Spontaneous tumor lysis syndrome in a case of B-cell non-Hodgkin’s lymphoma

Tumor lysis syndrome (TLS) is a group of metabolic abnormalities that are usually seen in cancer patients treated with chemotherapy although it can occasionally occur spontaneously without chemotherapy in patients with a high tumor burden. It is due to the rapid lysis of tumor cells resulting in the release of large amounts of intracellular contents in the blood stream. This results in the rapid development of high levels of phosphate, potassium and uric acid accompanied by a profound decrease in serum calcium. TLS usually occurs in bulky tumors with a high turnover such as leukemias and lymphomas. The malignancy can be undiagnosed at the time of development of TLS [1]. In this report we present a case in which the patient presented with spontaneous TLS (STLS) and was later diagnosed with high-grade B-cell non-Hodgkin’s lymphoma (NHL).

Case summary

A 75-year-old male with a history of prostate cancer (at the time under remission), diabetes mellitus, hypertension and chronic kidney disease (creatinine 1.4 mg/dL (124 µmol/L) in October 2011) presented to the hospital with abdominal pain of 1-month duration along with decreased urine output. Home medications included lasix, metoprolol, clonidine, atorvastatin, plavix, amlopidine, benazepril and omeprazole.

In the emergency room the patient was afebrile with a blood pressure of 130/70 mmHg and a pulse of 110/min. On clinical examination the patient was noted to have dry mucous membranes with abdominal distension and generalized abdominal tenderness.

Initial laboratory workup showed Hb 100 g/L (10 g/dL), platelet $322 \times 10^9$/L, potassium 6.1 mmol/L, Cl 95 mmol/L, CO$_2$ 24 mmol/L, BUN 32 mmol/L (89 mg/dL), creatinine 665 µmol/lt (7.52 mg/dL), Ca 2.5 mmol/L (10 mg/dL), PO$_4$ 2.06 mmol/lt (6.4 mg/dL), amylase 162 U/L, lipase 1064 U/L, LDH 447 U/L, CK 48 U/L, uric acid 886 µmol/L (14.9 mg/dL). His urinalysis was positive for blood, leucocytes, leucocyte esterase, 1+ proteinuria. Albumin creatinine ratio was 0.7. A renal ultrasound revealed normal sized kidneys and increased bilateral echogenicity with no hydronephrosis. Ascites was evident. Intravenous (IV) fluids were given for volume depletion. Lisinopril and furosemide were discontinued.

Computerized tomography (CT) scan of the chest and abdomen was done due to worsening abdominal distension and pain. It showed bulky lymphadenopathy in the chest with retroperitoneal lymphadenopathy in the abdomen.

TLS was suspected on account of the elevated serum phosphate, uric acid, and lactate dehydrogenase (LDH) and the CT findings. The differential diagnosis included acute tubular necrosis, acute interstitial nephritis and acute glomerulonephritis. Rasburicase was given intravenously to treat hyperuricemia. Uric acid decreased from 845 µmol/L (14.2 meq/lit) to 399 µmol/L (6.7 mg/dL) within 24 h. There was no improvement in his renal function. A retroperitoneal lymph node biopsy was consistent with B-cell NHL of germinal center cell origin (Figure 1). Hemodialysis was initiated due to the development of uremia. The ensuing clinical course was complicated by the development of confusion, hypotension, leukocytosis and sepsis. His family decided to pursue comfort care. He expired shortly afterwards.

Discussion

The incidence of TLS in hematological malignancies after chemotherapy is 4–42%. In a retrospective study, the rate of STLS (spontaneous TLS) was 1.08% in patients with diagnosed hematological malignancy. Risk factors include bulky tumors, high pretreatment uric acid level >446 µmol/L (7.5 mg/dL), preexisting kidney disease, exposure to nephrotoxins, oliguria, acidic urine and dehydration [2].

Patients with TLS demonstrate increased morbidity and mortality from acute kidney injury (AKI). Chemotherapeutic drug levels are usually elevated (due to decreased renal clearance) leading to extra renal toxicity such as skin and mucosal damage. The treatment of the underlying malignancy is also affected as chemotherapy is often withheld due to the development of AKI. Dialysis itself frequently results in increased clearance of chemotherapeutic agents leading to under treatment and reducing the chances of inducing a remission [3]. TLS caused AKI in 45% of cases and half of these patients needed dialysis with mortality rate of 40% [4].

Routine prophylaxis of TLS in patients with high or intermediate risk is believed to be beneficial to reducing the morbidity and mortality related to AKI. Aggressive intravenous hydration should be initiated prior to the onset of chemotherapy. Allopurinol has been shown to help prevent hyperuricemia due to chemotherapy although it does not reduce preexisting hyperuricemia. Rasburicase is a recombinant uric acid oxidase which directly causes conversion of uric acid into allantoin, a much more soluble substance. The effect of rasburicase starts within 4 h and uric acid normalized within 3–4 days. Coiffler et al. [4] reported 100 patients with NHL receiving chemotherapy and none needed dialysis when rasburicase was given with the first cycle of chemotherapy. Allopurinol failed to prevent AKI in 25% of cases with TLS [5].

Hemodialysis is needed in established cases of TLS with AKI complicated by severe oliguria, anuria, life-threatening hyperkalemia or hyperphosphatemia-induced hypocalcemia. In addition, hemodialysis is very effective in reducing the uric acid level when rasburicase is unavailable. Oliguria tends to improve once the uric acid level drops <595 µmol/L (10 mg/dL). Clearance for uric acid with hemodialysis is 70–100 ml/min. The clearance of uric acid with continuous venous hemo dialfiltration (CVVHDF) is 45 ml/min. Although the clearance of intermittent hemodialysis is greater than that of CVVHDF, over time CVVHDF is more effective as it is continuous and can be extended over prolonged periods and may be safer in
hemodynamically unstable patients. CVVHDF has been used as a prophylactic measure in patients with TLS who are at high risk to develop AKI [1].

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