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Case Report

Malignant Mesothelioma of the Testes with Retroperitoneal Recurrence and Resection in an 80-Year-Old Male and Review of the Literature

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Abstract
Malignant mesothelioma of the testes is an aggressive, yet rare urogenital malignancy, accounting for an infinitesimally small number of oncologic diagnoses. This infrequent occurrence is accompanied by a relative lack of knowledge surrounding this disease, thus limiting management options beyond surgical intervention. Oftentimes, these malignancies present with a poor prognosis despite early intervention and only worsen in the event of metastatic spread with poor survival and limited response to treatment, if any. Our case documents positive patient outcomes following the use of aggressive surgical intervention in the management of a metastatic testicular mesothelioma. A healthy 80-year-old male with sudden painless testicular swelling requiring radical orchidectomy following failed initial conservative management. Pathologically, the specimen was diagnosed as malignant mesothelioma of the right testis with involvement of the tunica albuginea and tunica vaginalis. Following disease recurrence at 82 years of age, the patient subsequently opted for an open right-sided template non-nerve sparing retroperitoneal lymph node dissection which was undertaken without complication. Malignant mesothelioma of the testes remains an ominous diagnosis with historically poor outcomes and for which surgical intervention remains the mainstay of treatment. The retroperitoneal lymphatic drainage represents the most common route of metastatic spread for testicular tumours; however, retroperitoneal lymph node dissection has rarely been employed in

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this patient population and never in an individual of this age. Our findings contribute to the growing literature surrounding these rare malignancies and outline the importance of considering both patient autonomy and the clinical picture in disease management.

Introduction

Malignant testicular mesothelioma is an exceedingly rare entity comprising 0.3–5% of mesothelioma diagnoses [1–3]. Since first described in 1957, this malignancy has been reported in fewer than 300 cases globally and metastatic disease described in less than 90 reports [4–6]. Given their anomalous nature, clinical understanding of prevalent risk factors and appropriate management strategies for these aggressive testicular neoplasms remains limited. Non-specific presentations of these tumours typically require that definitive diagnosis be made post-operatively and warranting local resection as the mainstay of treatment [2, 5]. Embryological origin of the testes designates the retroperitoneum as the primary route for lymphatic drainage, predisposing these lymph nodes as the central site for metastatic spread [7]. Such considerations paired with the aggressive nature of these malignancies and lack of evidence supporting systemic therapy have prompted arguments around the necessity of retroperitoneal lymph node dissection (RPLND) in disease management [5, 8, 9]. Here, we report a case of a surgically managed malignant mesothelioma of the tunica vaginalis testis with retroperitoneal recurrence requiring further intervention.

Case Presentation

The CARE checklist was completed by the authors for the present case report, and this is attached as online supplementary material (for all online suppl. material, see https://doi.org/10.1159/000531839). A healthy 80-year-old Caucasian male with minimal past medical history and no known history of asbestos exposure presented in September 2020 with sudden onset painless swelling of the right testis of approximately 3 weeks duration. Palpable inguinal or pelvic adenopathy was absent bilaterally and the left testis and hemi-scrotum were clinically normal. Following failed initial conservative management with antibiotics the patient underwent urgent ultrasonography which revealed a complex cystic-solid lesion in the right scrotum invading the right testicle (shown in Fig. 1). Testicular tumour markers, alpha-fetoprotein, lactate dehydrogenase, and beta human choriongonadotropin levels were within normal limits. Subsequent radical inguinal orchidectomy was undertaken without complication and the patient recovered well.

