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Kidney transplant and Klippel-Trenaunay-Weber syndrome: an unusual association

Trasplante renal y síndrome de Klippel-Trenaunay-Weber: una asociación insólita

Dear Editor,

Klippel-Trenaunay-Weber syndrome (KTS/KTWS) is a congenital disorder defined by the triad of capillary malformations of (haemangiomas or port-wine stains) and venous (varicose veins) and overgrowth of bone and soft tissue with or without lymphatic malformations. It has been described genetic association with the PIK3CA gene encoding the protein p110α, a subunit of the enzyme phosphatidylinositol 3-kinase (PI3K).[1–3] Major complications include coagulation disorders in the form of thrombosis, particularly in the renal vein or the central retinal vein, less common is the occurrence of deep vein thrombosis and pulmonary thromboembolism.[3]

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It has been associated with renal disease in three cases of nephrotic syndrome[4–6] (one with focal segmental glomerulosclerosis [FSGS]),[4] urological malformations (one with upper tract renal haemorrhage requiring nephrectomy[7]) and one case of unilateral polycystic kidney disease.[7,8] To our knowledge, there have been no previous reports of patients with KTWS who have received a kidney transplant.

We present the case of a 39-year-old male patient with a previous medical history of hypertension, insulin-dependent type 2 diabetes mellitus, obesity with a body mass index of 35 kg/m^2, hyperuricaemia with nephrolithiasis that required nephrectomy in 2003 and thrombophilia, with positive lupus anticoagulant antibody and antiphospholipid syndrome with thrombosis of the renal vein in 2015 and of the bilateral central retinal vein in 2016,[9] on treatment with Sintrom®.

Renally, the patient had clinical and biochemical nephrotic syndrome, diagnosed by renal biopsy in 2015 with perihilar FSGS secondary to obesity in a patient with a single kidney, and treated with anti-proteinuric measures. The chronic kidney disease progressed to stage V and he started haemodialysis in 2020.

In the context of KTS the patient presented with facial haemangiomas (port-wine stain), lymphoedema, hypertrophy of the lower limbs and vascular malformations.

For inclusion on the transplant waiting list, a computed tomography angiogram was performed, which revealed neoformed vessels surrounding the left iliac vessels with involvement of the left lower limb. All this was discussed in the renal transplant committee, in conjunction with vascular surgery, urology and radiology, and he was considered suitable for renal transplantation. Finally, the patient received a brain-dead donor cadaveric kidney transplant and as the recipient was at low immunological risk, immunosuppression was based on basiliximab and triple therapy with corticosteroids, tacrolimus and mycophenolate. In view of the patient's history of thrombophilia and the fact that KTWS could increase the risk of thrombosis, the following thromboprophylaxis strategy was applied: a change of treatment from Sintrom® to acetylsalicylic acid 100 mg/24 h since inclusion on the transplant list until transplantation. No blood transfusions were required during surgery, but the patient did need transfusions in the post-transplant period due to a drop in haemoglobin to 6.8 g/dl related to the presence of perirenal haematomas, which did not require surgical intervention. He was treated with transfusion of two units of red blood cell concentrate and darbepoetin 80 mcg/week. Subsequently, he was started with prophylactic treatment of low-molecular-weight heparin and finally switched to full-dose Sintrom®. The kidney transplant resulted in immediate renal function, with creatinine on discharge (and usual) of 2.3 mg/dl, glomerular filtration rates of 32 ml/min/1.73 m^2 (by CKD-EPI) and usual haemoglobin levels of 13 g/dl without darbepoetin treatment.

The association between KTWS and kidney disease has been described previously. In our patient the kidney disease did not seem to be related to KTWS, rather it was explained by his cardiovascular risk factors in a patient with a single kidney following nephrectomy.

To our knowledge, this is the first published case of renal transplantation and KTWS, and we should highlight that patients with KTWS are said to have a risk of vascular malformations; from abnormal neoformed vessels predisposing to bleeding to duplication of the vena cava.[2,10] They may also have an increased risk of lymphoedema and lymphoceles. We would therefore stress the importance of carrying out a thorough pre-transplant vascular study of the abdominal vessels, with computed tomography angiogram being recommended, both in arterial and venous phases, as well as a multidisciplinary assessment.

Another important aspect of the case was the strategy of early anticoagulation for thrombophilia, made worse by the KTWS.

With regard to immunosuppression, the use of mammalian target of rapamycin (MTOR inhibitors) would not be advisable due to their association with lymphatic complications, and a case has been described of a patient with KTWS who received treatment with everolimus (due to severely symptomatic vascular malformations) developing a pulmonary embolism despite being anticoagulated.[3]

In conclusion, patients with KTWS are not at increased risk of kidney disease, but if they need a kidney transplant, a detailed assessment of the abdominal venous tree must be made in order to plan an adequate surgical approach, and post-transplant use of MTOR inhibitors is not advisable, due to the risk of worsening thrombotic and lymphatic complications.

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