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Spontaneous bilateral renal aneurysm rupture secondary to Polyarteritis Nodosa in a patient with chronic myelomonocytic leukaemia: A case report study

Christiana Georgiou (MBBS)^{a,*}, Miltiadis Krokidis (MD PhD)^b, Natasha Elworthy (FRCA)^a, Stavros Dimopoulos (MD PhD)^a

^a John Farman ICU, Cambridge University Hospitals NHS Foundation Trust, Cambridge, United Kingdom

^b Department of Radiology, Cambridge University Hospitals NHS Foundation Trust, Cambridge, United Kingdom

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ABSTRACT

INTRODUCTION: Polyarteritis Nodosa (PAN) is a systemic vasculitis affecting small and medium size arteries resulting in microaneurysms formation. Bilateral renal aneurysm rupture is a rare and life threatening complication. Although uncommon, PAN has been associated with chronic myelomonocytic leukaemia (CMML).

PRESENTATION OF CASE: We report a case of a 77-year-old female with a known CMML, presented to hospital with abdominal pain. Left initially and right renal microaneurysm ruptures were shown in CT scan within one-week interval. Microaneurysms were treated with embolization with microcoils. A diagnosis of PAN was made and treated with successful outcome with steroids, cyclophosphamide.

CONCLUSION: Spontaneous bilateral renal haemorrhage as the initial manifestation of PAN in association with CMML is a rare condition and it can be associated in delays in diagnosis and treatment. Clinicians should be aware of this possible complication in their daily clinical practice.

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1. Introduction

PAN is a systemic vasculitis affecting small and medium size arteries causing microaneurysm formation. This can be complicated with microaneurysm rupture, haemorrhage, thrombosis and consequently organ ischaemia. There is a rare association between chronic myelo-monocytic leukaemia (CMML) and PAN; the mechanism of which is still unknown. Bilateral renal haemorrhage as a first presentation and complication of PAN is rare. The management of this complication is poor, often leading to permanent renal impairment, nephrectomies and even death. Here, we present a rare case of bilateral renal artery aneurysm rupture in a patient with PAN and CMML.

2. Case presentation

A 77-year-old lady with a background medical history of an uncomplicated and untreated type 1 chronic myelo-monocytic leukaemia (CMML-1), Platelet-Derived Growth Factor Receptor Beta (PD GFRbeta) gene translocation and systemic mastocytosis, presented at the Emergency Department of our Hospital after a staging CT scan, with generalised abdominal pain, unresponsive to common analgesic treatment. Patient also had a significant weight loss of 7 kg, reduced appetite, generalized weakness and diffused arthralgia during the last 3 months. She had no history of trauma.

On admission, she was afebrile with normal peripheral oxygen saturation (SpO₂ = 97%), mild arterial hypertension (systolic and diastolic arterial blood pressure of 160/95 mmHg) and tachycardia (100 beats per min). Cardiovascular examination was unremarkable with rhythmic regular heart sounds (S1, S2), no additional sounds/murmurs and palpable symmetrical bilateral pulses in upper and lower limbs. Respiratory examination showed good bilateral and symmetrical chest air entry. From her abdominal examination there was mild abdominal distension, diffuse tenderness at deep palpation, with hypoactive bowel sounds and negative Murphy, McBurney and Blumberg signs. Urine microscopic haematuria was present.

Laboratory tests showed an increased white blood cell count of $90 \times 10^9/L$ with $65.75 \times 10^9/L$ neutrophils, $7 \times 10^9/L$ lymphocytes

Abbreviations: PAN, Polyarteritis Nodosa; CMML, chronic myelo-monocytic leukaemia; CT scan, computerised tomography scan.

* Corresponding author at: John Farman ICU, Cambridge University Hospitals NHS Foundation Trust, Cambridge, United Kingdom.

