Malignant mesothelioma of the tunica vaginalis: a rare case report and description of multimodal treatment

Eric D. Andresen, MD,[1] Grant Henning, BS,[2] Matthew A. Uhlman, MD,[1] Amit Gupta, MD[1]

[1]Department of Urology, University of Iowa, Iowa City, Iowa, USA
[2]Carver College of Medicine, University of Iowa, Iowa City, Iowa, USA

ANDRESEN ED, HENNING G, UHLMAN MA, GUPTA A. Malignant mesothelioma of the tunica vaginalis: a rare case report and description of multimodal treatment. *Can J Urol* 2016;23(6):8585-8589.

Malignant mesothelioma is an uncommon neoplasm that develops from serous surfaces, and rarely from the tunica vaginalis. Although atypical in any location, paratesticular presentation is exceedingly infrequent as only 0.3% to 1.4% of mesothelioma cases arise from the tunica vaginalis. Fewer than 300 cases have been reported with very few descriptions of long term follow up and multimodal therapy. Here we describe a patient with 2 years of follow up for metastatic mesothelioma treated with orchiectomy, chemotherapy and robot-assisted laparoscopic retroperitoneal lymph node dissection.

Key Words: tunica vaginalis, mesothelioma, robotic RPLND, multimodal therapy

Introduction

Malignant mesothelioma is an unusual neoplasm that develops from serous surfaces such as the pleura, pericardium, peritoneum and tunica vaginalis. Although uncommon in any location, a paratesticular presentation is exceedingly rare as only 0.3% to 1.4% of mesothelioma cases arise in the tunica vaginalis.[1] Knowledge of the natural history of this unusual disease process and effective treatment options is limited, as fewer than 300 cases have been reported.[1] We describe a case and multimodal treatment of malignant mesothelioma of the tunica vaginalis. After presenting with a rapidly enlarging hydrocele over 2 years ago, the patient is currently being surveilled after undergoing orchiectomy, spermatic cord resection, chemotherapy and robot-assisted laparoscopic retroperitoneal lymph node dissection.

Accepted for publication September 2016

Address correspondence to Dr. Amit Gupta, Department of Urology, University of Iowa, 200 Hawkins Dr., 3 RCP, Iowa City, IA 52242-1089 USA

Case report

A 60-year-old man with a past medical history notable for super obesity (body mass index 50), diabetes mellitus and scleroderma, presented to an outside hospital with scrotal swelling and discomfort occurring over 2-3 weeks. He denied scrotal trauma or an inciting event.

Ultrasonography showed a large right-sided hydrocele with increased color flow of the left testicle compared to the right. The Doppler changes were felt to be of little significance given the lack of testicular pain. The testicles were otherwise normal and a diagnosis of a benign right hydrocele was made.

A hydrocelectomy was performed 3 weeks later. Intraoperatively, a possible cord lipoma and hernia sac were noted, dissected and reduced without mesh placement. No other intraoperative abnormalities were noted. Postoperatively the patient developed a wound infection with poor healing.

On pathological examination the hydrocele sac was noted as a fragment of tan-pink fibrous and adipose tissue with no identifiable lesions. However, histologic examination showed atypical mesothelial proliferation with haphazard infiltrative features and a large number

of gland-like formations. Immunohistochemistry showed strong positivity for calretinin with focal, weak positivity for CK5/6 and negativity for CEA and MOC-31 and a presumptive diagnosis of malignant mesothelioma was made.

After referral to our institution, the patient was found to have a history of asbestos exposure. Chest x-ray showed no evidence of pulmonary abnormalities or metastases. CT of the abdomen and pelvis showed limited non-specific pelvic lymph nodes with no evidence of metastases.

A right inguinal radical orchiectomy with wide local excision of surrounding tissues and hemiscrotectomy was performed approximately 2 months after presentation to our institution. Intraoperatively, the spermatic cord was notably thickened with a large amount of surrounding fatty tissue. Near complete fusion of the planes between the testicle and the surrounding scrotum was noted. Dissection of the spermatic cord cephalad was very difficult due to the patient's body habitus.

