May 5th, 12:00 AM

Management of Late-Stage Ewingoid Dedifferentiated Liposarcoma of the Spermatic Cord with Emergent Complications: A Case Report

Raeann Dalton
Rowan University

Abdullah Junayed
Rowan University

Brian Thomas
Rowan University

Young Son
Rowan University

Megan Donlick
Jefferson Health - NJ

Author(s)

Raeann Dalton, Abdullah Junayed, Brian Thomas, Young Son, Megan Donlick, Kathryn Goettle, Lance Earnshaw, and Thomas Mueller

Management of Late-Stage Ewingoid Dedifferentiated Liposarcoma of the Spermatic Cord with Emergent Complications: A Case Report

Raeann M. Dalton, Abdullah Junayed, Brian Thomas, Young Son, Megan Donlick, Kathryn Goettle, Lance Earnshaw, Thomas Mueller

Jefferson New Jersey Urology, 18 E. Laurel Rd., Stratford, NJ 08084

Background

Liposarcoma (LS), a malignant tumor of adipose origin, is the most common soft tissue sarcoma (STS), and can develop within any soft tissue. It rarely occurs in the paratesticular region, and accounts for 3-7% of spermatic cord tumors.[1] Dedifferentiated liposarcoma (DDLS) and well-differentiated liposarcoma (WDLS) account for two of the five subtypes of LS, with dedifferentiation occurring in 20% of cases.[2] There have been 66 cases of DDLS of the spermatic cord reported to date, but none present with a 22/22q trisomy without the fusion or rearrangement that commonly produces these aggressive tumors.

While WDLS shows proliferation of mature adipocytes with variation in cell size and nuclear atypia, DDLS shows an abrupt transition to a region of non-lipogenic sarcoma.[2] Amplification of 12q13-15, which contains the MDM2 gene, a key negative regulator of p53, is a common abnormality of the two subtypes.[2] WDLS and DDLS can be easily confused with their benign counterparts, lipomas, as well as other STSs such as Ewing sarcoma (EWS) based on clinical presentation and morphology. EWS is a tumor of osseous origin which is composed of small round cells expressing high levels of CD99, which contributes to its aggressive nature.[3]

Case Presentation

Initial Presentation

A 57-year-old male presented with a 3-month history of a painless, indurated, rapidly growing left inguinal mass. Three years prior, during a suspected left inguinal hernia repair, a solid mass was discovered attached to the left spermatic cord. The mass was extensively dissected from the spermatic cord, leaving the cord structures intact, and was histologically diagnosed as a lipoma. The patient remained asymptomatic for the next three years until he noticed this new mass in the same location. Family history was significant for a father with prostate, kidney, and colon cancer and a second-degree relative with Ewing's sarcoma.

CT of abdomen and pelvis with contrast detected a 11.7 x 7.3 x 6.5 cm solid mass with calcification in the left inguinal canal, with a second satellite mass measuring 2.7 x 2.6 cm adjacent to the sigmoid colon. An MRI confirmed this finding (Fig. 1). Chest x-ray findings were negative, however a subsequent CT chest showed multifocal bilateral pulmonary metastases up to 2.3 cm. ^{18}F-FDG-PET showed hypermetabolic activity in the two pelvic tumors and the pulmonary nodules.

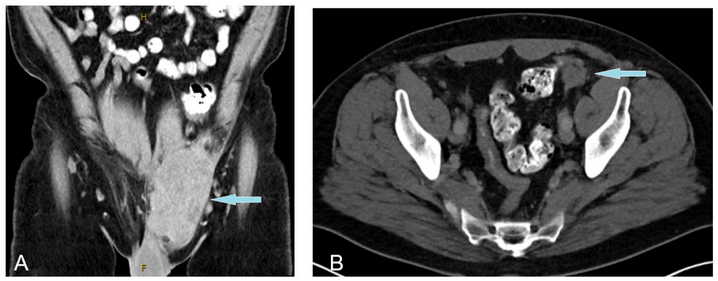

***Figure 1**: Primary tumor visualized on CT abdomen and pelvis in the coronal plane (A). Satellite lesion visualized in the transverse plane (B).*

Diagnosis and Management

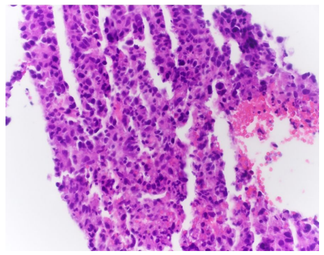

***Figure 2**: Core needle biopsy of left groin mass revealed a sheet of round cells, brisk mitotic activity, and extensive tumor necrosis, indicative of high grade round cell sarcoma most consistent with dedifferentiated liposarcoma. IHC was positive for FLI1 and CD99 and negative for AE1/AE3, Cam5.2, S100, desmin, TdTT, CD3, CD20, TLE1, CD34, and LCA.*

Re-examination of the original sample from 3 years prior revealed atypical morphologic features indicative of a well-differentiated liposarcoma with 71% of cells having MDM2 amplification at chromosome 12q15 on fluorescence in situ hybridization (FISH). Core needle biopsy of the current mass was performed (Fig. 3). FISH revealed that 94% of cells had MDM2 amplification. Staining showed diffuse positivity for FLI1 and CD99, and a third copy of EWSR1 was noted without evidence of rearrangement, suggestive of trisomy of 22/22q. These findings were consistent with a high grade dedifferentiated liposarcoma, in the context of the previously misdiagnosed well-differentiated liposarcoma. Surgical intervention was deemed infeasible due to the mass size, risk of seeding of malignant cells, and extended healing time delaying systemic therapy; therefore doxorubicin monotherapy was initiated.

