Case report

Successful treatment of Lipoid ProteinosisIn a Young Adult with Isotretinoin.

Abstract

Lipoid proteinosis (LP) is an extremely rare autosomal recessive genodermatosis, characterized by persistent hoarseness and classical skin lesions. Amorphous hyaline depositions may affect any organ, but mainly the face and extremities. These depositions cause limitations in tongue movement, and hence, difficulty speaking. Biopsies of skin lesions usually show massive deposits of homogeneous, acidic, hyaline-like material at the epidermal junctions and superficial dermis that stains positive for periodic acid-Schiff stain (PAS-D). At present, there is no specific treatment for this extremely rare disease, but some studies have reported that treatment with acitretin and etretinate results in some improvement. This paper reports on the effectiveness of isotretinoin for the first time for treatment of this disease.

Keywords: Lipoid proteinosis, hoarseness, periodic acid Schiff, isotretinoin

Introduction

Lipoid proteinosis (LP), or Urbach-Wiethe disease, is a very rare autosomal recessive skin disease that initially presents with laryngeal deposition of amorphous vitreous material, leading to persistent hoarseness at birth or in early childhood, as expressed by a soft cry[1]that is accompanied by classic skin changes such as scarring, fragility, discomfort, papules and/or nodules infiltrating the eyelid [2].

The deposition of an amorphous vitreous substance on the tongue usually limits the tongue's movements and causes speech difficulties. In addition, these infiltrates can lead to the appearance of papules and scars resembling chickenpox [3].It primarily affects the face and extremities. However, any organ in the body can be affected, such as the respiratory system, which causes airway obstruction, and the central nervous system, resulting in seizures [4].

There is currentlyno specific established therapeutic option to treat lipoid proteinosis, but this paper reports a positive response with treatment by isotretinoin.

Case Presentation

A 20-year-old man born to first degree consanguineous parents (48-year-old father and 43-year-old mother) presented with hoarseness that was noticed by his mother at birth and was clear when he was crying. This hoarsenesshas persisted until the current date.At the age of 17, recurrentskin lesions started to appear every 2-4 months on his face and upper extremities that left disfiguring lesions as scars when healed.

Clinical examinationsrevealedthat the patient had hoarseness while talking. On the first examination, lesions (mainly on the face) were described as multiple papulopustular with atrophic scars similar to chickenpox (Figure 1).Areas of friction (elbows, knees, hands, dorsae) developed verrucous hyperkeratotic plaques (Figure 2). Typical beaded papules (monilia

ornaments blepharosis) were also present on the eyelid margins (Figure 3), andthe patient had difficulty protruding his tongue (Figure 4).

The patient underwent ENTconsultation, which reported vocal cord thickening and hyaline depositionsat the larynx and posterior pharyngeal wall, oral cavity,and tongue. Laboratory investigations included a full blood count, measurement of serum glucose level, hepatic and renal function tests, and lipid profile, all of which were within normal levels. A skin biopsy from the upper backshowed massive deposits of homogeneous, eosinophilic, hyaline-like material at the dermal-epidermal junctions and at the superficial dermis (H&E) *that stains positive for periodic acid-Schiff stain* (PAS-D) (Figure 5).

Based on clinicaland histopathological findings, the patient was diagnosed with a case of lipoid proteinosis.He was started on isotretinoin 20 mg/day inAugust 2021, with follow up examinations every two months.The drug dose was adjusted according to body weight atevery follow-up visit.Baseline investigationswere also conducted and repeated every two months.Six months following treatment initiation, the hoarseness partially improved, and the tongue could be partially protruded.The skin lesions also decreased in number (figure 6). ENTfollow upreported decreased vocal cord thickening and decreased hyaline deposits in the larynx and oral cavity. One year after follow-up, no new lesions had appeared, and a 70% improvement in voice quality was noted.

Discussion

Lipoid proteinosis is a rare autosomal recessive disease caused by a homozygous mutation ofthe Q276X in the ECM1 gene, resulting in deposition of hyaline-like material in

multiple tissues [3].Usually, hoarseness during crying in infancy is the initial symptom noticed,along withacne acne likecutaneous lesions, papulopustular lesions, beaded papules along the eyelids, and oral mucosal lesions appearinglater in childhood, often after the age of 10[5].In agreement with this, the case study presented here shows a history of soft crying since birth,whichcontinued as hoarsenesswhentalkinginearly childhood. Skin lesions also appeared at age of 17 years as recurrent skin lesions every 2-4 months on his face and upper extremities that leftdisfiguring scars.

