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Acute allograft dysfunction – a severe case

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CASE REPORT

We report the case of a 49-year-old female patient, born in Cape Verde. She has arterial hypertension detected during her second pregnancy at the age of 25. The arterial hypertension has never been controlled and she started haemodialysis, in Portugal, at 36 years with the presumptive diagnosis of hypertensive nephroangioesclerosis.

Two years ago, at 47 years old, she received a deceased donor kidney, with five mismatches. She had panel reactivity antibodies of 77%; the cross match and donor specific antibodies (DSA) by Luminex was negative at zero time.

The initial prescribed immunosuppressive therapy was thymoglobulin, methylprednisolone, tacrolimus and mycophenolate mofetil. She presented an allergic reaction to thymoglobulin and the induction therapy was made with basiliximab.

The diuresis was null after the kidney transplantation. The allograft kidney echo doppler showed an increased resistance index in the renal artery.

At 48 hours after transplantation a borderline positive crossmatch developed and DSA (DR 13, MFI 1009) was detected by Luminex. Six day after transplantation an allograft kidney biopsy was made.

Figures 1 to 5 represent this first biopsy.

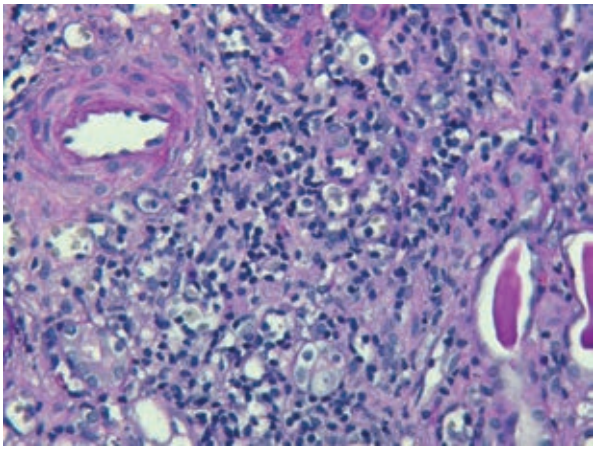

Figure 1
Periodic acid shift (PAS); x400.

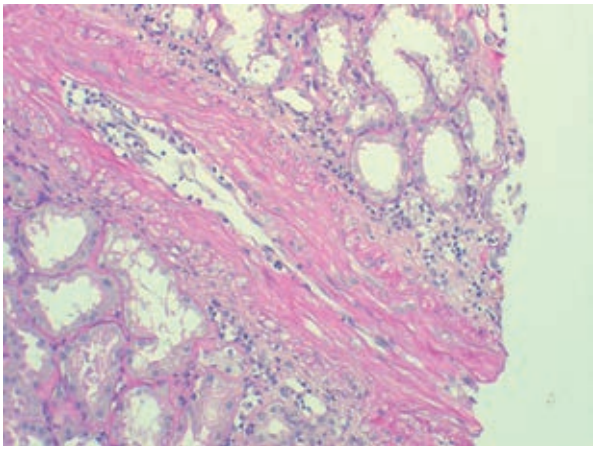

Figure 2
Periodic acid shift (PAS); x200.

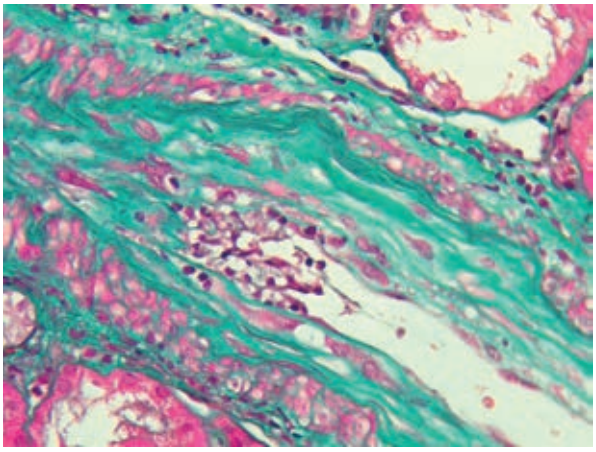

Figure 3
Masson Trichrome; x400.

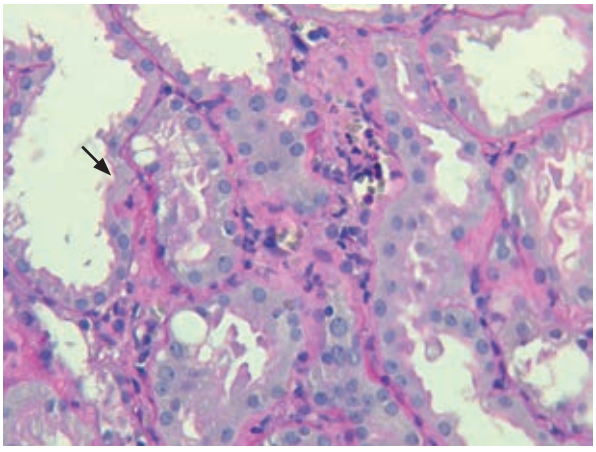

Figure 4
Periodic acid shift (PAS); x 400.

DISCUSSION

In Fig. 1 we can observe tubular basement membranes destruction by mononuclear inflammatory infiltrate. That lesion corresponds to tubulitis grade 3. A medium sized artery is visible without changes.

