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Case Report

Massive uric acid nephrolithiasis with progressive renal failure due to spontaneous tumour lysis syndrome

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Abstract

Tumour lysis syndrome (TLS) is a constellation of metabolic complications due to the rapid destruction of malignant cells, causing renal, cardiac or cerebral dysfunction. Electrolyte abnormalities include hyperuricaemia, hyperphosphataemia, hyperkalaemia and hypocalcaemia. TLS-induced renal failure is mainly caused by uric acid and calcium phosphate crystal deposition and usually develops following cytotoxic chemotherapy. Here, we present a case of spontaneous TLS in a patient with chronic myelomonocytic leukaemia (CMML) with massive uric acid stone and crystal formation and rapidly worsening renal failure. Autopsy revealed underlying tumourous kidney infiltration. Risk factors for occurrence of TLS and current therapeutic management are discussed.

Keywords: acute renal failure; therapy; tumour lysis syndrome; uric acid nephrolithiasis

Introduction

The term tumour lysis syndrome (TLS) describes metabolic derangements and organ dysfunctions caused by rapid destruction of malignant cells. It is classified into laboratory TLS (LTLS) and clinical TLS (CTLS) [1]. LTLS is characterized by elevated serum uric acid, potassium and phosphorus and low serum calcium. CTLS consists of LTLS together with renal, cardiac or cerebral dysfunction. Pathophysiologically, intracellular phosphorus, potassium and nucleic acids, which are then metabolized to uric acid, are rapidly released and overwhelm the body's homeostatic mechanisms. Once TLS-related renal failure occurs, clearance of these substances is impaired leading to their further accumulation. Hypocalcaemia results from complex formation and precipitation of calcium with phosphate. Intrarenal uric acid and calcium phosphate precipitation lead to acute crystal nephropathy, the latter being the predominant mechanism of acute renal failure (ARF) in spontaneous TLS [2].

Case report

A 73-year-old patient was admitted to a local hospital with uraemia (creatinine 1588 μmol/L, urea 56.2 mmol/L, potassium 6.0 mmol/L). He had a history of chronic myelomonocytic leukaemia (CMML) that was diagnosed 1 year earlier and was treated with dexamethasone 1 mg/day since then. Chronic renal failure of unknown origin (MDRD GFR 36 mL/min) was found at that time. On current admission, ultrasonography revealed post-renal obstruction with dilatation of both renal pelvises due to multiple concrements in the urinary tract, which were composed of uric acid as shown by x-ray diffraction. Serum uric acid was markedly elevated (1262 μmol/L). Despite the placement of bilateral transureteral catheters and treatment with allopurinol and rasburicase with consecutive rapid normalization of serum uric acid, creatinine and urea remained elevated (1051 μmol/L and 51.7 mmol/L). Metabolic acidosis persisted despite bicarbonate infusion. A bone marrow biopsy showed no evidence for progression of the underlying CMML (2% blasts and 9% promyelocytes/promonocytes versus 5% and 12.5% at diagnosis 1 year earlier). Eleven days later the patient was referred to our tertiary care nephrology clinic because of persistent renal failure. Elevated levels of phosphate (3.29 mmol/L), lactate dehydrogenase (LDH: 674 U/L; normal 150–420) and C-reactive protein (134 mg/L: normal <5) were found. The patient developed septic shock due to *E. coli* bacteraemia and died despite fluid resuscitation, antibiotic treatment and continuous haemodiafiltration. Autopsy showed massive amounts of uric acid concrements in the renal pylon (Figure 1A) and some crystal deposition in the papillae and tubules (Figure 1B). There were no urate tophi or calcium phosphate depositions. The bone marrow revealed myelodysplastic syndrome with leukaemic infiltrates in the kidneys (Figure 1C), liver, spleen, epicardium and lungs.

