CASE REPORT

Patient

A 20-year-old Hispanic male who is a semiprofessional soccer player with no medical history presented to the emergency department with 1 month of abdominal distension and 4 days of left lower extremity swelling. During initial interview, the patient offered that his testicle had been enlarged for approximately 4-6 years, without any workup or intervention. A firm nontender abdomen, enlarged left hemiscrotum, and left lower extremity swelling were noted on physical examination. A left supraclavicular lymph node was also palpable. Laboratory workup revealed a serum creatinine of 1.64 mg/dL and estimated glomerular filtration rate of 59. Tumor markers were drawn and elevated (alpha-fetoprotein, 350; human chorionic gonadotropin, 440; and lactate dehydrogenase 262) (Fig. 1). Lower extremity duplex ultrasound confirmed noncompressible occlusive venous thrombosis involving the left external iliac, common femoral, great saphenous, femoral, and popliteal veins. Severe right and moderate left hydronephrosis were visualized on renal-bladder ultrasound, along with a large compressive intraabdominal cystic mass compressing bilateral ureters. Scrotal ultrasound was obtained confirming a 9.8 × 6.8 × 8.2 cm heterogeneous left testicular mass. Positron emission tomography-computed tomography imaging revealed a large left testicular cystic mass; a large volume of multiseptated cystic mass filling the entire abdomen and pelvis, encasing the great vessels and their branches and displacing all intraabdominal organs anteriorly and superiorly; and a large left neck mass. Bilateral hydrenephrosis from extrinsic compression was also noted. Masses were hypometabolic on positron emission tomography imaging. There was no evidence of disease in the thorax or brain. Bilateral percutaneous nephrostomy tubes were placed with subsequent normalization of renal function. Biopsy of the retroperitoneal mass was performed and histopathological evaluation was consistent with immature teratoma. Oncology was consulted and the patient began his first of 3 cycles of bleomycin, etoposide, and cisplatin chemotherapy for International Germ Cell Consensus Classification Group good-risk disease. Anticoagulation with low molecular weight heparin was initiated for left lower extremity deep venous thrombosis. Repeat imaging performed after 3 cycles of bleomycin, etoposide, and cisplatin showed an increase in tumor burden despite normalization of tumor markers, with propagation of thrombus within the left common iliac vein, consistent with growing teratoma syndrome (GTS). Specifically, an 8-cm left neck mass was delineated with enlargement of large cystic, lobulated masses, which had displaced the entire abdomen and encased the aorta, vena cava, common iliac vessels, and bilateral renal hilum (Fig. 2). The decision was made to proceed with surgical extirpation for curative intent.

Preoperative Planning

Extensive discussion was held at genitourinary tumor board and with patient and family regarding the surgical approach and plan for retroperitoneal mass resection with left radical orchiectomy. As masses were encasing aorta, inferior vena cava, bilateral renal arteries, and veins, a discussion of the possibility of aortic resection with grafting, inferior vena cava resection, and unilateral vs bilateral nephrectomy requiring postoperative renal replacement therapy were held. The patient decided to proceed with surgery. Vascular surgery was called on standby, and otorhinolaryngology or head and neck surgery joined for concomitant dissection of the left supraclavicular mass.

Procedure

A midline incision was used and immediately upon entering the abdomen, a large-volume tumor was encountered displacing bowel into the left upper quadrant. Bilateral ureters were identified for protection first. Given the large volume of tumor and involvement of multiple compartments, it was evident that resection must occur in multiple packets, rather than en bloc. We encountered a complete thrombosis of the left common iliac and left external iliac veins, likely from longstanding extrinsic compression. The left common iliac vein was ligated distally and resected along with the tumor. All visible tumors
in the pelvis were thereafter completely excised and bilateral pelvic lymph node dissection was performed. A left radical orchiectomy was then successfully performed. The aorta and inferior vena cava were dissected free from the encasing tumor burden. The right kidney and renal vasculature were then freed of substantial tumor encasement, keeping the organ itself intact. A similar dissection was performed on the left, without damage to the left kidney, renal hilum, or ureter. Tumor dissection was continued in the bilateral retrocrural and left suprahilar regions. No residual tumor burden was visible in the abdominal cavity or pelvis on final exploration (Fig. 3). Otolaryngology or head and neck surgery concomitantly performed the left neck dissection and removed the left supraclavicular mass.

