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Case Report

Spontaneous bilateral kidney rupture during autologous stem cell transplantation in a patient affected by amyloidosis

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Abstract

Kidney spontaneous rupture is not a recognized complication neither for amyloidosis nor of autologous stem cell transplantation (ASCT). A 46-year-old white woman, affected by nephrotic syndrome, was diagnosed as AL amyloidosis by renal biopsy. We report the singular case of a bilateral spontaneous kidney rupture during ASCT for AL with renal rescue.

Keywords: amyloidosis; ASCT; kidney rupture; spontaneous rupture

Background

Immunoglobulin light-chain amyloidosis (AL) is a rare systemic disease characterized by progressive tissue and organ extracellular fibrillar deposition [1]. AL frequently presents with proteinuria, nephrotic syndrome and progressive renal failure. Kidney spontaneous rupture is not a recognized complication in amyloidosis or autologous stem cell transplantation (ASCT). We report the singular case of a bilateral spontaneous kidney rupture during ASCT for AL with renal rescue.

Case report

A 46-year-old Caucasian female, affected by nephrotic syndrome, was diagnosed with AL amyloidosis by renal biopsy (Figure 1), performed on the left kidney (maximal longitudinal renal axes 10.9 cm), in December 2006, with an IgG-λ as monoclonal protein. The data of laboratory examination at the time of diagnosis are listed in Table 1. Her past clinical history was unremarkable.

In July 2007, she was considered suitable for ASCT and started the stem-cell mobilization with G-CSF 10 g/kg/day, yielding 2.081×10^9NC/kg (8.323×10^6CD34+ cells/kg).

In September 2007, she was admitted to the Stem Cell Transplant Unit for ASCT. Laboratory parameters showed serum creatinine (sCr), serum cystatin C (sCys C), urea, haemoglobin (Hb) and platelets (Plt) levels in the normal ranges, Bence Jones proteinuria positive, 24-h proteinuria in nephrotic range (4.5 g), serum albumin level 2.1 g/dL, and white blood cells (WBC) 4050/μL (Table 1).

Just before transplantation, she was submitted to a conditioning regimen consisting—as protocol—of melphalan (200 mg/m^2, total dosage 340 mg) administered at Day 3 before transplant. One day before ASCT, the patient presented a sudden onset of flank abdominal pain with symptoms and signs of a severe haemorrhagic shock. An urgent computed tomography (CT) scan of the abdomen and pelvis showed a severe right renal capsular bleeding with a voluminous haematoma (20 cm) (Figure 2a). She underwent an urgent right nephrectomy. The pathological findings consisted of an ochre normal-dimension kidney (10.5 × 7 × 4.5 cm) with large haemorrhagic lesions in medium and apical regions and diffuse subcapsular haemorrhages, with vascular aspect of hilar venous thrombosis. Histologically, there were widespread amyloid deposits in the interstitium and vessel walls with a high intensive Congo red-stained positivity; no findings were found for vasculitis or for neoplastic.

Two days after surgical intervention, the patient underwent ASCT, and antimicrobial prophylaxis was started. However, she developed a sepsis due to pneumonia, in response to broad-spectrum antimicrobial therapy. During this time, renal function was preserved.

At Day +17 after ASCT, the patient presented a second haemorrhagic shock with left abdominal pain and anuria. At the time, coagulation times were within the normal range, while hyperfibrinogenaemia (fibrinogen 533 mg/dL) and a low Plt count were present (platelets 14 000/μL). A CT abdomen showed a left renal laceration with a vast haemorrhage (Figure 2b).

