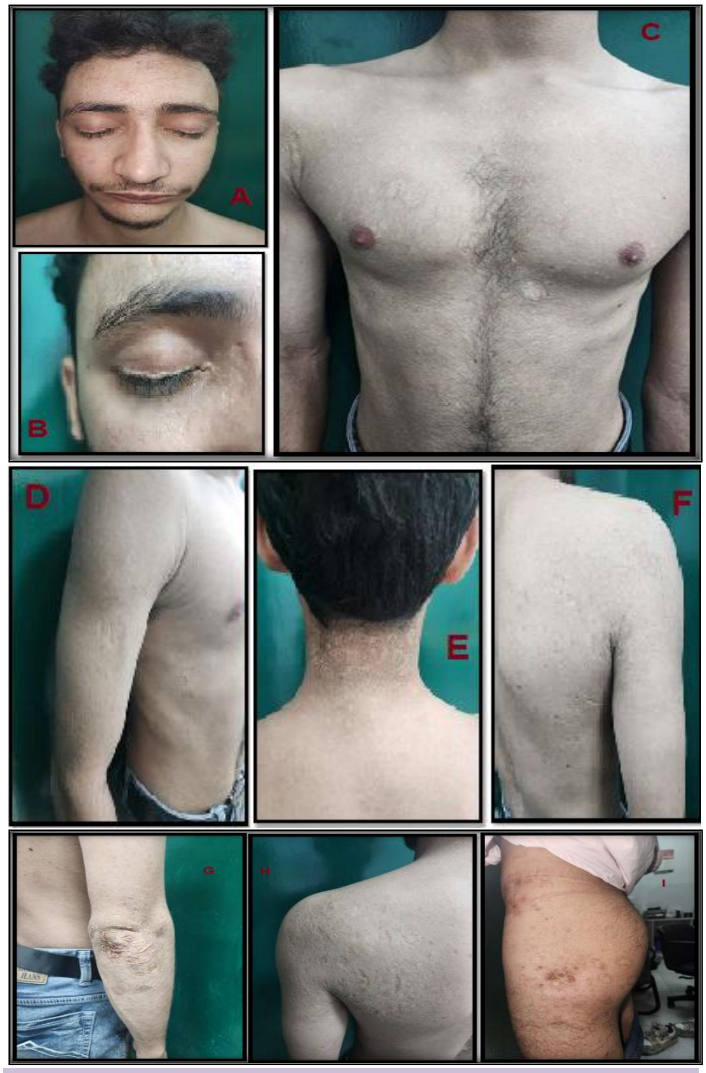
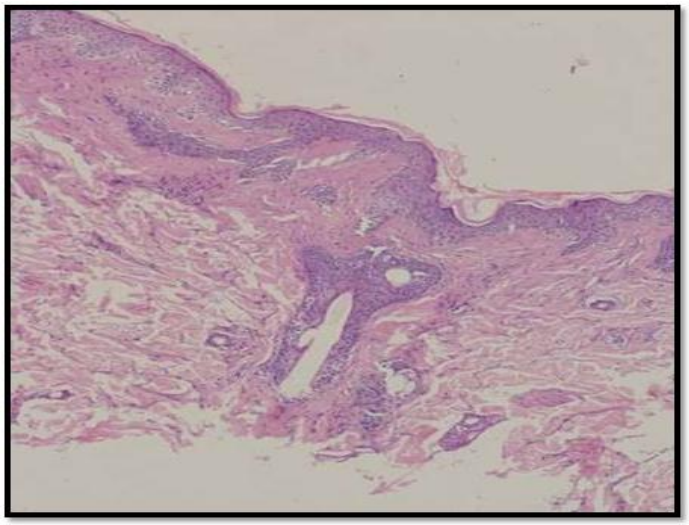
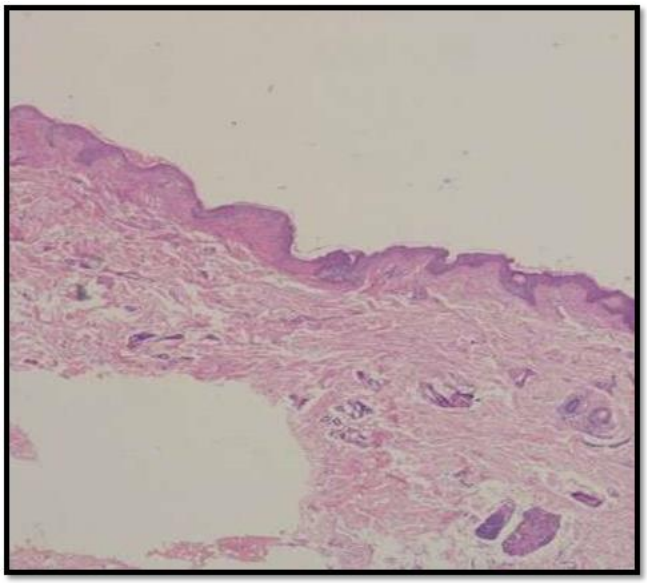