Cutaneous lesions of LP mainly affectsun-exposed areas: the face, elbows and hands. They appear characteristically in the form of thickened facial skin with a waxy texture covered with yellow, infiltrated, flat plaques, and papules amongdisfiguring scars [6].In the present case, skin lesions appeared on the face and the upper extremities during puberty, whichleft post-healing scars in the form disfiguring lesions.Infiltration of oral mucosa, the vocal cords and frenulumby an amorphous hyaline-like material also characterizes LP lesions, leading to hoarseness and restricted tongue protrusion. In addition, attacks of respiratory distress might occur, whereby the airway is affected[5].

Histopathological findings of LP include deposition of homogeneous, eosinophilic, hyaline-like material at the dermal-epidermal junctions and superficial dermis. In addition, the hyaline like-material is positive on periodic acid-Schiff stain (PAS-D)[7].The skin biopsy from the upper back of the present case showed massive deposits of homogeneous, eosinophilic, hyaline-like material at the dermal-epidermal junctions and at the superficial dermis (H&E). The hyaline like-material was positive on periodic acid-Schiff stain(PAS-D).

Because of the rarity of lipoid proteinosis, there is a serious limitation in terms of trials of therapeutic options. Of those that do exist, some studieshave reported good results with the

treatment of acitretin and etretinate[8-10].The present case was treated with isotretinoin and showed impressive improvement.

It is thought that retinoidsmodulate the metabolism of the connective tissue matrix of the dermal-epidermal junction and the dermis[11].At present, no previous studieshave been published to support the usefulness of isotretinoin on both cutaneous lesions and hoarseness[12].Therefore, isotretinoin may be a superior treatment to acitretin and etretinate, the former of which has the qualities of a tolerance, ease of dose modification and minimal side effects over the long term compared to other variants of retinoid. In a similar case that used acitretin, there was no obvious cutaneous improvement;however, there was significant improvement in hoarseness[9]. In another two young girls in Egypt treated with acitretin, there was complete remission of cutaneous lesions and improvement of the hoarseness after one year [13].Since there is limited experience with isotretinoin in treating LP, futurestudies are advisedto evaluate and monitorits effects on LP patients despite our experience with this case providing impressive results.

Conclusion: Isotretinoin perhaps considered a preferable treatment better than acitretin and etretinate, for the advantages of its feasiblity and shorter half life compared to acitritin, so in case of serious complications or lack of response can be discontinued immediately safely .

Ethical approval: IRB received

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Figures:

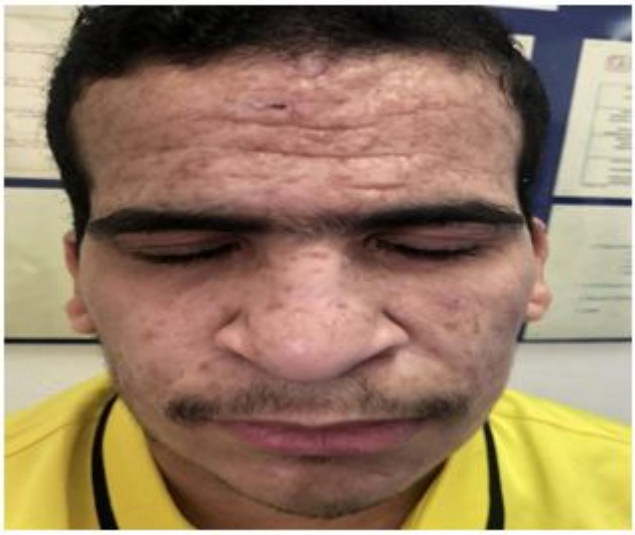


Figure 1: Skin lesion on the face

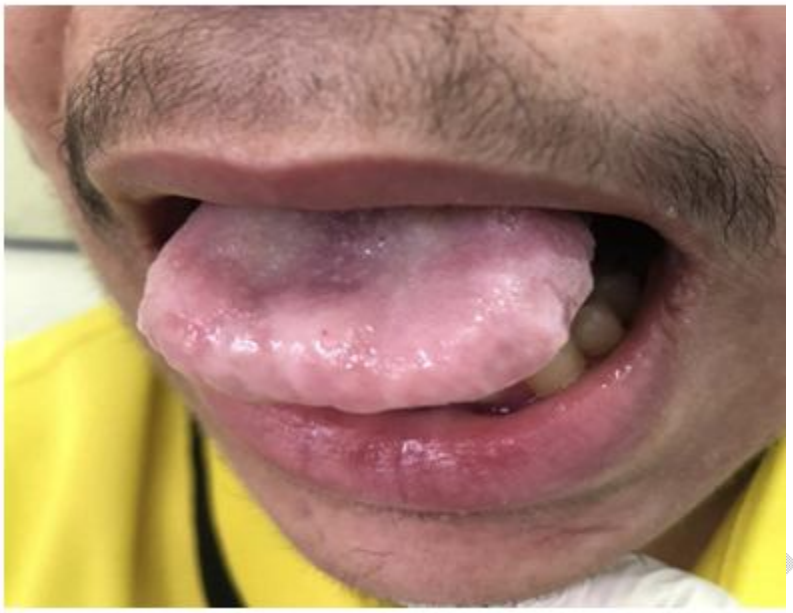


Figure 2: Difficulty in tongue protrusion

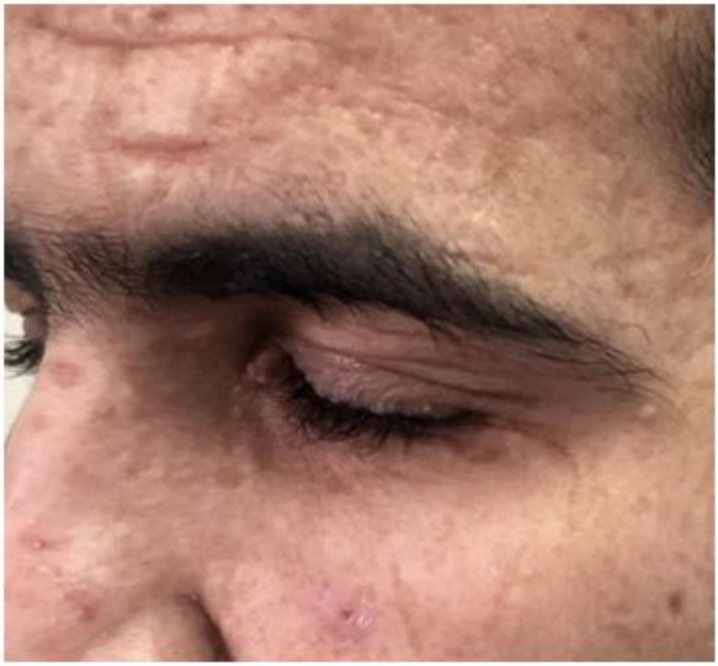


Figure 3: Typical beaded papules occur on the eyelid margins "moniliform blepharosis"