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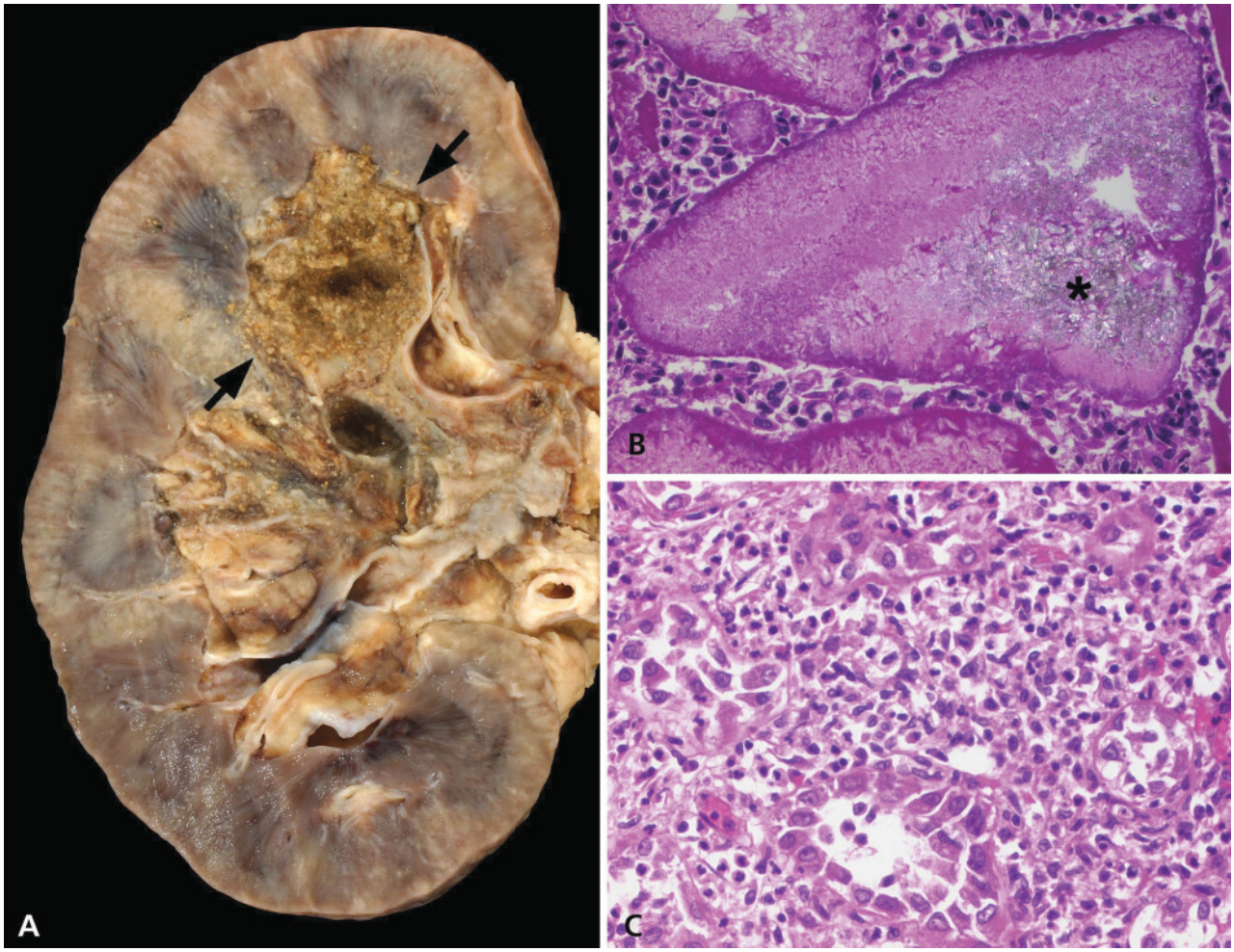

Fig. 1. (**A**) Extensive pelvic nephrolithiasis (between arrows) due to uric acid stone formation. (**B**) Light microscopy of renal tissue showing partly amorphous, partly rectangular and birefringent crystals (HE, original magnification ×260; birefringence marked with ∗). (**C**) Interstitial infiltrates of myeloid cells in the kidney at autopsy (HE, original magnification ×200).

