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Teaching Point
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Arteriovenous malformation in a kidney allograft

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Introduction

Arteriovenous aneurysms may be congenital (arteriovenous malformation, AVM) or acquired (arteriovenous fistula, AVF). AVFs after a renal transplant biopsy are seldom, but well recognized, usually harmless complications [1]. Congenital AVMs are usually of the cirsoid (racemose) type [2], characterized by a tangle of tortuous vessels of small diameter, with multiple varix-like communications between the artery and the vein, arteriovenous shunting and lack of intervening capillaries. AVMs may be associated with multiple intraparenchymal haemorrhagic foci, which are caused by ruptures of the vessel walls. Here we describe a case of spontaneous renal AVM in a kidney transplant patient who had undergone deceased-donor renal transplantation in 2005 for Alport syndrome and after <3 years presented with progressive renal failure. Allograft nephrectomy revealed classic cirsoid type congential AVM. A search of the literature did not yield any reports of congenital AVM in a renal allograft.

Case presentation

A 42-year-old man, who underwent deceased-donor kidney transplantation in March 2005 because of Alport syndrome, presented with peripheral oedema in the lower extremities and deterioration of kidney function. His past medical history included a diagnosis of myocardial infarction 13 years previously, prolonged arterial hypertension (>10 years) and chronic hepatitis B infection. The patient was receiving tacrolimus, methylprednisolone and mycophenolate mofetil as immunosuppressive drugs. His blood pressure was 130/70 mmHg, in both arms with no postural difference. His heart rate was 72/min and respiratory rate was 14 breaths per minute. The chest and heart examinations were unremarkable. Abdominal examination revealed a loud systolic–diastolic murmur above the kidney transplant, suggesting a vascular abnormality, and was otherwise unremarkable. Arterial pulses in the lower extremities were preserved and equal. We suspected acute renal allograft rejection, and the patient was scheduled to undergo a kidney allograft biopsy. An ultrasound examination before the biopsy revealed a large convoluted vessel in the caudal part of the transplant kidney. We initially suspected progression of a traumatic AVF after a previous kidney biopsy in 2005. However, we were puzzled by the fact that colour Doppler measurement revealed no typical fistula flow pattern. Although we observed a relatively high flow (peak flow, 150 cm/s) in some of the convoluted arterial vessels, typical arterial turbulences were generally not present. Moreover, we observed a significant within-breath modulation of venous blood flow in some venous convolute vessels. We carried out an abdominal MRT and MR angiography (Figure 1). Both examinations indicated AVM, but could not definitely exclude the presence of a highly vascularized renal cell tumour. Conventional contrast angiography suggested AVM, but demonstrated no possibility to perform an embolization of the malformation. There was no evidence of further AVMs in our patient. The kidney transplant function decreased further and haemodialysis was started. In view of a non-functional allograft with increased risk of haemorrhage, our surgical colleagues were not reluctant to operate on this patient. Nephrectomy of the kidney transplant was performed. The histological findings showed a classic cirsoid type AVM (Figure 2 Part I, panel A). There was no evidence of renal cell carcinoma. The caudal peripelvic region of the kidney was spongy, and occupied the medullary region up to arcuate arteries. The vessels were free of intravascular thrombi. There was no iron deposition as a correlate of a renal biopsy-induced haematoma. We propose that the AVM in our patient was congenital. The vessels in the AV convolute exhibited irregular wall thicknesses, fibromuscular wall thickening and elastic fibres, typical of arteries and veins, which is consistent with a congenital AVM (Figure 2 Part I, panels B and C). Notably, the cause of death of the kidney donor was intracerebral

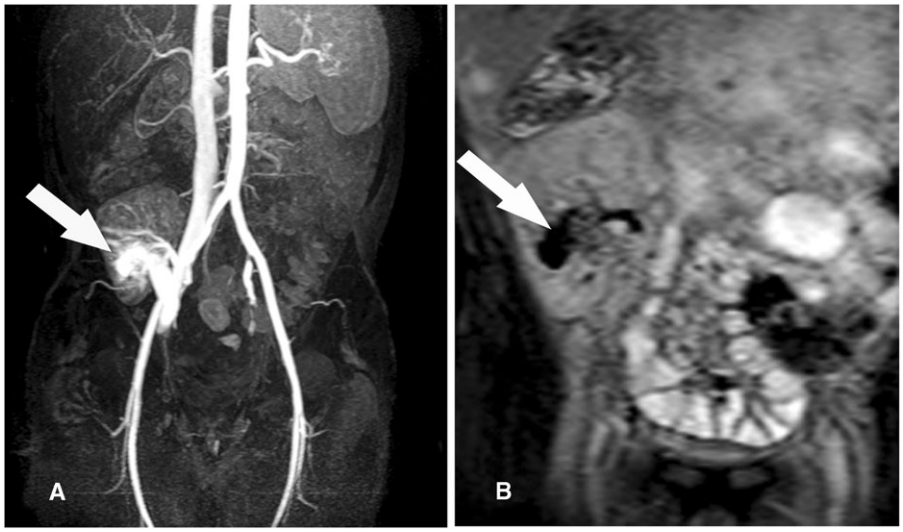

Fig. 1. Panel A: detection of AVM by MR-angiography. The arrow shows the AVM in the caudal region of the renal transplant allograft. Panel B: abdominal MRT. The arrow shows the dimensions of the AVM in relation to the renal transplant allograft.

