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Clinical Features and Outcomes of Tunica Vaginalis Mesothelioma: A Case Series from the National Institutes of Health

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Abstract

OBJECTIVE—To present our single-institution experience with management of seven patients with mesothelioma of the tunica vaginalis.

MATERIALS AND METHODS—Our institution database was queried from 2003 to 2014. Clinical, surgical and pathological features were retrospectively collected and evaluated.

RESULTS—Seven patients were identified with tunica vaginalis mesothelioma. Average age at the time of diagnosis was 63.6 years. Four patients presented with hydrocele, one with scrotal mass, one with inguinal mass, and one with spermatocele. Two (28.6%) patients reported possible asbestos exposure. Radical orchiectomy was performed in all patients. Two patients received adjuvant radiotherapy, one patient received both chemotherapy and radiation. All patients were followed up postoperatively with serial imaging detect for recurrence. One of 7 patients in our cohort experienced recurrence at 12 months. Our mean follow-up time on these patients is 52.2 months.

CONCLUSION—Previous reported cases have described poor prognosis of tunica vaginalis mesothelioma despite aggressive surgery and systemic therapy. Our single-institution experience

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suggests relatively good outcomes with surgery and limited adjuvant therapies. Post treatment surveillance is also imperative and should include imaging routinely within the first 2 years. Negative asbestos exposure screening during history should not eliminate clinical suspicion.

Keywords

Paratesticular mesothelioma; urologic oncology; case series

INTRODUCTION

Malignant mesothelioma of the tunica vaginalis is an exceedingly rare and aggressive neoplasm. Tunica vaginalis shares a common embryological origin with visceral pleura, peritoneum, and pericardium.¹⁻² Malignant mesothelioma of the tunica vaginalis is morphologically identical to of the peritoneum,¹⁻² however only 0.3% to 5% of all malignant mesotheliomas arise from this origin.² The pathophysiology of these neoplasms remains unclear, and it is difficult to obtain a preoperative diagnosis. Historically, this neoplasm has been associated with a poor prognosis and there is no guidelines for management due to its rarity. Herein we report a contemporary case series of seven patients that were diagnosed with malignant mesothelioma of the tunica vaginalis, our experience with early surgical management, and subsequent outcomes.

PATIENTS AND METHODS

Seven cases of histology confirmed malignant mesothelioma of the tunica vaginalis were identified between 2003 and 2014 on retrospective review of the National Institute of Health patient records. Clinical features, history of asbestos exposure, and primary therapeutic approach were collected and verified. Hematoxylin and eosin-stained slides for each case were reviewed with an expert pathologist and the histologic diagnosis of malignant mesothelioma was confirmed using established criteria. The tumors were then sub classified into epithelioid, or biphasic patterns on morphology. Immunohistochemically stains were reviewed. Follow-up data of patients were obtained by reviewing charts and corresponding with primary physicians.

RESULTS

Clinical Characteristics and Presentation

Clinicopathologic features of the series are summarized in Table 1. The mean age at diagnosis was 63.6 years (range 43 – 85 years). Initial presentation included: 4 (57.1%) hydroceles, 1 (14.3%) solid scrotal mass, 1 (14.3%) with an inguinal mass mimicking an inguinal hernia, and 1 (14.3%) spermatocele. All patients denied systemic and constitutional symptoms. 2 (28.6%) of patients reported possible asbestos exposure, and 2 (28.6%) other patients were smokers.

Therapeutic Approach and Pathology

Radical orchiectomy was performed in all patients. Two (28.6%) patients received adjuvant radiotherapy, 1 (14.3%) patient received both chemotherapy (pemetrexed and cisplatin) and

radiation. All patients were followed up postoperatively with serial imaging detect for recurrence. Pathologic diagnosis of malignant mesothelioma was confirmed for all 7 patients and summarized in Table 1.

Disease Course and Follow Up

All 7 patients were followed up annually/semiannually with scrotal ultrasound (US), Computed Tomography of chest-abdomen-pelvis (CT), and Positron Emission Tomography-Computed Tomography (PET/CT) to assess for recurrence. One patient developed local recurrence 12 months after primary surgical treatment and eventually passed away from his disease 5 years after initial diagnosis. CT imaging revealed new left-sided mesenteric masses and a poorly defined enhancing soft tissue mass surrounding the vessels within the inguinal canal and scrotum. Another patient was lost to follow-up after his radical orchiectomy. Average length of follow-up (excluding patient lost to follow-up after discharge) was 52.2 months (Range 15–155 months).

