Acute Myeloid Leukemia Complicated with Staghorn Calculus

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An 11-year-old girl who presented with hyperleukocytosis accompanied by significant increases in serum uric acid and lactate dehydrogenase levels was discovered to be suffering from acute myeloid leukemia (AML). Subsequently a staghorn calculus was identified 22 months after the start of chemotherapy. The diagnosis of staghorn calculi was suggested by plain abdominal X-ray and ultrasonography. This paper describes the course of an adolescent patient with AML and focuses specifically upon her urological complications. To the best of our knowledge, this is the first reported pediatric case of AML complicated with staghorn calculi, which developed following repeated episodes of septicemia.

Key words: acute myeloid leukemia – staghorn calculi – hemorrhagic cystitis – hyperuricemia – septicemia

INTRODUCTION

Renal calculi, both of the CaPO 4 and precipitated uric acid types, appear to occur frequently amongst patients with acute lymphoblastic leukemia who exhibit a high initial leukocyte count (1). On rare occasions, staghorn calculi may masquerade as hemorrhagic cystitis amongst the urological complications of acute myeloid leukemia (AML). Because of their similar clinical presentations, these two disorders should be diagnosed with caution.

CASE REPORT

An 11-year-old girl newly diagnosed with acute myeloid leukemia (FAB classification: M1) was treated at Chang Gung Children’s Hospital. Her admission laboratory findings were remarkable for hyperleukocytosis (leukocyte count of 552.6 × 10⁹/l, blasts 96.3%), hyperuricemia (860 μmol/l; reference range, 120–420 μmol/l) and a high serum lactate dehydrogenase (LDH) level (19.34 μkat/l; reference range, 0.82–2.66 μkat/l). Serum creatinine, calcium, phosphorus and immunoglobulin levels appeared to be normal. Cytogenetic examination revealed no chromosomal abnormalities. In order to prevent the consequences of tumor lysis syndrome (TLS), the patient was given allopurinol (10 mg/kg) and sodium bicarbonate for urinary alkalization during her early induction therapy. An alkaline diuresis was established before the start of chemotherapy to ameliorate significant increases in uric acid and phosphorus in her serum. TLS was eventually prevented with the anticipatory treatment.

The following day, induction chemotherapy was started with a 7 day infusion of cytosine arabinoside (AraC) 100 mg/m²/day i.v. and oral thioguanine 80 mg/m²/day as well as a 3 day program of epidoxorubicin 20 mg/m²/day i.v. A sonographic study was performed 1 month subsequent to admission owing to the presence of left abdominal pain associated with hypocalcemia (1.20 mmol/l; reference range, 2.20–2.50 mmol/l) and hypophosphatemia (0.75 mmol/l; reference range, 0.80–1.60 mmol/l), although only bilaterally increased renal echogenicity was demonstrated. Abdominal radiography revealed no evidence of radiopaque density.

The patient responded well to chemotherapy and hematological remission was achieved after 1 month. She received two courses of consolidation therapy with 3 days of etoposide, 200 mg/m²/day, followed by cyclophosphamide, 300 mg/m²/day, alternating every 3 weeks with 3 days of AraC and epidoxorubicin in the dosage described earlier. Gross hematuria, with symptoms of cystitis and negative urine cultures, occurred on two occasions following cyclophosphamide administration. Urinalysis revealed red blood cells that were too numerous to count, one to four leukocytes per high-power field and trace proteinuria, although no bacteria were isolated from the urine.

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Staghorn calculus and leukemia

The clinical findings were presumed to be hemorrhagic cystitis and she was treated with forced hydration.

The patient’s later clinical course was complicated by Pseudomonas aeruginosa and Klebsiella pneumoniae bacteremia over the subsequent 6 month period and bone marrow relapse 20 months later. Reinduction therapy was initiated, which was comprised of AraC, 1 g/m² every 12 h by a 3 h infusion, on days 1, 2, 8 and 9 and mitoxantrone, 8 mg/m²/day as a 30 min infusion on days 3, 4, 10 and 11. Her course was complicated with another episode of K. pneumoniae sepsis.

