

# Malignant Mesothelioma of the Tunica Vaginalis Testis in a Petrochemical Worker Exposed to Asbestos

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**Abstract.** *Malignant mesothelioma of the tunica vaginalis testis is a rare and aggressive asbestos-related malignancy that may pose difficult diagnostic problems. After 16 years of asbestos exposure, a 38-year-old petrochemical worker came to our notice with acute right testicular pain and swelling, simulating torsion of the spermatic cord. Histopathology of surgical samples of the tunica vaginalis revealed tubulopapillary, epithelioid neoplastic proliferation. Immunohistochemical staining for the epithelial glycoprotein Ber-EP4 was negative, whereas results were positive for mesothelial markers, thus leading to the diagnosis of epithelial mesothelioma. The tumour infiltrated the testicular surface and the epididymis, but no distant metastases were found. The patient was treated with radical inguinal orchidectomy without adjuvant therapy and is free from disease 15 months after diagnosis. Tunical mesothelioma may simulate metastatic carcinoma at routine histopathological examination. Immunohistochemistry and occupational anamnesis are helpful for the correct diagnosis, which, in turn, is important for prognosis and treatment, and in relation to legal issues when asbestos is involved in the causation of the disease.*

Malignant mesothelioma of the tunica vaginalis testis is an extremely rare neoplasm with potentially aggressive behaviour. Asbestos is the only established etiopathogenetic factor. Diagnosis is problematic and no definite treatment modality has been established (1-4).

We report an occupational case that came to our notice

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without distant metastases, which simulated acute torsion of the spermatic cord, and was favourably treated with radical inguinal orchidectomy.

## Case Report

A 38-year-old man without significant medical or surgical history was hospitalized for sudden onset of right testicular pain and swelling. A right hydrocele was found on examination. General physical examination, chest radiography, electrocardiography and routine blood/urine analyses were normal. Testicular tumour markers ( $\beta$ -human chorionic gonadotropin and  $\alpha$ -fetoprotein) were within normal limits.

The patient was employed from 22 years of age in the petrochemical industry. His duties included renovation, maintenance and demolition of asbestos-containing fuel tanks, exposing him to the inhalation of asbestos fibres. Additional exposure derived from the frequent use of fireproof asbestos coverings.

With the suspicion that he had suffered acute torsion of the spermatic cord, a surgical inspection of the right hemiscrotum was carried out, revealing thickening of the tunica vaginalis and clear effusion. The fluid was aspirated and the tunica resected. Histopathological examination of the surgical sample demonstrated multifocal epithelioid neoplastic infiltration with a tubulopapillary pattern (Figure 1). The cells were relatively uniform in morphology and dimensions, with a cuboidal aspect. They showed a moderate amount of eosinophilic cytoplasm with vesicular nuclei, prominent nucleolus and occasional, atypical mitotic figures. The nuclear proliferation marker Ki-67/MIB-1 was expressed in more than 10% of the neoplastic population. Immunohistochemical staining for the epithelial glycoprotein Ber-EP4 was negative, whereas results for the mesothelial markers [cytokeratins, calretinin (Figure 2), vimentine, and human bone marrow endothelia 1 (HBME-1)] were positive, leading to the diagnosis of (well

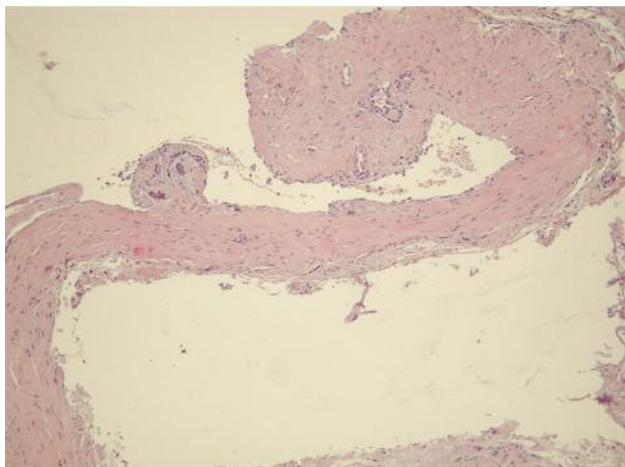


Figure 1. Section of the tunica vaginalis showing neoplastic proliferation with papillary and glandular features, and stromal infiltration. The superficial mesothelial lining presents hyperplasia and reactive fibrosis (hematoxylin-eosin; original magnification, x20).

differentiated) epithelial mesothelioma.

