Lipoprotein glomerulopathy with ApoE Kyoto mutation in an asymptomatic Chinese male patient: A case report

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Introduction

Lipoprotein glomerulopathy is a rare disorder predominantly affecting Chinese and Japanese. Patients usually present with proteinuria and renal insufficiency, and may progress to renal failure. Biochemical investigations typically reveal elevated serum apolipoprotein E (apoE) level and hyperlipidemia. The diagnosis is confirmed by renal biopsy. It is an autosomal dominant disease with incomplete penetrance caused by missense mutation of the apoE gene.

Clinical history

A 24-year-old asymptomatic Chinese male was found to have proteinuria during pre-employment checkup. He had unremarkable past health and no family history of renal disease. His blood tests showed deranged renal function (Creatinine 165 umol/L) and hyperlipidemia (Triglyceride 5.0 mmol/L, total cholesterol 9.5 mmol/L, HDL 1.0 mmol/L). 24-hour urine protein was 7.89 g/day. Screening for hepatitis B/C infection and autoantibodies were all unremarkable.

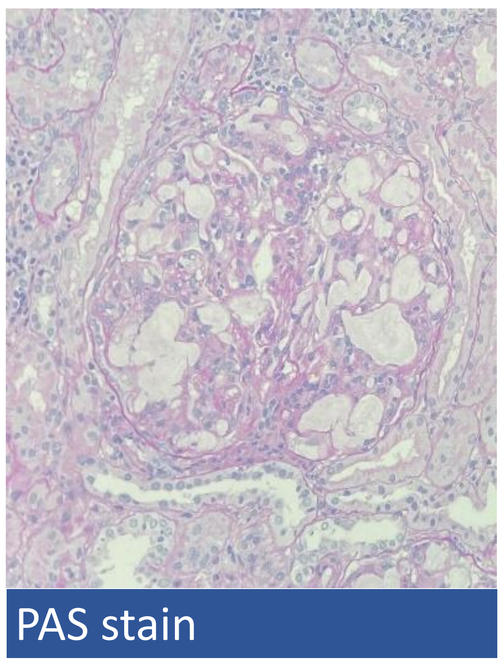
Pathological findings

Light microscopy of the renal biopsy showed glomerular capillary loops distended by thrombi (weakly PAS +, oil red O +, silver stain - and Congo red -). Mild to moderate degree of mesangial expansion and hypercellularity were evident. Silver stain showed focal segmental double contour of glomerular basement membrane.

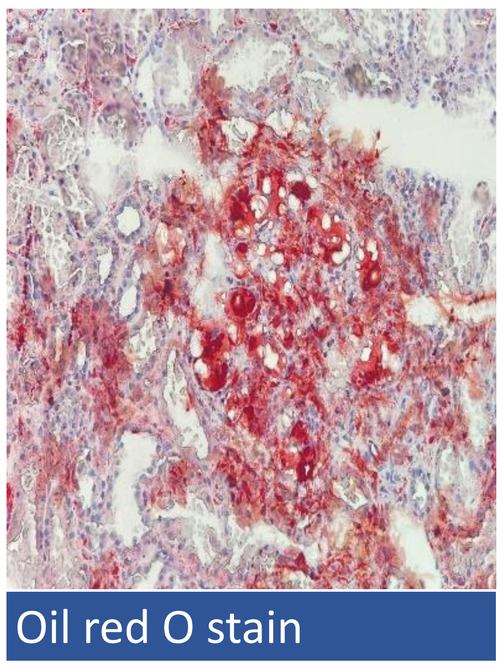
Direct immunofluorescence study showed trace mesangial granular staining for IgM. Staining for IgA, IgG, C3, C1q and fibrinogen were negative. No light chain restriction was demonstrated.

Electron microscopy showed concentric lamellated thrombi within the glomerular capillary loops. Small to moderate amount of mesangial, subendothelial and intramembranous lipid deposits were present.

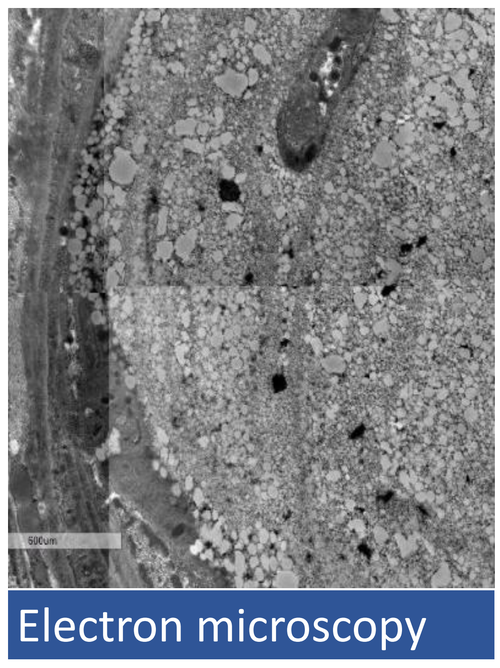
ApoE gene Sanger sequencing was performed in EDTA blood. Heterozygous apoE NM_000041.4:c.127C>T, p.(Arg43Cys) (legacy name: p.(Arg25Cys)) (ApoE Kyoto) was detected.



PAS stain



Oil red O stain



Electron microscopy

Discussion

The patient had deteriorating lipid profile but static renal function on 2-year follow up. His father was also tested positive for the mutation but had no proteinuria nor renal derangement, demonstrating incomplete penetrance of the disease. ApoE Kyoto mutation is associated with reduced binding capacity of apoE to LDL receptor, reduced catabolism of triglyceride-rich lipoproteins and their remnants and subsequent glomerular lipoprotein deposition. Lipoprotein glomerulopathy can co-exist with other glomerular diseases, such as membranoproliferative glomerulonephritis.

Fibrates, a lipid-lowering agent, help improve proteinuria and may result in clinical remission. On the other hand, corticosteroids are ineffective. For patients who progress to end stage renal failure, renal transplantation is not a practical option as recurrence is inevitable.

Conclusion

Lipoprotein glomerulopathy is a rare disorder with distinctive histological features. Pathologists should be aware of this unusual disease entity and genetic counselling is advised.

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