The pathology of the specimen was evaluated as malignant mesothelioma of the testis. Macroscopic examination revealed a hydrocele containing yellowish clear fluid along with a large primarily exophytic mass, measuring 5.2 × 4.5 × 0.5 cm, on the surface of the tunica vaginalis and tunica albuginea and predominantly involving the latter. The surface of tunica vaginalis was studded by multifocal papillary tumour nodules measuring 0.1–0.7 cm in diameter. Several small foci of stromal invasion were noted along with an additional 1.5 cm satellite lesion. The mass was negative for invasion of the testes, epididymis, and rete testis with negative resection margins of the spermatic cord for tumour involvement; however, lymphovascular invasion was positive. Microscopically, there was a malignant neoplasm with epithelioid cells arranged in a papillary, tubulopapillary and solid pattern. Cells were rounded

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Fig. 1. Ultrasonography of the testes displaying complex cystic-solid lesion invading the right testicle.

to cuboidal, containing eosinophilic cytoplasm and pleomorphic, prominent nuclei with significant mitotic activity. Cellular atypia of the mesothelial surface, indicative of in situ neoplasm was also noted. On immunohistochemistry (IHC) staining, the tumour was strongly positive for pan-cytokeratin, calretinin, D2-40, WT-1 with focal staining for CD99 while negative for cytokeratin 5 and 6, alpha-fetoprotein, MART-1, and inhibin. Staging computed tomography (CT) of the chest, abdomen, and pelvis was undertaken and revealed no definite evidence of metastatic disease, however, noted multiple indeterminate sub-centimetre periaortic nodules (shown in Fig. 2).

Considering the lack of significant evidence supporting systemic therapy paired with the negative resection margins, active imaging surveillance was initiated with follow-up on a 3-month basis. The patient remained well over the proceeding 16 months with negative testicular tumour markers, albeit slightly increased prominence of the retroperitoneal nodes on follow-up CT scanning (shown in Fig. 2). A positron emission tomography-CT scan undertaken in February 2022, shown in Figure 3, revealed multiple moderate to intensely fluorodeoxyglucose avid para-aortic and interaortocaval nodes larger than 1 cm and consistent with metastatic disease. After prolonged consideration, the patient subsequently opted for a RPLND aimed at delaying mortality while limiting age-related morbidity and complications. An open right-sided template non-nerve sparing RPLND was undertaken without complication approximately 6 months following metastatic presentation with the patient discharged home 5 days after the procedure without complications. Pathologic examination revealed identical morphology and IHC to the initial testicular mass. Six of sixteen interaortocaval nodes were positive for malignancy, with the largest focus measuring 3 cm in maximum dimension, while all four excised right paracaval nodes were negative for metastatic mesothelioma. Extranodal extension and large vessel invasion were present as excision of the right gonadal vein yielded positivity for malignancy along with one adjacent lymph node with metastatic disease. The patient is currently well and remains on active surveillance.

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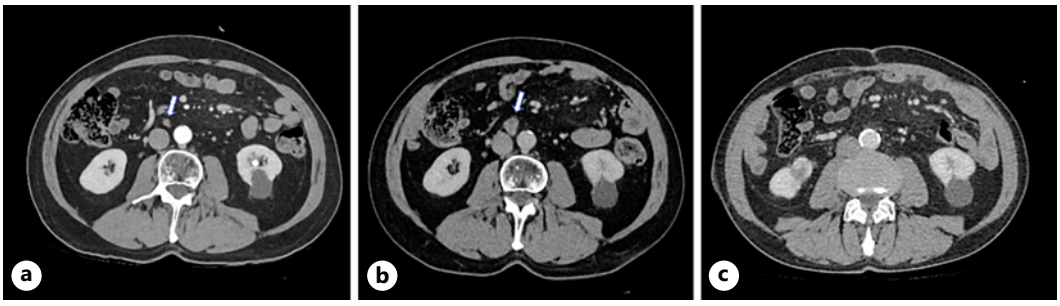

Fig. 2. Axial computed tomography (CT) showing metastatic disease progression (arrows indicate enlarging para-aortic lymph nodes). **a** Initial staging CT. **b** Pre-operative CT scan. **c** Post-operative CT scan.

