Case Report

Ophthalmic Presentation of Lipoid Proteinosis in Iraqi Siblings: Case Report

Ali Nema Abushnein[1], Khitam Fakhir Alhasseny[2]
[1-2]Ibn Al-Haithem teaching eye hospital

ABSTRACT

The present study highlights the clinical manifestations, progression, and conservative treatment of lipoid proteinosis in two patients from an Iraqi family. An abnormal buildup of glycoprotein in numerous organs is known as lipoid proteinosis (LP), an autosomal recessive disorder. Hoarseness of speech, skin lesions, scars, papules that bead up around the eyelids, is all potential symptoms. Epilepsy and neuropsychiatric diseases can result from calcifications of brain tissue. In this paper, two cases of 13 and 15-yearold Iraqi family siblings (born to consanguineous parents) are reported. They were presented to Ibn Al-Haithem Hospital with hoarseness and characteristic symptomatic moniliform eyelid lesions. Biopsy confirmed the diagnosis. Though ocular involvement in LP is rare, ophthalmologists may encounter diverse ocular complications. With the exception of possible acute respiratory or neurological sequelae, the disease runs a slowly progressive but otherwise benign course. The rarity of this disease motivated this report.

Key Words: Lipoid proteinosis, glycoprotein, moniliform blepharosis.

How to Cite this Article: Abushnein AN, Alhasseny KF. Ophthalmic Presentation of Lipoid Proteinosis in Iraqi Siblings: Case Report. Pak J Ophthalmol. 2023, **39 (2):** 161-166.

Doi: 10.36351/pjo.v39i2.1587

Correspondence: Ali Nema Abushnein
Ibn-Al-Haithem Hospital

Received: January 31, 2023
Accepted: March 30, 2023

INTRODUCTION

A dermatologist named Urbach and an otolaryngologist named Wiethe initially reported lipoid proteinosis in 1929.[1] It is also known as Urbach-Wiethe syndrome or hyalinosis cutis et mucosae. Due to a mutation in the extracellular-matrix protein-1 gene on chromosome 1q21, it is a rare autosomal recessive multisystem disorder with manifestations in the skin, ears, nose, eyes, and nervous system. It is distinguished by the deposition of an amorphous hyaline substance with a glycoprotein composition in a variety of body tissues, particularly the tongue, skin, and larynx.[2]Though this entity has been well known to dentists, dermatologists and otorhinolaryngologists, few reports have appeared in the ophthalmic literature with the eyelids involvement in the majority of cases.[3]The prognosis is, nonetheless, relatively good despite progressive nature of the disease until early adulthood. Two cases of lipoid proteinosis involving bilateral eyelids with pathognomonic moniliform blepharosis are described here.

CASE PRESENTATION

This study adheres to the guidelines in the Declaration of Helsinki and was carried out after receiving approval from the institutional human research ethics committee and written informed consent from the patients' parents.

A 13-year old lady, presented with painless skin lesions on her eyelids since she was 5-year old. She had delayed milestone (teething at 18th month, and walking at 24th month) and learning difficulties and hearing problems when she was 4 years old. She had husky voice at age two and feeble crying when she was an infant. She had a history of snoring during sleep at six for which surgery for nasal polyps was attempted with limited benefit. Since age 8, pinkish scaly lesions were noted in front and behind the ears and over the knees.

The patient complained of a recent history of gait abnormality due to lower limb weakness. No history of