Due to the high bleeding risk, surgical treatment was considered inappropriate, and the haemorrhage was self-tamponed. Because of the onset of acute renal failure, daily renal replacement therapy (RRT) in haemodiafiltration modality was started for a total of 10 sessions. Diuresis gradually restarted with large doses of furosemide, and

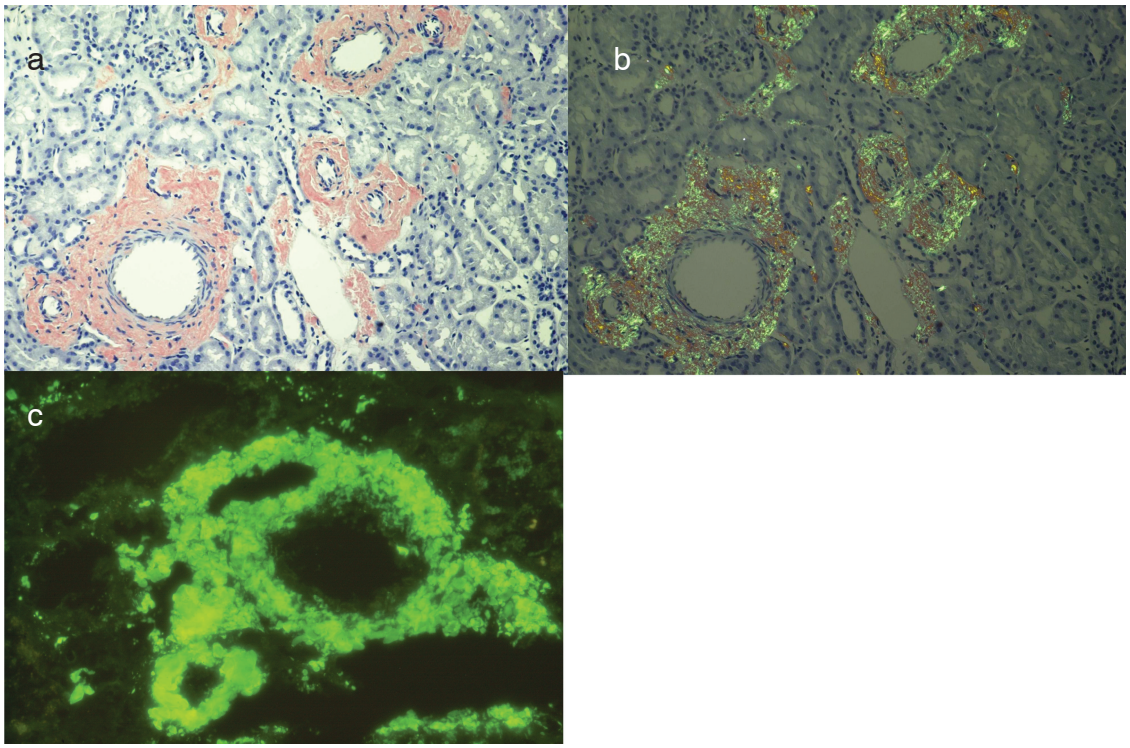

Fig. 1. A 46-year-old Caucasian female, affected by nephrotic syndrome, was diagnosed as AL amyloidosis by renal biopsy: (a) amyloid deposition (Congo Red staining) viewing by standard light microscopy and (b) polarized light microscopy; apple green birefringence is elicited on polarization (100×). (c) Immunofluorescence microscopy for lambda light chains of the same specimen (frozen tissue) (100×).

Table 1. Data of laboratory examinations at December 2006 (diagnosis of amyloidosis) and July 2007 (admission for ASCT)

	Normal value	December 2006 Value	July 2007 Value	Units
Hb	12–16	12.9	11.4	g/dL
WBC	4.5–10	6.150	4.050	10^3/μL
Plt	150–450	162	176	10^3/μL
Serum total protein	6.60–8.0	4.9	4.6	g/dL
Serum albumin	3.4–4.8	2.2	2.1	g/dL
24-h proteinuria	0.20–150	5020	4512	mg
24-h albuminuria	0–30	4548	3918	mg
sCr	0.4–1.1	0.63	0.85	mg/dL
Urea	10–50	37	41	mg/dL
sCys C	0.53–0.95	0.79	0.85	mg/L
λ Serum free light chain	0.15–4.53		7.25	mg/dL
λ Urine free light chain	0–0.9		11.1	mg/dL
λ Serum total light chain	90–120		318	mg/dL
λ Urine total light chain	<0.45		27.7	mg/dL

sCr, serum creatinine; sCys C, serum cystatin C.

