paper, referring to "ongoing therapeutic trials investigating inhibitors of components C3 and C5."[8]

However, recent data break this axiom and make it less rigid by introducing C1q as a possible building block in IgAN, suggesting both that it plays its own independent role (and we do not yet know whether this is mutually exclusive regarding alternative pathway activation as in our immunofluorescence findings)[4–6] and that C1q can therefore be considered in the ever-expanding landscape of IgAN target therapy. Finally, it confirms the role of microscopic examination of kidney biopsies (histopathology and immunofluorescence) not only for the prognostic aspects of the Oxford classification but also to identify cases where pathological glomerular IgA deposition is accompanied by C3 or C1q, thus differentiating patients with distinct potential therapeutic targets.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

Conflicts of interest

There are no conflicts of interest.

Gabriele Gaggero[1], Katia Mazzocco[1], Barbara Cafferata[1], Andrea Angeletti[2]

[1]Pathology Unit, [2]UOC Nefrologia Dialisi e Trapianto, IRCCS Istituto Giannina Gaslini, Largo Gerolamo Gaslini, Genova, Italy

Corresponding author:
Gabriele Gaggero, Pathology Unit, IRCCS Istituto Giannina Gaslini, Largo Gerolamo Gaslini, Genova, Italy. E-mail: gabriele.gaggero@outlook.it

References

1. Roberts LE, Williams CEC, Oni L, Barratt J, Selvaskandan H. IgA Nephropathy: emerging mechanisms of disease. Indian J Nephrol 2024;34:297–309.
2. Berthoux FC, Mohey H, Afiani A. Natural history of primary IgA nephropathy. Semin Nephrol 2008;28:4–9.
3. Trimarchi H, Barratt J, Cattran DC, Cook HT, Coppo R, Haas M, *et al*. Oxford classification of IgA nephropathy 2016: An update from the IgA nephropathy classification working group. Kidney Int 2017;91:1014–21.
4. Tian S, Yang X, Luo J, Guo H. Clinical and prognostic significance of C1q deposition in IgAN patients – a retrospective study. Int Immunopharmacol 2020;88:106896.
5. Tan L, Tang Y, Pei G, Zhong Z, Tan J, Zhou L, *et al.* A multicenter, prospective, observational study to determine association of mesangial C1q deposition with renal outcomes in IgA nephropathy. Sci Rep 2021;11:5467.
6. Hayashi A, Kawabe M, Yamamoto I, Ohki Y, Kobayashi A, Ueda H, *et al.* Clinical and pathological significance of mesangial C1q deposition in kidney transplant recipients with recurrent IgA nephropathy and patients with native IgA nephropathy. Nephron 2023;147(Suppl 1):80–8.
7. Suzuki H, Kiryluk K, Novak J, Moldoveanu Z, Herr AB, Renfrow MB, *et al.* The pathophysiology of IgA nephropathy. J Am Soc Nephrol 2011;22:1795–803.
8. Zhang Y, Zhang H. Current understanding and new insights in the treatment of IgA nephropathy. Nephrology (Carlton) 2024 (Epub ahead of print).

How to cite this article: Gaggero G, Mazzocco K, Cafferata B, Angeletti A. Mesangial C1q Deposition in IgA Nephropathy: Does the Classical Complement Pathway Play an Independent Role? Indian J Nephrol. 2025;35:116-7. doi: 10.25259/IJN_424_2024

Received: 27-07-2024; **Accepted:** 09-08-2024
Online First: 17-10-2024; **Published:** 04-01-2025

DOI: 10.25259/IJN_424_2024

Factor V Leiden Heterozygous Mutation and Hyperhomocysteinemia Presenting with Vascular Rejection and Renal Allograft Infarction

Dear Editor,

A 40-year-old male was diagnosed with end-stage kidney disease in 2020. He developed lower limb edema following femoral catheterization which resolved spontaneously. He underwent a kidney transplant in 2022. In October 2023, he presented with macroscopic hematuria and graft dysfunction. Graft biopsy revealed acute T-cell-mediated rejection (TCMR).

He was treated with methylprednisolone pulse and rabbit anti-thymocyte globulin. After initial response, his creatinine started increasing again. Graft biopsy revealed acute cortical necrosis with residual inflammation of TCMR. Doppler graft kidney and MRI revealed multiple cortical wedge-shaped infarcts [Figure 1].

Workup was negative for ANA and APLA, and complement levels were normal. Thrombophilia workup revealed hyperhomocsyteinemia 31.3 (1–5) micromol/L and factor V Leiden heterozygous mutation. There were no mutations in prothrombin gene (PGM) and MTHFR gene. Protein C and Protein S levels were normal. He was managed with oral Apixaban and folate. He stopped anticoagulation after a month and presented with recurrent DVT right lower limb and pulmonary thromboembolism.

