

## B-cell lymphoma presenting with renal failure associated to spontaneous tumor lysis syndrome and urinary tract obstruction

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### Summary

The acute tumor lysis syndrome (ATLS) may be a dramatic complication of anticancer treatment. It occurs mostly in haematological malignancies and less commonly in solid tumors. Spontaneous tumor lysis syndrome (STLS) has been reported more frequently in Burkitt's lymphomas than in other haematological tumors, and exceptionally in solid tumors like small-cell lung carcinoma and germ-cell tumors. We report on the case of a patient with a diffuse large B-cell lymphoma (DLBCL) of the urinary tract involved by acute renal failure due to STLS and complicated by obstructive uropathy subsequent to neoplastic infiltra-

tion of the bladder. Hyperhydration, urine alkalization, urate oxidase administration and continuous veno-venous haemodiafiltration (CVVHDF) permitted to control the initial renal failure and to administer chemotherapy. The patient then developed chemotherapy-induced tumor lysis syndrome (TLS) controlled by urate oxidase administration, hyperhydration and urine alkalization. The treatment of TLS and the differences between ATLS and STLS are discussed.

**Key words:** acute tumor lysis syndrome, large diffuse B-cell lymphoma, spontaneous tumor lysis syndrome, urinary tract, urinoma

### Introduction

STLS occurs when local conditions such as anoxia and necrosis are exceeding the tumor proliferating capacities. Few cases have been reported and most of them concern haematological malignancies such as acute leukaemia [1], Burkitt's lymphoma [2], and T-lymphomas [3]. Much less often STLS is seen in patients with solid tumors like germ-cell tumors [4], advanced gastric adenocarcinoma, lung adeno-

carcinoma [5] and breast cancer. Only one case of STLS associated with B-cell lymphoma localized in the colon has been described [6]. We report on a case of a B-cell lymphoma infiltrating the urinary tract.

### Case presentation

A 72-year-old former social worker was admitted as an emergency for abdominal pain. He had a 2-week history of progressively deteriorating abdominal pain and fatigue. He presented episodes of profuse sweating, mostly at night. Weight loss and urinary or digestive complains were not reported. Past history revealed hypercholesterolemia and bilateral cataract treated some years ago. He was a heavy smoker (20 cigarettes per day for 50 years) and he mentioned beer consumption limited to Friday evenings.

Physical examination revealed a normohydrated, normocoloured, overweighted male. Temperature was 36.6° C; blood pressure 145/80 mmHg; and pulse rate 82/min and regular. The following abnormal findings

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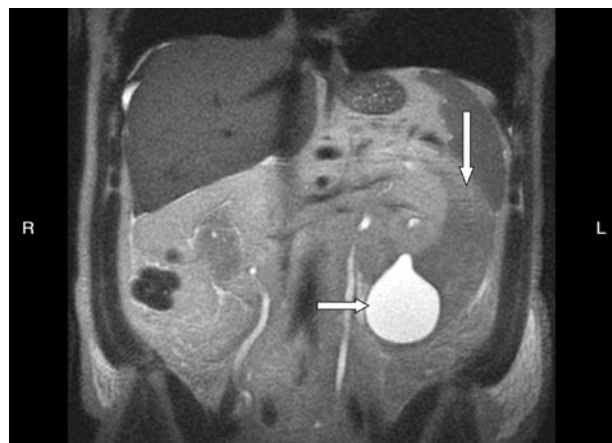
were noted: bilaterally decreased vesicular murmur and a huge left abdominal fullness going from the left hypochondrium towards the left groin. The percussion of the left costolumbar region was painful. There was no sign of peritoneal irritation; peristalsism was present and the cardiac and neurological examinations were normal. Diuresis was 415 ml/24 h.

The laboratory findings (Table 1) revealed mild normocytic anaemia with normal counts of platelets and white blood cells; serum creatinine was elevated at 1.6 mg/dl; LDH elevated at 750 UI/ml; and CRP was 8.32 mg/dl. Electrolytes and hepatic enzymes were normal. Urinalysis showed leukocytes (4.1/ $\mu$ l) and erythrocytes (28.2/ $\mu$ l), without crystals nor bacteria.