Figures 2 and 3 show a medium sized vessel, probably an arciform artery. These images illustrate mononuclear inflammatory cells beneath the endothelium artery denominated as endothelialitis or endarteritis. No transmural arterial inflammation or fibrinoide necrosis has observed in this biopsy. The presence of endothelialitis defines vascular rejection or acute cellular rejection grade II. When necrosis of the artery medial smooth muscle is present, the rejection is graded as III.

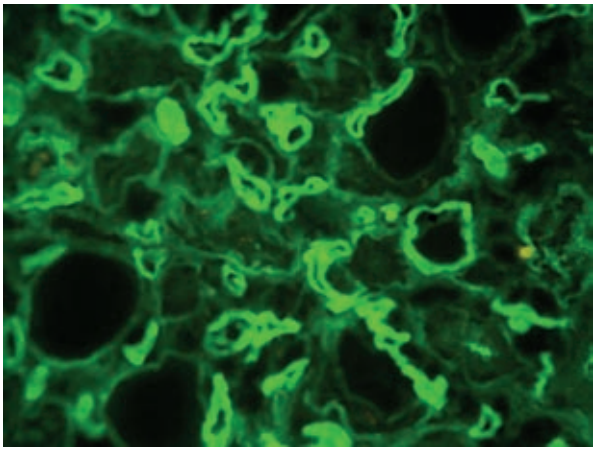

Figure 5
Immunofluorescence in frozen section for C4d; x400.

Figure 4 shows capillaritis; the presence of inflammatory cells in peritubular capillaries. The presence in more than 10% of the biopsy defines capillaritis. The number of inflammatory cells by peritubular capillary grades the Banff score of capillaritis. This patient presents a capillaritis grade 3. Some polimophonuclear cells are visible. The presence of neutrophils must be related as is a marker of worse prognosis.

Figure 5 shows diffuse and intense deposition of C4d in peritubular capillaries.

CLINICO-ANATOMICAL DIAGNOSIS

The presence of capillaritis, C4d in peritubular capillaries and the serum presence of donor specific antibodies allowed the diagnosis of acute antibody mediated rejection.

This patient presented acute cellular rejection IIa associated to acute antibody mediated rejection.

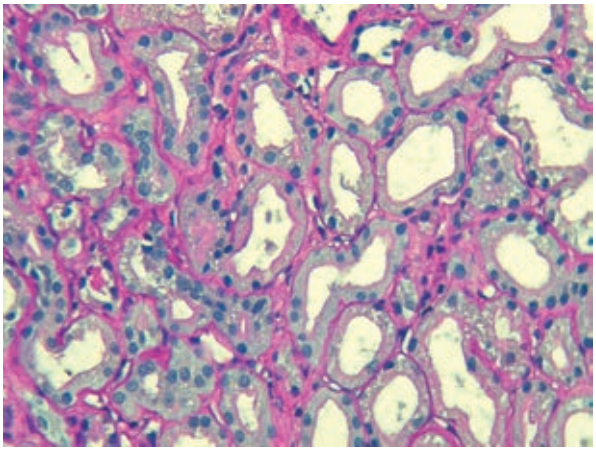

Figure 6
Periodic acid shift (PAS); x200.

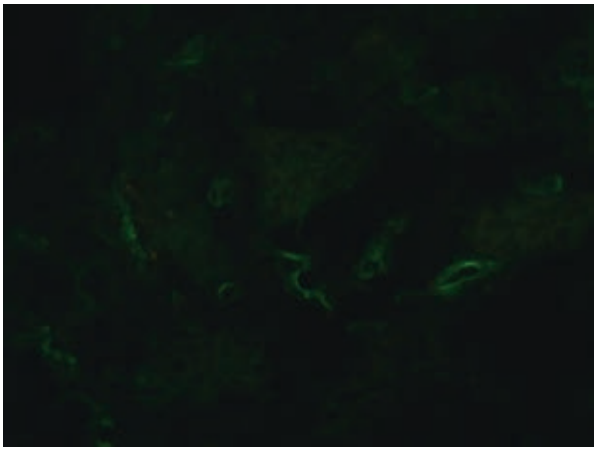

Figure 7
Immunofluorescence in frozen section for C4d; x400.

TREATMENT AND EVOLUTION

The allograft kidney biopsy was complicated by intraperitoneal haemorrhage, requiring surgical intervention.

The patient was treated with anti-thymocites globulin for 10 days. The DSA disappeared without improvement of the renal function.

Rituximab pulses were done at 18, 27 and 42 days after transplantation.

After the first rituximab pulse haemodialysis was stopped. A slow recovery of the renal function was observed.

A second allograft biopsy was done 47 days after transplantation (Figs. 6 and 7).

In Fig. 6 we can see a normal kidney and no deposition of C4d in Fig. 7.

Several acute allograft pyelonephritis infections occurred in the next months.

The patient underwent a new biopsy 21th months after transplantation for decline of the kidney function. That biopsy revealed interstitial fibrosis and tubular atrophy grade III, according to the Banff Classification. The immunosuppression was switched and currently the patient is under tacrolimus, everolimus and prednisolone, with a creatinine of 2.3 mg/dl.

References

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3. Haas M, Sis B, Racusen LC, *et al.* Banff 2013 meeting report: inclusion of C4d-negative antibody-mediated rejection and antibody-associated arterial lesions. Am J Transplant 2014;14(2):272-283.