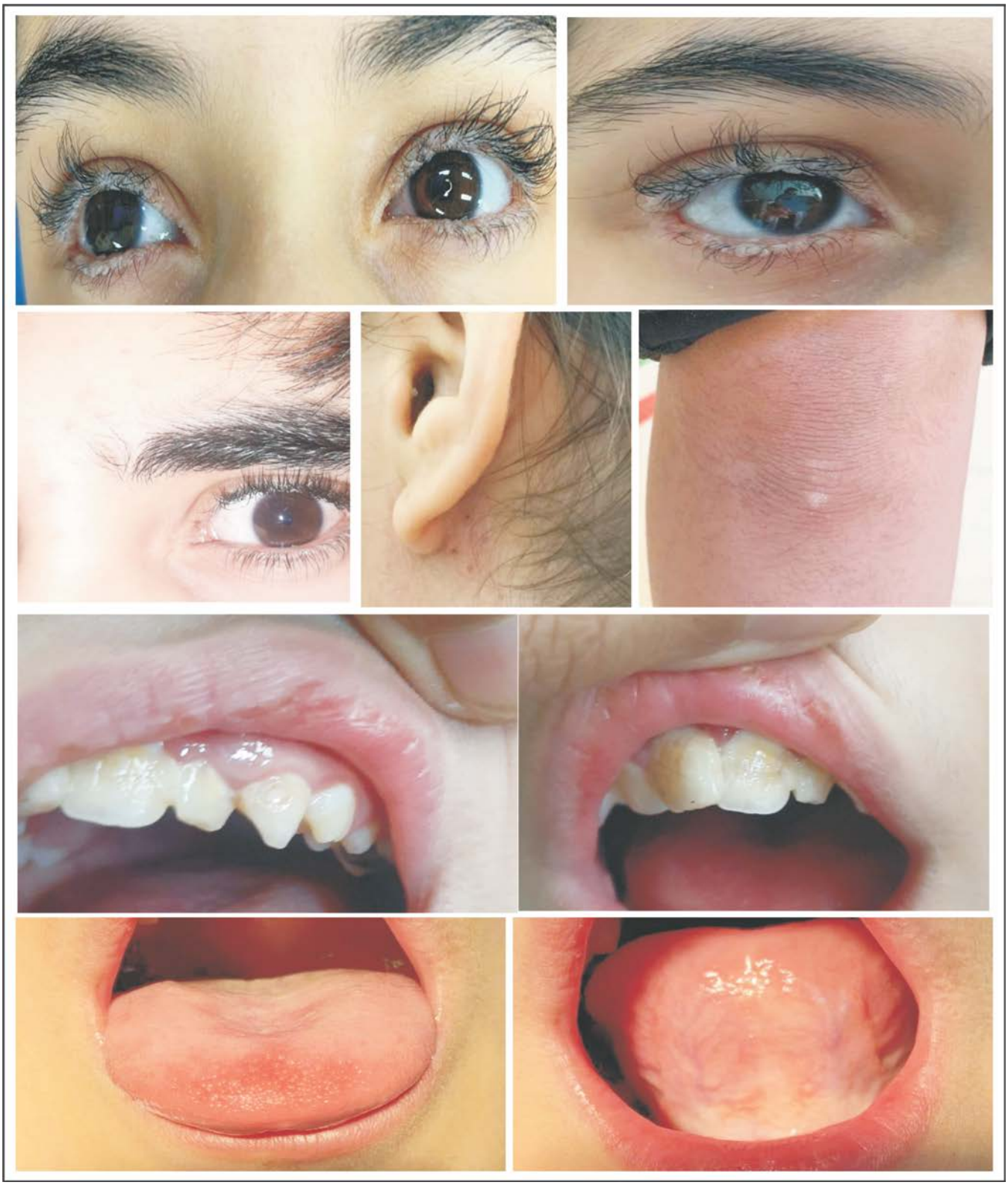

Figure 1: 1st Row; Lipoid proteinosis involving eyelids (left). Pathognomonic moniliform blepharosis with trichomegally and Madarosis (right)
2nd Row: Pathognomonic moniliform blepharosis (left). Pinkish scaly lesion behind the ear (middle).Pinkish scaly lesion over the knee (right).
3rd Row: Crowded teeth in patients with LP.
4th Row: Firm mucosa of the tongue. Free movement of the tongue with no deposition of proteinaceous materials over the dorsum of the tongue.

(epilepsy, tremor, headache, dizziness, or vertigo). There was loss of eye lashes associated with lid lesions. She was the 3rd child of a five member's family with cousin marriages. Her eldest brother complained of the same lid lesions. There was no family history of seizures or visual disturbances. Her parents were normal without manifestations of LP.

Best corrected visual acuity was 6/6 in each eye and IOP 14mm Hg OD and 16mm Hg OS. There were several small, waxy, skin-colored, flat-topped papules, 1 – 3 mm in size scattered along the whole lid margin on all eyelids, giving the lesions a distinctive beaded form upon close observation. Anterior segment evaluation revealed rows of yellow-white color, round or oval, bead-like excrescences on the margins of all four lids and the caruncle, resembling a string of pearls, the pathognomonic, moniliform blepharosis (Figure 1). Multiple attempts were made for excision of these lesions when she was 6, 8, and 10 years old; however, they showed no cure.

Neurologic examination revealed motor neuropathy (axonal motor neuropathy). Endoscopy of the larynx showed thickened vocal cords bilaterally and arytenoid swelling. There was firm mucosa of the larynx and tongue with free movement of the tongue. She has crowded teeth and few teeth have already been removed (Figure 1, 2 and 3).