haemorrhage, which might have resulted from rupture of a systemic vascular dysplasia, e.g. Osler–Rendu–Weber syndrome. Also of note, past medical history of the 61-year-old female donor included clip ligation of cerebral aneurysm 2 months previously. Other diagnoses included previous breast cancer and hepatitis B infection. Ultrasound examination of the donor's abdomen was unremarkable. Apart from a small cyst in the non-transplanted right kidney, both kidneys were normal on ultrasound. From Eurotransplant medical records, we also learned that other organs had not been transplanted. There was no information about possible telangiectasias in the donor.

A search of our pathology databank revealed only two cases of iatrogenic, traumatic AVF in kidneys; in one case a native and in the other a transplanted kidney was affected (Figure 2 Part II, panels A and B). Gross pathology showed haemorrhage or haematoma in the cortex. Higher magnification revealed focal destruction of the venous and arterial walls with continuity between both vessels. Due to rupture of the vessel wall, intrarenal haematoma (so called false aneurysm) may develop. Thus, the histologies of AVF and AVM are clearly different; in AVF, destruction of the vessels is a prerequisite; in AVM, malformation and remodelling of the dilated vessels is present.

Conclusions and discussion

Congenital AVM in the kidney is highly uncommon. The estimated rate in large autopsy series is less than 1 case per 30 000 patients [3]. Most AVMs belong to the classic cirsoid type. Congenital, cirsoid AVMs consist of arteries and dilated veins with a corkscrew appearance, much like a varicose vein. Cirsoid AVMs have not been reported in transplant kidneys to our knowledge. Acquired, traumatic AVF after a renal transplant biopsy are seldom, but well recognized, usually harmless complications [1]. In the histological study of such aneurysms, special elastic tissue stains are always necessary to differentiate between arteries and veins.

Our patient developed a classical cirsoid AVMs in his kidney allograft. The rapid growth within <3 years is remarkable. The AVM is congenital, although the aetiology is not clear. The histology of the AVM is distinct compared to traumatic, acquired AVF. Notably, the donor died from intracerebral haemorrhage, which might suggest a systemic vascular dysplasia, e.g. Osler–Rendu–Weber syndrome. The morphology of cirsoid AVM is entirely different from that of telangiectasias, dilated capillary vascular channels, which are usually seen in Osler–Rendu–Weber syndrome. However, three cases of cirsoid AVMs have been described in Osler–Rendu–Weber syndrome in the literature [4–6]. Osler–Rendu–Weber syndrome or hereditary haemorrhagic telangiectasia (HHT) is an autosomal dominant inborn error of vascular structure with multiple manifestations. Apart from the skin and mucous membrane, telangiectases and/or AVMs may be present in the lungs, intestinal tract, spleen, brain and rarely in the kidney [4–6]. Congenital cirsoid type AVMs in native kidneys have been associated with secondary hypertension [2,3]. Mutations of endoglin (*ENG*) genes and activin receptor like kinase type I (*ALK-1*) genes are involved in the genetic pathogenesis of HHT type 1 and HHT type 2, respectively. These genes are responsible for 60–90% of all clinical cases of HHT. Mice harbouring heterozygous *Eng* and *ALK1* mutations resemble HHT in humans. Unfortunately, our attempts to isolate the DNA failed. Thus, we were unable to perform a mutational analysis of *ENG* and *ALK-1*. Nevertheless, the finding of a classical cirsoid type AVM is suggestive for an inherited trait.