On pathological examination, the testis and epididymis were noted to be surrounded by "tan-yellow, firm, nodular tissue." While no invasion into the testis or epididymis was identified grossly, there was suspicion for extension into the spermatic cord and paratesticular soft tissue. Microscopic examination showed multiple microscopic foci of malignant mesothelioma involving the spermatic cord, paratesticular soft tissues with focal invasion into the testicular parenchyma, and a focus highly suspicious for lymphovascular invasion of the spermatic cord. However, no perineural invasion was noted, the proximal spermatic cord margin was uninvolved and right inguinal lymph node excision showed no identifiable tumor. Postoperatively, the patient again experienced delayed wound healing of his inguinal region.

The patient underwent CT of the chest, abdomen, and pelvis 3 weeks later. No enhancing nodules suggestive of residual disease and no evidence of distant metastases were found. Nonspecific bilateral inguinal and pelvic sidewall lymphadenopathy were noted to be stable.

Given the aggressive nature of malignant mesothelioma and lymphovascular invasion, medical oncology was consulted and recommended adjuvant chemotherapy with carboplatin (750 mg) and pemetrexed (500 mg/m^2). Pegfilgrastim was given to reduce infection risk and B12 injections with oral folic acid were administered. Four cycles if carboplatin/pemetrexed were completed and were well tolerated.

The patient underwent surveillance with CT of chest, abdomen, and pelvis every 3 months, in addition to routine follow up for poor healing of the scrotal/inguinal incision site.

Two years after his initial hydrocelectomy and 18 months after the final cycle of carboplatin/pemetrexed, minimal increase was noted in one retroperitoneal lymph node on CT, Figure 1. A follow up PET/CT was performed 2 months later and demonstrated uptake in two retroperitoneal lymph nodes. These nodes were deemed too small and difficult to biopsy.

A radiation oncology consultation was made, but due to the patient's history of scleroderma he was

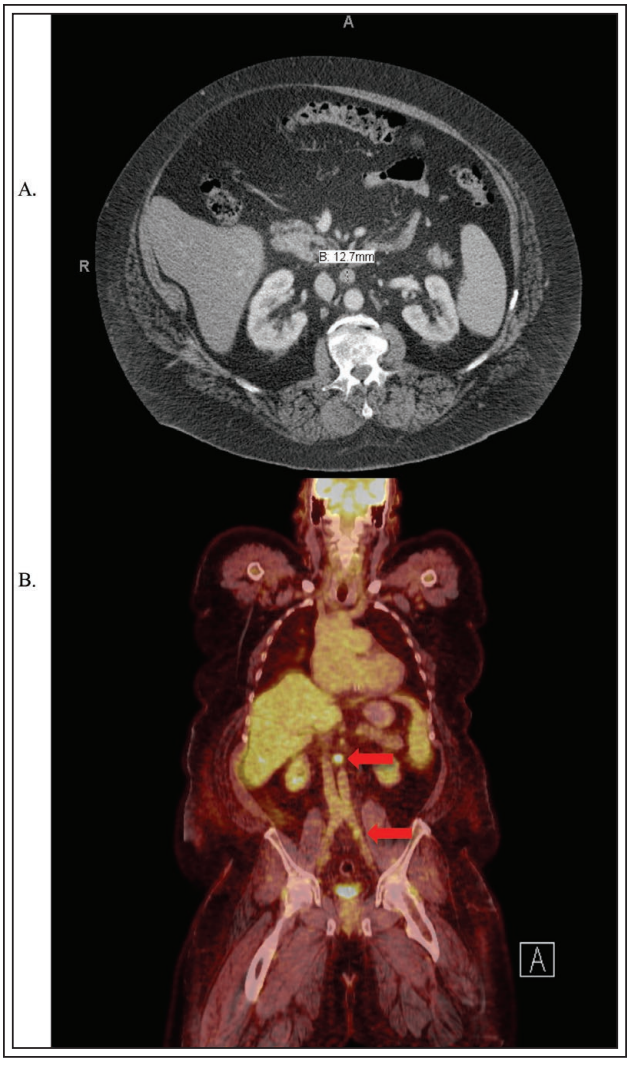

Figure 1. A. CT image showing increased size (13 mm) of a para-aortic retroperioneal lymph node. CT imaging 3 months prior showed node with short interval axis diameter of approximately 10 mm. **B.** Follow up PET/CT showing increased F-18 fluorodeoxyglucose uptake in a para-aortic lymph node and in a left iliac node (red arrows).

