

## Case report

## Tumor lysis syndrome in a patient with ovarian yolk sac tumor

Katherine VanHise<sup>a,\*</sup>, Alexa Swailes<sup>a</sup>, Michael Roche<sup>a</sup>, Jordan M. Newell<sup>b</sup>, Joshua P. Kesterson<sup>c</sup><sup>a</sup> Department of Obstetrics and Gynecology, Penn State College of Medicine, Milton S. Hershey Medical Center, United States<sup>b</sup> Department of Pathology, Penn State College of Medicine, Milton S. Hershey Medical Center, United States<sup>c</sup> Department of Obstetrics and Gynecology, Division of Gynecologic Oncology, Penn State College of Medicine, Milton S. Hershey Medical Center, United States

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## 1. Introduction

Ovarian yolk sac tumor is a subtype of germ cell tumor – a rare gynecologic malignancy comprising < 5% of all ovarian neoplasms (Shaaban et al., 2014). These tumors are characterized by high mitotic rates and rapid proliferation, often resulting in bulky tumor burden. Tumor lysis syndrome has been reported in association with germ cell tumors, typically following chemotherapy (Feres et al., 2008). Herein, we present the case of tumor lysis syndrome following low-dose, localized palliative radiation prior to chemotherapy exposure in a patient with a metastatic germ cell tumor.

## 2. Case presentation

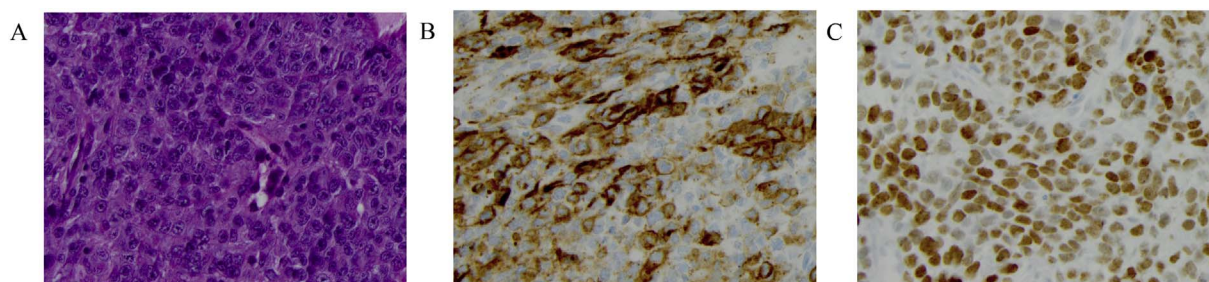
A 40-year-old nulliparous woman with history of heavy vaginal bleeding presented as a referral to Gynecologic Oncology after imaging at an outside hospital showed a pelvic mass and diffuse lymphadenopathy. This imaging was prompted by the patient's complaint of abdominal and neck pain, and rapidly enlarging neck mass. CT demonstrated a lobulated, hypo-enhancing heterogeneous endometrial mass measuring 9 × 8 cm as well as a 13 × 10 cm left adnexal mass and diffuse bulky lymphadenopathy, including a 7 × 6 cm superior mediastinal lesion. A CT-guided core biopsy of the abdominal mass was consistent with a poorly differentiated germ cell tumor with staining pattern and histologic features supportive of yolk sac tumor (Fig. 1). Surgical resection was not considered to be a feasible option in this patient given her considerable widespread tumor burden and poor functional status. Due to persistent vaginal bleeding, she received 9Gy of pelvic radiation in 3 doses. She subsequently developed acute kidney injury with a creatinine of 1.75 mg/dL (previously 0.9 mg/dL). Additionally, she was found to have uric acid elevated to 9.9 mg/dL

(47.5% increase from her baseline), phosphorous elevated to 5.6 mg/dL (51.4% increase from baseline), and potassium of 5.5 mg/dL (37.5% increase from baseline), raising the suspicion for tumor lysis syndrome. She met three Cairo-Bishop laboratory criteria (hyperuricemia, hyperphosphatemia, hyperkalemia) and one clinical criterion for tumor lysis syndrome (acute kidney injury), thus establishing the diagnosis (Cairo and Bishop, 2004). The tumor lysis syndrome resolved with aggressive intravenous hydration, allopurinol and a low potassium diet over a period of three days (Table 1). Chemotherapy was subsequently initiated consisting of bleomycin 30 units (days 1, 8 and 15), etoposide 100 mg/m<sup>2</sup> (days 1–5) and cisplatin 10 mg/m<sup>2</sup> (days 1–5) (Homesley et al., 1999). The dosage of cisplatin was reduced from the standard dose of 20 mg/m<sup>2</sup> to 10 mg/m<sup>2</sup> to prevent exacerbation of acute kidney injury (Homesley et al., 1999). Likewise, standard hydration was administered with chemotherapy; however, the total amount was decreased secondary to the patient's volume overloaded status. During the patient's hospital course, she developed sepsis resulting in multi-organ system dysfunction. She was treated aggressively with antibiotics and supportive measures, with which she improved. After undergoing a total of two cycles of bleomycin, etoposide and cisplatin, the patient developed sepsis again with multi-organ failure. She and her family elected for no further interventions, and she died on hospital day 63.

