Case Report

Partial renal vein thrombosis in a kidney transplant: management by streptokinase and heparin

Peggy W. G. du Bu" dhe Vereijken, Luuk B. Hilbrands and Jack F. M. Wetzes

Department of Medicine, Division of Nephrology, University Hospital Nijmegen, The Netherlands

Key words: infection; kidney transplantation; renal veins; thrombolytic therapy; thrombosis; streptokinase

Introduction

Acute renal vein thrombosis is a rare but dreaded late complication after renal transplantation. As a transplanted kidney usually has only one renal vein, occlusion of this vein mostly leads to graft loss. However, several recent reports have shown that local infusion of a thrombolytic agent can result in graft salvage [1–5].

We present a case in which a partial renal vein thrombosis was treated with selective intra-arterial administration of streptokinase, rescuing the kidney. The subsequent course was complicated by recurrent episodes of urosepsis.

Case report

A 38-year-old woman presented with fever and pain at the lateral margin of her renal transplant, positioned in the left iliac fossa. She had received a cadaveric renal allograft 11 months before, because of end-stage renal disease of unknown origin accompanied by hypertension. Her previous medical history was uneventful. The allograft had one artery, one vein and one ureter and the surgical procedure and postoperative course were uneventful. Immunosuppressive therapy consisted of cyclosporin and prednisone. Almost 4 months after the transplantation she was admitted because of a deep venous thrombosis of her left leg, extending from her calf up to the iliac vein, just below the entrance of the vein of her graft. The thrombosis was complicated by pulmonary embolism. She was treated with intravenous heparin for 7 days and received acenocoumarol orally.

At discharge her serum creatinine was 125 μmol/l. At that time a polycythemia was diagnosed. Her haematocrit had risen from 0.37 l/l at the time of transplantation to 0.50 l/l at the time of the deep venous thrombosis of her leg, and subsequently to 0.59 l/l at 7 months after the transplantation. For this reason a phlebotomy was performed once.

Now, 11 months after the kidney transplantation, she presented with cramping pain in the lower abdomen, a few hours later being most severe on the lateral margin of her renal allograft. She complained of general malaise, nausea and vomiting and had a low grade fever. Urine production had not changed. Six weeks before, acenocoumarol therapy was stopped because she had been treated for the deep venous thrombosis and pulmonary embolism for more than 6 months by then. She still used cyclosporin and prednisone as immunosuppressive therapy, as well as atenolol and amlodipine because of hypertension.

On physical examination we saw a moderately ill woman with a relatively low blood pressure of 106/64 mmHg, a pulse of 84 b.p.m. and a body temperature of 38.4 °C. Her body mass index of 29 kg/m² indicated mild obesity. Her graft was painful on examination. Further physical examination revealed no abnormalities. Her legs showed no signs of recurrent venous thrombosis. Laboratory investigation on admission showed a rise of serum creatinine from 125 μmol/l to 183 μmol/l, lactate dehydrogenase of 1265 U/l (normal limit 330 U/l), aspartate aminotransferase of 77 U/l (normal limit 25 U/l) and alanine aminotransferase of 55 U/l (normal limit 30 U/l). The leukocyte count was 25.7 × 10⁹/l, haemoglobin 18.8 g/dl, haematocrit 0.60 l/l and thrombocyte count 240 × 10⁹/l.

A renal vein thrombosis was suspected and an immediately performed Doppler ultrasonography showed neither an arterial nor a venous signal at the upper segment of the renal transplant. Subsequent arteriography showed unimpaired perfusion of the proximal arterial vasculature, but a segmental lack of perfusion in the upper part of the kidney, with a nearly absent venous phase. Arterial and venous perfusion of the lower segment of the allograft were normal, as well as the flow in the iliac vein (Figure 1). A partial
transplant renal vein thrombosis was diagnosed. In accordance with the publication of Chiu et al. we decided to treat this thrombosis with administration of streptokinase into the renal artery. We started approximately 15 h after the beginning of the patient’s complaints. A bolus of streptokinase of 100,000 IU was given in the first 30 min. The infusion was continued at a rate of 40,000 IU/h for the next 3 h, 30,000 IU/h for the following 4 h, and 25,000 IU/h as maintenance dose. Besides the thrombolytic therapy, cyclosporin was replaced by azathioprine because of the possible thrombogenic properties of cyclosporin. Medroxyprogesteronacetate was added to delay menstrual bleeding.

After 24 h the pain was less, but serum creatinine was still rising. Doppler ultrasonography of the kidney revealed no improvement in peripheral arterial perfusion. Although bleeding complications of the thrombolytic therapy had not occurred, we decided to stop the treatment with streptokinase because the risk of adverse events might outweigh the possible benefits. However, we continued anticoagulant therapy by means of heparin intravenously for 7 days and started acenocoumarol orally later on. Her recurrent polycythemia was treated with phlebotomies, performed twice on two consecutive days, removing 750 ml of blood and replacing it by 500 ml gelofusin and 250 ml normal saline. Follow-up of the perfusion of the renal allograft was performed daily by means of Doppler ultrasonography, which showed improvement from the third day. The rise in serum creatinine leveled off and a plateau of 504 μmol/l was reached on the fourth day.

