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Case Report

Urinary tract obstruction due to extramedullary plasmacytoma: report of two cases

Naïke Bigé[1], Bertrand Arnulf[2], Aurelie Hummel[1], Eric De Keyser[3], Virginie Royal[4], A. Buzyn[5] and Fadi Fakhouri[1]

[1]Nephrology Department, Université Paris Descartes, AP-HP, Necker Hospital, [2]Haematology Department, Saint Louis Hospital, [3]Radiology Department, [4]Pathology Department and [5]Haematology Department, Université Paris Descartes, AP-HP, Necker Hospital, Paris

Abstract

Extramedullary plasmacytomas (EMP) rarely occur during the course of multiple myeloma (MM). Most frequent reported sites are superior respiratory airways, pleura, lung, lymph nodes, skin, subcutaneous and soft tissues, testicles and liver. EMP involving the urinary tract are very uncommon and have been ill-described in the literature. We report two unusual cases of obstructive urinary tract EMP revealing a relapse of MM after allogeneic stem cell transplantation. Clinicians must be aware that EMP may be responsible for urinary tract obstruction even in the absence of medullary progression of MM.

Keywords: bladder; multiple myeloma; plasmacytoma; urinary tract

Introduction

Extramedullary plasmacytoma (EMP) rarely occurs during the course of multiple myeloma (MM). The incidence rate of extramedullary localizations in MM is around 4.6%, half at diagnosis and half during the course of the disease [1]. EMP seem to be more frequent during MM relapses after autologous and allogeneic stem cell transplantation (autoSCT and alloSCT) with an incidence ranging from 7 to 14% and 14 to 21%, respectively [2–5] Surprisingly, extramedullary relapses often occur without evidence of medullary progression of the disease [3]. Most frequent reported sites are upper respiratory airways, pleura, lung, lymph nodes, skin, subcutaneous and soft tissues, testicles and liver. Urinary tract involvement is very uncommon and has been ill-described in the literature [6–10].

Correspondence and offprint requests to: Fadi Fakhouri, Molecular Genetics and Rheumatology Section, Faculty of Medicine, Imperial College, Hammersmith Campus, London, UK. E-mail: fadi.fakhouri@nck.aphp.fr

We report two unusual cases of obstructive urinary tract EMP revealing a relapse of MM after alloSCT.

Cases

Case 1

A 62-year-old man with a history of ischaemic cardiopathy was diagnosed with stage III IgG kappa MM in 2002. He was first treated with three courses of vincristine adriamycine and dexamethasone (VAD)-chemotherapy, high-dose cyclosphamide and melphalan chemotherapy followed by autoSCT. He achieved partial remission as paraprotein level decreased from 30 to 15 g/L.

In January 2004, he presented a first MM relapse with an increase in IgGK level (30 g/L) without other sign of disease progression. He was treated with four courses of dexamethasone–thalidomide combination. In May 2004, he underwent non-myeloablative alloSCT with his brother as donor. Conditioning treatment included total body irradiation (TBI) and fludarabin. He achieved complete remission. Despite prophylaxis using ciclosporin and mycophenolate mofetil, he developed coetaneous and digestive GVHD controlled with corticosteroids.

In November 2004, a second relapse occurred. Treatment with bortezomib and dexamethasone led to partial remission with persisting monoclonal component around 15 g/L. Subsequently, a treatment with four courses of bortezomib–dexamethasone was started and was followed by donor lymphocytes injection. Monoclonal component dropped to 3.1 g/L.

In September 2006, the patient presented with acute renal failure and Laboratory tests showed serum creatinine (SCr) 233 μmol/L (glomerular filtration rate estimated using the MDRD formula at 26 mL/min/1.73 m^2) (versus 115 μmol/L 3 months earlier), kalaemia 4.4 mmol/L, serum HCO_3 27 mmol/L, calcaemia 2.27 mmol/L, haemoglobin 10.8 g/dL, proteinuria 0.7 g/day. There was no evidence of MM progression. Monoclonal component was stable in plasma (3.5 g/L) and lower than 0.2 g/day in