E-mail addresses: christiana.georgiou@doctors.org.uk, christiana_geo@hotmail.com (C. Georgiou), mkrokidis@hotmail.com (M. Krokidis), drnelworthy@hotmail.co.uk (N. Elworthy), stdimop@gmail.com (S. Dimopoulos).

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Fig. 1. CT abdomen with contrast in late arterial phase showing a bilateral perirenal haematomas. There is an area of contrast extravasation in the upper pole of the right kidney (arrow) that suggests active bleeding; presence of coils (arrowhead) in the area previously embolized in the left kidney.

and $17.93 \times 10^9/L$ monocytes. Haemoglobin initial value was 82 g/L and platelet count was $85 \times 10^9/L$. Prothrombin and activated partial thromboplastin times were within normal limits; 16.6 s, 34.4 respectively.

Inflammatory markers showed increased C-reactive protein of 76 mg/L. Renal function was within normal limits for age; urea 5.9 mmol/L and creatinine 90 $\mu\text{mol/L}$ and liver function showed; bilirubin 21 $\mu\text{mol/L}$, alkaline phosphate 169 U/L, ALT 278 U/L, albumin 29 g/L.

CT of the abdomen revealed a retroperitoneal haematoma with an area of contrast extravasation in arterial phase in the lower pole of the left kidney, suggesting active bleeding from a left renal artery microaneurysm rupture. Based on the clinical findings and the results of the CT, patient underwent angiography, and was successfully treated with embolization with microcoils of one of the segmental branches of the left renal artery.

One week later, the patient had a further episode of abdominal pain with associated rectal bleeding and haemoglobin level dropped to 40 g/L. Patient was stabilized with blood products transfusion and transferred to CT room. An arterial phase CT of the abdomen was repeated and revealed a new, right this time, retroperitoneal haematoma with an area of contrast extravasation in the upper pole of the right kidney, suggesting the rupture of a microaneurysm in this area (Fig. 1). The findings were confirmed angiographically after selective catheterization of the segmental

branches of the right renal artery; furthermore an arteriovenous fistula was noticed in communication with the pseudoaneurysm and successful embolization of the vascular lesion with microcoils followed (Fig. 2). A control angiogram was also performed in the left renal artery and confirmed satisfactory seal of the previously embolized area and the presence of another very small non-ruptured microaneurysm in the upper pole of the left kidney. Embolization was not retained necessary at that stage because the lesion was too small. Although embolization was successful in terms of control of haemorrhage the patient’s clinical condition deteriorated with multi-organ failure including systemic inflammatory response syndrome, acute kidney injury requiring renal replacement therapy and encephalopathy requiring ventilatory support. She was transferred to the intensive care unit (ICU) for further monitoring and treatment.

Patient was then thoroughly investigated for causes of bilateral non-traumatic renal artery aneurysms. There was a negative diagnostic serology tests for Hepatitis B and C, absence of anti-nuclear antibodies (ANA), anti-neutrophil cytoplasmic antibodies (ANCA), anti-glomerular basal membrane antibodies, negative rheumatoid factor and complements C3, C4 were within normal range limits. Serum immunoglobulin concentrations were also normal. No signs of infectious disease were noted with negative blood cultures and negative serology tests for Epstein-Barr virus (EBV), Cytomegalovirus (CMV), Varicella Zoster virus (VZV). The patient had no evident signs of neuropathy or livedo reticularis. Bone marrow biopsy was avoided because of patient’s haemostatic disorder.

Our patient had spontaneous bilateral renal haematomas and multiple renal microaneurysms confirmed by angiography, associated with a history of weight loss of greater than 4.5 kg, generalized weakness, arterial hypertension and despite initial normal renal function she developed acute kidney injury on admission to ICU with urea 15.6 mmol/L and creatinine 237 $\mu\text{mol/L}$. Based on the American College of Rheumatology, our patient scored 5 out of 10 criteria for the diagnosis of Polyarteritis Nodosa (PAN) with sensitivity and specificity of 82% and 85% respectively [1]. For these reasons, patient received subsequently treatment for PAN in addition to CMML treatment. The treatment regimen included steroids, cyclophosphamide and hydroxycarbamide.