Discussion

TLS commonly follows initiation of cytotoxic therapy for tumours with high proliferative rates, in patients with a large tumour burden and high sensitivity to therapy [3]. A recent retrospective analysis identified elevated pre-chemotherapy values of uric acid, creatinine, LDH and white blood cells as well as male sex and history of CMML as significant predictors for the occurrence of TLS during induction therapy for acute myelogenous leukaemia (AML) or advanced myelodysplastic syndrome [4]. Spontaneous TLS is rare. In one case series, patients with hyperuricaemic ARF due to spontaneous TLS represented ∼1% of all patients with ARF [5]. In CMML, TLS after starting mildly cytotoxic therapy with hydroxyurea has been described [6], but we are not aware of any report of spontaneous or steroid-induced TLS in CMML.

The mainstay of prophylaxis and treatment of TLS is vigorous hydration, which enhances excretion of uric acid and phosphate. If urinary output is not sufficient, diuretics should be added. Urine alkalinization to enhance the solubility of uric acid is not recommended in recently published guidelines because it increases the risk for calcium phosphate and xanthine (accumulating under allopurinol therapy) precipitation [7]. Hyperphosphataemia carries the risk of precipitation of calcium phosphate, resulting in nephrocalcinosis and nephrolithiasis. Treatment includes phosphate binders and dialysis. Hypocalcaemia commonly occurs in the setting of calcium phosphate deposition. Asymptomatic hypocalcaemia should therefore not be treated to avoid elevation of the calcium phosphorus product with further propagation of calcium phosphate precipitation. Hyperkalaemia must be treated according to its severity and concomitant cardiac abnormalities. Hyperuricaemia can be prevented by the xanthine oxidase inhibitor allopurinol. Recombinant urate oxidase (rasburicase) metabolizes uric acid to allantoin and very effectively lowers uric acid levels [3]. It is indicated in patients at high risk for TLS and also in established TLS [7]. If these measures fail, renal replacement therapy is needed.

Our case fulfils the criteria of CTLS. We consider this case as a spontaneous TLS, since it occurred in the context of low-dose steroid treatment that was not changed over more than 1 year. All risk factors for TLS described in patients undergoing induction therapy for AML were present [4]. Direct tumour cell infiltration of the kidney by CMML

has been reported previously and was possibly responsible for the pre-existing chronic renal failure in our patient [8]. Rapid correction of obstructive uropathy was not successful in restoring kidney function in our patient, which was also the case in four out of five patients undergoing such a procedure in a recently published series [5].

Taken together, this case illustrates that in patients with CMML, TLS can occur spontaneously without treatment changes or evidence for disease progression. Acute uric acid nephropathy in a patient with malignancy should trigger a search for TLS, even in the absence of cytotoxic therapy. If present, therapy should focus on rapid correction of metabolic abnormalities, which will often require renal replacement therapy. Patients with multiple risk factors for development of this syndrome may need close surveillance and even prophylactic treatment with allopurinol to reduce uric acid formation.

Conflict of interest statement. None declared.

References

1. Cairo MS, Bishop M. Tumour lysis syndrome: new therapeutic strategies and classification. *Br J Haematol* 2004; 127: 3–11
2. Kjellstrand CM, Cambell DC, von Hartitzsch B *et al*. Hyperuricemic acute renal failure. *Arch Intern Med* 1974; 133: 349–359
3. Rampello E, Fricia T, Malaguarnera M. The management of tumor lysis syndrome. *Nat Clin Pract Oncol* 2006; 3: 438–447
4. Mato AR, Riccio BE, Qin L *et al*. A predictive model for the detection of tumor lysis syndrome during AML induction therapy. *Leuk Lymphoma* 2006; 47: 877–883
5. Hsu HH, Chan YL, Huang CC. Acute spontaneous tumor lysis presenting with hyperuricemic acute renal failure: clinical features and therapeutic approach. *J Nephrol* 2004; 17: 50–56
6. Otrock ZK, Taher AT, Mahfouz RA *et al*. Acute tumor lysis syndrome secondary to hydroxycarbamide in chronic myelomonocytic leukemia. *Am J Hematol* 2006; 81: 220–221
7. Coiffier B, Altman A, Pui CH *et al*. Guidelines for the management of pediatric and adult tumor lysis syndrome: an evidence-based review. *J Clin Oncol* 2008; 26: 2767–2778
8. Robinson GT, Sundaram KR, Dilly SA *et al*. Renal failure in a patient with chronic myelomonocytic leukaemia. *Nephrol Dial Transplant* 1997; 12: 1500–1502

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