considered a poor candidate for radiotherapy. His case was then reviewed at a multidisciplinary conference and potential surgical intervention via retroperitoneal lymph node dissection (RPLND) was discussed. Consideration was also given to systemic therapy for relapsed mesothelioma. Overall, it was felt that a minimally invasive surgical approach with robot-assisted laparoscopic RPLND could be considered. After extensive counseling the patient decided to undergo surgery, with particular consideration given to his previous wound difficulties. Prior to surgery, an additional CT was performed and showed a mild interval increase in the retroperitoneal lymph nodes previously shown on PET, Figure 2.

Robot-assisted RPLND was performed with excision of pre-aortic, para-aortic, pre-caval, para-caval and inter-aortocaval lymph nodes. In addition, left common iliac lymph nodes were excised. Metastatic mesothelioma was found in 5 of 11 interaorto-caval nodes, 1 of 3 para-caval and pre-caval nodes, and 0 of 2 pre-aortic and para-aortic lymph nodes. Postoperatively, the patient underwent an uneventful hospital course and was discharged on POD 2. Three weeks following surgery, no surgical complications were noted and incision sites were found to be well healing, Figure 3. Follow up PET/CT was performed 3 months postoperatively and no evidence of recurrent tumor or metastasis was noted. We will continue to monitor for recurrence with PET/CT at approximately 4 month intervals.

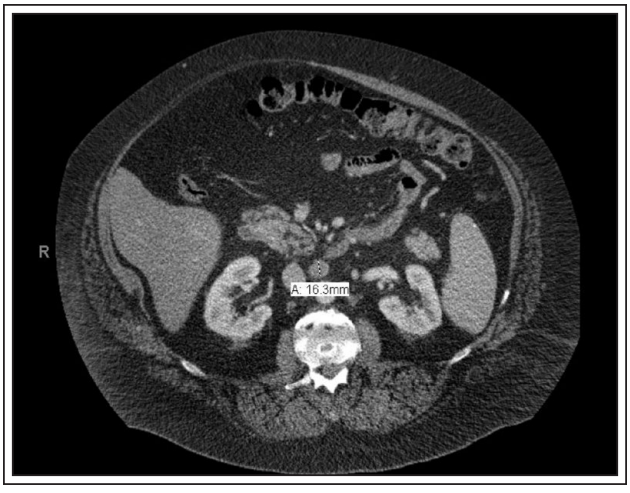

Figure 2. CT image showing increased size (16 mm) of a para-aortic retroperioneal lymph node. CT imaging 3 months prior showed node with a short interval axis diameter of approximately 13 mm.