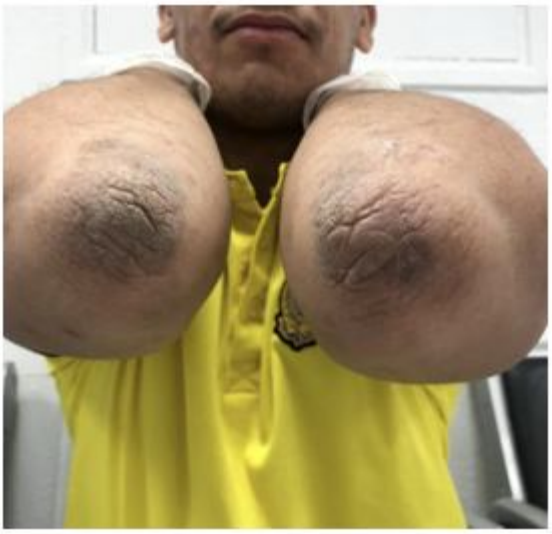


Figure 4: Elbows developed verrucous hyperkeratotic plaques

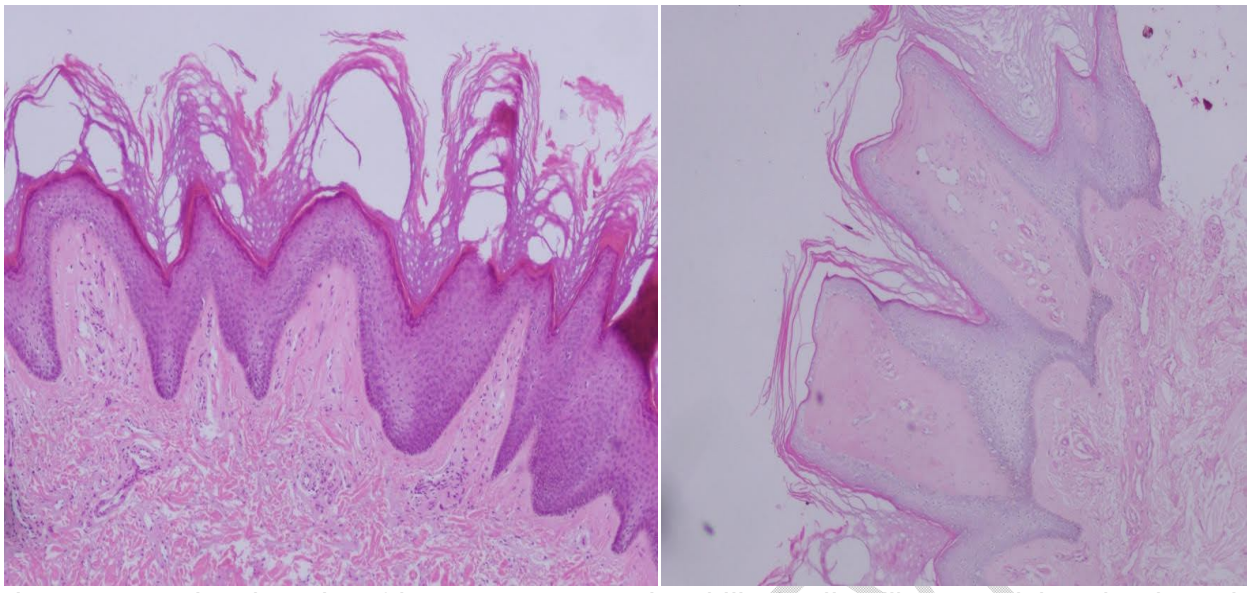
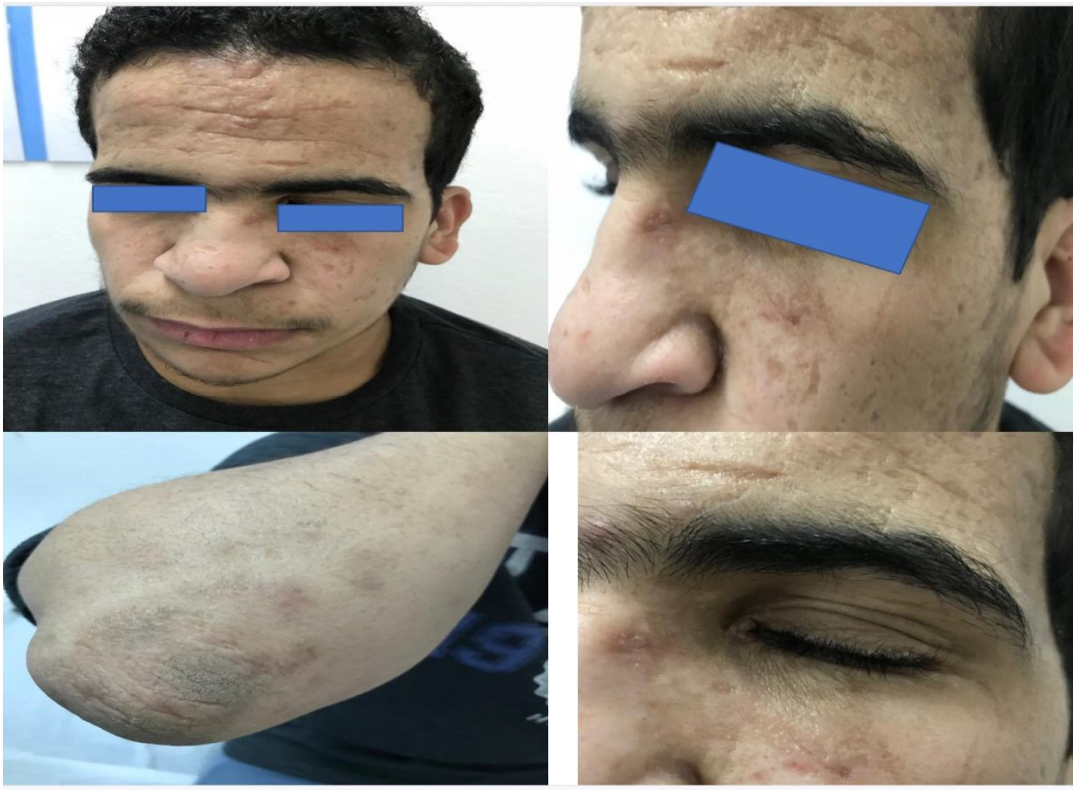


Figure 5: Massive deposits of homogeneous, eosinophilic, hyaline-like material at the dermal-epidermal junctions and at the superficial dermis (H&E).



(figure 6): Post treatment with isotretinoin showed improvement of skin lesions in termdecreased number and size.