Similar clinical features including pathognomonic moniliform blepharosis and hoarseness of voice were noted in her 15-year-old boy with the same lid features. He had history of surgery at age 6 for removal of nodules over the vocal cords to tackle the hoarse voice, followed years later by filler injection to the vocal cords. A vitiligo-like lesion covered his face and neck. He had alopecia areata and warty lesions over his fingers. Histopathological report showed hyperkeratosis, focal acanthosis and pseudo epithelial hyperplasia. Mild superficial dermal perivascular inflammatory cell infiltration. The histological finding was non-specific to be correlated with the clinical finding. The dermatologist regarded those lesions as viral warts and treated them accordingly. In contrast to his sister, his milestones were not delayed. He experienced normal teething, and he had no gait or hearing issues. Although he had dysphagia that was not present in his sister.

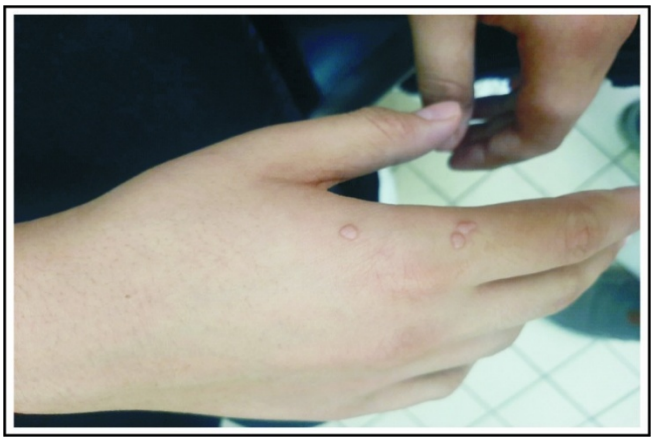

Figure 3: Warty skin lesion over the dorsum of hand in the patient with LP.

The characteristic lid lesions, besides the hoarse voice and positive family history, were suggestive of LP as a provisional diagnosis. A punch lid lesions biopsy was performed for the girl and the histopathological result wasconsistent with lipoid proteinosis.

The results of the complete blood count, serum glucose level, liver and kidney function tests, and porphyrin levels in serum, urine, and stool were all negative.MRI of the brain and cervical spine were normal. CT scan of brain revealed no calcification. A CT scan of the PNS showed polyp with mild mucosal

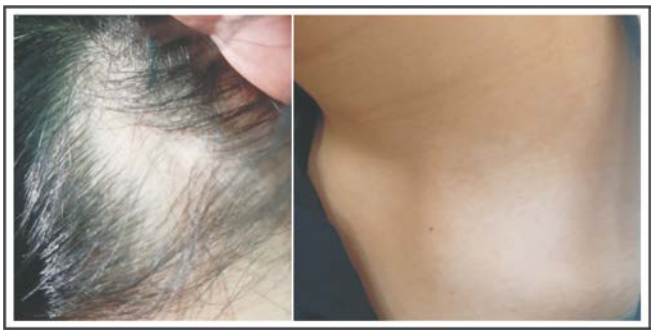

Figure 2: Alopeia areata in the patient with LP (left). Vitiligo-like skin lesion (right).

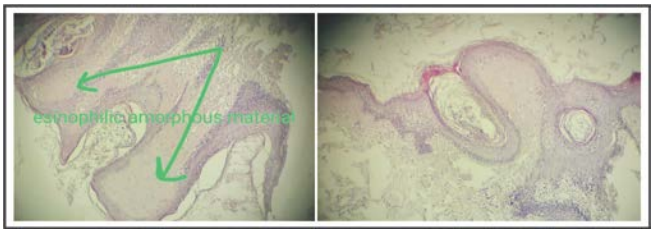

Figure 4: (H&E, x200)A normal looking epidermal layer, expansion of the papillary dermis and filled by amorphous eosinophilic acellular hyaline material, and extended around sweat glands (left). A normal looking epidermal layer, expansion of the papillary dermis and filled by amorphous eosinophilic acellular hyaline material, and extended around sweat glands (right).

thickening seen. EEG was also normal.

Diffuse motor nerve involvement in a length-dependent pattern (affecting both upper and lower limbs; the lower limbs are affected maximally). The main pathology is axonal degeneration of moderate degree with evidence of active ongoing degeneration and re-innervation signs. Electrophysiological study showed signs of motor neuropathy or neuropathy associated with peripheral nerve hyper excitability syndrome. However, her brother had no evidence of diffuse peripheral neuropathy or myopathy.

