Role of robot-assisted retroperitoneal lymph node dissection in malignant mesothelioma of the tunica vaginalis: case series and review of the literature

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Introduction: *The management of malignant mesothelioma of the tunica vaginalis (MMTVT) is not clearly defined. Retroperitoneal lymph node dissection has been reported as a potential management option. Herein we present our experience with robot-assisted retroperitoneal lymph node dissection (RARPLND) in our series of patients with MMTVT.*

Materials and methods: *The Mayo Clinic cancer registry was queried from 1972-present for all patients who had a diagnosis of MMTVT. Six patients were identified, five of whom were treated with RPLND, where four underwent RARPLND.*

Results: *In five patients who underwent RPLND, the median age was 50 years (IQR 34-51). Four patients originally presented with right sided symptomatic hydroceles, while one presented with right sided chronic epididymitis. Orchiectomy (one simple, two inguinal radical) was performed in three patients prior to presentation. Preoperative cross-sectional imaging, including PET-CT scan in three patients, was negative for lymphadenopathy or metastasis. RARPLND was performed in 4/5 (80%) cases and concomitant hemiscrotectomy in 4/5 (80%) cases. Full bilateral template was performed in three patients and right modified template was performed in the remaining two. Median lymph node yield was 29 (IQR 22-32) and median blood loss was 275 cc (IQR 200-300). Positive retroperitoneal lymph nodes were found in 3/5 (60%) cases. All patients who underwent RARPLND were discharged home on postoperative day one. Mean follow up was 27 months (range 3-47). No patients recurred.*

Conclusions: *Regardless of the approach, RPLND may provide a diagnostic benefit in patients who present with MMTVT, with the robotic approach affording a potentially expedited recovery.*

Key Words: mesothelioma, lymphadenectomy, surgical procedures, robotic

Introduction

Malignant mesothelioma of the tunica vaginalis of the testes (MMTVT) is a rare entity that is thought to comprise less than 5% of all mesothelioma cases.[1] There is a bimodal age of presentation, with the majority of patients presenting after the age of 50 and a smaller proportion of cases occurring at ages younger than 25.[2-4] Most patient present with a symptomatic hydrocele or scrotal mass.[3] Asbestos exposure is the greatest risk-factor and is associated with approximately 40% of cases.[5] The management of MMTVT is not completely understood, though reports have demonstrated success with orchiectomy/hemiscrotectomy and lymph node dissection in patients with radiologically suspicious lymph nodes.[2,3,6]

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The retroperitoneum is the most common lymphatic region affected by MMTVT.[2] There is some controversy regarding the role of retroperitoneal lymph node dissection (RPLND) in patients without clinical and/or radiological suspicion of metastasis, despite there being reports of metastatic disease being found in the retroperitoneum after RPLND in such patients.[3] Robot-assisted retroperitoneal lymph node dissection (RARPLND) has been found to be feasible in managing patients with metastatic testicular cancer, while also providing patients with the benefits of minimally invasive surgery (i.e. lower estimated blood loss, shorter hospital length of stay).[7-9]

This study reviews a small series of MMTVT patients treated with RARPLND and presents a review of the literature on this topic. It aims to demonstrate feasibility of RARPLND as an option for patients with MMTVT without demonstrable lymphadenopathy.

Materials and methods

Following institutional review board (IRB) approval, the Mayo Clinic cancer registry was queried from 1972-present for all patients who had a diagnosis of MMTVT. Six total patients resulted. Five of these patients underwent RPLND, four of which were RARPLND at our institution. The robotic cases were all performed by one surgeon, while the open case was performed by another surgeon. Data was collected on all pertinent demographic, preoperative data, perioperative data (RPLND template, nerve-sparing status and extent of nerve spare), pathologic data (diagnosis, margins, lymph node yield), postoperative outcomes, and follow up data (adjuvant therapies, cross sectional imaging results, recurrence). This data was collected from all patients with pathologically confirmed MMTVT between January 1989 and July