On the sixth day of admission the patient developed an *E. coli* urosepsis, treated with ceftazidim and later cefazolin intravenously for a total of 14 days. Renal scintigraphy showed moderate perfusion, and irregular dispersion of radionuclide activity in the allograft kidney with several photopenic areas in the upper and lateral part. Her serum creatinine rose again to 917 μmol/l on the tenth day of admission. She once needed haemodialysis on day thirteen. After this episode her renal function gradually recovered, serum creatinine being 253 μmol/l on discharge, 24 days after admission.

Six days after discharge she again developed pain in the lower abdomen with high fever, chills and cloudy urine. On physical examination there were no abnormalities except for a relatively low blood pressure of

Fig. 1. Arteriography showing unimpaired perfusion of the proximal arterial vasculature, but a segmental lack of perfusion in the upper part of the kidney transplant, with a nearly absent venous phase. Arterial and venous perfusion of the lower segment of the allograft, as well as the flow in the iliac vein, is normal.
110/60 mm Hg and a rapid pulse, accompanying her body temperature of 39°C. Laboratory investigations showed a rise in serum creatinine up to 421 μmol/l, and 752 μmol/l 1 week later. On admission her haemoglobin was 10.0 g/dl and the leucocyte count 6.4 × 10⁷/l, with 16% bands in the differential count. Blood and urine cultures again showed a non-resistant E. coli. This time renal scintigraphy showed adequate vascularization with improvement of the irregularly dispersed activity of the radiopharmacon in the kidney.

A CT-scan of the abdomen revealed several small, partly confluent, hypodense areas dispersed in the renal transplant, without enhancement of the margins of these areas after intravenous administration of a small amount of contrast fluid. These findings were interpreted as necrotic areas, possibly with infection or abscess formation. She was treated with cefazolin intravenously for 10 days, and subsequently with ciprofloxacin orally for 6 weeks. Her serum creatinine, being 584 μmol/l on discharge has improved to 213 μmol/l 18 months after the partial renal vein thrombosis. A repeated CT scan of the abdomen shows a decrease in the size of the hypodense, confluent areas in the renal allograft.

Discussion

Renal vein thrombosis in the direct postoperative period of a kidney transplantation is reported in a frequency of up to 4.2% and is thought to occur mainly due to surgical complications [6–8]. In addition, associations with acute rejection, immune-complex mediated thrombosis, use of cyclosporin, as well as expression of the gene for plasminogen activator inhibitor 1 have been reported [8–11]. The preferential treatment is urgent surgical exploration, mostly however resulting in nephrectomy [7,8].

The occurrence of allograft renal vein thrombosis several months after the transplantation is rare. In this condition use of cyclosporin, membranous glomerulopathy either with or without nephrotic syndrome, polycythemia, and embolic occlusion of a caval filter with subsequent renal, iliac and femoral vein thrombosis have been suspected as predisposing factors [1,4,12]. In our patient use of cyclosporin, previous thrombosis, polycythemia and mild obesity could be identified as possible risk factors.

Successful treatment of late renal vein thrombosis by regional thrombolysis, using either streptokinase [1,5] or urokinase [2–4] has been reported several times before. As discussed by Marder et al., each thrombolytic agent has its own advantages, regarding efficacy, safety, cost and ease of administration [13]. Delivery of the thrombolytic agent directly to the site of thrombosis couples the use of a lower dosage compared to systemic treatment, to a high rate of efficacy.

In cardiology the application of local, intracoronary thrombolysis seemed to be slightly more effective compared to intravenous therapy. However, because of the required specialized cardiac catheterization facilities and the delay in the initiation of thrombolytic therapy, intravenous therapy is generally preferred in acute myocardial infarction [14]. Furthermore, regional therapy does not prevent systemic effects with subsequent haemorrhagic complications [13]. In renal vein thrombosis however, angiography is mostly already performed for diagnostic purposes and regional therapy is therefore instituted more easily.

The site of administration of the thrombolytic agent in case of renal transplant vein thrombosis differs in literature: at the arterial site [1], at the venous site [2,4,5] or combined arterially and venously [3]. In this small number of observations catheter location did not seem to affect the success rate. In accordance with the report of Chiu we chose to treat our patient with local intra-arterial administration of streptokinase.

In contrast with others [1–5], we did not continue the thrombolytic agent for more than 24 h, because of lack of evidence of improvement in our patient in this period. Other authors concluded improvement from either the course of clinical parameters like relief of pain, decrease of graft swelling, or increase in graft function, or from improvement on early repeated radiologic investigations [1–4]. Remarkably, radiologic recovery mostly preceded clinical or biochemical improvement.

Like the other authors, we had no serious bleeding complication. However, our patient suffered from necrosis of kidney tissue, as indicated by the elevated serum levels of tissue enzymes. Probably this predisposed her to the recurrent infectious complications she went through. Despite stabilization of her kidney function after the thrombolytic therapy, these recurrent infections with hypotension led to deterioration of her kidney function twice, probably partly due to acute tubular necrosis. Although this patient never had urinary tract infections before, it can be questioned whether in case of necrotic kidney tissue prophylactic antibiotic therapy would be wise.

In summary, we report the successful treatment with intra-arterial administration of streptokinase of a (partial) renal vein thrombosis, occurring late after kidney transplantation. Unfortunately, our patient suffered from serious infectious complications, probably originating from necrotic areas in the graft. Adequate therapy eventually resulted in a reduced, but stable allograft function.

References


Received for publication: 1.10.97
Accepted: 8.10.97