## 3. Discussion

Tumor lysis syndrome (TLS) is an oncologic emergency characterized by metabolic derangements secondary to cell breakdown and release of intracellular contents. It often occurs in patients with hematological malignancies being treated with cytotoxic therapies (Cairo and Bishop, 2004). Treatment-induced widespread and rapid destruction of tumor cells results in a massive efflux of intracellular ions,

\* Corresponding author at: Penn State College of Medicine, 500 University Drive, Hershey, PA 17033, United States.  
E-mail address: [kvanhise@pennstatehealth.psu.edu](mailto:kvanhise@pennstatehealth.psu.edu) (K. VanHise).



**Fig. 1.** Immunohistochemical features supportive of ovarian yolk sac tumor. Sections demonstrate solid sheets of tumor cells with prominent nucleoli, a moderate amount of eosinophilic cytoplasm, and moderate cytologic atypia (A. H&E; 400 ×). Additionally, increased mitotic activity and necrosis were seen. Immunohistochemistry demonstrated the tumor cells to be strongly reactive for glypican-3 (B. 400 ×) and SALL-4 (C. 400 ×).

**Table 1**  
Laboratory changes establishing the diagnosis and resolution of Tumor Lysis Syndrome.

	Normal Values	Patient Baseline	Diagnosis of TLS <sup>a</sup>	Treatment Day 1	Treatment Day 2	Treatment Day 3 <sup>b</sup>
Uric acid	2.5–6.2 mg/dL	4.0 mg/dL	9.9 mg/dL	8.9 mg/dL	Not measured	7.1 mg/dL
Phosphorous	2.5–4.5 mg/dL	3.7 mg/dL	5.6 mg/dL	4.8 mg/dL	5.1 mg/dL	4.4 mg/dL
Potassium	3.5–5.1 mg/dL	4.0 mg/dL	5.5 mg/dL	4.8 mg/dL	4.1 mg/dL	3.6 mg/dL
Calcium	8.4–10.2 mg/dL	8.9 mg/dL	9.2 mg/dL	9.2 mg/dL	9.2 mg/dL	9.1 mg/dL

<sup>a</sup> Laboratory diagnosis requires two of the four laboratory changes: uric acid > 8 mg/dL or 25% increase from baseline; potassium > 6 mg/dL or 25% increase from baseline; phosphorus > 4.5 mg/dL in adults or 25% increase from baseline; calcium < 7 mg/dL or 25% decrease from baseline.

<sup>b</sup> On treatment day 3, the patient no longer met laboratory diagnostic criteria for Tumor Lysis Syndrome indicating successful resolution.

nucleic acids and metabolites into the bloodstream. Nucleic acids are broken down into uric acid leading to hyperuricemia; hyperkalemia, hyperphosphatemia and hypocalcemia also result. Hyperuricemia and hyperphosphatemia promote precipitation of uric acid and calcium phosphate crystals in the renal tubules causing self-perpetuating kidney injury. In addition to kidney injury, the efflux of ions into the bloodstream can trigger cardiac arrhythmias, seizures or death. Any such occurrence in the setting of large tumor burden with or without use of cytotoxic therapy constitutes a clinical diagnosis of TLS. A laboratory diagnosis of TLS is made using the Cairo-Bishop classification (Cairo and Bishop, 2004), which requires two of the four laboratory changes: uric acid > 8 mg/dL or 25% increase from baseline; potassium > 6 mg/dL or 25% increase from baseline; phosphorus > 4.5 mg/dL in adults or 25% increase from baseline; calcium < 7 mg/dL or 25% decrease from baseline. Such metabolic derangements seen in TLS often necessitate vigorous hydration, hypouricemic agents and hemodialysis—the mainstays of treatment (Cairo and Bishop, 2004).

Tumor lysis syndrome has been reported in patients with solid tumor malignancies including male germ cell tumors. Reports of cases in solid tumors are rare, and have been documented to occur both spontaneously and after chemoradiation (Feres et al., 2008; D'Alessandro et al., 2010; Pentheroudakis et al., 2001; Stuart and Auten, 2017). Herein, we presented a case of a young woman with large tumor burden who developed TLS prior to chemotherapy. Whether her palliative radiation was the inciting factor to development of TLS or if the TLS occurred spontaneously secondary to large tumor volume is uncertain. There have been rare reports of spontaneous tumor lysis syndrome occurring in germ cell tumors (D'Alessandro et al., 2010; Pentheroudakis et al., 2001). In such cases, marked hyperuricemia was seen prior to any cytotoxic therapy. In our patient, uric acid level prior to radiation treatment was within normal range, at 4.0 mg/dL.

An appreciation of the risk factors for TLS must be maintained so that prompt diagnosis and treatment can be initiated. Managing a patient with TLS proves to be challenging when planning for future cytotoxic therapy. The risks of using of nephrotoxic chemotherapeutic agents that could possibly worsen the acute kidney injury in TLS must be weighed against the alternative: progression of disease or no chance for cure. Ovarian germ cell tumors are most commonly treated with the

combination chemotherapy BEP - bleomycin, etoposide and cisplatin - with favorable outcomes; however, cisplatin is known to be nephrotoxic in a dose-related and cumulative fashion (Homesley et al., 1999). Ultimately, we decided to utilize BEP chemotherapy given the young age of our patient.

#### Patient consent

Written informed consent was obtained from the patient for publication of this case report. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

#### Conflict of interest statement

The authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

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