Esophageal Aperistalsis in a Patient with Lipoid Proteinosis

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ABSTRACT

Lipoid proteinosis is a rare disorder with autosomal recessive inheritance, characterized by progressive deposition of hyaline material in the skin, mucous membrane, and different organs of the body, resulting in a multitude of clinical manifestations. A 34-year-old woman presented with hoarseness, dysphagia, eyelid beeding, and acneiform scars on the facial skin and extremities. The patient was diagnosed clinically as having lipoid proteinosis, which was confirmed by laryngeal biopsy. The objective of the present report is to describe this rare entity. This case report also illustrates that lipoid proteinosis may show protean clinical features and yet may remain undiagnosed for many years.

KEYWORDS:
Acneiform scars, Eyelid beading, Hoarseness of voice, Hyaline material, Dysphagia

INTRODUCTION

Lipoid proteinosis (LP) or Urbach–Wiethe disease is a rare, autosomal recessive disorder, which was first reported in 1929 by Erich Urbach and Camillo Wiethe.¹ This disorder was characterized by hoarseness from early infancy and various cutaneous manifestations, such as acneiform scarring, waxy papules, moniliform blepharosis, and non-cutaneous manifestations attributed to infiltration of hyaline-like material in the skin, larynx, and other organs.² The hyaline-like material is periodic-acid Schiff (PAS) positive and diastase resistant leading to the deposition of non-collagenous proteins and glycoprotein.³

To our knowledge, esophageal motility disorders have not been reported as a part of this disorder. We describe the first case of LP who presented with dysphagia caused by concomitant esophageal aperistalsis.

CASE REPORT

A 34-year-old Bakhtiari woman who was a known case of LP based on clinical and pathological diagnosis, referred to our hospital with hoarseness and dysphagia accompanied by cutaneous lesions. She presented with hoarseness and typical skin lesions since adolescence. About 7 years ago she developed a gradually progressive dys-
phagia to solid food as a predominant symptom and complained of intermittent post-prandial chest pain without regurgitation or weight loss. She had no history of gastroesophageal reflux disease (GERD), seizures, visual disturbances, or respiratory obstruction. None of the other family members were affected. Examination revealed an otherwise healthy individual with typical clinical findings of LP (figure 1). Systemic examination and laboratory tests did not reveal any abnormalities. Upper gastrointestinal endoscopy showed widespread mucosal thickening and irregularity in the pharynx and larynx. Upper and middle parts of the esophagus were normal, but an esophageal ring with normal overlying mucosa was observed in distal esophagus (figure 2). High-resolution manometry showed absent peristalsis (figure 3).

**DISCUSSION**

LP or Urbach–Wiethe disease is an autosomal recessive genetic disorder, which is caused by mutations in chromosome 1q21 and the extracellular matrix protein 1 (ECM1) gene. The disease is diagnosed on the basis of clinical symptoms and histopathology. Affected indi-
individuals can be asymptomatic and carriers of the disease. The accumulation of hyaline material in the dermis and the thickening of the basement membranes in the skin lead to the dermatological manifestation. One of the typical dermatological signs of the disease is beaded papules on the eyelid, which was noted in our case.

Diffuse infiltration of the pharynx and larynx may cause respiratory distress, which requires tracheostomy but rarely LP is a life-threatening disease. Our patient presented with hoarseness, typical skin lesions, and progressive dysphagia to solid food, but she had no respiratory symptoms. Some other common extracutaneous manifestations of the disease include epilepsy, mental retardation, and neuropsychiatric disorders.

While gastrointestinal involvement is infrequent in LP, hyaline deposits have been shown in visceral biopsies and autopsy specimens from the esophagus, stomach, small bowel, and rectum. In the largest case series of LP reported from turkey (including 14 and 10 cases), no esophageal involvement was reported. Dysphagia has been described as a typical symptom of LP in two recent reports of cases with LP. Infiltration of the upper third of the esophagus and a medium-sized sliding hiatal hernia were the only abnormal findings on upper endoscopy. We could only find one patient with LP in whom esophageal manometry was reported. Lima and colleagues reported a Brazilian patient with LP who was referred for the evaluation of epigastric pain, postprandial fullness, and bloating without esophageal symptoms. Upper endoscopy showed multiple yellowish nodules throughout the esophagus, body of the stomach, and duodenum. Esophageal manometry was normal in this patient. An older report of a Chinese patient that dates back to 1988 did not describe any esophageal symptoms, but the authors assessed the esophageal transit time in their patient before and after treatment with dimethyl sulfoxide. Interestingly, the mean esophageal transit time (normal value: < 10 seconds) decreased from 36.8 seconds before treatment to 5.8 seconds after 3 years of treatment. However, no manometric findings were available in the latter report.

Infiltration of hyaline material in the muscular layer of the esophagus may be the cause of the motility disorder found in our patient, but it was not possible to acquire a tissue specimen from the deep esophageal layers for histological diagnosis in our patient.

There is no specific and curative treatment for Urbach–Wiethe disease. Current treatment includes oral steroids, dimethyl sulfoxide, D-Penicillamine, intralesional heparin, and etretinate, which are used for symptomatic treatment of disability and symptoms. Although acitretin was used there is no strong evidence on whether this drug is beneficial for the treatment of dysphagia. Some patients require tracheostomy due to the respiratory obstruction but it occurs rarely and life expectancy is usually normal.

