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Oral Presentation of Lipoid Proteinosis: A Case Report

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ABSTRACT

Lipoid proteinosis (LP) is a rare congenital metabolic disorder characterized by the abnormal accumulation of hyaline material in various organs. With only approximately 400 cases reported to date, LP presents a wide range of manifestations, from asymptomatic skin lesions to potentially life-threatening laryngeal obstruction. Clinical features include hoarseness of voice from infancy, mucocutaneous manifestations, moniliform blepharosis, and dental anomalies such as aplasia of teeth. While there is no definitive cure for LP, symptomatic treatment can help manage its symptoms. This case report describes a 28-years-old female previously diagnosed with LP presenting with recurrent skin lesions, hoarseness of voice, and moniliform blepharosis. Additionally, she is congenitally missing seven permanent teeth, has limited mouth opening, and localized mucosal thickening. Early diagnosis and management of dental complications associated with LP are crucial for preserving optimal oral health. A thorough understanding of LP's clinical features is essential for healthcare providers to enhance their care and expand our knowledge of this and similar congenital disorders.

KEYWORDS

Lipoid proteinosis; Dental; Aplasia; Metabolic

INTRODUCTION

Lipoid proteinosis (LP), or hyalinosis cutis et mucosae, was first documented by Urbach and Wiethe in 1929 [1]. This rare genetic disorder is characterized by the buildup of hyaline-like material in various tissues, leading to distinctive changes in the skin and mucous membranes [2]. LP can also impact the nervous, mental, and digestive systems [1]. The initial case report involved a brother and sister from an Austrian Jewish family, who exhibited thickened, yellowish skin plaques on the face, neck, and other areas, hoarseness of voice, beaded papules along the eyelid margins, recurrent respiratory infections, and swallowing difficulties, all common features of LP [3,4].

LP is inherited in an autosomal recessive pattern, often affecting individuals with a family history of the disorder [4]. Despite its global occurrence, LP is rare, with approximately 400 reported cases in medical literature [4,5]. The condition affects both genders equally and can occur in individuals of any race or ethnicity [5]. Interestingly, the Namaqualand region in South Africa has a notable number of LP cases sharing a common mutation, suggesting a founder effect [3]. Moreover, 25% of all reported cases have been observed in South Africa, where

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many of the patients are of Dutch or German ancestry [4].

The precise cause of LP remains elusive, and specific risk factors are not yet identified. The condition is primarily genetic, with mutations in the extracellular matrix protein 1 (ECM1) gene playing a central role [1,5,6]. Mutations that cause LP occur in areas of the ECM1 gene known as exon 6 and exon 7 [6]. These mutations disrupt protein-protein interactions and tissue homeostasis. However, not all individuals with ECM1 mutations develop LP, indicating potential involvement of other environmental or genetic factors [6]. Mutations in the ECM1 gene are also linked to other conditions like Dyschromatosis Universalis Hereditaria (DUH) and Lichen Sclerosus [5].

LP is frequently misdiagnosed or remains undiagnosed due to its involvement of multiple organ systems [7]. Healthcare providers can conduct thorough examinations to identify characteristic features of LP and may perform imaging studies to assess organ involvement, especially the larynx. Skin biopsies and genetic testing can confirm the diagnosis [7]. Due to its rarity and varied presentation, a multidisciplinary approach involving dermatologists, geneticists, and other specialists is often necessary for accurate diagnosis and management. Given the oral manifestations of LP, dental professionals should possess a thorough understanding of the genetic and clinical aspects of this and similar conditions to facilitate early detection, treatment, and genetic counseling.

CASE PRESENTATION

This report details the case of a 28-years-old female (she/her) with a confirmed diagnosis of LP who presented to Indiana University for preventive dental care. Her medical history includes numerous consultations with otolaryngologists during childhood for persistent hoarseness, though no definitive diagnosis or treatment was established at that time. Since the hoarseness did not interfere with daily activities or cause discomfort, obtaining a definitive diagnosis was not prioritized. At age 19, she was formally diagnosed with LP while seeking cosmetic treatment for atrophic facial scarring.

The patient's primary symptoms are a hoarse voice present since birth and cutaneous lesions that emerged during childhood, predominantly affecting her hands, elbows, and axillary regions. She also experiences chronic xerosis and scalp irritation, accompanied by hair thinning since childhood. Additional medical history includes plaque psoriasis, moniliform blepharosis, hypertrophic tonsils and adenoids (prior to surgical removal), and atrophic scarring. Apart from LP, the patient is in overall good health and does not report any other chronic medical conditions.

