Lipoid Proteinosis Mimicking Congenital Immunodeficiency: A Case Report

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CASE REPORT

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Abstract

Lipoid proteinosis is a rare congenital disorder that can present with a variety of symptoms. A nineteen year old Indian male with dysmorphic features was admitted with a twelve year history of recurrent ulcerations over the upper limbs and oral cavity. Although the initial presentation was strongly suggestive of a congenital immune-deficiency syndrome, all investigations for immunodeficiency disorders were negative. Subsequent evaluation yielded a diagnosis of lipoid proteinosis.

Key Words
Lipoid proteinosis, congenital immunodeficiency syndrome, recurrent ulcerations

Background

Lipoid proteinosis is an extremely rare, autosomal recessive genetic disorder. It can manifest in a variety of ways including unexplained hoarseness of voice, dermatological and mucosal manifestations, dental abnormalities, intracranial calcifications and recurrent parotitis. Once diagnosed, lipoid proteinosis carries a good prognosis, and usually does not progress beyond adulthood. We present the case of a teenage male whose initial presentation was strongly suggestive of a congenital immune-deficiency syndrome, but after evaluation was subsequently diagnosed with lipoid proteinosis.

CASE

A nineteen year old student presented with oral ulcers and recurrent ulcerations on his upper limbs over the previous twelve years. He also complained of persistent hoarseness of voice over this period. Previous treatment included thyroxine supplementation and intermittent intravenous injections for these complaints over many years, however the precise nature and duration of these injections could not be ascertained in the absence of any documentation. He was born to a consanguineous marriage (his father being his mother's uncle) and had one elder sister who was asymptomatic. There was no history of similar complaints in any of his family members. He reported no habits or addictions and denied any incident of unprotected sex, and described his academic performance during formal education as average.

On examination, the patient was found to be fully oriented, moderately built and nourished with a BMI of 18.8. Pallor, icterus, clubbing, cyanosis, pedal oedema and lymphadenopathy were all absent. General physical examination revealed facial dysmorphism (Figure 1) with alopecia over the left side of the head (Figure 2), polydactyly in all four limbs (Figures 3, 4), multiple ulcers with indurated margins and slough over both upper limbs (Figure 5), and shallow ulcerations over the buccal mucosa (Figure 6). Systemic examination was otherwise unremarkable.

Complete blood counts showed marginally elevated total leukocyte count (14,500 /mm^3), with other laboratory parameters including thyroid function tests within normal limits. HIV serology was negative. Considering the strong possibility of a congenital immunodeficiency syndrome, he was carefully evaluated for markers which would indicate immunodeficiency disorders. Serum immunoglobulin levels were marginally below normal (IgA:137 mg/dL (Normal range 200-280), IgG:1169 mg/dL (Normal range 1200-1480), IgM:69 mg/dL (Normal range 110-136)). CD4 count was normal (362). A nitroblue-tetrozolium test was performed to test for neutrophil function, and this was also normal. All investigations for

immunodeficiency thus failed to turn up any significant defect. An upper GI endoscopy was performed to look for mucosal lesions in view of his oral lesions and possible immunodeficiency but this was essentially normal. Duodenal biopsy showed no evidence of coeliac disease.

In view of his dysmorphic features, an echocardiogram was also undertaken to screen for congenital heart disease. Results showed a patent foramen ovale and mild mitral valve prolapse. A plain CT head was performed and this ruled out any intracranial calcification. A urine test for porphyrins was negative. An ENT opinion was taken because of the hoarseness of voice and a laryngeal web was found. He was advised to attend speech therapy to accommodate his difficulty with speaking.

A dermatology opinion was sought for the skin lesions, and a biopsy was performed on a papule on his neck. The biopsy showed orthokeratotic, hyperpigmented epidermis overlying amorphous, hyaline eosinophilic material in a thickened papillary dermis. Perivascular deposits were also seen, forming thick hyaline perivascular mantles. Similar deposits were seen around eccrine glands. The histology was therefore consistent with lipoid proteinosis. The case was subsequently reviewed by dermatologists, and as the clinical picture of multiple mucocutaneous lesions, hoarseness of voice and alopecia was compatible with this a final diagnosis of lipoid proteinosis was made. The patient was reassured, treated symptomatically and discharged.

Two weeks after this initial admission, the patient returned presenting with odynophagia. He was found to have extensive oral lesions and was readmitted for treatment. In consultation with oral surgeons, he underwent debridement of the affected areas and thereafter made a good recovery. He was subsequently discharged, is still on follow up and is doing well.