DISCUSSION

The initial clinical presentation of patients in this series coincides with what has been commonly reported in the literature. All of our patients presented with painless scrotal enlargement-spermatocele (14.3%), mass (28.6%), hydrocele (57.1%). Reported potential risk factors include exposure to asbestos, long-lasting hydrocele, trauma, and herniorrhaphy. Asbestos exposure has the most direct association with malignant mesotheliomas of all variations and has been well documented.^{5,14} Many studies have demonstrated that patients with malignant mesothelioma of the tunica vaginalis have a similar frequency of asbestos exposure as those with pleural mesothelioma, ranging from 34.2% to 41%.^{5,7} However, many of these cases do not specify whether the asbestos exposure was confirmed. Interestingly, only 2 out of 7 patients (28.6%) in this case series reported a potential asbestos exposure, which could not be confirmed. All other patients had no risk factor of asbestos exposure based on history. This is much lower than the frequency reported in the literature. As a result, based on these data we believe that a negative asbestos history should not exclude this diagnosis.

All patients in this series were referred to the National Institute of Health with the suspicion of having testicular malignancy. Diagnosis of malignant mesothelioma of the tunica vaginalis was confirmed on postoperative pathologic examination evaluated at our institution. Historically, the majority of other reported cases had also confirmed diagnosis postoperatively.⁵ Preoperative imaging studies such as scrotal US can be useful, as they may demonstrate tunical surface irregularities or soft-tissue masses within the tunica vaginalis.⁸ Likewise, color Doppler ultrasound may reveal the vascular characteristics of malignant mesothelioma, though its interpretation can be challenging.⁹ Recently there have been case reports of obtaining a correct preoperative diagnosis via US-guided fine-needle aspiration cytology of the suspected scrotal mass.¹⁰ None of the patients in this series received preoperative cytology.

Radical orchiectomy with complete histologic examination and follow up for an adequate duration is accepted as the optimal primary treatment option for malignant mesothelioma of

the tunica vaginalis.¹¹ Conservative surgical management such as local resection of the hydrocele wall has been associated with a local recurrence rate of 36% compared to 10.5% to 11.5% reported for radical orchiectomy.⁵ All patients in our cohort received radical orchiectomy and none were documented to have had retroperitoneal lymph node dissection. The necessity for lymph node dissection remains controversial.

The use of adjuvant therapy in our cohort was dependent on practice patterns at their referring institutions. The role of adjuvant therapy remains inconclusive due to the limited number of reported cases and absence of treatment guidelines. Radiotherapy, chemotherapy, or a combination of both has been utilized in the past. Cisplatin and pemetrexed has been considered in these patients due to their demonstrated effectiveness in treating pleural mesothelioma.^{5,6} role in tunica vaginalis derived mesothelioma is less certain. Plas et al. found that the given data did not strongly support chemotherapy as primary adjuvant therapy. However, due to the rarity of this disease, the numbers supporting this claim is limited. Adjuvant radiotherapy and combined chemotherapy-radiotherapy had slightly more favorable results and were found to be safer to use in patients with locally extended mesothelioma after resection of the tumor with negative margins, and also for patients with disseminated disease who are in good physical condition.^{5,12,13} Their true therapeutic benefit in the management of this disease has not been fully demonstrated.

All patients in this series received radical orchiectomy and none received lymph node dissections. Of the 3 patients who received adjuvant therapy, 2 patients received adjuvant radiotherapy only and the other received adjuvant radiotherapy and chemotherapy with pemetrexed and cisplatin; neither had evidence of disease recurrence in 8 years. However, 3 of the 4 patients who did not receive adjuvant therapy likewise had no evidence of recurrence. Thus, in accordance with the literature, our series does not demonstrate a clear benefit to providing adjuvant therapy or necessity for lymph node dissection. Unfortunately, due to the extreme rarity of this disease, robust studies to determine the role of adjuvant therapy are unlikely to ever be successfully completed.

Mesothelioma of the tunica vaginalis testis arises from the serosal membrane of the tunica vaginalis and has a mesenchymal origin. Gross examination often reveals a firm, yellow or white tumor with a solid or cystic-cut surface. The tunica vaginalis is usually thickened, or it is studded with nodules of varying size. Microscopically, most of the tumors are epithelial with papillary, tubulopapillary, or solid patterns. The neoplastic cells are classically cuboidal with scant to moderate amounts of eosinophilic cytoplasm and bland cytological features in the well-differentiated tumors; however, they may appear highly malignant in poorly differentiated tumors. Typically, the papillae have thick, hyalinized fibrovascular cores. Histology of mesothelioma can be categorized into epithelioid, sarcomatoid, or biphasic-with epithelioid being most common.² In few cases, the tumors are biphasic with epithelial and sarcomatoid patterns admixed.⁴ Prognosis has been reported to be better in epithelioid mesothelioma and worse in sarcomatoid disease.⁴ Prognosis in biphasic histology varies based on the mixture of epithelioid and sarcomatoid cells, and is more favorable when there is more epithelioid than sarcomatoid cells.⁴ All of the patients in our cohort had epithelioid (Figure 1) or biphasic (Figure 2) histology. Interestingly, the one patient who suffered adverse outcomes had epithelioid histology. The immunohistochemical profile of

mesotheliomas that arise from the tunica vaginalis testis is similar to those that arise from the pleura and is typically positive for calretinin, Wilms tumor antibody (WT1), D2-40, epithelial membrane antigen (EMA), thrombomodulin, and CK7, variably positive for CK5/6, and negative for carcinoembryonic antigen (CEA) and cytokeratin 20 (CK20).²⁰