Plain abdominal X-ray showed stercoral stasis. Abdominal CT scan without contrast demonstrated left nephromegaly with urinoma at the inferior pole, mild dilatation of the renal calyces and pelvis and infiltration of the perirenal fat reaching the ureter and limited to the retroperitoneal region.

A renal abscess due to calyx rupture was suspected and the patient received i.v. amoxicilline clavulanate and paracetamol. A renal scintigraphy confirmed the left urinary obstruction and on MRI (Figure 1) the CT scan findings were reconfirmed.

The following days the patient felt better except of abdominal cramps radiating to the scrotum. However, biological tests worsened (LDH, uric acid and creatinine rose respectively up to 2027 UI, 17.8 mg/dl and 2.6 mg/dl). A Doppler echography on day 8 excluded a renal infarction that could explain both elevated LDH and renal failure. Doppler of the arterial flow was normal. Fat infiltration and urinoma were unchanged on echography but there was bilateral pyelocalycectasis with an approximate diameter of 13 mm and important thickening of the bladder wall, also shown on CT scan (Figure 2).



**Figure 1.** MRI T2 sequences showing a voluminous urinoma 130 mm in diameter (short arrow) and the infiltration of the perirenal fat (long arrow).

A double J catheter was impossible to insert because the distal ureteral end was completely infiltrated. Biopsy of the bladder mucosa revealed a diffuse large B-cell lymphoma. The International Prognostic Index



**Figure 2.** CT scan without contrast showing enlarged bladder walls. The thickness of the walls ranges between 25 mm (anterior wall, long arrow) to 48 mm (posterior wall, short arrow).

**Table 1.** Biological tests of our patient (selected data): Initial admission on day 1 ; ICU admission on day 10 (start of urate oxidase administration) ; chemotherapy administration on day 16

	Normal range	Days							
		2	8	10	11	15	16	18	26
Na <sup>+</sup>	135-145 meq/l	138	137	141	140	136	135	143	139
Cl <sup>-</sup>	96-106 meq/l	106	100	98	99	100		102	108
K <sup>+</sup>	3.4-4.5 meq/l	4.1	3.6	4.8	4.4	3.7	5.5	4	3.8
Ca <sup>++</sup>	8.3-10.2 mg/dl	9.3	9.6	8.2	8.3		8.1	6.9	8.4
PO <sub>4</sub>	2.4-4.1 mg/dl	2.6	3		5.1	2.6	15.3	12.6	1
LDH	<470 IU	1008	2027	3107	4532	7260	9900	6435	1624
Uric acid	2.7-7.3 mg/dl	11.8	17.8	16.5	<0.2	1.6	6.3	3.7	1.9
Urea	<45 mg/dl	34	86	126	135	51	141	192	29
Creat	<1.2 mg/dl	1.9	2.6	5.6	5.1	1.5	2.9	2.1	0.7

was 5. A diagnosis of spontaneous TLS was made and the patient was transferred to the Intensive Care Unit (ICU) where urate oxidase was administered (0.2 mg/kg/day for 1 day). Uric acid fell below 0.2 mg/dl. As creatinine reached 5.6 mg/dl, continuous CVVHDF was started.

Renal function gradually improved and after 5 days, when creatinine levels declined to 1.5 mg/dl, CVVHDF was stopped and chemotherapy was started with a regimen consisting of rituximab, cyclophosphamide, adriamycin, cisplatin and prednisone. Subsequently, the patient developed a chemotherapy-induced TLS that was treated with hyperhydration, urate oxidase (0.2 mg/kg/day for 3 days) and urine alkalinization. There was no further deterioration of the renal function. During myelosuppression that followed chemotherapy, febrile neutropenia occurred which responded to antibiotics without further complications. Abdominal signs and symptoms gradually improved. On day 35 the patient was discharged in good condition.