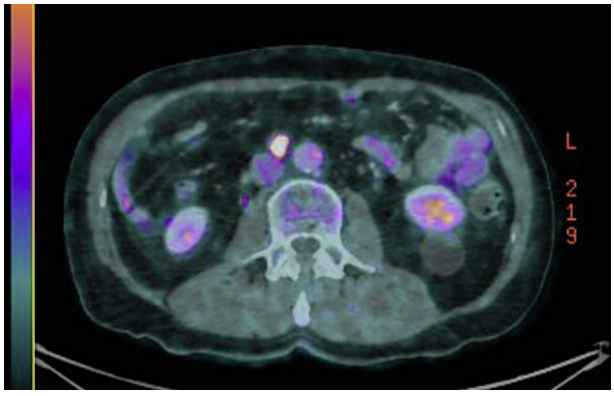

Fig. 3. PET-CT (February 2022) demonstrating a >1 cm fluorodeoxyglucose (FDG) avid lymph node consistent with metastatic disease.

Discussion

Mesotheliomas represent a relatively rare, yet aggressive subset of cancers arising from the serosal membrane lining the pleura, peritoneum, pericardium, and on rare occasions, originating from the tunica vaginalis of the testis. These malignancies, which may present at any age, are typically reported in males between 55 and 75 years with older patients having worse prognosis [4, 5]. While aetiology remains unclear, several risk factors including history of testicular trauma, herniorrhaphy, and various inflammatory processes of the inguinal region have been proposed as associated with the development of this malignancy [10, 11]. Further, morphological similarity to peritoneal and pleural mesotheliomas has postulated asbestos exposure as a predominant risk factor for development [12, 13]. Contrastingly, two independent reviews reported that only 30–40% of cases were likely associated with asbestos exposure [4, 14]. Our reported case of an 80-year-old male with no known history of asbestos exposure or previous testicular trauma provides limited support for these explanations. It is likely that incidence of these malignancies is a multifactorial occurrence; however, there have been several cases in the past that have presented without any evident underlying risk [1, 11, 12].

Testicular mesotheliomas remain diagnostically challenging with insidious onset and non-specific manifestation as a hydrocele or paratesticular mass with analogous presentation to various other gonadal complaints. Further complicating diagnosis is the ineffectiveness of testicular tumour markers in differentiating from otherwise benign occurrences as various reports, including our case, noted absence of elevation [5]. Physical examination and radiological evaluation may be of assistance in identification, with ultrasonography having the

greatest accuracy in detecting testicular tumours; however, diagnosis is rarely made pre-operatively [15]. Surgical management has been warranted as the mainstay of treatment for these malignancies and is predominantly accomplished via radical inguinal orchidectomy with hemiscrotectomy followed by primary retroperitoneal lymphadenectomy [2, 5, 16]. Post-operative pathological examination generally reveals an IHC profile comparable with other mesotheliomas and typically displays positivity for calretinin, WT-1, EMA, D2-40, thrombomodulin, cytokeratin (CK) 7, and variably expression for CK5/6. These indicators along with negative stains for CK20, Ber-EP4, carcinoembryonic antigen, Leu-M1 are used to differentiate from various adenocarcinomas [1, 3, 13]. It is important to note that initial primary retroperitoneal lymphadenectomy was not undertaken in our case due to the patients' advanced age, however, would be considered standard of care in younger patients in the prevention of aggressive metastases.

Adjacent to local resection, the rarity of these cases is accompanied by a lack of extant literature indicating a role for systemic therapy or other modalities in the management of disease. The use of radiotherapy remains controversial, however, may possess utility in preventing disease recurrence following margin-negative surgical resection [7, 11]. Similarly, the role of adjuvant chemotherapy remains poorly understood and typically utilizes regimens with a proven effectiveness in the management of pleural mesotheliomas. A combination of pemetrexed and cisplatin has been standard, utilized in several reports, while Gemcitabine has also been indicated as a viable alternative for patients with poor response to platinum-based chemotherapies [1]. Despite limited success in the management of testicular mesotheliomas, the use of such systemic therapies may delay mortality in select cases and warrant consideration in individuals with unfavourable prognosis. Our patient was not offered systemic therapy and remained well until disease recurrence at approximately 16 months.

