1. Introduction

Tumour lysis syndrome (TLS) is an oncologic emergency caused by the release of phosphate, potassium and nucleic acids into the systemic circulation after cytotoxic chemotherapy. It is most frequently a complication in patients with hematologic malignancies and is rarely encountered in adult patients with solid organ tumours (Howard et al., 2011). Patients with TLS commonly present within 7 days after chemotherapy with acute kidney injury (AKI), seizures and/or cardiac dysrhythmias. The diagnosis of TLS is made according to the Cairo-Bishop classification system which includes laboratory and clinical criteria. To confirm a laboratory diagnosis of TLS, patients must have uric acid > 476 (μ/L), phosphate > 1.45 mmol/L, potassium > 6.0 mmol/L and calcium < 1.75 mmol/L. The clinical criteria include serum creatinine 1.5 times the upper limit of normal, cardiac arrhythmia, seizure or sudden death (Cairo and Bishop, 2004).

2. Case report

2.1. Initial presentation

A 71 year old woman with a history of hypertension presented to the emergency department with increasing dyspnea on exertion and a 3 month history of malaise, anorexia, fatigue and progressive unintentional weight loss. She was found have new atrial fibrillation with heart failure and was referred to the internal medicine service for further investigation and management.

During admission, an abdominal and pelvic ultrasound performed for the investigation of clinical ascites revealed large bilateral adnexal masses with solid and cystic changes. Abdominal CT scan confirmed the adnexal masses, and demonstrated solid peritoneal deposits with moderate to large volume ascites (Fig. 1). Given these findings, an ovarian malignancy was suspected although her CA-125 level was low at 154 (μ/mL) which was not entirely supportive of this diagnosis.

After medical stabilization, the patient was discharged home with urgent follow-up at the regional cancer centre by the Gynecology service.

2.2. Outpatient clinic visit and initiation of chemotherapy

Five days following discharge, the patient was assessed at the gynecology-oncology clinic and a paracentesis was performed. The cytology revealed malignant cells suggesting poorly differentiated carcinoma or sarcoma with epithelioid morphology. Based on these results, her gynecologist planned for 3 cycles of Paclitaxel and Carboplatin followed by interval debulking for presumed epithelial ovarian cancer. She received the first dose of her chemotherapy at a subsequent clinic visit, eleven days after her first clinic visit. The patient did not receive allopurinol for TLS prophylaxis.

2.3. Re-admission to hospital

Four days after chemotherapy, the patient presented to the emergency department with diarrhea, fatigue and generalized weakness. On examination, the patient was afebrile and clinically dehydrated. Her blood work revealed the following (Table 1).

The patient’s vitals were as follows: temperature of 36.4 °C, irregular heart rate of 100, a blood pressure of 88/54, 96% oxygen saturation on room air and a respiratory rate of 26 at the time of our examination. She was admitted to hospital and received volume resuscitation for hypotension and pre-renal acute kidney injury (AKI). The patient was also pancytopenic and was treated with 2 units of PRBC (packed red blood...
cells), GCSF (Granulocyte colony stimulating factor) and prophylactic antibiotics.

2.4. Diagnosis of tumour lysis syndrome

In view of the patient's recent chemotherapy, new onset AKI, hypophosphatemia and hypocalcemia; a diagnosis of tumour lysis syndrome (TLS) was considered. A uric acid (UA) level was immediately drawn and was found to be considerably elevated at 1417. According to the Cairo-Bishop criteria, the patient met criteria for tumour lysis syndrome (TLS) with a serum phosphate ≥1.45mmol/L, uric acid level ≥476μmol/L and cytotoxic therapy within 7 days. The patient was promptly given a dose of Rasburicase 6mg IV and started on a maintenance dose of 0.5mg/kg daily.

2.5. ICU stay

The patient was transferred to the Intensive Care Unit (ICU) as she required intubation for progressive hypoxic respiratory failure secondary to volume overload and started on vasopressor support for septic shock. Continuous renal replacement therapy (CRRT) was initiated. Blood cultures grew Group B streptococcus and urine was positive for E. coli. Broad spectrum antibiotic therapy with piperacillin-tazobactam was continued.

Unfortunately, the patient remained dependant on CRRT and with no significant improvement in her haemodynamic state or respiratory status. The patient then developed a fungemia which led to further clinical deterioration. Given the patient's overall poor prognosis, the patient's family opted for comfort care. Life support was withdrawn and the patient passed away shortly thereafter.

2.6. Autopsy

Autopsy revealed an intramural uterine malignant neoplasm with extensive necrosis consistent with undifferentiated endometrial stromal sarcoma with metastatic involvement of the omentum, bowel, gastric mucosa and the pancreas. Examination of the kidneys reveals marked autolytic changes with numerous granular casts within proximal distal tubules (Fig. 2).