RRT was stopped. However, 48 h after the last dialysis session the patient presented a septic shock status with *Aspergillus* pneumonia, plus the onset of acute respiratory distress syndrome and anuria. She was submitted to non-invasive respiratory support and aggressive antifungal therapy; cardiocirculatory system was maintained by vasoactive therapy, and new sessions of CRRT (in high-volume haemofiltration modality) were started. Net ultrafiltration rate was adjusted in each session according to the body weight and the better haemodynamic compliance. Blood pressure and renal and respiratory functions gradually improved, and CRRT was stopped.

At Day +36 post-transplant, the patient was discharged with preserved diuresis, and laboratory tests for renal function were as follows: sCr 2 mg/dL, urea 69 mg/dL, 24-h proteinuria 2.2 g, Hb 13.4 g/dL, Plt 47 000/μL, WBC 3410/μL, and serum λ free light chain 9.13 mg/dL in urine. The follow-up at 24 months showed sCr 1.48 mg/dL, urea 76 mg/dL, 24-h proteinuria 196.5 mg, absence of Bence Jones proteinuria and serum λ free light chain 2.03 mg/dL.

Discussion

The deposition of immunoglobulin light-chain fragments damages several organs causing their progressive failure and death. The kidney is involved in 40% to 73% of patients [2,3–5], and proteinuria is by far the most common manifestation [1]. If on dialysis, these patients have a poor survival rate. Although rare, spontaneous organ ruptures occur [6–8], and seem to be due to the loss of vascular integrity leading to spontaneous bleeding and subsequent rupture [9].

Spontaneous kidney rupture is not reported as a complication in amyloidosis or ASCT. Spontaneous subcapsular or perinephric bleeding of the kidney is described as a rare complication in renal cell carcinoma, angiomyolipoma and vascular diseases such as periarteritis nodosa; moreover, rarely are spontaneous renal haematomas reported in chronic haemodialysed patients, particularly in those who have acquired renal cystic disease [10].

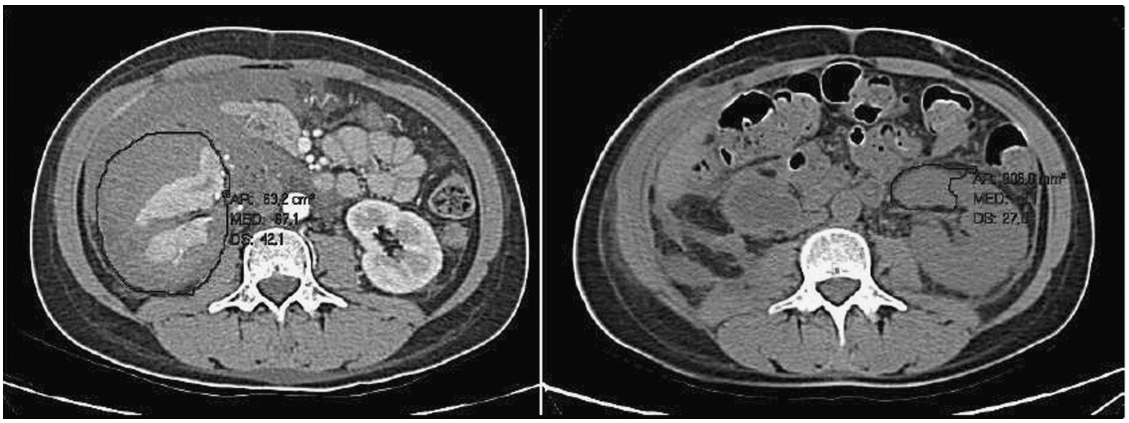

Fig. 2. a. CT scan of the abdomen and pelvis showed a severe right renal capsular bleeding with a voluminous haematoma (20 cm). **b**. CT abdomen showed a left renal laceration with a vast haemorrhage.

In our patient, the CT scans performed to evaluate the eligibility for ASCT and then again to explain the rupture of kidneys did not show neoplastic lesions; moreover, the immunological screening and the renal biopsy showed amyloidosis and excluded any kind of vasculitis or other immunological disorders. Therefore, it is possible that the spontaneous renal rupture could be due to amyloidosis or to ASCT.