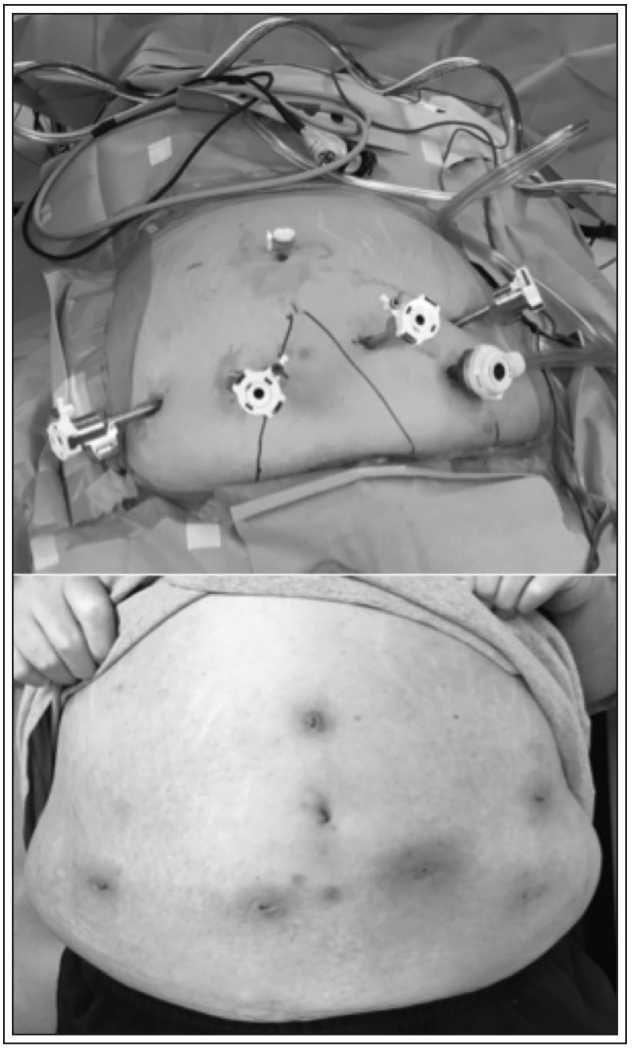

Figure 3. Photographs showing robotic port placement immediately following surgery (above) and incision sites 3 weeks postoperatively (below).

Discussion

Although the exact pathogenesis remains unclear, asbestos exposure is considered the main risk factor for developing mesothelioma. It has been suggested that cases of peritoneal mesothelioma arise after asbestos fibers are ingested or inhaled and work their way through the lymphatic system to the peritoneum. Once in the peritoneal layers, fibers are trapped and cause irritation/inflammation, ultimately leading to cancer development of mesothelial cells.[2] It is plausible that similar inflammation associated with asbestos fibers could be involved with development in the tunica vaginalis. However, it is clear that asbestos is not the sole risk factor, as only about one-third of patients

(34.2%) with mesothelioma of the tunica vaginalis report a history of asbestos exposure.[3] Chronic inflammatory processes of the groin such as epididymitis, hydrocele, hematocele, and inguinal hernias, have also been suggested as causes of reactive hyperplasia of the mesothelial lining that may lead to tumorigenesis and ultimately malignant mesothelioma.[4]

Regardless of pathogenesis, the diagnosis of malignant mesothelioma of the tunica vaginalis can be difficult to make given its rarity and low clinical suspicion. Factors contributing to such diagnostic difficulty include variability in presenting symptoms, age at diagnosis, and ultrasonography findings. Initial clinical presentation is nonspecific, most often presenting as a hydrocele (49.5%), but also as a testicular tumor (36.6%), inguinal hernia (5.9%), epididymitis (3%), spermatocele (2%), testicular torsion (2%), and traumatic testicular injury (1%).[3] While nearly 50% of patients with malignant mesothelioma of the tunica vaginalis are diagnosed between the ages of 55 and 75, it has been found in patients ranging from 7 to 87 years of age.[5] Ultrasonography is a valuable tool for assessment of scrotal masses, yet a variety of appearances have been described for malignant mesothelioma, limiting its diagnostic utility. Hydroceles containing echogenic fluid with hypervascular parietal vegetations have been described as the most common finding on ultrasonography, yet other cases have shown solid masses not associated with hydrocele.[6]

Diagnosis is typically determined intraoperatively and established by postoperative pathology.[5] The immunohistochemistry profile of malignant mesothelioma of the tunica vaginalis is similar to that of pleural mesothelioma and is predictably positive for calretinin, epithelial membrane antigen, thrombomodulin, Wilms tumor antibody, D2-40 and CK7, with variable positivity for CK5/6, while being negative for carcinoembryonic antigen (CEA) and cytokeratin 20. In our patient, the hydrocele sac specimen was highly suspicious for mesothelioma, given the positivity for calretinin and CK5/6 and negativity for CEA.

Although few cases have been reported, accurate preoperative diagnoses have been made when a hydrocele is found in association with a paratesticular tumor on ultrasonography. When such findings occur, fine needle aspiration with cytology may be of diagnostic aid. Cytologic examination may show several growth patterns of malignant mesothelioma including highly differentiated epithelial, biphasic, sarcomatoid and anaplastic tumors.[7] Yet when combined with features of cellular atypia and immunohistochemistry staining, suspicion for mesothelioma can be sufficiently raised. However, considering the relatively low sensitivity of cytology and potential added risk of metastasis, routine use of fine needle aspiration is under debate and surgical exploration with pathological examination and immunohistochemistry is often warranted for definitive diagnosis.