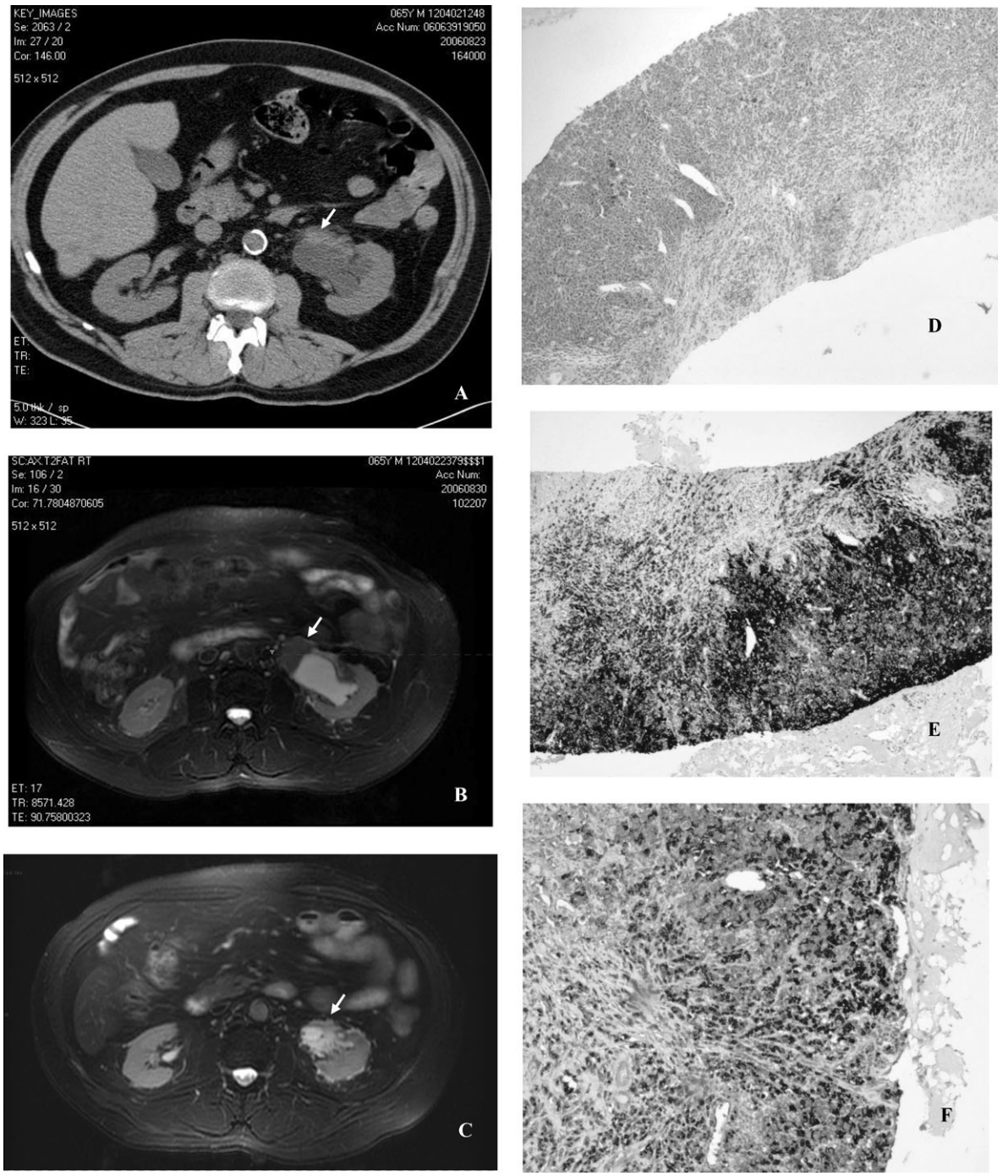

Fig. 1. Patient 1 with a history of IgG kappa multiple myeloma presented with acute renal insufficiency. Non-enhanced CT-scan (panel **A**) and MRI (panel **B**; Té weighted) showed a retroperitoneal mass (arrow on CT scan and MRI) infiltrating the left proximal ureter and the renal pelvis. Following treatment, the mass regressed and only mild residual infiltration of the left proximal ureter (arrow) was noted on a control MRI performed 2 years later (panel **C**). A biopsy of the mass revealed the presence of plasma cell proliferation (panel **D**, light microscopy, haematoxylin phloxine saffron staining, ×50) that stained positive for CD 138 (panel **E**) and kappa light chain (panel **F**).

