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Short Communication

Malignant Mesothelioma of Tunica Vaginalis: Can Ultrasound Assist in Pre-Operative Diagnosis?

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Abstract

Malignant mesothelioma (MM) of tunica vaginalis testis is a rare aggressive tumor with around 100 reported cases. Since most common presentation of this malignancy is asymptomatic hydrocele, majority of the cases are diagnosed either intraoperatively or on final pathology, leading to incomplete resection or scrotal violation. Through this review we aim to describe the clinical features and pathological characteristics of MM of tunica vaginalis. We further discuss the use of scrotal ultrasound with doppler in pre-operatively suspecting this uncommon malignancy.

INTRODUCTION

Mesotheliomas are relatively rare tumors of the serosal membranes of pleura, pericardium and peritoneum. Mesothelioma of tunica vaginalis, an outpouching of peritoneum, is even rare and constitute only 0.3-5% of mesothelioma cases. Malignant Meosothelioma (MM) of tunica vaginalis is an aggressive tumor with approximately 100 reported cases [1-3]. It is found to occur in a wide age range of patients (6 to 91 years), though more common in individuals between 55 to 75 years of age [4]. MM presents mostly as an enlarging or recurrent hydrocele developing over a period of months to years [5,6] and less likely as a testicular mass [4,7] or acute scrotum[8,9]. Although it is usually unilateral, there are reports in the literature with bilateral synchronous presentation [8,10]. Tumors mimicking inguinal hernia or other inguino-scrotal masses [11,12] have also been reported. Approximately 15% of the patients present with primary metastatic disease [4].

Risk factors

Asbestos exposure is the only consistently found risk factor in MM of tunica vaginalis and has been reported in around 35% of patients [4,13]. Interestingly, asbestos exposure has been linked to a higher percentage (50-70%) of pleural and peritoneal mesothelioma [14]. As with mesothelioma at other sites, MM of tunica vaginalis has been shown to exhibit long latency periods explaining increased incidence in older adults [4]. Other suggested risk factors of MM of tunica vaginalis are herniorapphy, trauma, and long standing hydrocele, [15-17] however these etiologies have not been validated in the recent literature. Radiation, radiotherapy, viral infections, deletions at chromosomes 1p, 3p, 6q, 9q and monogamy of chromosome 22 have been reported to be associated with development of mesothelioma at other sites [18,19] but have not been implicated in the development of MM of tunica vaginalis.

Pathology

On gross examination, MM appears as multiple, firm white nodules often with papillary excrescences on the internal surface of hydrocele sac [4,20]. When presenting as a mass, they appear as firm yellow or white tumor with solid or cystic cut surface [3]. Histologically, the tumors are similar to their counterparts in pleura and peritoneum with 60-70% being epithelial, 30-40% biphasic and rest sarcomatous. These tumors often show significant nuclear atypia, mitotic activity, and invasion of the epididymis, spermatic cord, lymphatic spaces, or the fibrous tissue of the tunica [21]. The immunohistochemical profile of MM of tunica vaginalis is similar to pleural mesothelioma. Most widely used positive markers for confirmation of diagnosis are calretinin, thrombomodulin, epithelial membrane antigen and Cytokeratin 7 and Cytokeratin 5/6. Calretinin is a marker of mesothelial cells and serve as an important marker in distinguishing it from metastatic adenocarcinoma [22]. MM is negative for expression of carcino-embryonic antigen, leuM1 and CK20 [20]. Keratin antibodies were also consistently positive in cases where reported [20]. A combination of microscopic examination and immunohistochemistry is essential to differentiate MM from other paratesticular lesions. While

benign pathology such as reactive mesothelial hyperplasia and adenomatoid tumor can be excluded by presence of invasion and cellular atypia, immunohistochemistry is useful to distinguish it from metastatic adenocarcinoma.