CONCLUSION

Beaded papules along the margin of eyelids, thickened protuberant lips, and hoarseness of voice, confirm the diagnosis of LP. Dysphagia as a clinical manifestation was not reported previously in LP but our patient presented with dysphagia and esophageal aperistalsis.

ETHICAL APPROVAL

There is nothing to be declared.

CONFLICT OF INTEREST

The authors declare no conflict of interest related to this work.

REFERENCES

1. Urbach E, Wiethe C. Lipoidosis cutis et mucosae. Virchows Archiv für pathologische Anatomie und Physiologie und für klinische Medizin 1929;273:285-319.
2. Black MM. Lipoid Proteinosis, Metabolic and nutritional disorders. In: Champion RH, Burton JL, Burns DA, Breathnach SM, editors. Rook/Wilkinson/Ebling Textbook of Dermatology. 6th ed. Oxford: Blackwell Science; 1998. pp. 2460-2.
3. Touart DM, Sau P. Cutaneous deposition diseases. Part I. J Am Acad Dermatol 1998;39:149-71. doi: 10.1016/S0190-9622(98)70069-6.
4. Hamada T, McLean WH, Ramsay M, Ashton GH, Nanda A, Jenkins T, et al. Lipoid proteinosis maps to 1q21 and is caused by mutations in the extracellular matrix protein 1 gene (ECM1). Hum Mol Genet 2002;11:833-40. doi: 10.1093/hmg/11.7.833.
5. Hamada T. Lipoid proteinosis. Clin Exp Dermatol 2002;27:624-9. doi: 10.1046/j.1365-2230.2002.01143.x.
6. Ramsey ML, Tschen JA, Wolf JE. Lipoid Proteinosis. Int J Dermatol 1985;24:230-2. doi: 10.1111/j.1365-4632.1985.tb05443.x.
7. Hamada T, Wessagowit V, South AP, Ashton GH, Chan I, Oyama N, et al. Extracellular matrix protein 1 gene (EMC1) mutations in Lipoid Proteinosis and genotype – phenotype correlation. *J Invest Dermatol* 2003;120:345-50. doi: 10.1046/j.1523-1747.2003.12073.x.

8. Caplan RM. Visceral involvement in lipoid proteinosis. *Arch Dermatol* 1967;95:149-55. doi:10.1001/archderm.1967.01600320005001.

9. Baykal C, Topkarci Z, Yazganoglu KD, Azizlerli G, Baykan B. Lipoid proteinosis: a case series from Istanbul. *Int J Dermatol* 2007;46:1011-6. doi: 10.1111/j.1365-4632.2007.03115.x.

10. Dertlioglu SB, Calık M, Çiçek D. Demographic, clinical, and radiologic signs and treatment responses of lipoid proteinosis patients: a 10-case series from Şanlıurfa. *Int J Dermatol* 2014;53:516-23. doi: 10.1111/ijd.12254.

11. Ajdarkosh H, Shirzad S, Taher M, Daryani NE Zaman F. Lipoid Proteinosis: A Case Report Urbach & Wiethe Disease. *Govaresh* 2011;16:200-3.

12. Malekzad F1, Rahimi H, Lotfi S, Qaisari M. Lipoid Proteinosis in two Iranian Sisters: A Case Report and Review of Literature. *Iran Red Crescent Med J* 2011;13:280-2.

13. Lima JC, Nagasaki CK, Montes CG, Kamata Barcelos IH, de Carvalho RB, Mesquita MA. Gastrointestinal Involvement in Lipoid Proteinosis: A Ten-Year Follow-Up of a Brazilian Female Patient. *Case Rep Med* 2014;2014:952038. doi: 10.1155/2014/952038.

14. Wong CK, Lin CS. Remarkable response of lipoid proteinosis to oral dimethyl sulphoxide. *Br J Dermatol* 1988;119:541-4. doi: 10.1111/j.1365-2133.1988.tb03260.x.

15. Di Giandomenico S, Masi R, Cassandrini D, El-Hachem M, De Vito R, Bruno C, et al. Lipoid proteinosis: case report and review of the literature. *Acta Otorhinolaryngol Ital* 2006;26:162-7.

16. Bakry OA, Samaka RM, Houla NS, Bashia MA. Two Egyptian cases of lipoid proteinosis successfully treated with acitretin. *J Dermatol Case Rep* 2014;8:29-34. doi: 10.3315/jdcr.2014.1168.

17. Gündüz Ö, Şahiner N, Atasoy P, Şenyücel Ç. Acitretin treatment for lipoid proteinosis. *Case Rep Dermatol Med* 2012;2012:324506. doi: 10.1155/2012/324506.

18. Van Hougenhouck-Tulleken W, Chan I, Hamada T, Thornton H, Jenkins T, McLean WH, et al. Clinical and molecular characterization of lipoid proteinosis in Namaqualand, South Africa. *Br J Dermatol* 2004;151:413-23. doi: 10.1111/j.1365-2133.2004.06076.x.