**Outcome**

Surgical pathology revealed fibrosis and mature teratoma from all 9 tumor specimens, including the left supraclavicular mass and the left testicle. Postoperatively, tumor markers remained normal. Subsequent imaging at 2 months revealed postoperative seromas, and repeat imaging with a computed tomography scan at 8 months

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**Figure 1.** Tumor markers before chemotherapy, after chemotherapy, and after surgery. AFP, alpha-fetoprotein; beta-hCG, beta-human chorionic gonadotropin; BEP, bleomycin, etoposide, and cisplatin; LDH, lactate dehydrogenase.

**Figure 2.** Preresection. (A-C) Computed tomography imaging demonstrates large-volume tumor burden in the left neck and abdomen. Note the significant displacement of the aorta in (B) by tumor. (D) Intraoperative tumor burden before resection of the mass. (Color version available online.)
postoperatively demonstrated no evidence of disease recurrence (Fig. 3).

**DISCUSSION BY SIAMAK DANESHMAND, M.D.**

**Growing Teratoma Syndrome**

In the era of cisplatin-based chemotherapy, the survival rate of metastatic nonseminomatous germ cell tumors exceeds 90%. Nevertheless, approximately one-third of patients treated with chemotherapy will have residual retroperitoneal disease. Less than 10% of these patients will have a chemo-resistant disease with persistent tumor growth. GTS is characterized by the following 3 criteria: (1) normalization of elevated serum alpha-fetoprotein and human chorionic gonadotropin, (2) tumor growth during or after systemic chemotherapy after a significant reduction in tumor burden or a disease-free interval, and (3) histologic presence of only mature teratoma during tumor marker resection. The chemo-resistant nature of GTS renders additional cycles of chemotherapy ineffective. Early recognition is critical to prevent further systemic therapy and to allow for surgical planning. Despite large-volume tumor burden, complete resection is often curative. Failure to intervene appropriately leads to mortality from either compression of vital organs or subsequent malignant transformation. Herein, we presented a case of GTS with a significant tumor burden, for which complete surgical extirpation has thus far been curative.

While nonseminomatous germ cell tumors have an excellent cure rate, patients experiencing relapse have a poor 5-year prognosis estimated at 30%. The majority of patients (67%-85%) with mature teratoma in the retroperitoneum harbor teratoma in the testicular primary. Teratomas are generally indolent and chemo-resistant, but if left alone have the potential for growth or malignant transformation. First described in 1982, GTS describes the rare scenario of a growing metastatic mass during or shortly after chemotherapy despite normalization of tumor markers. While there may be considerable variability in growth patterns, the median linear growth rate has been shown by Lee et al to be 0.5 cm/mo with a volume growth rate of 9.2 cm³/mo. While it is recommended to complete the intended course of chemotherapy, delay in postchemotherapy surgery may result in increased morbidity and mortality from significant growth with extrinsic compression of vital organs. Circumferential involvement of essential vasculature was observed in this case and is common in high-volume retroperitoneal disease, defined as longest tumor axis exceeding 10 cm. Caval resection is necessary in 7% of cases, and nephrectomy from renal hilum involvement is necessary in up to 31% of cases. Vascular surgical expertise is a prerequisite of surgical resection, given the often significant involvement of the great vessels or common iliac vessels. Complete extirpation of tumor burden is critical and often curative; recurrence rates as high as 83% have been reported in patients with incomplete resection. The size of the residual mass and International Germ Cell Consensus Classification are the significant predictors of disease recurrence after postchemotherapy retroperitoneal lymph node dissection. Complete tumor resection is associated with a 10-year recurrence-free survival of 80%.

Medical management of GTS is a growing topic of discussion. Vaughn et al reported on the treatment of 3 patients with recurrent tumor burden despite surgical extirpation of GTS. Cyclin-dependent kinase (CDK) mediated phosphorylation of retinoblastoma has been shown to be necessary for cell growth in mature
As such, patients in this small case series were treated with a selective CDK inhibitor, with either disease response or stable disease for 18-24 months, suggesting therapeutic benefit of CDK inhibitors in inoperable or recurrent GTS. A follow-up phase II study of 12 patients with unresectable mature teratoma treated with selective CDK inhibition with a median follow-up of 38 months demonstrated a median progression-free survival of 5.3 months and event-free survival of 16.2 months, suggesting clinically meaningful delay in disease-related major clinical events. Further work is necessary to elucidate the benefits of medical management in these patients.

Although an unusual clinical entity, early recognition of GTS is critical to avoid further systemic chemotherapy that may be ineffective. Despite considerable volume of metastatic chemo-refractory disease and encasement of vital vasculature and organs, complete surgical excision may reverse an otherwise fatal prognosis. A multidisciplinary approach involving oncologic and surgical expertise is necessary. Patients with GTS should be recognized as early as possible and referred urgently to centers of excellence for the management of germ cell tumors.

References