urine. Ultrasonography showed dilatation of the left renal pelvis and proximal ureter. CT scan and abdominal MRI (Figure 1) revealed an 8 cm obstructive retroperitoneal tumour infiltrating the left ureter and renal pelvis and responsible for ureterohydronephrosis. A transparietal biopsy of the tumour was performed. Pathology examination showed a proliferation of large plasmablastic cells that stained positive for CD138 and kappa light chains and negative for lambda light chains and CD20 (Figure 1). Diagnosis of ureteral EMP was made. A double-J ureteral stent was inserted and treatment with lenalinomide and dexamethasone was started. One month after the start of chemotherapy, SCr

had decreased to 150 μmol/L. Control MRI showed the regression of EMP with mild residual periureteral infiltration (Figure 1).

At last follow-up in August 2008, the patient is still in partial remission. SCr is 150 μmol/L with a monoclonal component is around 1 g/L. Control MRI showed stability of the left ureteral infiltration without reappearance of any EMP.

Case 2

A 31-year-old man without any medical history was diagnosed with IgA lambda (23.4 g/L) stage I MM in November 1993.

Ten years later, in February 2003, he presented with a retrosternal EMP, lysis of the lower extremity of the sternum, mediastinal adenopathies and bilateral pleural effusion. Paraprotein level had risen to 30 g/L. He received three courses of VAD-chemotherapy followed by high-dose cyclophosphamide and melphalan and autoSCT. He achieved partial remission: all EMP regressed and paraprotein level dropped to 9.5 g/L. On March 2004, maintenance therapy with thalidomide and dexamethasone was introduced.

On November 2004, he presented a first relapse with sacral EMP and increased paraprotein level (14.4 g/L). Treatment combined local radiotherapy and VAD-chemotherapy followed in June 2005 by a second autoSCT. However, paraprotein level persisted around 9 g/L.

On October 2005, paraprotein level increased to 15.9 g/L. He underwent alloSCT with non-myeloablative conditioning therapy (fludarabin, cyclophosphamide and TBI). Ciclosporine and mycophenolate mofetil were used to prevent graft-versus host disease (GHVD). One month later, relapse of sacral EMP was diagnosed. Three courses of bortezomib and dexamethasone regimen and local radiotherapy were performed.

On August 2006, the patient started complaining of dysuria and hypogastric pain. Subsequently, he presented with acute urinary retention. Laboratory tests showed SCr 100 μmol/L (GFR estimated using the MDRD formula) at (versus 70 μmol/L 2 months earlier) calcaemia 2.31 mmol/L, lactate dehydrogenase (LDH) level 1266 IU/L (normal <600 IU/L), haemoglobin 12.2 day/dL, platelets 168000/mm^3, leucocytes 7500/mm^3, monoclonal paraprotein level at 23.7 g/L on electrophoresis with the absence of monoclonal component in urine. Abdominal CT-scan (Figure 2) and MRI revealed thickening of the bladder wall and a tumour (5 × 9 cm) infiltrating both ureters and psoas muscles and leading to bilateral dilatation of pyelocaliceal cavities.

Urethral catheter was inserted and SCr decreased to 75 μmol/L. A cystoscopy and biopsies of the bladder tumour were performed. Histological examination showed monotypic plasma cell proliferation invading the chorion and detrusor and staining positive for CD138 and CD79, and negative for CD20, CD30 and KL1. The diagnosis of bladder EMP was made.

The patient received three courses of chemotherapy consisting of bortezomib, adriamycin and dexamethasone. Urethral catheter was removed rapidly. Monoclonal component disappeared. Subsequently, he received maintenance therapy with three courses of lenalinomide and dexamethasone. At last follow-up in April 2008, the patient was still in complete remission.