On September 10th, 2022, we started Acitretin tablet 0.4 mg/kg body weight for both siblings. Both siblings' LFT and lipid profiles had already been measured and were normal. In addition, we suggested CO2 laser treatment for the lid lesions, which was commenced by the dermatologist in conjunction with the ophthalmologist at the Baghdad Medical City Hospital. The result after 6 months of using Acitretin was disappointing; i.e., no improvement regarding both the skin and mucosal manifestations (including the hoarse voice). There was a subjective improvement with CO2 laser therapy for the lid papules; however, multiple sessions were recommended to achieve a desirable improvement. The otorhinolaryngologist advised speech therapy for the girl as she has a problem with phonation. The neurologist suggested conservative treatment with frequent follow up.

DISCUSSION

Lipoid proteinosis usually starts in infancy or early childhood due to the involvement of upper aerodigestive tract mucosa with hoarseness of voice as a presenting feature, and may be accompanied by swelling of the tongue and lips, with associated difficulty in swallowing and respiratory distress in some cases. Some cases show skin rash (not in our patients), involving the face, scalp, and trunk with a thickened, pale yellow-brown, pock-marked appearance of the lesions.[4] It may also involve the axilla (not seen in our case) or the extensor surfaces (elbows and knees), which were noticed in our patients with marked hyperkeratosis in response to minor trauma. Neurological manifestations include longstanding memory impairment, paranoia, rage attacks, mental retardation, and temporal lobe epilepsy.[5]

Although ocular involvement of lipoid proteinosis is rare, an ophthalmologist may identify various signs of lipoid proteinosis in any area of the eye, including the cornea, conjunctiva, sclera, trabecular meshwork, iris, pupil, lens, zonular fibers, retina, and nasolacrimal duct. Since eyelid lesions are among the most prevalent ocular lesions, moniliform blepharosis is regarded as one of the most pathognomonic features of lipoid proteinosis.[6]This feature is particularly well known as a potent diagnostic clue and typically manifests as microscopic papules on the eyelid borders, such as a string of yellowish and waxy beads. In addition to their diagnostic value, lid lesions are known to accompany the infiltration of the Zeiss, Moll, and Meibomian glands and to cause madarosis (as in our case), trichiasis, and occasionally distichiasis (there was trichomegaly in our case).

Thirty to fifty percent of patients develop drusen and the macula displays localized degeneration. Uncommon ocular manifestations of lipoid proteinosis include glaucoma (caused by the deposition of hyaline inclusions in the trabecular meshwork or by the hyalinization of scleral trabeculum with the deposition of glycoproteins), cataracts, and lens-related complications (lens dislocation or subluxation).[6] There are retinal complications (the association of retinitis pigmentosa, impaired color vision, and light hypersensitivity) and corneal manifestations (corneal ulceration brought on by trichiasis, corneal opacities, Keratoconus, as well as the deposition of hyaline on the cornea, especially at Descemet's membrane), iris- and pupil-related complications, unilateral or bilateral uveitis, dry eye or epiphora, nasolacrimal duct obstruction, and transient visual loss.[7]

Since lipoid proteinosis has a chronic, benign, but progressive course, there is no effective treatment. The type of visual manifestation with symptomatic improvement in the clinical disease is typically targeted for management. Similar to how we treat our patients, eyelid lesions are treated with artificial tear supplements, antihistamine eye drops, and in some circumstances, surgical removal and CO2 laser therapy.[8] A multidisciplinary team of specialists, including ophthalmologists, dentists, dermatologists, otorhinolaryngologists, and neurologists, has provided patients with additional advice and counseling regarding the disease's chronic nature, various ocular manifestations, multisystem involvement, and the need for follow-up.

In a case treated with oral dimethylsulfoxide, remarkable clearance of cutaneous and laryngeal lesions was reported, but no improvement was seen in

three additional cases.[9,10]One patient has reported experiencing positive results from etretinate.[11] D-penicillamine was used by Kaya et al, to successfully treat a girl over the course of two years.[12]

Literature shows that Acitretin may be helpful for lipoid proteinosis patients, for both cutaneous and mucosal lesions, an observation that requires further research.[13]

CONCLUSION

Ophthalmologists may encounter a variety of ocular complications, as mentioned above, even though ocular manifestations of lipoid proteinosis are uncommon. As a result, they play a more significant role in the diagnosis and treatment of patients with this disease as a member of a multidisciplinary team of physicians. The ocular manifestation of a rare and unusual systemic illness in patients from an Iraqi family is described in our case report. The ophthalmologist should be alerted by the appearance of distinctive lid papules to look for the patient's hoarse voice; if it is present, the diagnosis will be highly likely, especially if a biopsy of the lid lesions confirms a positive finding. The consultation with dermatologists, neurologists, otorhinolaryngologists, and dentists was beneficial in verifying the diagnosis and building a plan for subsequent therapy. A normal life span is compatible with lipoid proteinosis' benign course. Infant mortality is exclusively brought on by laryngeal deposits that restrict breathing. It is crucial that parents of affected children receive counseling about the risks of having other affected children, regardless of how the disease develops and how symptomatic therapy is used. Up until now, the focus of treatment has been on symptom relief and patient quality of life.