TABLE 1. **Patient characteristics, treatment, and outcomes**

	Patient 1	**Patient 2**	**Patient 3**	**Patient 4**	**Patient 5**
Age	51	79	34	19	50
Body mass index	26.4	26.9	30.6	23.2	38.3
Asbestos exposure	No	No	Yes	No	No
Presentation	Right hydrocele	Right chronic epididymitis	Right hydrocele	Right hydrocele	Right hydrocele
T stage	T2	T2	T2	T2	T2
Tumor size (cm)	N/A	N/A	0.5	7	N/A
Surgery performed	RARPLND, orchiectomy	RARPLND	RARPLND, orchiectomy	RARPLND	RPLND, left PLND
Hemiscrotectomy	Yes	No	Yes	Yes	Yes
OR time (min)	212	243	362	421	309
Estimated blood loss	50	200	300	50	900
RPLND template	Modified right	Bilateral	Modified right	Bilateral	Bilateral
Nerve spare	Yes	No	Yes	Yes	Yes
Nodes yielded	22	29	32	21	70
No. positive nodes	2	5	2	0	0
Scrotal margin	Negative	N/A	Negative	Negative	Negative
Length of stay	1	1	1	1	6
Follow up since surgery (mo)	3	26	37	27	47
Adjuvant chemo	No	No	Yes	No	No

OR = operating room
RARPLND = robotic assisted retroperitoneal lymph node dissection
mo = months; min = minutes; PLND = pelvic lymph node dissection

2017. The technique of RARPLND used in this series has been described in our previous report.[8] Descriptive analysis was performed to report patient postoperative and early oncological outcomes.

Results

Six patients with MMTVT were evaluated. In the patient who did not undergo RPLND, the patient presented initially at 80 years of age in 1989 with a hydrocele on the right side and during surgery, there were suspicious testicular lesions, prompting surgeons to proceed with an orchiectomy. The resulting pathology was consistent with MMTVT. The patient subsequently underwent right hemiscrotectomy. Initial cross-sectional imaging was negative and the patient was followed conservatively. Sixteen months after the index surgery, retroperitoneal lymphadenopathy was appreciated, suggestive of metastasis. The patient elected to be followed conservatively and subsequently passed away 19 months after the index surgery due to the disease.

In five patients who underwent RPLND, Table 1, the median age was 50 years (IQR 34-51) and median body mass index was 26.9 kg/m^2 (IQR 26.4-30.6). Four patients originally presented with right sided symptomatic hydroceles, while one presented with right sided chronic epididymitis. Orchiectomy (one simple, two inguinal radical) was performed in three patients and hydrocelectomy in the other two patients prior to presentation. All outside pathology was reviewed by a genitourinary pathologist. Preoperative cross-sectional imaging, including PET-CT scan in three patients, which was negative for lymphadenopathy or metastasis. The CT scan in the open case (patient 5) did reveal an indeterminate pelvic lymph node. RARPLND was performed in four cases and concomitant hemiscrotectomy in 4/5 (80%) cases. Hemiscrotectomy was not done in one patient who previously underwent radical inguinal orchiectomy. The ipsilateral spermatic cord was removed in all cases. Groin dissection was deferred, due to lack of clinically suspicious nodes.

Full bilateral template was performed in three patients and right modified template was performed in the remaining two. The open RPLND case also included an ipsilateral pelvic lymphadenectomy due to concerns about an indeterminate pelvic lymph node. Patient 2 was impotent and requested a maximally aggressive oncological operation, with no interest in a nerve-sparing approach. As such, this was the only patient who underwent a non-nerve sparing procedure. During surgery, there was no evidence of grossly involved lymph nodes. Median lymph node yield was 29 (IQR 22-32) and median blood loss was 275 cc (IQR 200-300). Positive retroperitoneal lymph nodes were found in 3/5 (60%) cases. Out of the three patients who had preoperative negative PET-CT scans, two were found to have lymph node involvement after RPLND. In the four hemiscrotectomy specimens, one was positive for disease, with negative margins. Those who underwent RARPLND were discharged home on postoperative day one. One patient received four cycles of adjuvant Cisplatin and Pemetrexed. Mean follow up was 27 months (range 3-47). No patients recurred.

Discussion

In this series of six patients who presented with MMTVT, we demonstrate that RPLND can be a useful diagnostic and potentially therapeutic option in managing these patients. All five patients who underwent RPLND had negative preoperative cross-sectional imaging for metastasis however, lymph node dissection yielded nodal involvement in 60% of these patients, suggesting a potential role for upfront RPLND in these patients. The robot provides a plausible minimally-invasive option for these patients.