Historically, patients were found to have a median survival of 23 months and a recurrence rate of 52.5%, with the majority of recurrences occurring within 2 years of follow-up.^{5,7} Age at diagnosis (<60 years old) is the only prognostic factor associated with increased survival ($p<.01$).^{5,7} In our series, only 1 out of 7 (14.3%) had documented recurrence, which occurred 12 months after primary treatment; the patient was diagnosed at age 43. These results do not strongly correlate with the existing prognostic data and the disease-free survival is higher than what has been previously reported.

CONCLUSION

Malignant mesothelioma of the tunica vaginalis is a rare but aggressive malignancy rarely diagnosed preoperatively, and historically associated with a poor prognosis. Absence of a history of asbestos exposure should not rule out this diagnosis if clinical presentation is supportive. Aggressive surgical management should be first-line treatment; as more conservative options may increase the risk of recurrence. The patients in our series had a higher disease free survival and lower rate of recurrence than what has been reported in the literature which may support the utilization of aggressive surgery and surveillance for localized cases.

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CLINICAL PRACTICE POINTS

- Mesothelioma of the tunica vaginalis is a rare malignancy presenting often as a painless testicular mass.
- Previous reported cases have described poor prognosis of tunica vaginalis mesothelioma despite aggressive surgery and systemic therapy.
- Aggressive surgical management should be first-line treatment; as more conservative options may increase the risk of recurrence
- There is currently limited data supporting the benefit of adjuvant therapies such as radiation or chemotherapy.
- Post treatment surveillance is also imperative and should include imaging routinely within the first 2 years.
- Negative asbestos exposure screening during history should not eliminate clinical suspicion.

Figure 1. Infiltrating malignant mesothelial cells of the tunica vaginalis, epithelioid type. A) Low power, green arrows indicate tumor, yellow arrows indicate normal spermatic tubules. B) intermediate power C) High power, nests of cells with high nuclear to cytoplasmic ratio.

Summary of clinical, therapeutic, and outcomes for patients with Tunica Vaginalis Mesothelioma

Table 1

Age	Ethnicity	Asbestos	Smoking	Presenting Syndrome	Histology	Immunohistochemistry Staining	Surgical Therapy	Adjuvant Therapy	Disease Free Survival (Months)
74	Caucasian	N	Y	Hydrocele	Biphasic	Positive for calretinin, WT-1, cytokeratins A1/A3, and mesothelin (in 30% of tumor cells), and negative for cytokeratin 5/6 and CEA.	1. Hydrocelectomy 2. Left radical orchi with excision of scrotal scar	None	Lost to FU
67	Caucasian	Y	N	Scrotal mass	Biphasic	Positive for AE1/AE3, EMA, calretinin, WT-1, CK5, BERP4, D240 and focally positive for CD15. Negative for MOC-31, CEA, B72.3.	1. Left radical orchiectomy	None	+47
58	Caucasian	N	Y	Spermatocele	Epitheloid	Positive for calretinin, WT-1, cytokeratins A1/A3, cytokeratin 7, and mesothelin (2+ in 30% of tumor cells), and negative for cytokeratin 5/6, cytokeratin 20.	1. Right inguinal orchiectomy	Radiation and Chemotherapy	+65
43	Caucasian	N	N	Scrotal mass	Epitheloid	N/A	1. Right groin exploration inguinal herniorrhaphy 2. Right orchiectomy and hemiscrotectomy	None	12 Recurrence in peritoneum (14 mo FU)
47	Caucasian	N	N	Hydrocele	N/A	N/A	1. Right orchiectomy 2. Left orchiectomy prophylactically	Radiation	+155
85	Caucasian	Y	N	Hydrocele	Epitheloid	Positive for cytokeratins AE1/AE3, Calretinin and WT-1. Negative for CK5/6. Mesothelin is positive, 2+ in 30% of tumor cells.	1. Hydrocelectomy 2. Inguinal incision excision of scrotal scar and Right orchiectomy	Radiation	+19
71	Caucasian	N	N	Hydrocele	N/A	Positive for CK5, CK7, CK20, CD31, CD34, calretinin, MOC-31 Ber-EP4, vimentin and WT1.	1. Hydrocelectomy 2. Radical left rechiectomy	None	+15