Published online 2023 December 26.

Lipoid Proteinosis, Its Symptoms, and Oral Manifestations: A Case Report and Review of Literature

Parmiss Omidsalar 101, Maryam Koopaie 102,* and Parisa Akhbari 101

¹Dental School, Tehran University of Medical Sciences, Tehran, Iran

²Department of Oral Medicine, School of Dentistry, Tehran University of Medical Sciences, Tehran, Iran

^{*}Corresponding author: Department of Oral Medicine, School of Dentistry, Tehran University of Medical Sciences, Tehran, Iran. Email: mariakoopaie@gmail.com

Received 2023 October 16; Revised 2023 December 03; Accepted 2023 December 04.

Abstract

Introduction: Lipoid proteinosis (LP), also known as Urbach-Wiethe disease, is an autosomal recessive disorder characterized by the deposition of glycoproteins in mucous membranes, skin, and organs. Symptoms typically begin in childhood, persist throughout life, and encompass hoarseness, skin inflammation, scarring, and ulcers, resulting in a waxy appearance. Oral manifestations present as white plaques and ulcers, significantly impacting the oral cavity. To date, approximately 400 cases have been reported worldwide.

Case Presentation: Herein, we present the case of a 36-year-old female diagnosed with LP who sought a dental implant evaluation. Her medical history revealed tooth decay, which necessitated extractions, and she had previously undergone maxillary implant placement and mandibular bone grafting. Upon general examination, the patient exhibited voice hoarseness, hyperkeratosis on the elbows and hands, and papules on the fingers. Oral examination revealed firm and fibrotic mucosa, papillomatosis, and limited mouth opening. Hyposalivation and the absence of the left parotid duct orifice were noted. No significant abnormalities were observed on the eyelids or face. Salivary gland assessment indicated a reduced flow rate (1 ml in 5 minutes). This case highlights the importance of conducting a comprehensive evaluation and tailoring management strategies to the individual needs of patients with LP.

Conclusions: Lipoid proteinosis is a rare mucocutaneous disorder characterized by a slow and benign course, with varying prevalence in different regions. Early recognition of oral symptoms is crucial, as they often precede skin and neurological manifestations. Although typical oral signs usually include tongue firmness and an inability to protrude, these were not observed in the present case. Xerostomia and dental agenesis, though uncommon, have been reported in previous cases, consistent with the findings of the present case, although different areas of the oral cavity might be involved in some instances.

Keywords: Lipoid Proteinosis, Xerostomia, Oral Manifestations

1. Introduction

Lipoid proteinosis (LP), also known as Urbach-Wiethe disease, is a rare inherited metabolic disorder that follows an autosomal recessive pattern of inheritance. Lipoid proteinosis hallmark feature is the deposition of glycoprotein, forming an amorphous hyaline-like substance in various tissues, such as the skin, mucous membranes, salivary glands, and internal organs (1, 2). Characteristic histopathological findings include melanin incontinence and hyperkeratosis in the basal layer. Additionally, periodic acid-Schiff (PAS)-positive hyaline deposits are typically found in the upper dermis, often localized around blood vessels and sweat glands (3, 4).

In many affected individuals, the first clinical

manifestation is a hoarse or completely voiceless condition, which can become apparent either at birth or later in life (2, 5). Clinical manifestations typically commence during childhood and progress with age. Skin manifestations encompass acne, inflammation, scarring, and ulcers. The presence of amorphous hyaline deposits in these ulcerated areas results in a thick, waxy skin texture. Furthermore, the ulcers tend to leave atrophic scars resembling chickenpox marks (6). Lipoid proteinosis predominantly affects the oral cavity (7), with nearly all oral tissues exhibiting infiltrated white plaques and chickpea-sized ulcers. These ulcers often appear before adolescence and gradually increase in size (8).

Macroglossia, characterized by a firm, wood-like

Copyright © 2023, Annals of Military and Health Sciences Research. This open-access article is available under the Creative Commons Attribution-NonCommercial 4.0 (CC BY-NC 4.0) International License (https://creativecommons.org/licenses/by-nc/4.0/), which allows for the copying and redistribution of the material only for noncommercial purposes, provided that the original work is properly cited.

consistency of the tongue tissue and difficulty protruding the tongue, is a common feature of LP (8). Approximately half of LP patients display rows of yellowish papules around all four eyelids (9). Despite LP being a sporadic disease, it occurs globally, with approximately four hundred reported cases (6). Lipoid proteinosis is a slowly progressing disorder, and although it follows a benign course, extensive skin lesions, dry mouth, and hoarseness can lead to severe psychosocial complications. This study presents a case report detailing the oral and skin manifestations of this syndrome in a 36-year-old female, along with a brief review.