Conflict of Interest

Authors declared no conflict of interest.

REFERENCES

1. **Hofer PA.** Urbach-Wiethe disease (lipoglycoproteinosis; lipoid proteinosis; hyalinosis cutis et mucosae). A review. Acta Derm Venereol Suppl (Stockh). 1973; **53:** 1-52.
2. **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 (3):** 162-167. PMID: 17063986; PMCID: PMC2639960.
3. **Abtahi SM, Kianersi F, Abtahi MA, Abtahi SH, Zahed A, Fesharaki HR, et al.** Urbach-wiethe syndrome and the ophthalmologist: review of the literature and introduction of the first instance of bilateral uveitis. Case Rep Med. 2012; **2012:** 281516. Doi: 10.1155/2012/281516.
4. **Bakry OA, Samaka RM, Houla NS, Basha MA.** Two Egyptian cases of lipoid proteinosis successfully treated with acitretin. J Dermatol Case Rep. 2014; **8 (1):** 29-34. Doi: 10.3315/jdcr.2014.1168.
5. **Emsley RA, Paster L.** Lipoid proteinosis presenting with neuropsychiatric manifestations. J Neurol Neurosurg Psychiatry, 1985; **48 (12):** 1290-1292. Doi: 10.1136/jnnp.48.12.1290.
6. **Mandal S, Dutta P, Venkatesh P, Sinha R, Kukreja M, Garg S.** Bilateral lens subluxation in a case of lipoid proteinosis. J Cataract Refract Surg. 2007; **33:** 1469–1670.
7. **Acar U, Yildiz EH, Yuksel D, Ustun H, Unlu N.** Keratoconus in a case of lipoid proteinosis. Eye Contact Lens, 2013; **39 (4):** e25-27. Doi: 10.1097/ICL.0b013e3182657dc6.
8. **Rosenthal G, Lifshitz T, Monos T, Kachco L, Argov S.** Carbon dioxide laser treatment for lipoid proteinosis (Urbach-Wiethe syndrome) involving the eyelids. Br J Ophthalmol. 1997; **81 (3):** 253. Doi: 10.1136/bjo.81.3.252b.
9. **Wong CK, Lin CS.** Remarkable response of lipoid proteinosis to oral dimethyl sulphoxide. Br J Dermatol. 1988; **119 (4):** 541-544. Doi: 10.1111/j.1365-2133.1988.tb03260.x.
10. **Ozkaya-Bayazit E, Ozarmağan G, Baykal C, Uluğ T.** Orale DMSO-Therapie bei 3 Patienten mit Lipoid proteinose. Ergebnisse einer Langzeittherapie [Oral DMSO therapy in 3 patients with lipoidproteinosis. Results of long-term therapy]. Hautarzt. 1997; **48 (7):** 477-481. German. Doi: 10.1007/s001050050613.
11. **Gruber F, Manestar D, Stasic A, Grgurevic Z.** Treatment of lipoid proteinosis with etretinate. Acta Derm Venereol. 1996; **76 (2):** 154-155. Doi: 10.2340/0001555576154155.
12. **Kaya TI, Kokturk A, Tursen U, Ikizoglu G, Polat A.** D-penicillamine treatment for lipoid proteinosis. Pediatr Dermatol. 2002; **19 (4):** 359-362. Doi: 10.1046/j.1525-1470.2002.00104.x.
13. **Bakry OA, Samaka RM, Houla NS, Basha MA.** Two Egyptian cases of lipoid proteinosis successfully treated with acitretin. J Dermatol Case Rep. 2014; **8 (1):** 29-34. Doi: 10.3315/jdcr.2014.1168.

14. **Hamada T.** Lipoid proteinosis. Clin Exp Dermatol. 2002; **27 (8):** 624-629.
Doi: 10.1046/j.1365-2230.2002.01143.x.

Authors' Designation and Contribution

Ali Nema Abushnein: Ophthalmology Specialist: *Concepts, Design, Literature search, Data analysis, Statistical analysis, Manuscript preparation, Manuscript editing, Manuscript review.*

Khitam Fakhir Alhasseny: Pediatric Ophthalmologist: *Design, Data analysis, Manuscript preparation.*