In the presented case, the association of two kidney ruptures is singular.

In the first event, the nephrectomized right kidney showed only hilar venous thrombosis. Renal vein thrombosis could be explained by nephrotic syndrome, a well-recognized condition associated with a hypercoagulability state. In fact, despite the underlying causes of the hypercoagulable state in patients with nephrotic syndrome that are not well understood, a variety of haemostatic abnormalities have been described, including decreased levels of antithrombin and plasminogen (due to urinary losses), increased platelet activation, hyperfibrinogenaemia, inhibition of plasminogen activation, and the presence of high-molecular-weight fibrinogen moieties in the circulation [11]. Amyloidosis, however, is characterized by an increased bleeding risk, but Adamu *et al.* [12] suggests many putative factors implicated in the pathogenesis of thrombosis during paraproteinaemias. Nevertheless, renal vein thrombosis is not recognized as a possible cause of renal rupture; so with regard to the right kidney, we could speculate a spontaneous rupture secondary to vessel amyloidosis leading to venous thrombosis. A second hypothesis, is that the hilar venous thrombosis, due to nephrotic syndrome, was the possible cause of renal rupture.

In the second episode of spontaneous renal rupture (in which there was no nephrectomy), we can suggest other causes. First, a renal vein thrombosis cannot be excluded due to the same procoagulant mechanisms suggested in the first rupture; nevertheless, after a few days, diuresis restarted, so we must consider a spontaneous resolution of thrombosis after renal rupture; moreover, the platelet count was very low because of the bone marrow suppression as a result of chemotherapy, and in this scenario, it is difficult to evoke a thrombotic cause. Second, before the second kidney rupture, the patient was submitted to ASCT and therefore to granulocyte colony-stimulating factor (G-CSF). In the literature, organ spontaneous rupture secondary to ASCT is often related to an increase in organ size as a result of extramedullary haematopoiesis [1]. The kidney is not a haematopoietic organ, and in the literature, there are extremely rare reports [13–15] about the occurrence of a renal extramedullary haematopoiesis. In fact, it usually occurs in the reticuloendothelial system, involving the liver, spleen and lymph nodes, in association with some haematological disorders (in particular myelofibrosis), as a response to erythropoiesis failure in bone marrow. In our patient, we did not report any failure of bone marrow erythropoiesis before chemotherapy, nor did renal histological findings (for the right nephrectomized kidney or the left kidney) support this rare possibility. Third, a spontaneous renal rupture attributed to acute tubular necrosis could be considered, but in the literature, this complication is related only to allograft kidneys [16]. Finally, without any histological support, we were not able to determine the definitive cause of the second renal rupture, but a loss of vascular integrity leading to spontaneous bleeding and subsequent rupture is suggestive.

In any case, suggested therapeutic approaches in kidney rupture are contrasting. Some authors advocate radical nephrectomy due to the possibility of a small clinically unapparent renal cell carcinoma. In contrast, others have advised a conservative approach when diagnostic studies fail to demonstrate a significant pathology and clinical signs are stabilized [17]. Nevertheless, in many cases, the severe haemorrhage necessitates surgical exploration.

In our patient, the first haemorrhagic event required nephrectomy to control the haemodynamic status. In the second event, a conservative approach was chosen because of the single-kidney status and the high bleeding risk. This strategy allows the patient to maintain a residual renal function without the need for dialysis.

In conclusion, spontaneous renal rupture is a medical and surgical emergency which needs a rapid diagnosis and prompt treatment, and AL amyloidosis should be included in the differential diagnosis.

Conflict of interest statement. All the authors have any financial interests or arrangements with a company whose product was used in this study or is referred to in a manuscript, any financial interests of arrangement with a competing company, any direct payment from any source to an author(s) for the purpose of writing the manuscript, and any other financial connections, direct or indirect, or other situations that might raise the question of bias in the work reported or the conclusions, implications or opinions stated—including pertinent commercial or other sources of funding for the individual author(s) or for the associated department(s) or organization(s), personal relationships, or direct academic competition.

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