2. Case Presentation

A 36-year-old female case who had been diagnosed with LP and confirmed through genetic testing sought evaluation at the Department of Oral and Maxillofacial Medicine, Faculty of Dentistry, Tehran University of Medical Sciences, Tehran, Iran, on October 31, 2023. The case presented with complaints of dry mouth and difficulty in speaking and swallowing. She expressed the need to drink water frequently to moisten her mouth. Her xerostomia had started approximately 10 years ago and had progressively worsened, significantly impacting her ability to communicate and sleep. She reported that her xerostomia was particularly severe at night, often disrupting her sleep. In her medical history, it was noted that she had been taking vitamin D, calcium, and the medication "Prolia" (denosumab). The patient also reported that her teeth had severely decayed around 1.5 years ago, ultimately leading to the extraction of all her teeth.

Upon general examination, several findings were observed, including voice hoarseness, hyperkeratosis on her elbows and hands (Figure 1), and multiple papules on her fingers (Figure 2). The oral and maxillofacial examination revealed limitations in mouth opening (with a maximal incisal mouth opening of 30 mm), along with firm, fibrotic, dry mucosa and multiple papules on the tongue. Her tongue appeared desiccated and depapillated (Figure 3).

The left parotid duct orifice could not be located, and dry mouth and hyposalivation were evident. Saliva collected from the patient appeared frothy and hazy, and the tongue blade test yielded a positive result. The patient did not exhibit any significant abnormalities in her eyelids or face. Furthermore, there were no signs or symptoms of temporomandibular joint disease, such as muscular tenderness, joint sounds, or pain, suggesting that reduced skin elasticity was the primary cause of her restricted



Figure 1. Hyperkeratosis of the case's elbow



Figure 2. Multiple papules on the case's fingers



Figure 3. Depapillated tongue with multiple papules

mouth opening. There was no history of seizures, visual disturbances, or disorientation.

Regarding her family history, there were no reports of consanguineous marriages. The case hailed from a middle economic and social class and had no siblings. None of her family members displayed similar symptoms. To assess salivary flow rate, unstimulated whole saliva was collected, with the patient instructed to collect her saliva and spit it out every minute for a total of 5 minutes, yielding a flow rate of 0.2 mL/min. The patient was educated on the importance of sipping a mixture of water, one tablespoon of fresh lemon drops, and one teaspoon of olive oil throughout the day. She was also advised to use a room humidifier at night to stimulate her parotid and submandibular glands 4 - 5 times daily and to rinse her mouth with olive oil before bedtime. The patient was cautioned against consuming alcohol, sugar, or strongly flavored substances that could irritate her dry and sensitive mucosa. On a follow-up contact one month later, the patient reported an improvement in her symptoms.

We searched MEDLINE, Scopus, Web of Science, and Cochrane databases with the following keywords. ((((lipoid proteinosis[Title]) OR (lipoid proteinosis syndrome[Title])) OR (Urbach-wiethe syndrome[Title])) OR (Urbach-wiethe disease[Title])) OR (Hyalinosis cutis et mucosae[Title]))) AND (((oral manifestations[Title])) OR (oral[Title])) OR (oral manifestation[Title])). Table 1 shows a summary of LP oral manifestation reports.

3. Discussion

Lipoid proteinosis typically follows a slow and benign course and exhibits varying prevalence rates across different regions, with a higher incidence reported in Sweden and South Africa (12). The oral symptoms of this rare syndrome tend to manifest earlier than other skin-related signs (10). Therefore, raising awareness among dentists about the oral indicators of this syndrome can lead to early identification and effective mitigation of its impact. One of the initial telltale signs of this condition is the hoarse voice and weak crying of a child immediately after birth (14, 23, 24). Additional symptoms encompass the presence of papules on the skin, eyelids, elbows, and hands, along with hyperkeratosis and scarring (12, 25). Prominent oral signs include tongue firmness and the inability to protrude the tongue due to hyaline deposition in the tongue and its frenum. This results in a thick and rough tongue texture, along with the formation of palatine and infratemporal papules.

In contrast to the current case, no signs of tongue thickness, inability to protrude the tongue, or ankyloglossia were observed. Xerostomia, tooth agenesis, and excessive gingival growth are infrequent oral manifestations of this disease (26). Xerostomia has been previously reported in LP cases, as evidenced in the case described here. Notably, non-specific salivary gland inflammation has been observed in LP patients, emphasizing the importance of ruling out conditions such as sialadenitis and Sjögren's syndrome. In the present case, the right parotid papilla could not be located, and the salivary gland flow rate was less than 1 mL in 5 minutes.