A right high inguinal orchidectomy was performed. Pathological analysis disclosed multifocal neoplastic localizations on the testicular surface and the epididymis. Staging total body computed tomography (CT), abdominal echography and total body positron emission-tomography (PET) showed no evidence of lymph nodal or visceral metastases. No adjuvant chemotherapy or radiotherapy was administered. The patient has been followed up for 15 months and is currently free from disease.

## Discussion

Most cases of malignant mesothelioma occur in the pleural or peritoneal cavity. The scrotal localization was first described in the 1950s (5, 6). Since then, approximately 100 cases have been reported in the literature, usually in patients older than 45 years, although, as in the case described here, the disease may also be observed in younger patients (1-4, 7).

The diagnosis of tunical mesothelioma is always difficult (especially preoperatively), due to the rarity of the tumour, its non-specific clinical manifestations (scrotal masses, hydrocele, scrotal discomfort or pain), and its morphological variability (1-4). In the patient reported here, the picture was dominated by acute testicular pain, simulating torsion of the funicle. Normality of  $\beta$ -human chorionic gonadotropin and  $\alpha$ -fetoprotein initially excluded the presence of a tumour. Definition of the neoplastic nature of the disease required exploratory surgery, and routine histologic examination was not sufficient for a conclusive diagnosis. With hematoxylin-eosin staining, epithelial (or

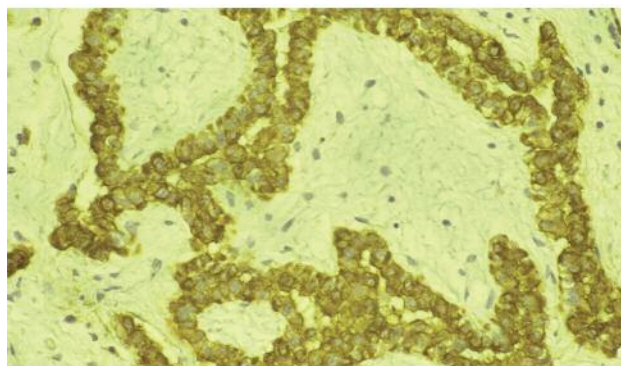


Figure 2. Sample of neoplastic tissue showing immunohistochemical reaction for calretinine (original magnification, x200).

epithelioid) mesothelioma (the most common histopathological subtype) often presents the same morphology as glandular carcinomas, as in this case. Especially in the pleural or peritoneal localization, epithelial mesothelioma may erroneously suggest metastatic invasion by occult adenocarcinoma. Sarcomatous (or sarcomatoid) mesothelioma, apparently reported only once in the tunica vaginalis (8), may in turn simulate sarcomas originating from connective tissue. The only pathognomonic histotype is the mixed (or biphasic) mesothelioma, where epithelioid and sarcomatoid tissues coexist (1-4, 9).

In this patient, the negative results of Ber-EP4 immunohistochemistry excluded reactivity of the surgical sample with epithelial-binding proteins, whereas results for cytokeratins, calretinin, vimentine and HBME-1 indicated reactivity of the neoplastic tissue with antibodies that preferentially bind cells of mesothelial origin. As a discriminant marker, calretinin (a calcium-binding protein) shows high sensitivity and specificity for mesothelioma, particularly for the epithelial subtype (7, 9). Thus, immunohistochemistry allowed us to formulate the correct diagnosis of primary malignant mesothelioma (epithelial subtype, well differentiated), excluding metastatic adenocarcinomatosis.