The patient has a familial predisposition to LP, evidenced by her older brother also exhibiting symptoms of the condition. Notably, her brother's son shows no clinical manifestations of LP. No other immediate family members, including another sibling, display symptoms of LP. The family's ethnic background comprises Germanic, Scottish, and Northwestern European origins.

After the initial diagnosis, the patient was prescribed Isotretinoin to reduce nodular acne and improve facial scarring, which yielded favorable outcomes. She has also used erythromycin ophthalmic ointment as needed since childhood for the prevention and early intervention of hordeolums. Additionally, she has received multiple laser resurfacing treatments aimed at diminishing facial scarring. Currently, she does not undergo any direct treatment for LP beyond cosmetic Botox injections in the forehead area, Fluocinonide for scalp plaque

psoriasis, and daily application of Adapalene and various emollients. She was recently prescribed Triamcinolone Acetonide cream for use on elbows by a dermatologist; however, she reports little impact on the appearance of the lesions associated with LP.

Well-documented oral manifestations associated with LP include thickening of oral mucosal tissue, mucosal and tongue scarring, restricted mouth opening, and aplasia of permanent teeth [8]. This patient exhibits congenital absence of teeth #4, #12, #13, #17, #20, #29, and #32 (Figure 1). Orthodontic treatment was administered during adolescence to create sufficient spacing for subsequent prosthodontic restoration. Notable scarring is observed on the buccal mucosa, tongue, and labial regions, likely resulting from the use of orthodontic brackets and habitual cheek biting. Furthermore, post-infectious scarring is present in the posterior oropharyngeal region, following multiple episodes of streptococcal pharyngitis during childhood (Figure 2). The patient reports that chronic infections resolved following the surgical removal of the tonsils at age 13.

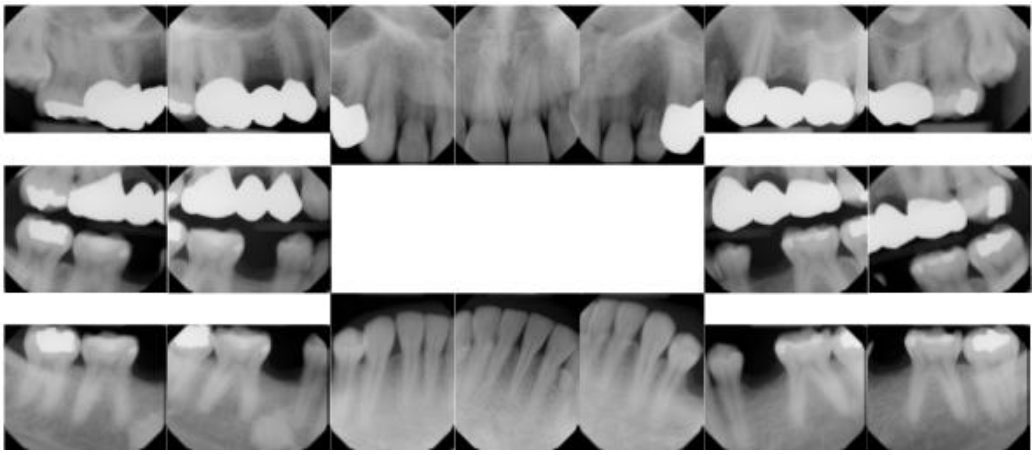

Figure 1: Full mouth radiographic series.

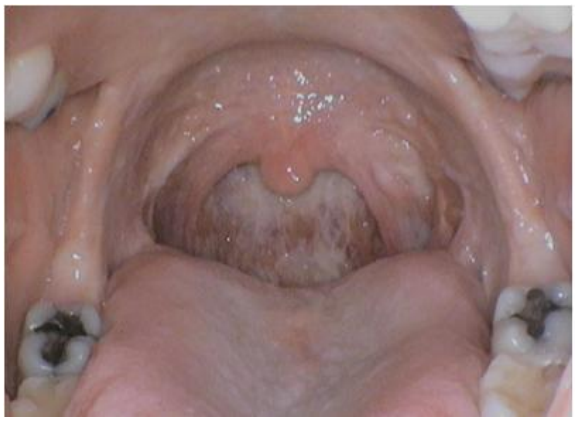

Figure 2: Scarring of posterior oropharyngeal region.

