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CASE REPORT

Spontaneous Tumour Lysis Syndrome Secondary to Metastatic Gallbladder Adenocarcinoma: a Case Report and Reflection

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Abstract

Tumour lysis syndrome (TLS) is a well-recognised oncological emergency caused by rapid destruction of cancer cells. Despite most commonly occurring in haematological malignancies or following initiation of chemotherapy, rarely, it occurs in solid tumours without any trigger. Release of nucleic acids during cell breakdown produces large amounts of uric acid resulting in crystallisation within the renal tubules, clinically manifesting as severe acute kidney injury. We hereby discuss the first reported case of lethal spontaneous TLS in a 77-year-old patient admitted with newly diagnosed metastatic gallbladder adenocarcinoma and reflect on the importance of considering rarer causes of severe AKI in patients with solid organ cancers.

Keywords Gallbladder · Tumour lysis · Surgical oncology · Oncologic emergencies · Acute kidney injury

Tumour Lysis Syndrome Secondary to Metastatic Gallbladder Adenocarcimona

A 77 year-old female presented to the acute surgical receiving unit with a 3-day history of right upper quadrant pain, radiating through to the back and associated with nausea and vomiting. Her past medical history included a perforated duodenal ulcer and hypertension but no other significant illnesses or prior hospitalisations. Regular medications included Amitriptyline, Simvastatin, Amlodipine and Valsartan. There were no recent changes to her medications, and no use of over-the-counter medicines. Physical examination was unremarkable, apart from right upper quadrant abdominal tenderness. Initial ultrasound (US) imaging revealed suspicious appearances of the liver in keeping with malignant infiltration. A CT scan confirmed large bi-lobar liver metastases and malignant infiltration as well as a slightly thick-walled gallbladder, with a suspicious focal lesion protruding into the gallbladder lumen. This can be seen in Fig. 1 (arrow for the mass). The patient was discharged with a supply of dihydrocodeine for analgesia and brought back to hospital 4 days later to undergo US-guided liver biopsy. She re-presented to hospital feeling well and underwent an uneventful liver biopsy, but routine pre-biopsy blood tests revealed a stage 3 acute kidney injury (AKI) with a creatinine of 248 µmol/L on a previously normal baseline. Within the next 12 h, the patient developed worsening nausea, vomiting and confusion.

On examination the patient was apyrexial, well perfused and haemodynamically stable with no evidence of fluid overload, abdomen was soft with some mild tenderness over the right upper quadrant and right renal angle. An ECG showed normal sinus rhythm. An indwelling urinary catheter was inserted to monitor urine output, which deteriorated from 40 to 10mls/h despite vigorous fluid resuscitation.

An ultrasound scan of the kidneys and collecting system performed as part of AKI investigations showed normal appearance of the renal parenchyma, with no evidence of hydronephrosis. Urinalysis was negative with 2 sets of negative urine cultures. Other investigations included a negative HIV and hepatitis serology, negative COVID PCR, negative blood cultures and a mildly elevated creatine kinase at 581 units/L. CA125 and CEA were within normal values (15 KU/L and < 2 ug/L respectively) and CA199 was raised at 44 kU/L.

A repeat set of blood tests performed several hours later revealed a further deterioration in renal function with a

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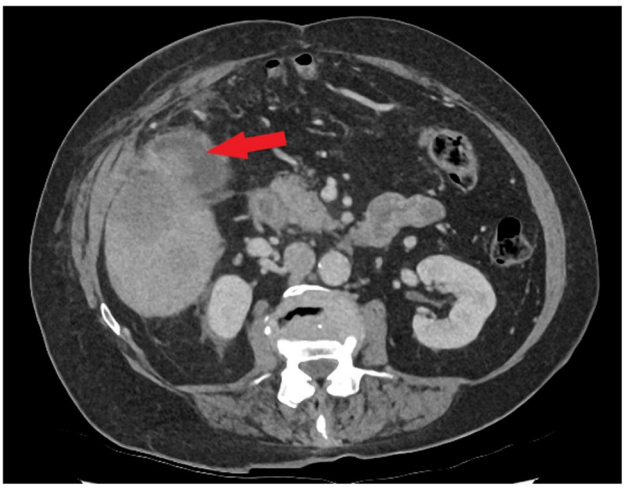

Fig. 1 Abnormal soft tissue mass in gallbladder lumen (see arrow) and metastatic liver disease

creatinine of 386 µmol/L and a potassium of 6.2. A venous blood gas showed a severe high anion gap metabolic acidosis with pH 7.13, with a lactate of 13 mmol/L. Plasma urate and phosphate levels were elevated at 1.06 mmol/L and 2.9 mmol/L respectively.

A diagnosis of spontaneous tumour lysis syndrome was made based on the Cairo-Bishop criteria for diagnosis of TLS [1]. Specifically, our patient met criteria for both biochemical and clinical tumour lysis syndrome with a urate level of 1.06 mmol/L (equivalent to 17.8 mg/dL), a phosphate of 2.9 mmol/L, potassium of 6.2 mmol/L, calcium 2.1 mmol/L and creatinine of 386 µmol/L. The patient was managed according to recommendations outlined in guidance focusing on management of TLS in haematological malignancies [2]. Given the rarity of solid-organ tumour lysis syndrome, there is a lack of guidance specific to this. She received vigorous IV fluid resuscitation, empirical broad-spectrum antibiotics, rasburicase, IV sodium bicarbonate and insulin-dextrose for hyperkalaemia but eventually progressed to requiring renal replacement therapy.