As a general rule, malignant mesotheliomas of all patterns and localizations are highly aggressive neoplasms, scarcely responsive to available treatments (4, 9). Tunical mesothelioma is no exception. This tumour may invade the adjacent scrotal structures (such as the testis and epididymis, as in the case presented), and disseminate to lymph nodes (retroperitoneal or, less frequently, inguinal and iliac) and distant organs, such as the lungs and liver. The extension of disease at the time of diagnosis is the main prognostic factor. When distant metastases are present, the survival is usually of few months, whereas locally confined

tumours may be completely resected and present a better prognosis, especially in younger (<60 years) patients (1, 2).

In case of localized disease, radical inguinal orchidectomy is the optimal primary surgical approach, while the utility of inguinal lymph node dissection, and of adjuvant chemotherapy and radiotherapy (alone or combined), has not been clearly determined for the limited number of reported cases. After surgery, the risk of disease relapse is maximal during the first two years, requiring close (*e.g.* 3-monthly) imaging follow-up. Later on, patients should be examined on a yearly basis for at least 5 years. Life-long follow-up should also be offered, due to the possibility of late tumour recurrence (1, 2, 4).

The patient had an occupational history of prolonged (16 years) asbestos exposure in the petrochemical industry. Asbestos is the only established risk factor for testicular mesothelioma, although its implication in the causation of the disease is less evident than in the pleural or peritoneal localization (10). Other hypothetical causes (absent in this case) include local trauma, viral infections and exposure to ionizing radiation (1, 2). How asbestos fibres reach the tunica vaginalis is unclear, and the mechanisms underlying asbestos-induced oncogenesis are not completely understood (10). Apparently, asbestos acts as a complete carcinogen on mesothelial cells and oxygen-free radicals play a pivotal role in the process, exerting direct and indirect genotoxic effects (11).

Besides malignant mesotheliomas, occupational and environmental asbestos exposure may cause benign pleural abnormalities, asbestosis (interstitial lung fibrosis), and lung cancer, with a risk proportional to the duration and intensity of exposure (12, 13). Beginning in the 1970s, the European Community, USA and Japan progressively introduced restrictive laws concerning the sale and use of asbestos, which was present in a variety of industrial processes. Italy definitively banned its extraction, import/export and use in 1992. However, asbestos continues to represent a major public health concern for several reasons (12-14). Firstly, people exposed in the past are still at risk, since asbestos-induced disease (especially cancer) may develop up to 40 years after exposure. Secondly, removal of preexisting asbestos, as well as maintenance, renovation and demolition of old buildings or structures, are current sources of exposure. Thirdly, a large portion of the asbestos utilized in the past is still present in the general environment, and inevitably causes fibres release into the air, due to aging and disintegration. Since a safety threshold for the risk of mesothelioma is apparently lacking, low asbestos doses, insufficient to cause asbestosis or lung cancer, may express pathogenetic potential for mesothelioma. Accordingly, epidemiological data indicate that the incidence of this aggressive malignancy is increasing (12, 15).

Thus, physicians should be aware of the possibility of malignant mesothelioma of the tunica vaginalis testis among workers previously exposed to asbestos. In such cases, careful occupational anamnesis may disclose a causal link between exposure and disease, with legal implications. The case described had to be reported to the Judicial Authority (as established by the Italian Penal Code) and was referred to the Italian Workers' Compensation Authority.

## Conclusion

This case illustrates the clinical problems posed by tunical mesothelioma. The epithelial subtype of this unusual tumour may simulate metastatic adenocarcinoma at routine histopathological examination. In such cases, the diagnostic doubts can be resolved using immunohistochemistry. In the absence of distant metastases, radical inguinal orchidectomy is the optimal primary treatment, while the utility of adjuvant therapy is undetermined. Life-long follow-up is advisable, due to the possibility of late tumour recurrence. When asbestos is involved in the causation of the disease, occupational anamnesis is crucial in relation to legal issues and occupation-related compensation claims.

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