CASE REPORT

Tumour lysis syndrome in a patient with intravascular spread from a recurrent epithelial ovarian cancer

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SUMMARY

Tumour lysis syndrome is a potentially life-threatening oncological emergency most commonly encountered in patients with rapidly proliferating, treatment-responsive haematological malignancies. It is rarely observed in solid tumours and, to our knowledge, this is the first time that it has been reported in a cancer with an intravascular tumour extension. In this report, we describe a case of a woman who presented with recurrent ovarian cancer and was found to have tumour invading into her vasculature. The patient subsequently developed tumour lysis syndrome after receiving chemotherapy. The case highlights the importance of considering tumour lysis syndrome prophylaxis when treating patients with intravascular involvement from a solid malignancy even if, as in this case, it is a recurrent tumour. Included is a brief review of the literature. We propose that 'intravascular tumour invasion is recognised as an important risk factor for the development of tumour lysis syndrome.

BACKGROUND

Tumour lysis syndrome (TLS) is an oncological emergency and a potentially life-threatening complication of anticancer treatment that most commonly occurs in patients with rapidly proliferating, treatment-responsive haematological malignancies such as acute leukaemia and non-Hodgkin's lymphomas.^{1–2} In these patients, it develops either spontaneously or within 12–72 h of treatment with cytoreductive chemotherapy, when large numbers of neoplastic cells are simultaneously lysed, releasing their intracellular ions and metabolic by-products into the systemic circulation overwhelming the body's normal homeostatic and excretory capabilities. The cardinal signs of TLS are hyperuricaemia causing uric acid nephropathy, hyperphosphataemia with secondary hypocalcaemia and hyperkalaemia. Clinical complications such as acute kidney injury, cardiac arrhythmias and seizures can develop and ultimately may even lead to death due to multiorgan failure.¹

TLS rarely occurs following treatment of solid tumours, although it has been described in individual patients treated for small cell lung cancer, breast cancer, germ cell tumours and malignant melanoma.^{3–4} There are three case reports describing TLS following treatment for epithelial ovarian cancer.^{4–7} To our knowledge, our case is the first to report TLS occurring in the context of intravascular extension of a solid tumour.

CASE PRESENTATION

A 63-year-old woman with a history of serous ovarian cancer that had been in remission for 9 years presented to her general practitioner with symptoms of increasing dyspnoea. She had first been diagnosed with grade 3, International Federation of Gynecology and Obstetrics (FIGO) stage III serous ovarian cancer in 2001 and underwent total abdominal hysterectomy and bilateral salpingo-oophorectomy followed by treatment with six cycles of carboplatin and docetaxel. Five months after completing treatment, her disease recurred with small pulmonary metastases and para-aortic lymphadenopathy, whereupon she received three cycles of liposomal doxorubicin (which was discontinued due to toxicity) followed by nine cycles of topotecan, completing treatment to a partial response in 2003. Remarkably, her disease remained stable for 9 years, during which time she underwent regular oncological review.

In 2012, the patient noticed increasing dyspnoea and was investigated with a contrast-enhanced CT scan of her chest, abdomen and pelvis. This demonstrated a 2.5 cm upper mediastinal mass as well as extensive retroperitoneal lymphadenopathy, both areas being strongly fluorodeoxyglucose (FDG)-avid on positron emission tomography imaging. Image-guided biopsy of her retroperitoneal nodal mass showed it had histological features consistent with recurrent grade 3 serous ovarian adenocarcinoma (CK7+, CK20–, WT-1+). She was also noted to have pulmonary emboli and started on low molecular weight heparin and antibiotics for a lower respiratory tract infection. However, her dyspnoea worsened and her imaging was repeated. This not only confirmed disease progression within the mediastinum, but new pulmonary nodules and extensive intravascular tumour extension involving the right pulmonary arteries, right atrium, inferior vena cava and pelvic veins (figures 1 and 2). Although para-aortic nodes were involved, there was no visible pelvic mass.

Removal of the clot by open cardi thoracic surgery or thrombolysis was considered but dismissed owing to the high risk of life-threatening complications. The patient was offered chemotherapy and started a combination of 3 weekly carboplatin (AUC5) with weekly paclitaxel (75 mg/m²). She was treated as a hospital inpatient and kept under close clinical observation. Two days after receiving her first dose of chemotherapy, she developed hyperkalaemia (6.1 mmol/l (normal range

To cite: Camarata M, Davies R, Copley S, et al. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2013-009532

Figure 1 Axial fused FDG¹⁸ CT/positron emission tomography demonstrating increased tracer uptake within the inferior vena cava and bilateral para-aortic lymph nodes.

3.5–5.3 mmol/l), hypocalcaemia (2.09 mmol/l (normal range 2.15–2.6 mmol/l)), hyperphosphataemia (1.69 mmol/l (normal range 0.8–1.5 mmol/l)), raised lactate dehydrogenase (758 IU/l (normal range 125–243 IU/l)) and blood urate level (0.83 mmol/l (normal range 0.14–0.37 mmol/l)). Arterial blood gas sampling demonstrated a metabolic acidosis pH 7.27 (7.34–7.44), BE 5.8 (–2 to +2), HCO₃[–] 20.3 (22–26 mEq/l). A clinical diagnosis of TLS was made with concurrent acute kidney injury and a metabolic acidosis.