There have been less than 300 cases of MMTVT reported in the literature.[5,10] Patients have a propensity to recur and survival rates are unfavorable. For instance, in an analysis of the National Cancer Institute's SEER database of patients with testicular mesothelioma, Nazemi et al reported 5 and 10 year disease-specific survival rates of 58% and 45%, and 5 and 10 year overall survival rates of 49% and 33%, respectively.[11] Management approaches have varied, though some clinical principles are being developed. For instance, once MMTVT is diagnosed, it was found in earlier cases that patients had greater than a three-fold higher local recurrence rate when they underwent a hydrocelectomy versus orchiectomy (35.7% versus 10.5%). This is important as local recurrences have been associated with a 9 month lower median survival.[2] Consequentially, orchiectomy with or without concomitant hemiscrotectomy in patients suspected to have MMTVT is seen as the standard of care in order to mitigate the risk of positive surgical margins, which is especially desired in this disease because positive margins were found to be associated with significantly worse cancer-specific survival in the series by Recabal et al.[3]

Outside of wide-local excision of the diseased testicle in patients with MMTVT, there are mixed reports on the use and efficacy of additional treatments. Due to the rarity and poor prognosis of this disease, much of the adjuvant data available is on patients with already disseminated disease. These cases have reportedly had

some success with either adjuvant radiotherapy[12] to affected sites or combined chemotherapy-radiotherapy therapy,[13] but results are not consistent. Chemotherapy data is limited, as numerous agents have been studied, though in the data available, little benefit of systemic chemotherapy is seen in this setting.[2,14] Lymph node dissection for the management of MMTVT is controversial. It is not clear which patient will benefit from the procedure and what should be the extent of dissection. RPLND has inherent risks of complication and may require referral to a tertiary center with expertise in performing the procedure. Second, MMTVT affects tunica vaginalis and thus the expected drainage should be to the pelvic lymph nodes. However, most of these patients will have some form of scrotal violation[2] (e. g. hydrocelectomy, scrotal orchiectomy and or needle aspiration) which could lead to alteration of the lymphatic drainage and thus, possible subsequent involvement of inguinal and retroperitoneal lymph nodes.[15-18]

In a systematic review of 74 patients by Plas et al, 15% of patients presented with clinically suspicious metastasis and the lymph node dissections performed revealed that the retroperitoneum was the most commonly affected area (8.5%), followed by the inguinal (5.1%) and iliac lymph nodes (3.4%). This review recommended against routine lymph node dissection in patients with no clinical suspicion for metastasis because the six patients who underwent lymph node dissection in otherwise negative preoperative metastatic work ups had no evidence of metastasis.[2] Conversely, in a more recent series by Recabal et al, only 2/15 (13%) patients had evidence of lymphadenopathy on cross-sectional imaging prior to surgery, but 7/8 (87.5%) RPLNDs, 1/7 (14.3%) pelvic dissections, and 10/10 groin dissections were positive for metastasis. All patient with groin dissections had suspicious findings on clinical exam.[3] This is congruent to our findings that despite negative clinical staging, patients may be affected with metastatic lymph node disease, as evidenced by the three patients with negative preoperative imaging, including two PET-CT scans, who were found to have lymph node involvement after RPLND. It also calls into question the utility and reliability of cross-sectional imaging such as CT scan and PET-scan, which were used in the present series. It should be noted, however that cross-sectional imaging has been useful for detecting disease progression/recurrence when used as a surveillance tool and thus should be integrated in a patient with MMTVT who has received primary treatment.[1,2,19,20]

Because the retroperitoneal lymph nodes are most common nodes affected by MMTVT, we decided to perform an RPLND in our modern series of patients. We elected to perform the minimally-invasive approach for which we have extensive experience.[8,9,21] Of note, this approach has been previously described in one case of a patient with MMTVT.[10] This approach was preferred due to the reported efficacy and feasibility in managing testicular cancer, with previously published favorable oncologic outcomes, low intraoperative estimated blood loss, low rates of postoperative complications, and shorter hospital length of stay (LOS) when compared to the open approach.[7-9,22] At our center we perform RARPLND even in the more challenging cases such as post-chemotherapy testis cancer cases and therefore application in this patient cohort was straightforward. As a result, it was employed in the MMTVT series and similarly resulted in low perioperative morbidity, short hospital LOS, and low recurrence in our variable follow up periods. The technical advantages of RARPLND are again appreciated in these cases, which include the superior visualization with the three-dimensional magnification, increased dexterity, increased control around the great vessels and the fact that all our patients went home postoperative day 1.[8,21,23] Though the standard at our institution is to perform RPLND using the robotic approach for patients who require the procedure, an open approach is often preferred due to the decreased frequency of these procedures and need for centralization at high volume centers. Despite the benefits of the robotic approach described here and in our previous reports,[8,9,21] one of the perceived drawbacks may include a steep learning curve. RPLND is not as common a procedure as other urological surgeries where use of the robot has become widespread (e.g. prostatectomy), which may make it more difficult for surgeons to build up experience with the approach. In addition, though the short and intermediate outcomes reported have been comparable to the open approach, more long term data is needed to confirm oncological equivalence to the open approach.[8,9,21]

