Post-transplant nephrotic syndrome: Besides the obvious

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Posttransplant glomerulonephritis (GN) is a significant cause of morbidity after kidney transplant (KT). Moreover, it has been shown that the incidence of *de novo* GN is higher after KT when compared to native kidney patients[1]. Although the reason for this observation is not fully understood, a recent body of evidence suggests alloimmunity may play a role[2]. We present a case we believe exemplifies the interplay between alloimmunity and *de novo* GN.

A 38-years-old Caucasian male with X-linked Alport Syndrome COL4A5 p.(Gly1448Arg) received an unrelated living donor KT with 4 HLA mismatches. Immunosuppression consisted in Basiliximab, Tacrolimus, Mycophenolate Mofetil (MMF) and Prednisolone. Posttransplant period was unremarkable until two years after KT when persistent diarrhea lead to MMF suspension. Diagnostic workup returned positive for Giardiasis that was successfully treated with metronidazole. One month later, the patient was admitted for nephrotic syndrome (NS) with preserved kidney function. Immunological study was remarkable for low C4 and normal C3 levels. Donor-specific antibodies (DSA) were negative. KT biopsy revealed a full house immune-complex mediated GN (IC-GN), mesangial proliferation, mild peritubular capillarity with positive C4d (also present in the glomeruli) and humps (Figure 1). No evidence of posttransplant anti-glomerular basement membrane disease was found. Spontaneous resolution of NS occurred and, one month after discharge, *de novo* DSA led to a second KT biopsy. Active antibody mediated rejection (AMR) and resolving foot process effacement with persistence of mainly subepithelial IC deposition and a full house pattern were observed, without evidence of transplant glomerulopathy. Treatment for subclinical AMR resulted in disappearance of DSAs. Later, complement consumption recovered.

Parasitic infections including Giardiasis have been associated with NS. However, most of the cases described in the literature report to the developing world and only rarely kidney biopsy results are shown[3]. Our patient presented with *de novo* IC-GN that we attributed to Giardiasis. The recent infection, spontaneous resolution of NS and exclusion of more common culprits including other infectious, auto-immune or oncologic diseases support this diagnosis. However, there might be more to the first biopsy than initially thought. Recently, Khairallah et al[2] showed that patients with *de novo* GN after KT had higher concurrent rates of AMR and higher DSA titers at time of diagnosis when compared to patients with recurrent GN. We believe C4d positivity with capillarity in the first biopsy was a clue for an underlying humoral process elicited by MMF suspension. The diagnosis of AMR one month later is in line with this observation. We hypothesize that the humoral process may have been the potential trigger for this rare infection-related GN. Nevertheless, the pathophysiology underlying the association between alloimmunity and *de novo* GN is still unknown and deserves further investigation.

Conflict of interests

The authors have no conflict of interests to declare.

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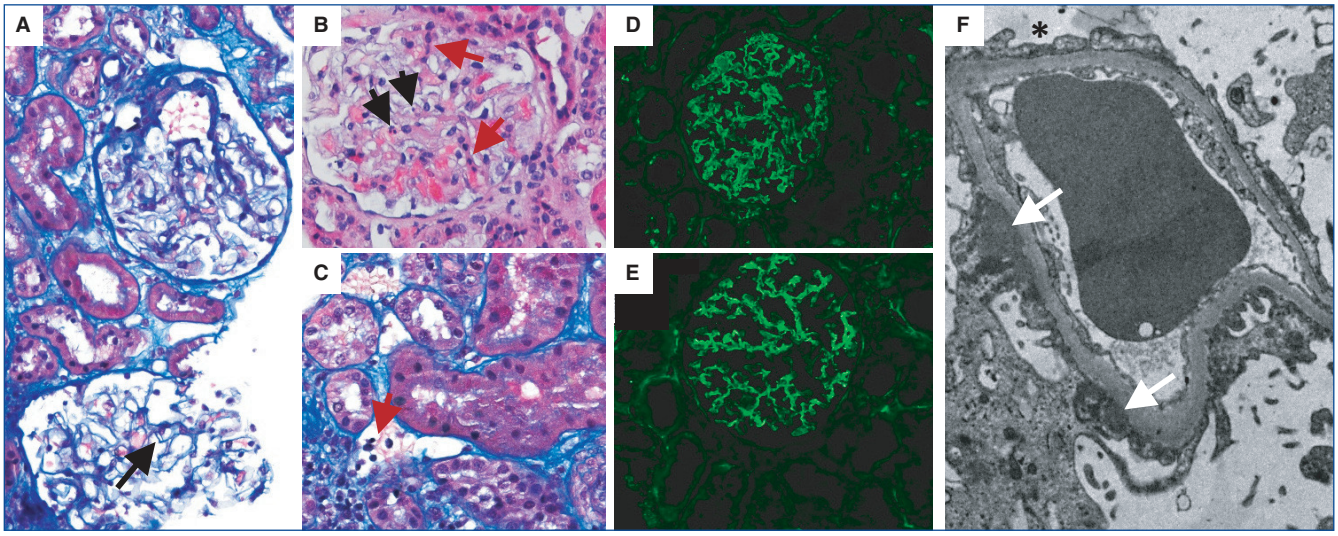

Figure 1. First Biopsy findings. A) Light Microscopy (Trichrome Masson stain, 400x) with focal glomerular capillary double contours (black arrow). B) Light Microscopy (Hematoxylin-Eosin stain, 400x) with glomerulitis (black arrows) and mild mesangial proliferation (red arrows). C) Light Microscopy (Trichrome Masson stain, 400x) showing capillarity (red arrow); D-E) Immunofluorescence microscopy showing a with diffuse granular IgG staining (D) and positive C4d in glomeruli and peritubular capillaries (E); F) Electron Microscopy revealing diffuse foot process effacement (*) and manly subepithelial immune-complex deposition forming *"humps"* (white arrows).

REFERENCES

1. Lim WH, Shingde M, Wong G. Recurrent and de novo glomerulonephritis after kidney transplantation. Front Immunol. 2019;10: 1944. doi: 10.3389/fimmu.2019.01944.
2. Khairallah P, Kamal J, Crew RJ, Serban G, Vasilescu ER, Dube GK, et al. The Association Between Post–Kidney Transplant De Novo Glomerulonephritis and Alloimmunity. Kidney Int Rep. 2021;6: 813–6.
3. Date A, Neela P, Shastry JCM. Membranoproliferative glomerulonephritis in a tropical environment. Ann Trop Med Parasitol. 1983; 77:279–85.