CASE REPORT

A tumour lysis syndrome in a chemotherapy naïve patient with metastatic pancreatic adenocarcinoma

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SUMMARY

A 56-year-old woman with a new diagnosis of metastatic pancreatic cancer presents to the emergency room with generalised fatigue. The patient is afebrile, however, hypotensive and tachycardic. Physical examination shows diffuse lymphadenopathy. Initial laboratory tests indicate that the patient has hyperkalaemia, hypocalcaemia, with a high lactate dehydrogenase and high uric acid. The patient was also in renal failure. On the basis of the clinical presentation, the patient was diagnosed with spontaneous tumour lysis syndrome, despite the syndrome never having been reported in metastatic pancreatic cancer. The patient was treated appropriately with intravenous hydration, allopurinol and rasburicase. All laboratory abnormalities were corrected by day 3 of treatment.

BACKGROUND

Tumour lysis is one of the most common oncological emergencies. Spontaneous tumour lysis syndrome (TLS) is rarely seen in solid tumours. We present the first case of spontaneous TLS in a patient with metastatic pancreatic cancer prior to receiving any systemic treatment for her disease. The importance of this case report is that it sheds light on the importance of making a diagnosis based on the clinical presentation of a patient and not solely on the prevalence of a syndrome.

CASE PRESENTATION

A 56-year-old woman presented to the outpatient clinic with generalised fatigue, abdominal pain and weight loss of 6 months duration. Her medical history was significant for chronic idiopathic pancreatitis since 2001 (figure 1). CT of the abdomen and pelvis demonstrated extensive intra-abdominal and retroperitoneal lymphadenopathy with a 6.7×10 cm mesenteric mass inseparable from the uncinate process of the pancreas (figure 2). Extensive hepatic metastases were also seen with the largest measuring 4.5×4.1 cm (figure 3). An ultrasound-guided biopsy of one liver mass revealed poorly differentiated pancreatic adenocarcinoma, staining positive for CK8/18, CK7, carcinoembryonic antigen (CEA), CA125 and negative for CK20, hepatocyte marker, AFP, CDX2, TTF1, PAX-8, CD31, synaptophysin and chromogranin. Her cancer markers at diagnosis were: CA19-9 3458.6 U/mL (0.0–35.0), CEA 25.8 µg/L (0.0–4.9), CA125 1793 U/mL (0–35). Prior to receiving chemotherapy, the patient presented to the emergency department for generalised weakness. Vital signs showed a temperature of 36.6°C, blood

Figure 1 Axial view of a CT of the abdomen and pelvis showing swelling of the distal body and the tail region of the pancreas in keeping with chronic pancreatitis.

Figure 2 Axial view of a CT of the abdomen and pelvis demonstrating extensive intra-abdominal and retroperitoneal lymphadenopathy with a 6.7×10 cm mesenteric mass inseparable from the uncinate process of the pancreas.

Figure 3 Axial view of a CT of the abdomen and pelvis showing extensive hepatic metastases, with the largest measuring 4.5×4.1 cm.

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pressure 89/55 mm Hg, heart rate 120 bpm, respiratory rate 18 and oxygen saturation of 95% on room air. The jugular venous pressure was below the sternal angle. Otherwise the physical examination was notable for diffuse lymphadenopathy. Medications were intravenous saline for volume expansion and morphine 2.5 mg every 8 h as needed for pain.

INVESTIGATIONS

Laboratory analysis revealed a creatinine of 146 µmol/L (reference range (RR) 40–85 µmol/L), potassium of 7.5 mmol/L (RR 3.5–5.0 mmol/L), phosphate of 2.10 mmol/L (RR 0.80–1.45 mmol/L), ionised calcium of 1.02 mmol/L (RR 1.15–1.32 mmol/L), uric acid of 857 µmol/L (RR 147–353 µmol/L) and lactate dehydrogenase of 379 U/L (RR 110–210 U/L). A venous blood gas showed a pH of 7.31 (RR 7.34–7.44). A presumptive diagnosis of TLS was performed. Acute pancreatitis and rhabdomyolysis were excluded biochemically. The ECG showed normal sinus rhythm without changes of hyperkalaemia.

TREATMENT

The patient received urgent medical treatment for her hyperkalaemia and acute renal insufficiency. She was also started on sodium polystyrene, allopurinol 100 mg daily, and was given rasburicase 3 mg intravenously. Normalisation of the creatinine, potassium, phosphate and uric acid levels was achieved after 3 days of treatment. The rasburicase was discontinued and the patient was continued on allopurinol 100 mg daily.