Similarly, previous reports have documented hyperkeratosis in specific body regions that are subject to continuous trauma, such as the hands (22, 27). Recently, Frenkel et al. conducted an extensive review of the oral manifestations in LP patients, analyzing 133 cases within 1948 and 2016. Frenkel et al. observed that the most commonly affected oral areas in this condition were the lingual (68%), the floor of the mouth (56%), the labial (43%), the buccal mucosa (40%), the palate (25%), and the gingival (6%) (27). However, in the present case, only the buccal mucosa was affected, presenting as firm and papillomatous.

Furthermore, there was no observed tongue involvement or any reports of such symptoms by the patient. Certain articles have reported findings, such as microdontia of permanent molars and congenital absence of lateral incisors and second premolars in LP cases (28). However, in this instance, the patient had already lost all her teeth during the examination, making it impossible to assess dental agenesis. It is crucial to recognize that LP can manifest differently in each case, with variations in clinical presentations and oral involvement. Therefore, a comprehensive examination by healthcare professionals plays a pivotal role in accurately diagnosing and managing the condition.

Table 1. Summary of Lipoid Proteinosis Oral Manifestations Reports		
Authors (y)	Oral Manifestations	Case
Jahanimoghadam and Hasheminejad (2022)(3)	Restricted mouth opening	- 10-year-old male
	Teeth hypoplasia or aplasia	
Lee et al. (2018) (10)	Pallor and fibrotic texture with induration of the lingual and buccal mucosa	10-year-old Asian female
	Maximal inter-incisal opening 20 mm	
	Loss of the dorsal tongue papillae	
	A thick sub-lingual frenum	
	Multiple atrophic papules extending from the soft and hard palates to the crypts of the tonsillar	
	Microdontia of the maxillary permanent premolars with congenitally missing teeth	
Ravi Prakash et al. (2012) (11)	Firm, thickened, and pale tongue with large crenations with cobble stoning with yellow to white papules	- 32-year-old male
	Nodular and thickened mucosa with hyperkeratosis of the buccal, labial, and palatal mucosa	
Aroni et al. (1998) (12)	White to yellow patches with micro-papules on the labial, dorsum of the lingual, faucal, and uvula mucosa	37-year-old female
	Thickened oral mucosa on palpation with inflamed and flabby appearance	
	Shortened and indurated lingual frenulum	
	The patient could not protrude her tongue	
	Ivory-colored depositions and bulging in the region of the sublingual gland	
	Enlarged gingiva	
Xanthinaki et al. (2008) (13)	The oral mucosa appeared nodular, diffusely enlarged, and thickened due to infiltration with waxy-yellowish-white plaques and nodules.	- 14-year-old male
	Thickened, furrowed appearance of the skin with several skin scars, eyelid nodules, loss of eyelashes, and voice hoarseness	
Hofer (1975) (14)	Lingual ulceration	27-year-old female
	Lingual stiffness with reduced mobility and depapillation	
	Partially everted lips and fissures at the corner of the mouth	
	Xerostomia	
	Agenesis of teeth 12 and 22	
Sabater-Abad et al. (2019) (15)	Well-defined ulcer with fibrin coating on the dorsum of the tongue	 50-year-old female
	No dental anomalies	
	Difficulty when protruding the tongue	
	Tongue and lips were thickened and indurated	
Finkelstein et al. (1982)(16)	Leathery, fibrotic, and thickened gingiva, lips, and tongue	5-year-old white female
Kabre et al. (2015) (7)	Scrapable whitish patches on the bilateral buccal, floor of the mouth, and palate mucosa	19-year-old male
	Missing 4 second premolars	
	A super-numerary tooth between 16 and 14	
Kabre, V., et al. (2015) (7)	Lingual ulcerations	- II-year-old male
	Voice Hoarseness started in infancy	
	Buccal mucosa ulcerations	
	Recurrent throat pain and dysphagia for the past 2 to 3 years	
Anil et al. (1993) (17)	Inability to protrude the tongue, crenated borders	18-year-old female
	Irregular nodules on lower lips	
	Lips were thickened, firm, and sclerotic	
	Ulcerations on gingiva	
	Gingival hypertrophy	
Deshpande et al. (2015) (18)	Crenations of an enlarged tongue	28-year-old male
	Sublingual frenum stiffness and reduced lingual movement	
	Yellow waxy papules in all of the mouth	
Mahalingam et al.(2015)(19)	Crenations of an enlarged tongue	61-year-old male
	Sublingual frenum stiffness and reduced lingual movement	
	Yellow waxy papules on lips	
Mittal et al. (2016) (20) Jansen et al. (2016) (21)	Sublingual frenum stiffness and reduced lingual movement	6-year-old male 22-year-old female
	vesicules and ulcers of the thickened lips mucosa	
	Actoscollina Destroyed dentition	
	Sublingual framm stiffnass and raduced lingual movement	
Kartal et al. (2016) (22)	Subingua inciditi stituces and reduced ingual moveillelli	42-year-old female
	Vallow and wave namulas on the line	
	renow and way papers on the nps	