Clinical course

MM is a locally aggressive tumor with high predilection for metastatic spread. In an analysis of 73 cases of MM of tunica vaginalis, Plas et al found tumor recurrence after primary surgery in 52.5% of the patients with 84% of patients with recurrence progressing to disseminated disease [4]. Local recurrences can occur on the scrotal incision or in inguinal lymph nodes. Distal recurrences have been noted at retroperitoneal LNs (14%), lungs (10%), liver (4%), pleura, omentum and others (10%). Primary metastatic disease is found in 15% of the cases and usually involves retroperitoneal, inguinal and iliac LNs in the order of frequency. 38% of the patients died during the median follow up of 23 months. The treatment of locally advanced and disseminated disease has not been standardized with studies presenting varied success with adjuvant chemotherapy, radiotherapy or both [7,23]. Retroperitoneal or inguinal LNs dissection as prophylaxis and a part of the staging procedure was advocated by some authors [11,24] while others only chose to follow patients closely to look for any signs of recurrences. Carp et al. [25] in 1990 suggested early surgical resection of the recurrences rather than as a salvage when other modalities have failed.

Pre-operative diagnosis

Radical orchiectomy through an inguinal approach is the recommended primary surgical treatment as there are higher chances of local recurrences after trans-scrotal resection [4,17,26]. Plas et al observed that there is three times more likelihood of local recurrence after resection of hydrocele wall alone as compared to radical orchiectomy. Since most of the cases (around 94%) of MM are found either intra-operatively or at the final pathology, many have incomplete resection of tunica vaginalis and/or scrotal violation. In these cases a second surgery in form of hemiscrotectomy with broad resection margins is usually performed later to decrease the chances of recurrences. Pre-operative diagnosis, thus, is essential for proper and adequate treatment of the patients. The major impediment for a pre-operative diagnosis is the absence of any specific clinical symptoms or diagnostic studies. There are only a handful of instances in literature where the diagnosis was made pre-operatively [7,27-31]. Four of them were diagnosed using either cytology of hydrocele fluid or FNAC of the suspected lesions, while scrotal ultrasound with Doppler was diagnostic in one case. Doo et al made the diagnosis using a combination of scrotal ultrasound and computed tomography scan. However, none of the above reported cases had long term follow up of the patients.

Aspiration cytology and FNAC are low yield methods that are useful only if positive and do not exclude malignancy if negative. Further, they, theoretically, put the patients at a risk of local dissemination of tumor. Ultrasound provides the first clue to the presence of any paratesticular tumor which may be associated with a simple or complex hydrocele. Sonographic appearances can vary from multiple extra-testicular nodular masses or papillary projections of variable echogenicity and sizes [29,32,33] to focal irregular thickening of tunica vaginalis [29,34]. However, ultrasound alone cannot reliably differentiate it from other benign conditions such as reactive mesothelial hyperplasia, adenomatoid tumor and well-differentiated papillary mesothelioma. That's where the Doppler study becomes essential.

We have previously reported a case of 73 year old man where a diagnosis of MM was made using scrotal ultrasound with Doppler [35]. Our patient had several small tumors arising from the tunica vaginalis with a central core and stalk configuration. The tumors were shown to have higher vascularity than the surrounding testicular tissue on the doppler examination. These findings led to the suspicion of malignancy. He underwent early inguinal orchiectomy which was attributed to improved survival in his case. Boyum et al described similar findings in their patient which was later confirmed by pathology [30]. The tumor was excised using inguinal approach. They discussed that the presence of increased vascularity in a paratesticular mass should increase the suspicion of malignancy as most common benign paratesticular masses - adenomatoid tumors are hypovascular on Doppler examination. Others have reported hypovascularity in mesothelioma masses at atypical locations in testis and epididymis, [24,26,33] which could be due to diminished sensitivity of the doppler at these locations.

To conclude, MM of tunica vaginalis is an aggressive cancer with dismal prognosis once advanced. In contrary to mesothelioma of pleura and peritoneaum, MM of tunica vaginalis can be completely resected. The treatment of the disease, however, is compounded by delayed diagnosis and incomplete resection as the most common presentation is of a benign hydrocele without much symptoms. Pre-operative suspicion of MM would lead to an early inguinal orchiectomy and may result in lower recurrences. It may also have an impact on prognosis as the tumor recurrences usually do not respond well to adjuvant chemotherapy, radiotherapy or even to surgical resection. We believe that the doppler study in combination with scrotal ultrasound may aid in suspecting MM of tunica vaginalis pre-operatively. Any para-testicular mass detected in the ultrasound should undergo a doppler study to check for the vascularity and if it is increased, then it should be treated by radical orchiectomy through inguinal approach. While doppler may not detect increased vascularity in all the mesothelioma masses, particularly if they are at atypical locations, other factors such as asbestos exposure and location of the mass should be considered while making a prudent decision.

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