Twenty days after the episode of K. pneumoniae sepsis, she had intermittent right flank pain and gross hematuria. Laboratory studies revealed the following profile: leukocyte count, 1.5 x 10⁹/l; segmented neutrophils, 47%; monocytes, 7%; lymphocytes, 41%; atypical lymphocytes, 5%; hemoglobin, 97 g/l; platelets, 113 x 10⁹/l; and normal levels of serum electrolytes, creatinine, calcium, phosphorus and coagulation studies. A staghorn stone about 4 cm in length was detected in the right kidney by both radiographic and sonographic studies (Fig. 1), this stone being detected 22 months subsequent to the diagnosis of leukemia. The follow-up abdominal radiograph revealed a reduced stone burden following supportive treatment. Idiopathic hypercalciuria was not evident for the patient when tested after this issue. However, following two further episodes of Escherichia coli bacteremia with urinary tract infection (UTI), the patient died of multisystem failure in a relapsed state 28 months subsequent to initial diagnosis.

**DISCUSSION**

For leukemic patients, a high leukocyte count may contribute to the deposition of uric acid crystals, especially whilst the patient is undergoing chemotherapy (1), although uric acid stone formation appears to be rare (2). For our case, a large tumor burden was reflected by a high LDH and uric acid concentration. Uric acid gravel in the kidneys may occur in the absence of any radiological evidence of calculi (3). Although no evidence of renal stones was noted from ultrasonography following induction chemotherapy, the valuable role of ultrasonography in the serial evaluation of chronic stone formation, as was the case for our patient, would appear to be indisputable (4).

It is likely that hemorrhagic cystitis resulted from preceding cyclophosphamide administration because of the assortment of clinical findings. However, the presence of hemorrhagic cystitis is difficult to determine because a sonogram of the bladder did not show focal areas of thickening or adherent clot. Subsequently, forced hydration used to treat this disease may preclude adequate urine collection for bacterial and viral cultures. Conversely, the time required for development of hemorrhagic cystitis after completion of chemotherapy varies, ranging from a few weeks to several years (5). Staghorn calculi in patients with leukemia may masquerade as hemorrhagic cystitis. Correct diagnosis of hemorrhagic cystitis can only be achieved by careful clinical observation and a combination of thoroughly scrutinized laboratory tests.

Despite its foreboding size and ominous consequences, a staghorn calculus in a child may be asymptomatic and discovered by evaluation for non-renal abdominal disorders (2,6). Staghorn calculi are infrequent and generally are infected stones. Struvite or apatite calculi are embedded with Gram-negative bacteria such as Proteus and Klebsiella (7,8). Recent studies have suggested that urease-negative bacteria or those reflecting weak urease activity might also be involved in the formation of struvite (9,10). The treatment of leukemic patients suffering from staghorn calculi remains a challenging problem. If symptoms are few, it appears hard to justify aggressive surgical procedures in order to render the patient stone free, although management with antibiotics and supportive measures is not considered a viable option except for a patient who is otherwise too ill to tolerate surgical stone removal.

The treatment options for patients with staghorn calculi other than simple observation include open surgery, percutaneous nephrolithotomy (PNL) and extracorporeal shock-wave lithotripsy (ESWL) (11). The need for blood transfusion is greater for open surgery and PNL, whereas ESWL carries a high

![Figure 1. (a) Plain film of the abdomen revealing a staghorn calculus filling the collecting system of the right kidney (arrow). (b) Ultrasonography revealing a non-opaque stone with posterior acoustic shadows (arrowheads).](https://academic.oup.com/jjco/article-abstract/32/9/365/850327/366)
probability of a need for an unplanned secondary procedure (12). From the patient’s viewpoint, a complication may have the same importance as a secondary anesthetic procedure. Therefore, the choice of available treatment options for this patient was watchful waiting with further action being dependent upon clinical status.

Our case raises a theoretical concern with respect to hyperuricemia for leukemic patients. Hyperleukocytosis at initial diagnosis may be considered a risk factor for the development of uric acid nephropathy and urolithiasis years after chemotherapy (1). Over time, uric acid calculi can act as the core for the calculus (13). When the infection is due to urea-splitting organisms such as *Klebsiella* and *Pseudomonas*, release of ammonium raises urine pH and predisposes to calcium stone formation (2,3), which is termed staghorn because of its characteristic shape. The present case indicates that this serious urological complication may occur under neutropenic conditions induced by intensive chemotherapy for leukemia.

**References**