Discussion

Lipoid proteinosis was first described in 1929 by two Viennese, E. Urbach and C. Wiethe[1], a dermatologist and an otorhinolaryngologist, for whom the condition is eponymously known as the Urbach-Wiethe syndrome[2]. The condition, also known as hyalinosis cutis et mucosae[3], shows no racial or sexual predilection. Less than 300 cases have been reported in literature, with a higher prevalence in South Africa and Sweden. However, there is no clear data regarding prevalence of this disorder in India, despite infrequent anecdotal reports of this condition. The autosomal recessive nature of the condition is demonstrated by the increased incidence in those born to consanguineous marriages, as was the case in our patient. Genome wide linkage analysis studies have mapped the disorder to 1q21[4]. A loss-of-function mutation in the extracellular matrix protein 1 gene (ECM1) has been implicated, although the normal biological function of this gene has still not been elucidated.

Lipoid proteinosis classically manifests at birth with unexplained hoarseness of voice [5], and this symptom was observed in this instance. Shortly afterwards, the child develops typical dermatological manifestations i.e. papular, nodular or diffuse yellow, waxy lesions that are usually seen over the face, as well as over pressure areas of the skin where the skin can become diffusely thickened and hyperkeratotic. Pruritus over the affected areas predisposes the lesions to scarring which may be either acneiform or varioliform. Nodular lesions on the elbows resemble xanthomas. The tongue, gingival and buccal mucosa and the eyelid margins are classically affected although this may not be the case in all affected individuals; the eyelid margins were not affected in our patient. Lesions on the scalp may cause alopecia, similar to those in this patient. Mucosal involvement is characterised by firm yellowish white infiltrates, which manifests via severe hoarseness of the patient's voice, as noted above, due to laryngeal involvement, and difficulty in protruding the tongue due to shortening of the frenulum. Both these symptoms were present in this case. Systemic manifestations of the disorder include dental abnormalities [6], intracranial calcifications [7] which predispose to seizures and recurrent parotitis. In fact, virtually all organ systems of the body have been known to be affected by this condition [8]. Fortunately, in our patient such systemic involvement was not seen.

Important differential diagnoses for lipoid proteinosis include erythropoietic protoporphyrias, congenital hypothyroidism and myxedema, amyloidosis and mucopolysaccharidoses. Protoporphyrias show photosensitivity and are not associated with hoarseness, whereas amyloidosis and mucopolysaccharidoses involve visceral organs and may be associated with hepatosplenomegaly. Congenital myxedema can easily be ruled out by means of thyroid function testing, which proved normal in this instance. The main diagnostic tool available for the diagnosis of lipoid proteinosis is biopsy of the skin lesions, and this was performed in the case of our patient. Fully developed lesions show papillomatosis and hyperkeratosis of the epidermis, whilst the superficial and deep dermal vessels show a thick, homogeneous, eosinophilic hyaline perivascular deposit which is periodic acid-Schiff (PAS) positive and alcian blue positive[9], all features observed in this patient's dermal sample.

Currently, there is no effective therapy for lipoid proteinosis [10]. Therapeutic strategies that have been employed with varying degrees of success include topical glucocorticoids, oral dimethyl sulphoxide [11], etretinate [12] and penicillamine [13] to alleviate mucocutaneous lesions. Surgical options include blepharoplasty, carbon dioxide laser therapy [14], plastic surgery and dermabrasion [15] for skin lesions, and microlaryngoscopy and vocal cord dissection for relief of hoarseness. Although reasonably successful, these procedures can predispose to progression of the disease as trauma leads to further deposition of the pathologic material.

Being an exceedingly uncommon disease, it is not unsurprising that lipoid proteinosis may be confused clinically with an immunodeficiency state, especially in the presence of a history of recurrent oral and skin ulceration from infancy. Indeed, our patient had received intermittent thyroxine supplementation, having been erroneously diagnosed to have hypothyroidism. This patient had serum immunoglobulin levels which were marginally below normal. Although these levels were not sufficiently low to make a diagnosis of an immunodeficiency syndrome, this was nevertheless in sharp contrast to the increased immunoglobulin levels reported in most cases, presumably secondary to chronic inflammation. The low immunoglobulin levels suggest at least an element of relative immunodeficiency – yet another unreported association with lipoid proteinosis. Furthermore, our patient had several dysmorphic features such as polydactyly that, to the best of the knowledge of the authors, have never been reported previously in association with lipoid proteinosis.