3. Discussion

TLS is very rarely encountered in solid organ tumours. To date, only 45 cases of TLS have been described in solid organ tumours. The most common neoplasms in which TLS was diagnosed were as follows: small cell carcinoma (13 cases), hepatocellular carcinoma (12 cases), breast carcinoma (10 cases), melanoma (9 cases) and sarcoma (6 cases) (Vodopivec et al., 2012).

TLS is even rarer in patient with uterine neoplasms with one case in a patient with uterine epithelioid leimyosarcoma (Hiraizumi et al., 2011) and another with recurrent endometrial cancer (Godoy et al., 2009). This is the first case to report a diagnosis of TLS in a patient with undifferentiated endometrial stromal sarcoma post chemotherapy with Carboplatin and Paclitaxel.

There are certain factors that place patients with solid organ tumours at higher risk of developing TLS which include: large tumour burden, extensive metastases, highly proliferative tumour, high sensitivity to anticancer therapy, pre-existing nephropathy, or pretreatment hyperuricemia, hyperphosphatemia, or LDH > 1500 IU/L².

This case illustrates that TLS is life threatening oncologic emergency that should be recognized in patients that have recently undergone chemotherapy and present with the hypocalcemia, hyperkalemia, hyperuricemia and hyperphosphatemia. Unfortunately, our patient had a highly proliferative malignancy with large tumour burden with extensive necrosis which placed her at a significantly higher risk of developing TLS.

Table 1

| Parameter | Normal ranges | Before chemotherapy | After Chemotherapy (Day 4, 5, 6) |
|-----------|--------------|---------------------|-----------------------------------|
| CBC       |              |                     | Day 4 7:00 PM | Day 5 2:26-11:15 PM | Day 6 2:20 AM |
| Leukocytes × 10⁹/L | 4.0–11.0 | 27.1 | 10.8 | 0.3 | 0.2 |
| Neutrophils × 10⁹/L | 2.0–7.5 | 25.5 | 10.6 | 0.1 | 0.1 |
| Lymphocytes × 10⁹/L | 1.5–4.0 | 1.2 | 0.2 | 0.2 | 0.1 |
| Monocytes × 10⁹/L | 0.2–0.8 | 0.3 | 0.0 | 0.0 | 0.0 |
| Hemoglobin × 10¹²/L | 115–165 | 92 | 91 | 82 | 85 |
| Platelets | 150–400 | 377 | 125 | 38 | 65 |
| Chemistry |            |                     |                   |                   |                   |
| Potassium (mmol/L) | 3.5–5.0 | 3.6 | 5.8 | 4.7 | 4.8 |
| Phosphate (mmol/L) | 0.80–1.45 | – | 3.15 | 3.16 | 3.30 |
| Calcium (mmol/L) | 2.15–2.55 | 2.01 | 1.48 | 1.31 | 1.28 |
| Albumin (mmol/L) | 35–50 | 18 | 12 | 11 | 10 |
| BUN (μmol/L) | 3.5–7.2 | – | 46.0 | 45.3 | – |
| Creatinine (μmol/L) | 50–98 | 71 | 250 | 242 | 238 |
| Uric acid (μmol/L) | 155–357 | – | – | – | 1417 |
| LDH (IU/L) | 100–220 | 597 | – | 1557 | – |
The management of TLS principally involves aggressive intravenous rehydration to preventing AKI since this minimizes toxic accumulation of uric acid, phosphate and potassium thus delaying progression of disease. Hypouricemic therapy with Rasburicase should be started promptly. Patients with TLS require treatment in the intensive care unit with cardiac monitoring, electrolytes every 6 h and accurate measures of urine output. Symptomatic hyperkalemia and hypocalcaemia should be treated and there should be a low threshold for initiating renal replacement therapy (Howard et al., 2011; Davidson et al., 2004).

4. Conclusion

Especially with the recent recognition of increasing TLS prevalence in solid organ tumours, it is important to consider TLS as a possibility even in patients with non-hematologic cancer with metastatic disease, and recent cytotoxic therapy.

Conflicts of interest statement

The authors do not have any conflicts of interest to disclose.

Author contributions

1. Zeeshan Ahmed – primary author. Performed the literature review and wrote the case report.
2. Ahmed Barefah – second author who assisted in literature review and writing of the case report.
3. Parveen Wasi – malignant Hematologist who provided guidance on the diagnosis and management of tumour lysis syndrome.
4. Graham Jones – ICU attending who contributed to historical details regarding the patient’s ICU course and also reviewed the manuscript.
5. Jennifer Ramsay – Pathologist who provided the pathology slides with their accompanying analysis. Also served as a primary reviewer for the manuscript.

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