The patient retained primary tooth H, with tooth #11 naturally erupting in place of tooth #12. Fixed bridges were utilized to address other maxillary spaces. Prior to bridge placement, the patient underwent a second course of orthodontic treatment in her early 20s, aimed at mesializing the molars to close the premolar sites. However, during an attempt to place a temporary anchorage device (TAD) into the bone of the palate, it was determined that the bone density was too high to safely place the device

without surgical intervention. Interestingly, a radiopaque lesion is observed apically to missing tooth #29, which was biopsied in 2019 and diagnosed as osseous fragments. Future treatment plans include implant placement to replace teeth #20 and #29. The patient currently presents with no active dental diseases, maintaining excellent oral hygiene practices and regular access to preventive dental care.

DISCUSSION

LP is a rare autosomal recessive disorder characterized by the accumulation of hyaline-like material in various tissues, resulting in distinctive clinical features affecting the skin, mucous membranes, and occasionally other organ systems. The case presented here aligns with the typical clinical manifestations of LP, including hoarseness of voice since birth, cutaneous lesions predominantly on the extremities, and oral abnormalities.

The diagnostic journey for LP often involves challenges due to its diverse and overlapping symptomatology across multiple organ systems. Early diagnosis can be elusive, as evidenced by the patient's prolonged medical history before a definitive diagnosis was established at age 19. This delay underscores the importance of heightened clinical suspicion and comprehensive evaluation, including genetic testing, when necessary, to confirm the diagnosis. Moreover, given the unusually high number of congenitally missing teeth and mucosal lesions, dental providers could have facilitated early intervention by referring the patient to diagnostic specialists.

Treatment of LP remains largely symptomatic and supportive, targeting specific manifestations such as cosmetic concerns related to facial scarring and cutaneous lesions. In this case, Isotretinoin therapy and laser resurfacing treatments were employed to manage facial scarring with favourable outcomes. Treatment plans should be personalized based on disease manifestations and the patient's healthcare goals. Systemic retinoids, such as acitretin or etretinate, have shown efficacy in treating cutaneous and laryngeal lesions by reducing hyaline-like deposits in the dermis [9]. Long-term acitretin therapy has been reported to improve various LP symptoms, including skin lesion healing, tongue size reduction, decreased hoarseness, and softening of hyperkeratotic papules and nodules [9]. However, response to retinoids can vary, with some patients experiencing improved voice quality but limited cutaneous improvement [9]. Surgical interventions, such as microlaryngoscopy and carbon dioxide (CO_2) laser procedures, may be successful for vocal cord involvement and impaired phonation but carry risks like postoperative complications and the need for follow-up interventions [10]. Cosmetic procedures, including CO_2 laser, dermabrasion, blepharoplasty, and erbium-doped yttrium aluminium garnet ablative laser, can be used to minimize scarring and moniliform blepharosis.

Few reports have explored a potential correlation between periodontal diseases and lipoid proteinosis (LP). Similarly, the patient in this case shows no evidence of periodontal inflammation or destruction. However, given that the oral mucosa of individuals with LP can become nodular and thickened, gingival tissues may be at risk for enlargement or inflammation [8]. The absence of functional ECM1 protein impairs binding between ECM1 and other proteins, resulting in an unstable extracellular matrix, which weakens cells in the skin and other tissues [6]. This compromised extracellular matrix may cause neighboring cells to overproduce proteins and other materials, further contributing to tissue instability [6]. These factors suggest that individuals

with LP who also have risk factors for periodontal disease, such as poor oral hygiene, diabetes, or substance use, may have an increased susceptibility to periodontal complications. Further research is warranted to elucidate the exact mechanisms and prevalence of periodontal disease in patients with LP and similar genetic conditions. Currently, there is no evidence to suggest that LP is a direct risk factor for periodontal infections.

CONCLUSION

This case report contributes to the broader understanding of LP's clinical spectrum, genetic basis, diagnostic challenges, and multidisciplinary management strategies. Further research into the genetic mechanisms underlying LP and its variable phenotypic expression is essential for advancing targeted therapies and improving outcomes for affected individuals. Efforts to enhance awareness among healthcare providers, facilitate early diagnosis, and optimize holistic care remain paramount in mitigating the impact of rare genetic disorders on patients' quality of life.

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