OUTCOME AND FOLLOW-UP

Owing to the unusual TLS presentation with no previous cases reported in treatment-naïve pancreatic patients with cancer and the new rapidly enlarging and diffuse lymphadenopathy, the patient underwent an excisional biopsy of a left infraclavicular lymph node to exclude concomitant high-grade lymphoma. Pathology showed anaplastic carcinoma with negative staining for lymphoid markers. The patient subsequently suffered from a very rapid functional decline due to her progressive disease and was deemed no longer a candidate for chemotherapy. She was provided with palliative care and died shortly thereafter.

DISCUSSION

One of the most common oncological emergencies is TLS. The rapid and sudden apoptosis and cell rupture of cancer cells release the cellular components into the blood circulation and causes sudden metabolic derangements.^{1–4}

There are numerous metabolic consequences: (1) hyperkalaemia, secondary to the release of intracellular potassium, which may lead to cardiac arrhythmias and sudden cardiac death. (2) Hyperuricaemia, secondary to the catabolism of purine nucleic acids to hypoxanthine and xanthine and then to uric acid via the enzyme xanthine oxidase.² The overproduction of uric acid may then contribute to an acute kidney injury by crystal precipitation in the tubules in addition to other mechanisms.³ (3) Hyperphosphataemia, secondary to its high concentration in malignant cells, which can cause calcium phosphate crystal deposition in the renal tubules and worsen kidney injury.^{2–4} (4) Secondary hypocalcaemia due to the binding of calcium to phosphate, which can precipitate in the heart and lead to cardiac arrhythmias.

TLS is most commonly seen in patients with high-grade lymphomas, particularly Burkitt's lymphoma, after the initiation of systemic treatment with cytotoxic therapy. However, TLS has been also reported in tumours with a high proliferative index (ie, High Ki67 index), large tumour burden, or in tumours with

high sensitivity to chemotherapeutic agents. Rarely, TLS may occur spontaneously before administration of the therapy, which has been described in haematological malignancies,⁵ as well as rarely in solid malignancies such as cholangiocarcinoma, renal cell carcinoma, hepatocellular carcinoma,⁶ small cell lung cancer, germ cell tumours and breast cancer.^{7–9}

The symptoms seen in TLS reflect the associated metabolic abnormalities. These include nausea, vomiting, diarrhoea, lethargy, heart failure, cardiac arrhythmias, seizures, muscle cramps, tetany, syncope and possible sudden death.¹

In 2004, the Cairo-Bishop criteria for TLS were defined.¹⁰ These are specific laboratory criteria for the diagnosis of TLS both at presentation and within 7 days of treatment. They are subdivided into laboratory or clinical TLS. Laboratory TLS is diagnosed if the levels of two or more of potassium, phosphate, calcium or uric acid are greater than or less than normal at presentation, or if they change by 25% within 3 days before or 7 days after the initiation of treatment. Clinical TLS is defined by the presence of laboratory TLS in addition to the following significant clinical complications: renal insufficiency, seizures and/or cardiac arrhythmias/sudden death.

TLS may be prevented in high-risk patients with aggressive intravascular hydration and prophylaxis against hyperuricaemia through the use of the xanthine oxidase inhibitor allopurinol or the recombinant urate oxidase rasburicase. Treatment of TLS aims to clear high plasma potassium and uric acid levels and to avoid or limit the acute renal failure. This may be achieved by giving potassium-lowering agents, use of allopurinol (although it has a limited use in acute TLS) or rasburicase, intravenous hydration and diuresis, and, if needed, renal replacement therapy.

To the best of our knowledge, this is the first reported case of TLS in a treatment-naïve patient with metastatic pancreatic adenocarcinoma. In pancreatic cancer TLS is rare, with only one case of TLS published, and that was in a patient who had already received chemotherapy.¹¹ Our patient received early-directed intervention and the fatal complications of this oncological emergency were prevented. Though the outcome was ultimately poor, our case highlights the importance of maintaining a high index of suspicion when presented with signs of symptoms of TLS.

Learning points

- ▶ Tumour lysis syndrome is uncommon in non-haematological malignancies.
- ▶ While uncommon, the condition can occur and requires the astute clinician to recognise the syndrome.
- ▶ The diagnosis of tumour lysis syndrome is mainly clinical relying on history, physical examination and laboratory results.
- ▶ Tumour lysis syndrome is an oncological emergency.
- ▶ If detected early, this potentially fatal condition can be medically managed.

Contributors RRS, JR and TCL were involved in the study concept and design. RRS, JR were involved in the acquisition of data. RRS, JR, TCL were involved in the drafting of the manuscript. TCL was involved in the study supervision.

Competing interests None.

Patient consent Obtained.

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