Teaching points

Be aware of the following:

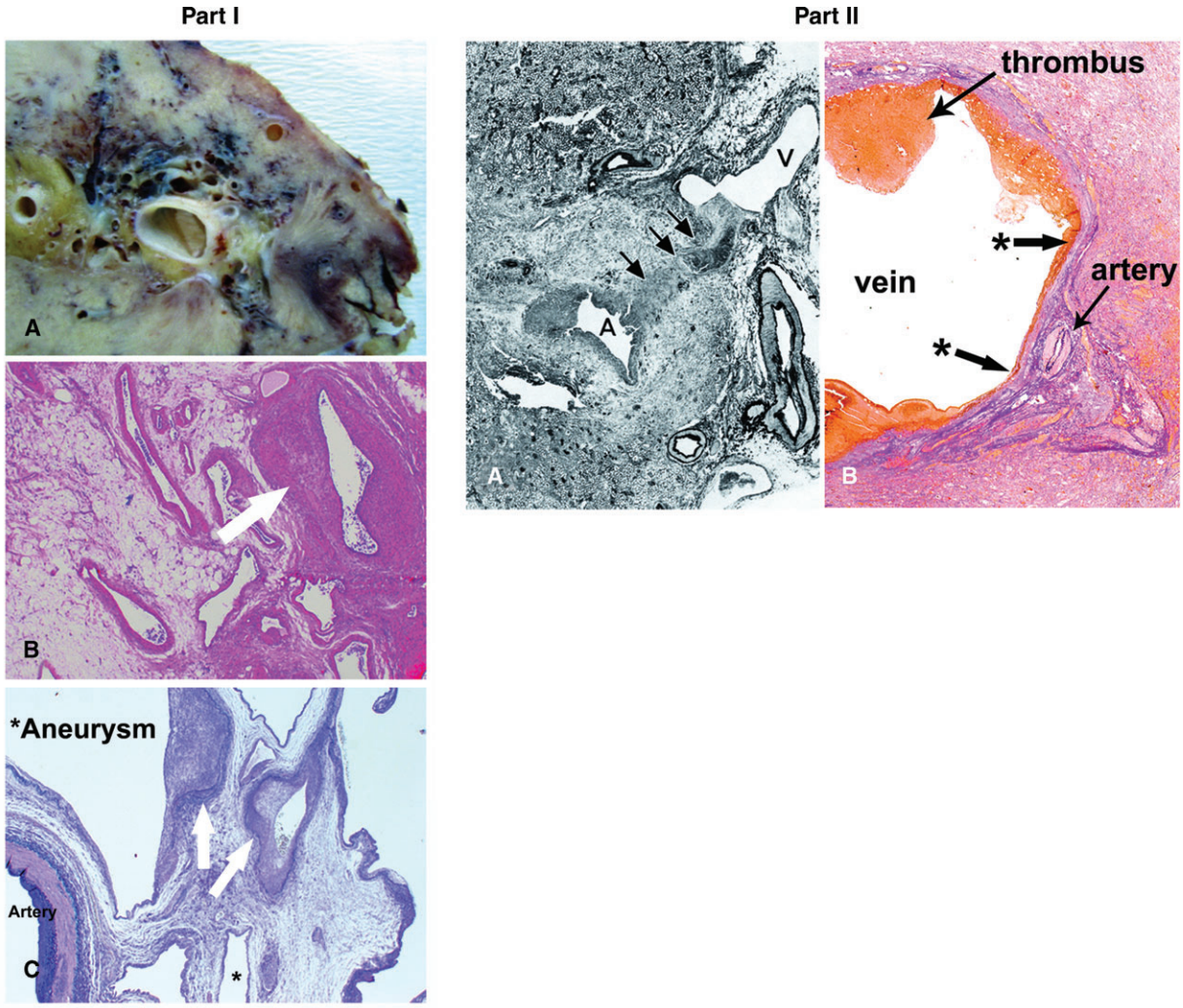

Fig. 2. Part I. Panel **A**: gross pathology showing the cirsoid type of AVM (marked red) in the caudal peripelvic region of the kidney. Panels **B** and **C**: classical cirsoid type AVM: numerous partly thin, partly thick walled vessels with the characteristics of arteries and degenerative damage of veins. A, HE stain, B, Elastica van Gieson stain. **Part II.** Traumatic AVF after a renal biopsy in a kidney allograft (**A**) and a native kidney (**B**). Panel A shows complete necrosis of the artery with communication via necrotic tissue with the dilated vein. Panel A was previously pictured (Zollinger H U and Mihatsch M J Renal pathology in biopsy, Springer Publisher Berlin Heidelberg New York, 1978). Panel B shows a false venous aneurysm, i.e. the wall of the aneurysm is formed by compressed renal and fibrous tissue with remnants of the venous wall (between arrows with asterisks). In a deeper sectioning plane of this area, a damaged artery was present as well. A and B, Elastica van Gieson stain.

1. Congenital renal cirsoid AVMs are extremely rare lesions, but may be present even in an allograft kidney.
2. Do not forget to bring your stethoscope! The most reliable indication of the presence of a significant renal AVF/AVM is a continuous bruit over the kidney's abdominal area. Advanced imaging techniques may help in the differential diagnosis.
3. Cirsoid AVMs have also been reported in Osler–Weber–Rendu syndrome and should stimulate genetic analysis.

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Conflict of interest statement. None declared.

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