One month after admission to ICU, the patient was discharged to ward care clinically improved and stable without the need for ongoing renal replacement therapy. Creatinine levels returned back to patient’s baseline levels of 90 $\mu\text{mol/L}$ Further CT abdomen with contrast, 4 months later, showed both her kidneys to be well perfused (Fig. 3). Patient was followed up for 26 months. During that period, she was on immunosuppression; azathioprine 25 mg three times a day and prednisolone 5 mg once a day. Follow up CT scans

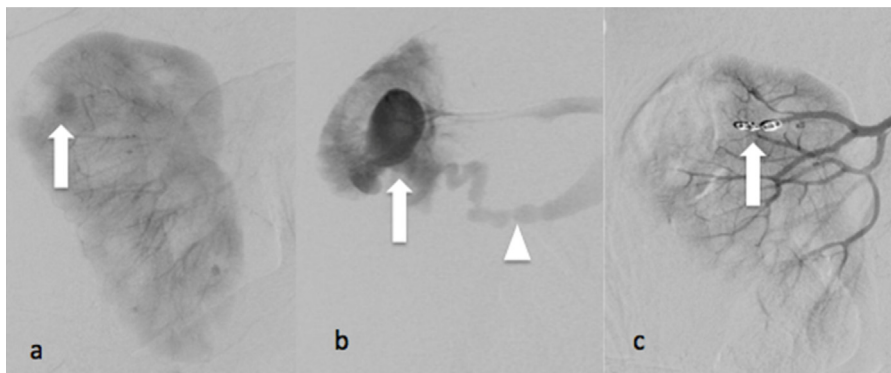


Fig. 2. a) Angiogram in late nephrographic phase after from a catheter placed in the right renal artery that shows the presence of a contrast blush from the upper pole of the right kidney (arrow). There is also presence of multiple very small other similar areas. b) Angiogram after superselective catheterization of the feeding branch confirms the presence of the pseudoaneurysm (arrow) and of an arteriovenous fistula (arrowhead). c) Angiogram that confirms the satisfactory exclusion of the lesion with coils and preservation of the vascularity of the residual renal parenchyma.



Fig. 3. Follow up CT abdomen scan with contrast showing reduction of the size of the perirenal haematomas, and no further area of bleeding. The coils are shown by the arrows.

were performed monthly for 2 months, then after 5 months and then after 12 months. All were unremarkable. At 19 months, a follow up CT scan showed a small subacute haematoma on the right kidney, which was resolved on its own without the need for any intervention. At 25 months CT showed bleeding from the liver. Further embolization in two sites was needed. Currently, patient is alive and stable with normal kidney function, creatinine 90 $\mu\text{mol/L}$, not requiring renal replacement therapy.

3. Discussion

PAN is known for its association with various conditions and in particular with hepatitis B [2] possibly due to an immune complex mechanism; however the role of the immune complexes in non-Hepatitis B related PAN remains unclear. Other associations include infectious organisms such as VZV, CMV, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* as well as certain syndromes such as Rheumatoid arthritis.

CMML association with vasculitis may be more common than initially thought. Hamidou et al. [3] described 8 cases of CMML associated with systemic ANCA-negative PAN. Patients presented in various ways such as fever of unknown origin, alveolar pneumonia, abdominal pain, sensory hearing loss, cutaneous lesions, peripheral neuropathy, eosinophilia in the setting of myelodysplastic syndrome. All fulfilled the American College of Rheumatology criteria for diagnosis of PAN as our patient did.

Fain et al. [4] analyse 60 patients with vasculitis associated malignancies. Vasculitis was more frequently associated with haematological malignancies rather than solitary tumours with frequency of PAN of 36.7%. Systemic ANCA-negative PAN type vasculitis seemed to be closely associated with CMML as it was found in 22% of the patients. Therefore, although CMML and PAN association is rare, there is undoubtedly a close association between them.