Despite management on the renal high-dependency unit, with one session of haemodialysis, the patient continued to deteriorate. Based on metastatic disease with an unknown primary (at the point of AKI) and continued deterioration despite RRT, the decision was made to withdraw active treatment and the patient passed away 8 days following initial presentation to hospital.

Review of liver histology obtained during ultrasound-guided biopsy, a few days after the patient's demise, showed liver tissue infiltrated by a focally necrotic, poorly differentiated carcinoma with variable but focally strong cdx2 expression, favouring an origin from the gastrointestinal tract. This is demonstrated in Figs. 2a, b and c.

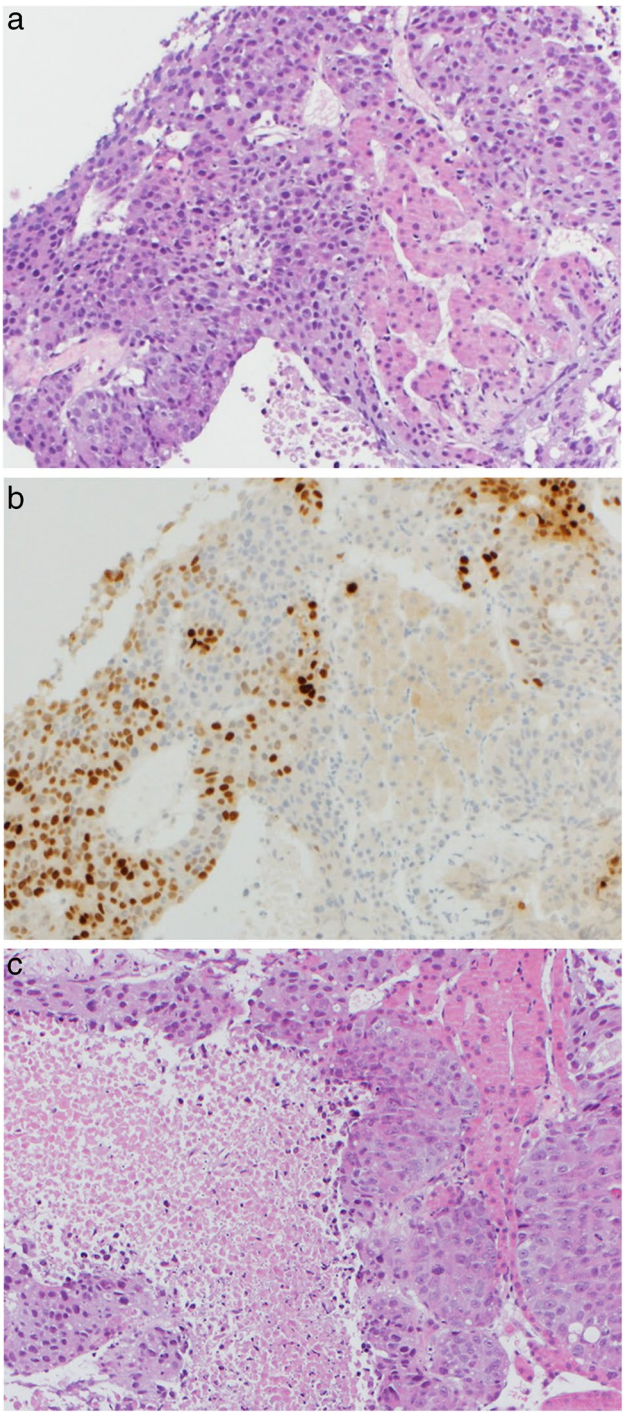

Fig. 2 **a** H&E-stained section of the liver biopsy showing infiltration by metastatic carcinoma. **b** Immunohistochemistry demonstrating nuclear cdx2 expression in a proportion the tumour cells. **c** Infiltration by metastatic carcinoma, and associated necrosis (the necrosis is mainly on the left side of this photo)

The CT imaging showed large bi-lobar liver metastases with a slightly thick-walled gallbladder with a suspicious focal lesion protruding into the gallbladder lumen. No gross bowel, gastric or pelvic abnormalities were seen (Fig. 1). The patient had also undergone a recent gastroscopy and local colon cancer screening with no abnormal results. Retrospective multi-disciplinary discussion reviewed both liver histology and radiological imaging and favoured a primary gall-bladder carcinoma with metastatic disease of the liver.

To our knowledge, this is the first report of a case of spontaneous tumour lysis syndrome associated with primary gallbladder carcinoma. A recent literature review showed the abdominal pain or discomfort was the most common presenting complaint in spontaneous tumour lysis syndrome in nearly half of cases. They also demonstrated that mortality in these cases could be as high as 69% [3]. The take home message from this case is that spontaneous tumour lysis syndrome is a rare, but extremely important differential to consider in patients with newly diagnosed malignancy who develop unexplained severe renal impairment.

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