Complications

Fourteen days into his 2nd chemotherapy cycle, the patient felt a pop in his left inguinal region and confirmed scrotal pain and swelling. CT abdomen and pelvis with contrast showed enlargement of the primary mass to 15.7 x 8.3 x 9.3 cm and a portion herniating into the scrotum with significant inflammatory changes (Fig. 3).

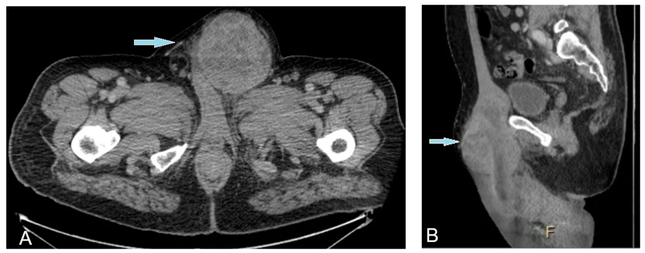

***Figure 3**: Transverse (A) and sagittal (B) views on CT abdomen and pelvis at emergency visit documenting tumor herniation with significant mass effect and inflammatory changes.*

On examination, the mass was incarcerated with local scrotal swelling causing phimosis and urinary retention (Fig. 5). Ultrasound confirmed severe left hydrocele, minor right hydrocele secondary to mass effect, and asymmetric arterial waveforms suggesting possible compression of left testicular artery. Aggressive surgical intervention was considered to decompress the testicular artery, however shared decision making resulted in forgoing aggressive treatment with accepted risk of testicular loss. Conservative measures with lower urinary tract drainage were employed along with hematology and oncology follow-up for continuation of chemotherapy.

Discussion

Misdiagnosis of the original WDLS led to improper surgical resection and allowed for the recurrence and dedifferentiation of the tumor. First line recommendation for DDLS is complete *en bloc* resection of the tumor with high ligation of the spermatic cord with radical orchiectomy to achieve negative margins.[4] This patient's mass, however, was deemed unresectable and the patient and care team opted for systemic chemotherapy with the goal of eliminating metastatic disease and shrinking the tumor to a resectable size. In reviewing the pathology in this case, the morphologic appearance of small round blue cell sarcoma, in the context of the patient's family history of EWS, make EWS or Ewing-like sarcoma reasonable considerations. However, a comprehensive sarcoma and solid tumor sequencing analysis detected no characteristic gene fusions of EWS, thus further exploration into the immunohistochemical markers is helpful in this case:

Table 1: Analysis of Immunohistochemical Markers

EWSR1	▪ *Frequently translocates to produce tumorigenic chimeric proteins* ▪ *Reported in EWS as well as other STSs*[5] ▪ *Trisomy = point of genetic instability; "Ewingoid" phenotype*
FLI1	▪ *EWSR1-FLI1 is the most common translocation in EWS*[5] ▪ *Fusion □ uncontrolled EPO signal transduction and growth □ rapid tumor growth*
CD99	▪ *Pro- or anti-inflammatory depending on splicing pattern* ▪ *Pro-inflammatory CD99 reported in 90% of EWS cases*[6] ▪ *Explains severe inflammation and disruption of fascial planes to produce swelling in penis and bilateral scrotum*
MDM2	▪ *Inhibits p53 tumor suppressor gene □ loss of apoptosis and cell-cycle arrest*[7] ▪ *High MDM2 amplification is specific for WDLS/DDLS* ▪ *Confirms diagnosis of WDLS □ dedifferentiated into a Ewingoid tumor*

Metabolic sarcomas are traditionally responsive to the anthracycline class of chemotherapeutics such as doxorubicin, and combination therapy with other agents have failed to show a difference in overall survival in locally advanced, metastatic, or unresectable STS with a higher toxicity burden.[2,8] The newer classes of systemic therapies being studied such as PD1 inhibitors, XPO1 inhibitors, MDM2 inhibitors, and CDK4 inhibitors suggest that such an investigation is worthwhile, as new targets for unique aspects of DDLS biology may lead to a change in the current treatment paradigm.[9]

Conclusion

Accurate diagnosis of LS of the spermatic cord is difficult but imperative for effective treatment. Misdiagnosis leads to ineffective management and poor outcomes, as seen in this case. This is the first reported case of DDLS showing 22/22q trisomy without fusion or rearrangement, and though its clinical significance is unclear, the complications arising from this spermatic cord LS were severe with significant implications for nearby anatomical structures. As this tumor's aggressive features demonstrated the potential for requiring emergent treatment, a review of the literature surrounding management of DDLS of the spermatic cord with advanced disease at time of presentation was found to be lacking and management poorly defined. We hope that understanding malignant changes in tumors like the one presented in this case will help guide therapies currently in development that will take advantage of specific biological targets implicated in DDLS.

References

1. Chalouhy, C et. al. (2017) Molec and Clin Onc. 6:438-440.
2. Singer S et. al. (2018) In: Cancer. DeVita VT, Rosenberg SA, Lawrence TS. Wolters Kluwer.
3. Grünewald TGP et. al. (2018) Nat Rev Dis Primers. 4(5):1- 22.
4. Shaban Y et. al. (2020). Int J Surg Case Reports. 72:418-422.
5. Thway K et. al. (2019) Surg Path Clinics. 12(1):165-190.
6. Manara C et. al. (2018) Genes. 9(3)159-175.
7. Oliner JD et. al. (2016) Cold Spring Harb Perspect Med. 6(6):a026336.
8. Tap WD et. al. (2017) The Lancet Onc. 18(8):1089-1103.
9. Gahvari Z et. al. (2020) Curr Treat Options in Oncol. 21(15):1-14.