Successful local arterial urokinase infusion to reverse late postoperative venous thrombosis of a renal graft

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Introduction

Graft renal vein thrombosis is fortunately rare, ranging between 1 and 4% of recipients [1,2]. This event usually occurs in the early postoperative period and is associated with surgical complications, acute vascular rejection, and probably some immunosuppressive regimens, particularly OKT3, although the role of cyclosporin remains controversial [3,4]. Unfortunately, acute thrombosis generally results in permanent graft loss, unless thrombectomy and postoperative anticoagulation are promptly started.

The occurrence of allograft vein thrombosis several months after kidney transplantation is infrequent. When the diagnosis is made early, streptokinase infusion can result in successful thrombolysis [5,6].

We present a case in which a partial renal vein thrombosis was successfully treated by combined intraarterial and venous infusion of urokinase.

Case

A 61-year-old woman was admitted 50 months after a cadaver renal transplant into the left iliac fossa, to evaluate swelling in her left thigh. Her primary renal disease was adult dominant polycystic kidney disease (ADPKD). Immunosuppressive therapy consisted of cyclosporin, prednisone, and azathioprine. The early post-transplant course had been complicated by an episode of acute rejection without late complications (baseline creatinine was 1.5 mg/dl). On admission, the patient showed induration of the left thigh that extended to the inguinal region. The renal allograft was somewhat tender and painful on examination. Laboratory investigation showed a slight increase in serum creatinine (1.8 mg/dl) and absence of proteinuria. Platelet count and function, prothrombin time, partial thromboplastin time, thrombin time and antithrombin III levels were all normal. The functional test for the determination of activated protein C resistance, performed with factor V-depleted plasma, was negative. The anticoagulant lupus factor was also negative. Protein C or protein S abnormalities were not investigated. A Doppler study of the iliac and allograft veins revealed thrombosis of the left iliac venous system. Emergency iliac and caval computed tomography (angio-CT) demonstrated an occlusive thrombus extending from the proximal left common femoral vein to the distal iliac vein with partial thrombosis of the renal allograft vein (Figure 1A). In addition the CT study showed a marked reduction of the lumen of the left common iliac vein because it was pushed towards the vertebra (Figure 2) by the left common iliac artery. After the placement of a temporary vena cava filter because of concerns of possible clot migration, i.v. infusion of heparin (1000 U/h) was started. At the same time, a catheter was positioned within the thrombus via the contralateral femoral vein. Urokinase infusion was begun at a rate of 75,000 U/h. Forty-eight hours after thrombolytic treatment was initiated, selective renal allograft arteriography did not show significant changes in kidney perfusion. The venous phase was virtually absent. Using the catheter that had been placed within the renal artery, local urokinase infusion (50,000 U/h) was started and the doses of heparin and the transcatheter regional venous urokinase were reduced to 500 U/h and 50,000 U/h respectively.
continue thrombolytic therapy and to remove both catheters. Venography showed partial recanalization of both left iliac and renal allograft veins. During this period the renal function deteriorated slightly (serum creatinine 2.5 mg/dl) without significant reduction of diuresis. Seven days later the patient was discharged, and subcutaneous low PM heparin (4000 U daily) and oral acenocoumarol were prescribed.

After one month, heparin therapy was discontinued and the patient began to walk again without symptoms. Thirty days later Doppler ultrasonography showed patency of the transplant renal artery and vein and of the left iliac vein, whereas remnants of the thrombus in the left femoral vein were present. Two weeks later angio-CT confirmed the total patency of the previously thrombosed veins (Figure 1B) and a slight extension of renal artery lumen owing to the slit of the wall.

**Discussion**

Late post-operative renal vein thrombosis in kidney transplant patients is rare, particularly in the absence of inciting factors, e.g. proteinuria, cyclosporin therapy, membranous nephropathy either with or without nephrotic syndrome, and polycythaemia [7,8]. In our patient the only conceivable inciting factors are immunosuppressive therapy and the stenosis of the left iliac vein. Despite reports that cyclosporin causes platelet activation and hyperaggregability, the relationship to late renal allograft vein thrombosis remains
Urokinase for venous thrombosis of renal graft

2227

controversial [4]. In our view, reduced blood flow in the left iliac vein, which had been pushed against the vertebra, potentially in conjunction with a rise in blood viscosity during an episode of hypovolaemia, might have favoured thrombosis of the femoral–iliac venous segment with involvement of the vein of the allograft.

Although surgery remains the treatment of choice for acute allograft renal vein thrombosis, the risk of irreversible damage to the graft and the difficulty of finding a new vascular anastomosis prompted us to use thrombolytic agents.

Different approaches have been reported for the administration of thrombolytic drugs: arterial [5], venous [6,9], or combined arterial and venous administration [10]. After 48 h of urokinase infusion via a catheter placed directly into the thrombus, we administered the thrombolytic agent via the renal artery. Although treatment had to be terminated prematurely because of complications, Doppler ultrasonography and angio-CT performed 3 months later showed almost complete patency of the left iliac and femoral veins with the recanalization of the renal allograft vein. We hypothesize that local arterial infusion of urokinase prevented backward extension of the thrombotic process with complete blockade of the renal vein. Early administration of systemic heparin sodium to maintain the partial thromboplastin time between 80 and 100 s and late (at the time of discharge) therapy with oral acenocoumarol may be necessary to allow endogenous lysis to self-repair the lesion.

Because the selective intra-arterial administration of urokinase is not a treatment without complications, i.e. the slit of the arterial wall in our patient, we believe that the thrombolytic agent infusion should not continue for more than 24–48 h.

References


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