Figure 5C, 5D, 5E, 5F, 5G, 5H, 5I: Atrophic scars over neck B/L upper limb, chest, back, B/L buttocks.

HISTOPATHOLOGY IMAGES



Deposition of eosinophilic, amorphous hyaline material in the superficial dermis and perivascular area



Presence of acanthotic epidermis with the deposition of eosinophilic, amorphous hyaline material in the papillary dermis and perivascular areas

Discussion

Lipoid Proteinosis is a rare autosomal recessive genodermatosis with variable presentation in the affected individuals.[1] It is caused due to the loss-of-function mutation in extracellular matrix protein 1 which binds to heparin sulphate proteoglycans in various tissues. This loss of these essential protein-protein interactions results in the abnormal degradation of glycolipids and sphingolipids, accumulation of basement membrane collagens and deposition of amorphous hyaline material in dermis and submucosa, hence the name "hyalinosis cutis et mucosae".[3,4]

The most classical presentation is hoarseness of voice in infancy which occurs due to laryngeal infiltration, which over time can progress to a hoarse whisper. In severe cases, respiratory obstruction might occur.[1] Various mucosal features include oral infiltrative yellow-white deposits with cobble-stoning of the mucosa, shortening of frenulum causing limited tongue protrusion (characteristic feature), dental impressions on lateral tongue and xerostomia. Various cutaneous manifestations are seen in the form of characteristic beaded eyelid papules (moniliform blepharosis) which are usually present only about two-thirds of the patients and might be very subtle in others.[1,4] Others include waxy, yellowish papulo-nodules with generalized thickening of the skin, hyperkeratosis of the extremities, blistering of skin caused by minor trauma which resolves with pock like or acneiform scarring especially on the face and extremities, alopecia and increased risk of bacterial infections. There is also an increased incidence of infections caused by human papilloma virus.[5]

Involvement of eyes, upper respiratory tract, neuro-psychiatric involvement, blood vessels and lymphatic tissue can occur.[1]

Various treatment modalities including retinoids, D-penicillamine, oral steroids, dimethyl sulfoxide, Oral and topical retinoids surgical procedures, carbon dioxide laser and dermabrasion have been tried.[1,6-8] Although the results are unsatisfactory, there is known improvement in hoarseness, palmer hyperkeratosis, planter hyperkeratosis, reduction in skin blistering and oral ulceration.[9] The clinical manifestations are also known to improve with time. The surgical treatment should be reserved for patients with a compromised airway.[10] The prognosis is variable; however, it is better in cases where the treatment is administered before the age of 11 years.[4,9] Despite the progressive nature of disease, the course is usually benign with normal life expectancy except the possible risk of death from respiratory obstruction in infancy.[1,9,10]

Herein, we are reporting these cases due to the rarity of the disease entity and to add to the existing literature, especially on Indian patients. We would also like to highlight the presence of variable clinical manifestations as can be seen from our cases, and that not all features might be present in all patients.

Conclusion

This case series highlights the clinical presentation, diagnostic challenges, and management of lipoid proteinosis in four patients, emphasizing the heterogeneity of the disease and the importance of early recognition. This series underscores the importance of a multidisciplinary approach to managing lipoid proteinosis, particularly in addressing skin and mucosal changes; and monitoring for potential neurological deterioration.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) guardian 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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Nil.

Conflicts of interest

There are no conflicts of interest.

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