## Discussion

We presented the case of a patient with a urinary tract diffuse large B-cell lymphoma, complicated by acute renal failure due to STLS and obstructive uropathy subsequent to neoplastic infiltration of the bladder. TLS is known to happen after cytotoxic treatment for high turnover neoplasms such as acute haematological malignancies. Development of TLS has been reported in patients with small-cell lung carcinoma, ovarian cancer [7], breast cancer [8], sarcoma [9], and squamous cell carcinoma of the vulva [10]. Yet, STLS is a rare condition and only few cases have been described. Most of them concern Burkitt's lymphoma [2], acute leukaemia [1], some T-cell lymphomas [3], and much less often solid tumors like germ-cell tumors [4], advanced gastric adenocarcinoma, lung adenocarcinoma [5] and breast cancer. Only one case of STLS in a patient with B-cell lymphoma of the colon has been reported [6]. Those cases of STLS usually are presented with unspecific symptoms like lethargy and alteration of the renal function due to acute uric acid nephropathy; the outcome of these patients is generally poor, even with extrarenal replacement.

At the best of our knowledge, this is the first case describing STLS in a patient with diffuse large B-cell lymphoma of the urinary tract. The particularities of our case were its tricking clinical signs and the renal failure induced by acute uric acid nephropathy and worsened by an obstructive component due to neoplastic infiltration of the bladder.

STLS occurs when local conditions, such as anoxia and necrosis, are exceeding the tumor proliferating capacities. It is difficult to predict when it will occur. In a small study comparing 10 different cases of STLS, the serum levels of LDH seemed to correlate with the risk of acute renal failure (ARF) [11], as it is the case in post-treatment TLS and acute renal failure seen in non-Hodgkin's lymphoma [12]. Even though it seems logical that elevated LDH, reflecting the tumor size and aggressiveness, may predict ARF in STLS, this has to be reconfirmed in further studies. In our case, the differences between STLS and induced ATLS should be discussed. Altered levels of phosphorus and calcium are characteristic for the diagnosis of ATLS but hyperphosphatemia and hypocalcemia are not specific in STLS since such changes mostly depend on the ability of the tumor to reutilize released phosphorus for resynthesis of new tumor cells which cannot occur in posttreatment TLS where all malignant cells are destructed at the same time [13].

Hyperhydration, urine alkalinization, urate oxidase administration and CVVHDF resulted in the control of the initial renal failure of our patient and allowed us to begin chemotherapy 5 days later. Indeed, the key point in the management and prevention of ARF in TLS is the control of uric acid, both in blood and urine, to prevent renal failure. Vigorous hydration with alkalinization of urine is recommended to maintain the glomerular filtration, and, thus, to increase renal excretion of uric acid and phosphate, and prevent the risk of uric acid crystals precipitation [14]. However, the use of sodium bicarbonate is controversial since it may lead to metabolic alkalosis and urine alkaline pH increases the solubility of urates but decreases the solubility of xanthine crystals [14, 15]. Indeed, urine alkalinization is not risky if urate oxidase is used instead of allopurinol. The use of urate oxidase leads to very fast decrease of uricemia [3]. Urate oxidase also has the advantage to prevent posttreatment renal failure, as it has been reported with allopurinol which causes accumulation of oxypurines leading to tubular precipitation of xanthine crystals that cannot be prevented with urine alkalinization [16, 17].

In our patient, those measures were efficient enough to prevent chemotherapy-induced ATLS but were not sufficient to control the initial ARF due to STLS. A technique of extrarenal replacement was necessary just after his admission to the ICU. Haemodialysis is more efficient for the clearance of uric acid than continuous haemofiltration [15]. However, CVVHDF offers greater haemodynamic stability and better volume control than conventional haemodialysis [18]. For these reasons we use CVVHDF in our unit.

In summary, we report the first case of STLS in

a primary urinary tract diffuse large B-cell lymphoma. Its unusual clinical presentation delayed diagnosis. Hyperhydration, urine alkalinization, urate oxidase administration and CVVHDF permitted us to control the initial renal failure and begin chemotherapy. The patient then developed a chemotherapy-induced ATLS, effectively treated by urate oxidase administration, hyperhydration and urine alkalinization. There is a need to differentiate the two types of TLS and prevent induced ATLS after STLS if a treatment is undertaken.

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