Lipoid proteinosis is a noteworthy and rare mucocutaneous disease primarily observed in infancy and early childhood. Given that oral manifestations of LP often precede skin and neurological symptoms, general dentists and dental specialists are ideally positioned to diagnose LP early, initiate appropriate referrals, and manage the condition effectively, thereby reducing its complications and morbidity.

Footnotes

Authors' Contribution: Maryam Koopaie, Parmis Omidsalar, and Parisa Akhbary conceived and designed the evaluation and drafted the manuscript. Maryam Koopaie and Parmis Omidsalar re-evaluated the clinical data, revised the manuscript, performed the review search, and revised the manuscript.

Conflict of Interests: There is no conflict of interest.

Funding/Support: There is no grant for the present study. **Informed Consent:** Written informed consent was obtained.

References

- Shirani AM. Cryosurgery (N2O) application to remove lip lesions of lipoid proteinosis syndrome: A case report. J Dental Research, Dental Clinics, Dental Prospects. 2008;2(2):68.
- Staut CC, Naidich TP. Urbach-Wiethe disease (Lipoid proteinosis). Pediatr Neurosurg. 1998;28(4):212–4. [PubMed ID: 9732251]. https://doi. org/10.1159/000028653.
- 3. Jahanimoghadam F, Hasheminejad J. Oral manifestations and dental management considerations of lipoid proteinosis: A case report and review of literature. *Journal of Dentistry*. 2022;**23**(3):321–6.
- Brar BK, Jain S, Brar SK. Lipoid proteinosis: A case with distinct histopathological and radiological findings. J Cutan Pathol. 2017;44(10):887–91. [PubMed ID: 28685839]. https://doi.org/10.1111/ cup.13002.
- Yakout YM, Elwany S, Abdel-Kreem A, Abou Seif S. Radiological findings in lipoid proteinosis. J Laryngol Otol. 1985;99(3):259–65. [PubMed ID: 3973495]. https://doi.org/10.1017/s0022215100096651.
- Mofarrah R, Ghasemi M, Mofarrah R, Emadi S, Rostamian F. Lipoid proteinosis: A systematic presentation of an unusual disease. J Cosmet Dermatol. 2022;21(10):4237–40. [PubMed ID: 35176194]. https://doi.org/ 10.1111/jocd.14861.
- Kabre V, Rani S, Pai KM, Kamra S. Lipoid proteinosis: A review with two case reports. *Contemp Clin Dent.* 2015;6(2):233-6. [PubMed ID:26097361]. [PubMed Central ID: PMC4456748]. https://doi.org/10.4103/0976-237X.156053.
- Chaudhary SJ, Dayal PK. Hyalinosis cutis et mucosae. Review with a case report. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 1995;80(2):168–71. [PubMed ID: 7552879]. https://doi.org/10.1016/s1079-2104(05)80196-9.
- 9. Muda AO, Paradisi M, Angelo C, Mostaccioli S, Atzori F, Puddu P, et al. Lipoid proteinosis: clinical, histologic, and ultrastructural investigations. *Cutis*. 1995;**56**(4):220–4.
- Lee KC, Peters SM, Ko YCK, Kunkle TC, Perrino MA, Yoon AJ, et al. Oral manifestations of lipoid proteinosis in a 10-year-old female: A case

report and literature update. Oral Surg Oral Med Oral Pathol Oral Radiol. 2018;**126**(4):e228-32. [PubMed ID: 29548668]. https://doi.org/10.1016/j. 0000.2018.01.025.