The mechanism of CMML causing vasculitis is unknown. One possible theory might be the abnormal stimulation of T and B lymphocytes by antigen dysplastic bone marrow stem cells. Despite the involvement of B and T cells, macrophage clearance of antigens may be greatly reduced, leading to enhanced levels of circulating immune complexes [5]. In CMML, a high number of circulating monocytes might also contribute to vessel inflammation [6]. By this case report, however, we did not find any explanatory pathophysiological mechanism; the association between CMML and PAN needs further investigation.

Renal aneurysms and unilateral renal haematoma are known complications of PAN. However, very few cases in the literature have described bilateral renal haemorrhage as a first presentation

and complication of PAN. From those cases, the outcome was poor; most patients died, others underwent nephrectomies and required renal replacement therapy and very few reported that patients survived without the need of renal support.

Schmidt et al. first reported perirenal haematoma as a complication of PAN, in 1908 [7].

Aslangul-Castier et al. [8] described 2 cases of spontaneous bilateral renal haemorrhage associated with PAN. Unlike our patient, both of these patients were presented initially with other complications such as calculus cholecystitis and aortic dissection. They then progressed into a sudden spontaneous bilateral renal haemorrhage and died 2 months later, despite embolization and corticosteroid treatment.

Agarwal et al. [9] presented a case of a 22-year-old girl with a known positive Cytomegalovirus who developed bilateral renal haemorrhage and a diagnosis of PAN was made. Unlike our patient, PAN was associated with CMV rather than CMML. Despite embolization, corticosteroid and cyclophosphamide, she died 10 days later with multi-organ failure.

Madhoun et al. [10] described a case of a previously fit and well 32-year-old man presenting with a right renal haemorrhage requiring right nephrectomy. He was diagnosed with PAN and he subsequently developed a left renal haemorrhage that was embolized. Unlike our patient, this man did not have an initial CMML. Although alive, he underwent unilateral renal nephrectomy and required long-term renal replacement therapy.

One of the cases described by Hamidou et al. [3] was a 58-year-old man with CMML and PAN that was admitted with pleuropericarditis and neuromeningeal involvement. He then developed spontaneous bilateral perirenal haemorrhage, successfully treated with embolization and corticosteroids. This was a rare case where patient survived with marked improvement in his renal function.

Our patient had an uncomplicated, stable CMML associated with PAN which first presented with spontaneous bilateral renal haemorrhage and was still alive 26 months after treatment with normal renal function.

4. Conclusion

By this case study presentation we have shown that diagnosis of PAN in association with pre-existent CMML might be challenging for clinicians, while early diagnosis of complications might confer better outcome. A multidisciplinary approach is necessary to manage similar cases. Particularly important is the role of interventional radiology to diagnose and treat complications such as bleeding and microaneurysms. Close follow-up with imaging is important to detect disease relapse and have appropriate treatment.

In conclusion, we described a rare case of bilateral renal haemorrhage due to renal artery aneurysm rupture caused by PAN in association with pre-existent CMML. The patient was treated initially with artery embolization and subsequently with steroids and cyclophosphamide and she managed not only to survive but also to regain a normal renal function with no need for further renal replacement therapy. Clinicians should be aware of this possible complication in their daily clinical practice. Further evidence is required to elucidate the mechanisms of the possible association of PAN and CMML.

Conflicts of interest

The authors declare that they have no conflict of interest.

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Ethical approval

No ethical approval needed.

Author contribution

MK performed the artery embolization. CG designed and wrote the manuscript. SD and NE assisted in drafting and editing the manuscript and reviewed the article. All authors read and approved the final manuscript.

Consent

Written informed consent was obtained from the patient for publication of this case report and any accompanied images. A copy of the written consent is available for review by the Editor of this journal on request.

Guarantor

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The work has been reported in line with the CARE criteria [11].

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