This case study details a unique example of an individual presenting with lipoid proteinosis, with features that have not previously been described such as polydactyly and possible immunodeficiency appearing in conjunction with the standard dermal features associated with the syndrome. It therefore represents a unique manifestation of an already rare disease.

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CONSENT

The authors declare that

1. They have obtained informed consent for the publication of the details relating to the patient in this report.
2. All possible steps have been taken to safeguard the identity of the patient.
3. This submission is compliant with the requirements of local research ethics committees.

PEER REVIEW

Not commissioned. Externally peer reviewed.

CONFLICTS OF INTEREST

The authors declare that they have no competing interest.

FIGURE LEGENDS

Figure 1: Facial dysmorphism with low set ears, oral lesions are observable on the dorsum of the tongue. Note coarsening of facial features due to thickening of skin.

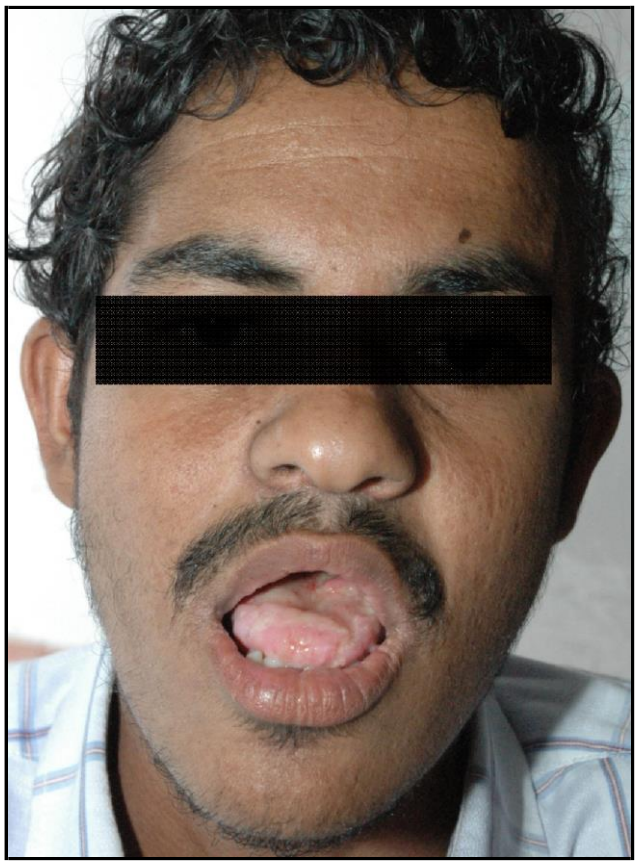
Figure 2: Alopecia due to lesion on scalp.

Figure 3: Polydactyly evident on hands. The extra digit in the right hand was extremely small and underdeveloped; it is not seen from this particular angle. Note hyperkeratotic lesions over the knuckles.

Figure 4: Polydactyly evident on both feet.

Figure 5: Hyperkeratosis and plaque-like lesions on the elbow typical of lipoid proteinosis.

Figure 6: Yellowish-white oral plaque-like lesions visible over dorsum of tongue.



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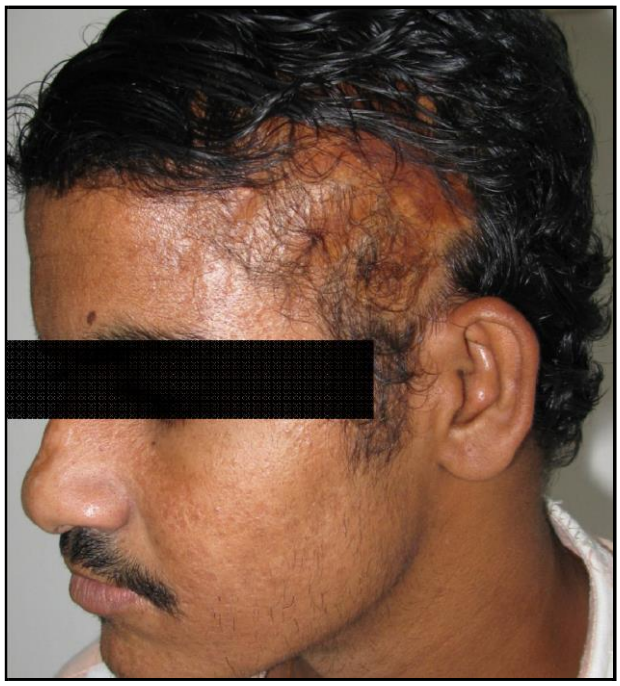
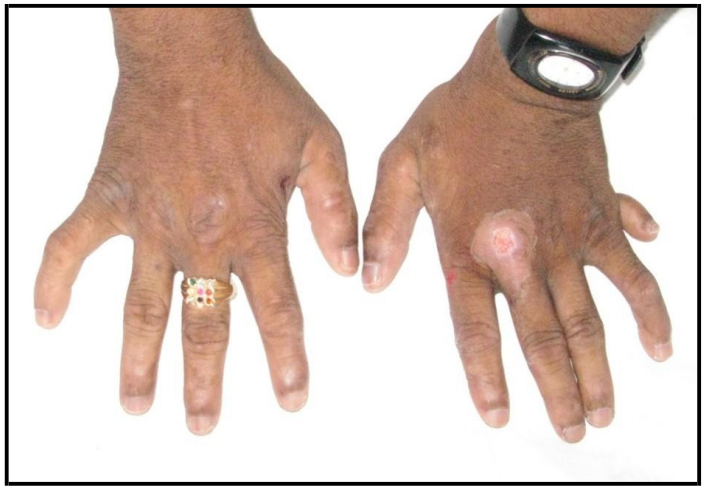