- Ravi Prakash SM, Verma S, Sumalatha MN, Chattopadhyay S. Oral manifestations of lipoid proteinosis: A case report and literature review. Saudi Dent J. 2013;25(2):91-4. [PubMed ID: 23960561]. [PubMed Central ID: PMC3723256]. https://doi.org/10.1016/j.sdentj.2012.12.004.
- Aroni K, Lazaris AC, Papadimitriou K, Paraskevakou H, Davaris PS. Lipoid proteinosis of the oral mucosa: Case report and review of the literature. *Pathol Res Pract*. 1998;**194**(12):855–9. [PubMed ID: 9894251]. https://doi.org/10.1016/S0344-0338(98)80088-5.
- Xanthinaki AA, Donta C, Gatou V, Tsichlakis C. Hyalinosis cutis et mucosae: Diagnosis based on oral manifestations-report of a case. J Clin Pediatr Dent. 2008;33(2):171–4. [PubMed ID: 19358387]. https://doi. org/10.17796/jcpd.33.2.u2v6362312467465.
- 14. Hofer P. Urbach-Wiethe disease (lipoglycoproteinosis; lipoid proteinosis; hyalinosis cutis et mucosae). A review. *Acta dermato-venereologica. Supplementum.* 1973;**5**:1–52.
- Sabater-Abad J, Matellanes-Palacios M, Pont-Sanjuan V, Miquel-Miquel J, Navarro-Conde P, Gimeno-Carpio E. Oral ulcer-a disabling manifestation in a patient with lipoid proteinosis. *JAMA Dermatol.* 2019;**155**(8):977–9. [PubMed ID: 31188408]. https://doi.org/10.1001/ jamadermatol.2019.0805.
- Finkelstein MW, Hammond HL, Jones RB. Hyalinosis cutis et mucosae. Oral Surg Oral Med Oral Pathol. 1982;54(1):49–58. [PubMed ID: 6956826]. https://doi.org/10.1016/0030-4220(82)90416-9.
- Anil S, Philip T, Jacob O, Beena VT. Hyalinosis cutis et mucosae a case report. J Pierre Fauchard Acad. 1993;7(3):89–92.
- Deshpande P, Guledgud MV, Patil K, Hegde U, Sahni A, Huchanahalli Sheshanna S. Lipoid proteinosis: A rare encounter in dental office. *Case Rep Dent.* 2015;2015:670369. [PubMed ID: 25874136]. [PubMed Central ID: PMC4383431]. https://doi.org/10.1155/2015/670369.
- Mahalingam S, Sadaksharam J, Karthikeyan B, Kessavalou S. Lipoid proteinosis with oral manifestation in a geriatric patient: A unique case report. *J Indian Academy Oral Medicine Radiology*. 2015;27(3). https: //doi.org/10.4103/0972-1363.170492.
- Mittal HC, Yadav S, Malik S, Singh G. Lipoid Proteinosis. *Int J Clin Pediatr Dent*. 2016;9(2):149–51. [PubMed ID: 27365938]. [PubMed Central ID: PMC4921886]. https://doi.org/10.5005/jp-journals-10005-1353.
- Jansen S, Quante G, Luers J, Beutner D. Urbach-Wiethe disease in a young woman: A case report. ENT: Ear, Nose & Throat Journal. 2016;95(1).
- Kartal D, Çınar SL, Kartal L, Saka OS, Borlu M. Lipoid proteinosis. Acta Dermatovenerologica Alpina Pannonica et Adriatica. 2016;25(1). https:// doi.org/10.15570/actaapa.2016.5.
- Kaya TI, Gunduz O, Kokturk A, Tursen U, Ikizoglu G. A life-threatening exacerbation of lipoid proteinosis. J Eur Acad Dermatol Venereol. 2002;16(3):286-8. [PubMed ID: 12195576]. https://doi.org/10.1046/j.1468-3083.2002.00487_3.x.
- Batra K, Safaya A, Aggarwal K. Lipoid Proteinosis (Urbach-Wiethe Disease): A Case Report from India. *Ear, Nose & Throat Journal*. 2008;87(9):531–6. https://doi.org/10.1177/014556130808700914.
- Touart DM, Sau P. Cutaneous deposition diseases. Part I. J Am Acad Dermatol. 1998;39(2 Pt 1):149–71. quiz 172-4. [PubMed ID: 9704823]. https://doi.org/10.1016/s0190-9622(98)70069-6.
- Disdier P, Harle JR, Andrac L, Swiader L, Weiller PJ. Specific xerostomia during Urbach-Wiethe disease. *Dermatology*. 1994;**188**(1):50–1. [PubMed ID: 8305758]. https://doi.org/10.1159/000247086.
- Frenkel B, Vered M, Taicher S, Yarom N. Lipoid proteinosis unveiled by oral mucosal lesions: A comprehensive analysis of 137 cases. *Clin Oral Investig.* 2017;**21**(7):2245–51. [PubMed ID: 27900487]. https://doi.org/10. 1007/s00784-016-2017-7.
- Al-Ekrish A, Al-Sadhan R. Lipoid proteinosis: A case report with recurrent parotitis and intracranial calcifications. *King Saud Univ J Dental Sci.* 2012;3(1):13–9. https://doi.org/10.1016/ji.ksujds.2011.10.002.