TREATMENT

The patient was given insulin Actrapid (10 units in 50 ml of 50% dextrose) and 10 ml of 10% calcium gluconate to correct her hyperkalaemia and hypocalcaemia. She was treated with intravenous fluids (0.9% normal saline at 125 ml/h), rasburicase (12 mg) and urinary alkalinisation with sodium bicarbonate (1.26% at 125 ml/h) aiming for a urinary pH of 7–7.5 to increase excretion of metabolic waste products. However, owing to

Figure 2 Axial fused FDG¹⁸ CT/positron emission tomography (PET) demonstrating increased tracer uptake within the right atrium and both lungs. PET scan of the heart showing right atrial tumour extension.

high-output cardiac failure, she developed pulmonary oedema following intravenous fluid rehydration. With multiorgan involvement and a high requirement for support and monitoring, she was admitted to the intensive care unit (ICU) where her diuresis was promoted with intravenous frusemide (1–4 mg/h) and pulmonary oedema treated with intravenous glyceryl trinitrate (1 mg/h). The following day she developed worsening type 2 respiratory failure and was started on non-invasive ventilation. She deteriorated clinically with the development of abdominal pain, deranged liver function tests with a raised bilirubin (28 (<17 µmol/l)), a raised alanine aminotransferase (229 (<37 IU/l)), worsening coagulopathy (prothrombin time of 22.7 (10–12 s) and a platelet count of 39 (150–400 × 10⁹/l)). A CT scan demonstrated ischaemic hepatitis, hepatic vein thrombosis and colonic infarction due to tumour fragments within the superior mesenteric vein and a filling defect in the main portal vein.

OUTCOME AND FOLLOW-UP

The patient died from multiorgan failure on day 2 of her ICU admission.

DISCUSSION

TLS is an oncological emergency resulting from tumour cell breakdown, which causes a rapid release of intracellular contents into the systemic circulation leading to metabolic abnormalities and clinical manifestations that can ultimately be life threatening. In 2004, Cario and Bishop modified the original definition of TLS published by Hande and Garrow⁸ and produced what is considered to be the current classification system⁹ with the addition of three further refinements proposed by Howard *et al.*¹ The current classification system of TLS (table 1) is divided into lab tumour lysis syndrome (LTLS) and clinical tumour lysis syndrome (CTLS).⁹ To fit the definition of LTLS, two or more of the metabolic abnormalities illustrated in table 1 must occur simultaneously within 3 days before or up to 7 days after the initiation of therapy.⁹ CTLS is defined as the presence of LTLS and any one or more of the clinical manifestations illustrated in table 1 that is not attributed to a therapeutic agent.⁹

Table 1 Tumour lysis syndrome definition⁹

Lab tumour lysis syndrome*		
Element	Value	Change from baseline†
Uric acid	≥476 µmol/l	25% increase
Potassium	≥6.0 mmol/l	25% increase
Phosphorus	≥1.45 mmol/l for adults	25% increase
Calcium	≤1.75 mmol/l	25% decrease
Clinical tumour lysis syndrome‡		
► Symptomatic hypocalcaemia ¹		
► Increase in serum creatinine greater than or equal to 1.5 times the institutional upper limit of normal		
► Cardiac arrhythmia		
► Seizure		
► Sudden death		

*Two or more of the metabolic abnormalities must occur simultaneously within 3 days before or up to 7 days after the initiation of therapy.

†Criterion only if outside the normal range.

‡Clinical tumour lysis syndrome is defined as the presence of lab tumour lysis syndrome and any one or more of these clinical manifestations not attributed to a therapeutic agent.

Box 1 Risk factors for development of tumour lysis syndrome in solid tumours²

- ▶ High tumour burden with metastatic disease
- ▶ Liver metastasis with or without liver impairment
- ▶ Elevated serum lactate dehydrogenase and uric acid levels
- ▶ Response to chemotherapy or other anti-neoplastic treatment
- ▶ Pre-existent renal insufficiency
- ▶ Treatment with nephrotoxic agents
- ▶ Underlying problems, such as infection and dehydration

The principles of management of TLS include the initiation of preventative therapy in high-risk patients and, on diagnosis, the prompt management of metabolic and renal complications. This includes the initiation of supportive measures such as intravenous hydration, haemodialysis where indicated and administration of catalytic agents such as allopurinol or the recombinant urate oxidase, rasburicase. Identifying patients at risk of TLS is essential because it may occur rapidly and is preventable with vigorous hydration and antihyperuricaemic therapy.¹⁰ Furthermore, the resulting complications can compromise the efficacy and/or subsequent administration of chemotherapy and have an adverse impact on morbidity and mortality.¹⁰

In 2006, Gemici² proposed risk factors for the development of TLS in solid tumours (box 1). In 2010, an expert consensus panel published recommendations on the evaluation of risk and prophylaxis of TLS in adults and children.¹⁰ Solid tumours were classified as having a low risk for the development of TLS with the caveat that bulky, solid tumours sensitive to chemotherapy be considered as an intermediate risk. For this group, they proposed the following prophylactic measures: monitoring for TLS and complications, increased hydration with 3 l/m² fluid per day and allopurinol 100–300 mg orally given 8 hourly.¹⁰ We propose that patients with solid tumours with an intravascular extension be included in the classification as being at high risk for the development of TLS even if the tumour itself is not.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

Learning points

- ▶ We describe an unusual case of a tumour lysis syndrome in a patient with recurrent metastatic ovarian cancer with an intravascular tumour extension that occurred following treatment with paclitaxel and carboplatin chemotherapy.
- ▶ We hypothesise that progression to florid clinical tumour lysis syndrome is more likely in the presence of an intravascular solid tumour extension, especially in patients with a long treatment-free interval.
- ▶ Such patients should be managed with prophylactic rasburicase, vigorous hydration and close clinical and biochemical monitoring in a high dependency environment.¹
- ▶ Where possible, these patients may also benefit from a treatment prophase, in which they receive low-intensity initial therapy for a week prior to the start of therapy to allow the renal homeostatic mechanisms to clear the high burden of metabolites before they accumulate and cause organ damage.¹

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