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A Rare Cause of Nephrotic Syndrome: The p.Leu364Pro Mutation Associated with Familial Lesitin Cholesterol Acyl Transferase Deficiency

Nuri Barış Hasbal[1], Fatih Palıt[2], Murat Yaşar Taş[2], Seyhun Solakoğlu[3], Işın Kılıçaslan[4], Gürsel Yıldız[5]

[1]Division of Nephrology, Department of Internal Medicine, Koc University School of Medicine, Istanbul, Türkiye
[2]Clinic of Nephrology, Basaksehir Cam and Sakura City Hospital, İstanbul, Türkiye
[3]Department of Histology and Embryology, Istanbul University School of Medicine, İstanbul, Türkiye
[4]Department of Pathology, Istanbul University School of Medicine, İstanbul, Türkiye
[5]Department of Nephrology and Renal Transplantation, Health Sciences University Başakşehir Cam and Sakura Health Application Research Center, İstanbul, Türkiye

Corresponding author: Nuri Barış Hasbal ✉ nhasbal@ku.edu.tr or nbhasbal@gmail.com

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To the Editor,

Lecithin-cholesterol acyltransferase (LCAT) deficiency is a rare genetic disorder characterized by abnormal lipid metabolism, leading to a spectrum of clinical manifestations primarily affecting the eyes, lipid metabolism, and kidneys.[1] Lecithin-cholesterol acyltransferase, an enzyme crucial for the esterification of cholesterol in high-density lipoprotein, plays a pivotal role in reverse cholesterol transport, facilitating the removal of cholesterol from peripheral tissues to the liver for excretion. Genetic mutations in the LCAT gene can result in either complete LCAT deficiency, known as familial LCAT deficiency (FLD), or partial deficiency, referred to as fish-eye disease (FED). Familial LCAT deficiency and FED share some common clinical features, including corneal opacifications and dyslipidemia, but differ significantly in their impact on kidney function and cardiovascular health.[2]

In this context, we report a mutation in the LCAT gene identified in a patient presenting with features consistent with FLD.

A 36-year-old male patient presented with nephrotic syndrome at the outpatient nephrology clinic. The swelling in his legs had begun approximately 2 weeks prior, and he was referred due to the detection of nephrotic-range proteinuria subsequently. He reported no significant medical history other than an episode of visible, transient hematuria approximately 10 years ago. His parents were consanguineously related, sharing a common paternal lineage as their mothers were half-sisters.

Physical examination revealed no hypertension, bilateral pretibial edema, and bilateral corneal clouding (Figure 1). While serum creatinine and urea levels were within the normal range, the patient exhibited hypoalbuminemia (albumin concentration: 2.3 g/dL) and dyslipidemia, evidenced by an elevated low-density lipoprotein cholesterol level of 197 mg/dL. Furthermore, significant proteinuria, quantified at 8.2 g/day, along with albuminuria of 6.3 g/day, was noted on the 24-hour urine collection. Kidney ultrasound findings did not reveal any abnormalities. Kidney biopsy identified 18 glomeruli, 2 of which exhibited sclerosis and were devoid of immunofluorescent deposits. A diffuse vacuolated, foamy appearance within the endothelial cells was noted, raising suspicions of a storage disease, specifically LCAT deficiency (Figure 2). Written informed consent was obtained from the patient who agreed to take part in the study.

pLeu364Pro (C.1091T>C) homozygous mutation in the LCAT gene was found in the DNA sequence analysis.

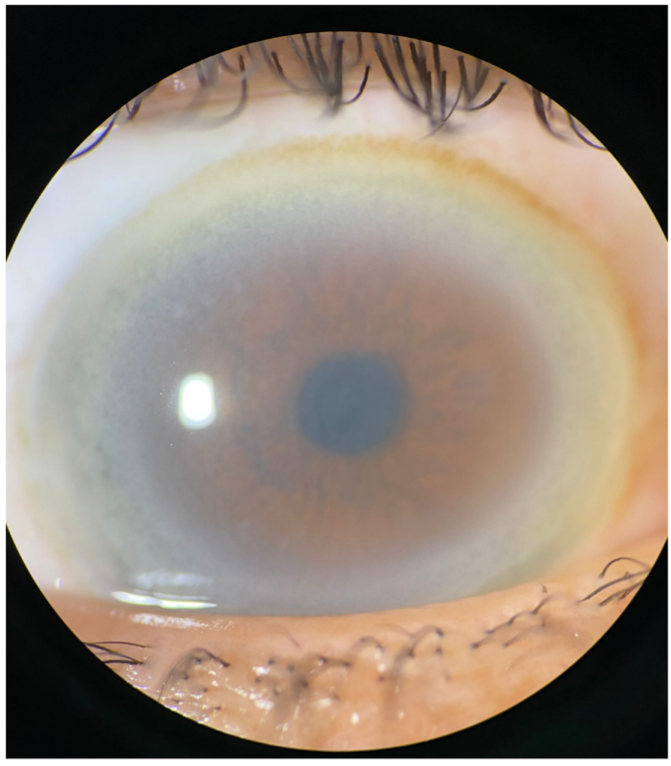

Figure 1. Slit-lamp examination showing corneal opacities.

Despite being first described over 5 decades ago, LCAT deficiency remains a challenge in clinical practice due to its rarity and the heterogeneity of its presentation. Over hundred mutations in the LCAT gene have been identified, contributing to the diverse clinical spectrum observed among affected individuals.

There are 2 other case reports from Türkiye and 1 report of 2 patients of Turkish origin in the literature. Ustaoglu et al[3] presented 2 cases with FED with different mutations [p.Asn29Ser and c.1052A.G (p.Tyr351Cys)] in the LCAT gene. Ozkok A. et al[4] presented a patient with nephrotic syndrome, corneal opacities, and a novel homozygous mutation in the LCAT gene splice site region (IVS1+1G>C[c.154+1G>C]). Last, Stoekenbroek RM et al[5] reported 2 brothers with FLD, homozygous carriers of an ACG to ATG mutation, resulting in the p.T345M substitution.[5]

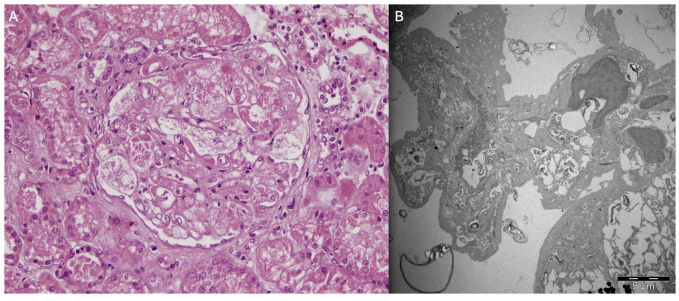

Figure 2. A. Advanced swelling and vacuolar appearance in endothelial cells (hematoxylin and eosin ×300). B. Electron microscopic examination shows lipid vacuoles and multilamellar inclusions in endothelial cells (uranyl acetate–lead citrate).

Nephrologists should be encouraged to consider LCAT enzyme deficiency in patients presenting with nephrotic syndrome and corneal opacity.

Informed Consent: Written informed consent was obtained from the patient who agreed to take part in the study.

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