Figure 2: Alopecia due to lesion on scalp.



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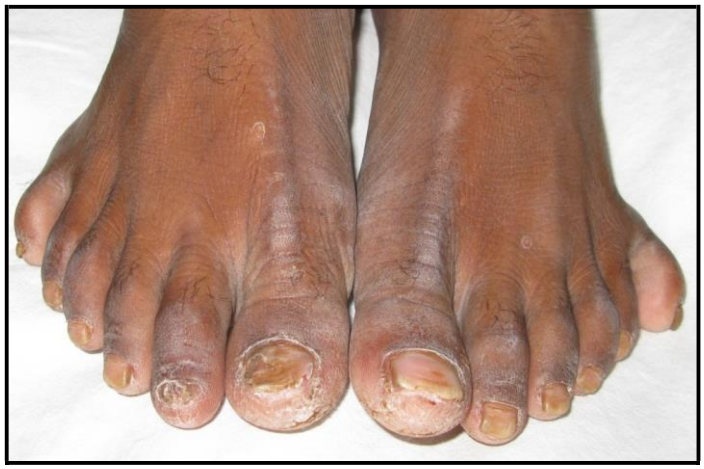
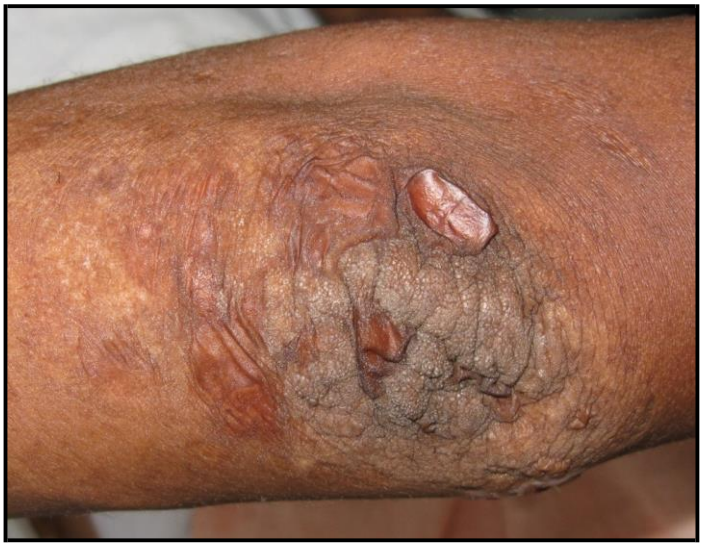


Figure 4: Polydactyly evident on both feet.



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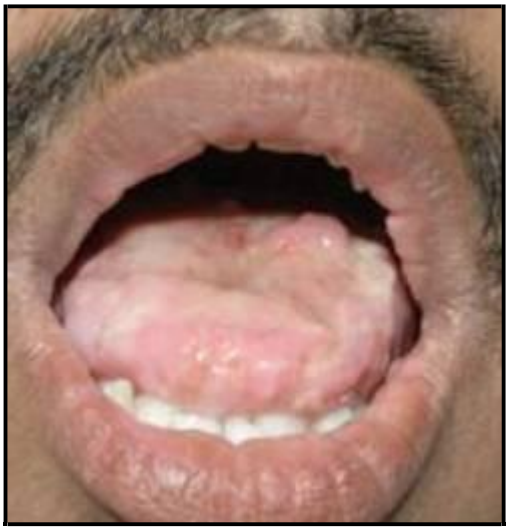

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