There is no accepted standard of treatment for malignant mesothelioma of the tunica vaginalis and the prognosis is generally described as poor, with median survival being reported at 24 months.[4] Radical orchiectomy is thought to be optimal and is used as first-line treatment, with local recurrence rates reported in 10.5%-11.5% of patients compared to 36% when local resection of the hydrocele is performed alone.[5] Despite mesothelioma being considered relatively chemoresistant, the combination of pemetrexed and cisplatin or carboplatin has been a widely accepted systemic therapy for malignant pleural mesothelioma, with the addition of folic acid and vitamin B12 being found beneficial for reducing chemotherapy related toxicity.[8] However, the true efficacy of such treatment for mesothelioma of the tunica vaginalis is yet to be determined and it is difficult to determine the value of a multimodal therapy approach. Our patient completed four cycles of pemetrexed and carboplatin, yet metastatic lymph nodes were found by PET/CT 18 months after completion of his last chemotherapy cycle.

While some have encouraged RPLND as part of definitive management,[9] others have suggested that staging should first be done with thoracic and abdominal CT, with lymph node dissection being recommended only in regions where metastases are suspected.[3,5] Lymphatic drainage of the testicle first goes to retroperitoneal lymph nodes, while the scrotum drains to the superficial inguinal nodes. As such, lymph node metastases can arise in multiple areas with retroperitoneal lymph node involvement being most common, followed by inguinal and iliac lymph nodes.[7] Although the presence of positive lymph nodes at the time of diagnosis is correlated with shorter survival,[5] few cases of lymph node dissection have been described.[5,9] Our patient was at very high risk for surgical complications due to his scleroderma and super obesity. His inguinal and scrotal wounds took several months to heal and as such it was felt that he was at high risk for developing severe wound related complications with an open approach. Hence, we decided to perform a robotic-assisted laparoscopic RPLND and minimize the potential morbidity for this patient.

The exact role of RPLND for para-testicular mesothelioma is controversial and the decision for RPLND needs to be individualized. Minimally invasive approaches to RPLND may be considered at select centers. □

References

1. Esen T, Acar O, Peker K, Sarman K, Musaoglu A, Tefekli A. Malignant mesothelioma of the tunica vaginalis: presenting with intermittent scrotal pain and hydrocele. *Case Rep Med* 2012; 2012:189170.
2. Ahmed I, Ahmed Tipu S, Ishtiaq S. Malignant mesothelioma. *Pak J Med Sci* 2013;29(6):1433-1438.
3. Segura-Gonzalez M, Urias-Rocha J, Castelan-Pedraza J. Malignant mesothelioma of the tunica vaginalis: a rare neoplasm--case report and literature review. *Clin Genitourin Cancer* 2015; 13(6):e401-e405.
4. Yen CH, Lee CT, Su CJ, Lo HC. Malignant mesothelioma of the tunica vaginalis testis: a malignancy associated with recurrent epididymitis? *World J Surg Oncol* 2012;10:238.
5. Plas E, Riedl CR, Pfluger H. Malignant mesothelioma of the tunica vaginalis testis: review of the literature and assessment of prognostic parameters. *Cancer* 1998;83(12):2437-2446.
6. Bertolotto M, Boulay-Coletta I, Butini R et al. Imaging of mesothelioma of tunica vaginalis testis. *Eur Radiol* 2016;26(3): 631-638.
7. Bandyopadhyay A, Bhattacharya S, Konar K. Preoperative cytological diagnosis of malignant mesothelioma of tunica vaginalis. *Diagn Cytopathol* 2015;43(10):850-854.
8. Habib EE, Fahmy ES. Chemotherapy management of malignant pleural mesothelioma: a phase II study comparing two popular chemotherapy regimens. *Clin Transl Oncol* 2013;15(11):965-968.
9. Smith JJ 3rd, Malone MJ, Geffin J, Silverman ML, Libertino JA. Retroperitoneal lymph node dissection in malignant mesothelioma of tunica vaginalis testis. *J Urol* 1990;144(5):1242-1243.