In order to construct an ideal treatment approach for MMTVT, it is important to understand the disease's natural history to determine what treatment approach should be established. Due to what is known of malignant mesothelioma and testicular pathologies, various treatment approaches have been attempted for MMTVT. Malignant mesothelioma has been previously found to be responsive to chemotherapy,[24] radiation,[25] and surgical resection.[26] As a result, all three treatment strategies have been attempted in MMTVT, but conclusive data is difficult to obtain secondary to the poor prognosis and rarity of MMTVT.

As mentioned above, chemotherapy has had mixed results in these patients, radiation therapy has conferred some benefit, and sole surgical resection of the primary tumor in the form of an orchiectomy is associated with early recurrence rates. Aside from the histopathology, the involvement of testicular structures introduces an additional question of whether to treat these patients like certain testicular tumors, such as non-seminomatous germ cell tumors. In such patients, RPLND provides very high cure rates and as a result, excellent long term disease-specific and overall survival.[27-29] However, there is little data on long term efficacy of this technique in MMTVT patients, but in the series by Recabal et al, two patients with confirmed retroperitoneal lymph nodes after RPLND are alive after 6 and 8 years, with no evidence of recurrence.[3] Our series supports this notion that RPLND may be beneficial in these patients, as no patients have recurred with up to 47 months follow up.

Limitations in this study include its small sample size and retrospective nature. The short follow up is also a limitation, especially in the one patient who was recently treated and has had minimal follow up. Though the mean follow up we report is short (27 months), most recurrences (> 60%) occur within 24 months, and a vast majority (> 90%) within 60 months according to previous reports.[2,3] Another limitation is the inability to have more accurate surveillance methods to monitor disease recurrence, as many cases of metastatic disease, including some patients in our series, are missed with cross-sectional imaging. Despite these limitations, RPLND for patients with MMTVT provides a diagnostic benefit by identifying lymph node metastases that may have otherwise gone undetected. Additional management approaches can be proposed based on available literature and modern series, Table 2. Longer term outcomes and controlled studies are needed to identify if RPLND translates into improved

TABLE 2. **Proposed management recommendations in patients who present with MMTVT**

Treatment option	Recommendation level*	Clinical basis
Hemiscrotectomy	Highly recommended	Most cases are diagnosed with initial scrotal violation surgery. Local recurrence has significant implications on early survival after surgery. Positive-margins are associated with significantly worse cancer-specific survival, which makes hemiscrotectomy a valuable option to obtain negative margins.
Retroperitoneal lymph node dissection	Highly recommended	MMTVT affects the tunica vaginalis, but due to the intimacy to the tunica albuginea, retroperitoneal involvement is not uncommon. Various figures exist regarding involvement, but this is the most common area involved and was involved in 60% of cases with negative cross-sectional imaging in the present and in 7/8 (87.5%) of patients where only 2/15 (13%) had suspicious nodes on imaging.
Pelvic lymph node dissection	Optional	Uncommonly involved in select series. Only 1 patient in present series had PLND done that was negative. Additional series with 7 PLND found 1/7 (14.3%) with positive nodes. Would recommend in radiologically suspicious cases
Inguinal node dissection	Optional	Most data on inguinal dissection is based on surgery performed when clinical suspicion is present (i.e. groin mass). Would recommend in clinically suspicious cases.
Chemotherapy	Optional	Little benefit described in studies evaluating the benefits of chemotherapy.
Radiation	Optional	Scant data on the role of adjuvant radiation therapy to affected sited. Scant data on the efficacy of combined chemotherapy and radiation in patients with metastatic disease.

*based on literature review and expert opinion

survival outcomes in these patients. Because of the rarity of this case and the paucity of published RPLND series for MMTVT, this series can contribute to the cumulative experience of studies previously published to assist clinicians in better understanding this entity. Given the perioperative morbidity associated with open RPLND, the minimally-invasive approach can be presented as an option to patients and may potentially increase their interest in proceeding with surgery as a primary intervention.

Conclusions

MMTVT is a very rare malignancy with high potential for retroperitoneal lymph node dissemination. Regardless of the approach, RPLND may provide a diagnostic benefit, with the robotic approach affording a potentially expedited recovery. □

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