Median survival time in those diagnosed with testicular mesothelioma is approximately 24 months which further reduces to 14 months in those with recurrent disease. Age greater than 60, higher tumour stage, and disseminated disease at presentation have all been negatively correlated with overall survival [5, 7]. The development of lymphatic and distant metastases has been frequently observed, with more than 60% of relapses occurring within the first 2 years. The retroperitoneal lymph nodes are the primary lymphatic drainage in testicular diseases and represent the most common site of metastatic spread, as seen in our case [5, 7]. A recent review by Grogg et al. [5] (2021) found that complete remission in the metastatic setting of these mesotheliomas has been reported in only 5 cases while suggesting that surgical intervention alone may be insufficient for cure [7]. Similar to primary tumour management, there is a lack of clear therapeutic recommendation regarding nodal metastases with aggressive surgical intervention comprising the majority of reported recommendations [5, 9]. RPLND remains a staple in the management of testicular germ cell tumours; however, this procedure is documented in fewer than 15 cases of testicular mesothelioma.

Despite the paucity of extant literature, our patient opted to undergo RPLND following disease progression as this provided the best chance to limit morbidity and outlast the dismal prognosis associated with this rare malignancy. While the potential for complications of invasive procedures is increased for an individual this age, prolonged consideration of the patient's physiological status and minimal past medical history deemed this most appropriate management option. We ultimately opted for a right template RPLND as opposed to full nodal dissection as associated histology for left-sided lymphatic spread would likely be less aggressive than seen with traditional testicular germ cell tumours. Further, given the patient's age this right-sided approach reduced operative time, which also contributed to the decision to perform non-nerve sparing surgery, and allowed for quicker post-operative recovery. While chemotherapies have also been employed in the metastatic setting, they have met with limited success in testicular mesotheliomas and are commonly utilized in palliative management.

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Employment of a chemotherapeutic regimen in our patient would have caused significant renal burden and likely instituted a palliative sequelae of disease, whereas such management would possess equivocal utility in the case of failed surgical intervention. Our case is the first to employ this invasive procedure in a patient of this age following recurrence of this rare malignancy and highlights the importance of the clinical picture along with patient autonomy in management. There remains limited evidence to support adjuvant treatment following disease recurrence with current literature supporting continued follow-up with clinical examinations and regular imaging via CT scanning assessing for additional metastatic spread.

Conclusion

Malignant mesothelioma of the testis is a rare, yet aggressive urogenital malignancy with a poor prognosis even in the event of early-stage surgical intervention. The exact nature of development for these malignancies remains unknown; however, metastases to the retroperitoneal lymph nodes are a well-documented route of spread. Our case is one of the few to employ a RPLND in managing metastatic spread of testicular mesothelioma and the first to implement such a measure in an individual of this age. Our findings contribute to the growing literature surrounding these malignant mesotheliomas and further highlight the importance of the clinical picture paired with patient autonomy in the management of this rare disease.

Statement of Ethics

This case report was conducted according to the guidelines of the Declaration of Helsinki. This study protocol was reviewed by Memorial University's Health Ethics Research Board and deemed exempt from ethics approval. Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Conceptualization, patient consent, and supervision were provided by Dr. Sohaib Al-Asaaed. The composition of the main manuscript text was undertaken by Ian Janes. Ian Janes and Dr. Paul Johnston prepared the enclosed figures. Dr. Sohaib Al-Asaaed, Dr. Paul Johnston, and Ian Janes reviewed and edited the final manuscript.

Data Availability Statement

All data generated or analysed during this study are included in this article and its online supplementary material files. Further enquiries can be directed to the corresponding author.

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