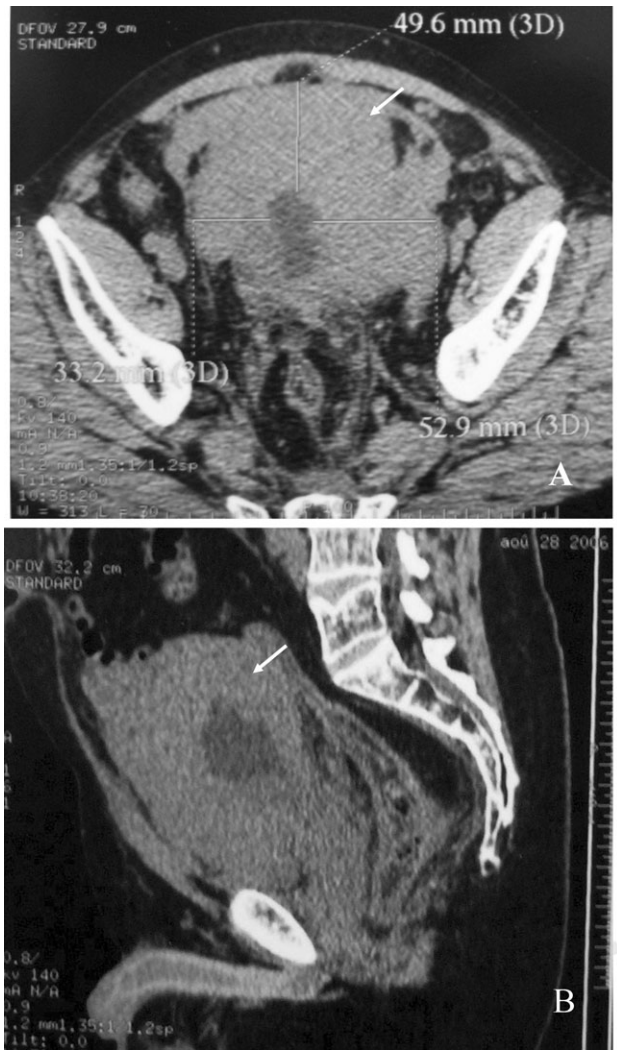

Fig. 2. Patient 2 with a history of IgA lambda multiple myeloma presented with acute urine retention. CT-scan (panel **A** and **B**) showed the presence of a mass (arrows) massively infiltrating the bladder.

Discussion

Renal involvement is frequent in the setting of MM. Renal failure is observed in 20–40% of newly diagnosed cases of MM [11] and is mainly due to myeloma cast nephropathy [12]. Amyloidosis, light chain deposit disease (LCDD) and Fanconi syndrome occur less frequently in MM patients. Moreover, these disorders are not exclusive and might coexist in the same patient.

EMP rarely occurs in the urinary tract during the course of MM. Only 19 cases of bladder plasmacytoma have been reported in the literature including one case in a renal transplant recipient. Among these, six were solitary plasmacytomas and six were associated with MM. Status for MM was unknown in seven patients [7–10]. None of these

patients presented with bladder obstruction. EMP occurring in the renal parenchyma are even rarer with only seven cases described in the literature [8].

To the best of our knowledge, we report the first two cases of ureteral and bladder obstructive EMP arising during the course of MM. In both cases, EMP occurred after alloSCT in patients experiencing GVHD. Indeed, EMP tend to be more frequent after SCT, particularly in alloSCT patients experiencing GVHD. The occurrence of GVHD usually requires intense immunosuppression that leads to the loss of the graft versus myeloma (GVM) effect and to the persistence of plasma cells sanctuary sites and/or of particularly resistant plasma cell clone. Reduced-intensity conditioning regimen may also increase the risk of EMP [3,5].

The occurrence of EMP relapse after HSCT does not impact patients overall and progression-free survival compared to the occurrence of MM medullary relapse. Patients' prognosis after MM relapse following HSCT is poor with a median survival of 25 and 40 months in the allo-HSCT and the auto-HSCT groups, respectively, regardless of the relapse site [4]. However, both patients presented herein had a rapid and sustained complete response to chemotherapy with no MM relapse after 24 and 20 months' follow-up. No surgical resection of the EMP had been necessary.

In conclusion, the occurrence of EMP in the urinary tract during the course of MM is rare. However, clinicians must be aware that EMP may be responsible for acute obstruction of urinary tract even in the absence of medullary progression of the disease. Chemotherapy may prove efficient in inducing remission and regression of the tumour without surgical resection.

Conflict of interest statement. None declared.

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