Several studies have described FVL mutation and increased risk of transplant RVT. FVL mutation leads to fourfold rise in allograft thrombosis.[1] FVL mutation also predisposes to acute vascular rejection.[2,3] Possible mechanism involves delayed inactivation of FVL leading to microthrombi

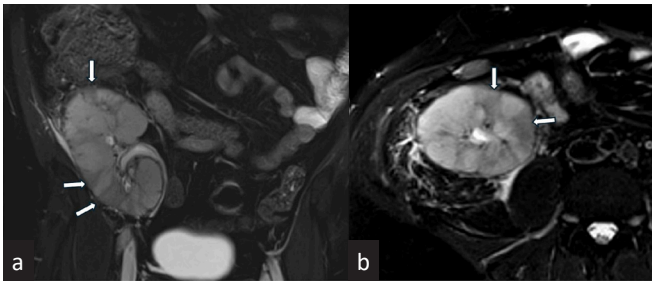

Figure 1: A T2 weighted MRI images of the transplant kidney. (a) Coronal and (b) axial images shows multifocal, wedge-shaped areas of T2 hypointensities (white arrows) suggestive of cortical infarcts.

formation in ischemic graft endothelium. There is a link between hypercoagulable state induced by FVL mutation and immunological injury to graft vasculature.

In our patient, thrombophilia profile led to vascular rejection and ACN. Any patient with history of DVT/PTE should be properly screened before transplant as thrombophilia can lead to RVT, microvascular thrombosis, and precipitate rejection. This can be prevented by pretransplant screening for FVL in high-risk patients and perioperative and posttransplant anticoagulation.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

Conflicts of interest

There are no conflicts of interest.

Taruna Pahuja[1], Sukhwinder Singh Sangha[2], Akash Sarkar[1], Raj Kanwar Yadav[1]

[1]Departmet of Nephrology, All India Institute of Medical Sciences, Ansari Nagar, New Delhi, [2]Departmet of Nephrology, Command Hospital, Cariappa Road, Lucknow Cantt, Lucknow, India

***Corresponding author:** Raj Kanwar Yadav, Department of Nephrology, All India Institute of Medical Sciences, Ansari Nagar, New Delhi, India. E-mail: Rkyadavnephrology@gmail.com*

References

1. Irish AB, Green FR, Gray DW, Morris PJ. The factor V Leiden (R506Q) mutation and risk of thrombosis in renal transplant recipients. Transplantation 1997;64:604-7.
2. Heidenreich S, Dercken C, August C, Koch HG, Nowak-Göttl U. High rate of acute rejections in renal allograft recipients with thrombophilic risk factors. J Am Soc Nephrol 1998;9:1309-13.
3. Ekberg H, Svensson PJ, Simanaitis M, Dahlba È ck B. Factor V R506Q mutation (activated protein C resistance) is an additional risk factor for early renal graft loss associated with acute vascular rejection. Transplantation 2000;69:1577-81.

How to cite this article: Pahuja T, Sangha SS, Sarkar A, Yadav RK. Factor V Leiden Heterozygous Mutation and Hyperhomocysteinemia Presenting with Vascular Rejection and Renal Allograft Infarction. Indian J Nephrol. 2025;35:117-8. doi: 10.25259/IJN_330_2024

Received: 24-06-2024; **Accepted:** 09-08-2024; **Online First:** 12-09-2024; **Published:** 04-01-2025

DOI: 10.25259/IJN_330_2024

Varia

Why We Transplant?

I want to share the story of our first renal transplant, way back in 2005. We were novices then, me and Dr. V Srinivas (my first boss and partner), with only our training to fall back on and with no "hands on experience".

I first met Ms. M in Srinivas' chamber, a shy, comely young girl of 18. She was visibly upset then, as she had just lost her father, who was her pillar of strength, to an myocardial infarction. She had been battling chronic kidney disease for some time. Her brother would also be diagnosed with chronic kidney disease later (a familial FSGS). Appropriate consent was obtained. They were preparing for a transplant. Coming from a traditional but well-connected family, they were spoilt for choices regarding the centers for transplant (both in Hyderabad and Visakhapatnam). However, they reposed their faith us, being fully aware that this would be our first transplant–credit to the days when patients had implicit faith in their doctors. A few words about my boss here would not be amiss. Sometime during his youth, he developed a spontaneous mutation of his "anger gene", leaving him unable to react angrily to any situation. He genuinely had the interest of his patients at heart and most patients did stick to him for a lifetime. He was the go-to person for patients for all their problems; some approached him unabashedly for their monetary requirements. When I saw the long line of familiar faces outside his chamber, I often wondered how many had come for a review and how many had come with pockets to fill. All carried a promise to return the money "soon", but I suspect very few did.

The mother came forward to donate, and the surgery went through uneventfully. I did "bedside" night duties for a few days, which were, of course, full of anxious