CASE REPORT

Peritoneal Mesothelioma Mimicking Ovarian Malignancy: The Critical Role of Immunohistochemistry in Diagnosis – A Case Report

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ABSTRACT

Peritoneal mesothelioma is a rare and aggressive cancer that may mimic other intra-abdominal malignancies, making the diagnosis challenging, particularly epithelial ovarian cancer. Immunohistochemistry (IHC) plays a vital role in distinguishing malignant mesothelioma from other cancers with overlapping features. This case highlights the importance of a comprehensive IHC workup in differentiating between mesothelial and ovarian neoplasms. We present a 74-year-old female who initially presented to the ED with neurological symptoms due to venous sinus thrombosis diagnosed by CT scan and MRV. This reflects that the patient's initial presentation was neurological, seizures, and hemiparesis due to venous sinus thrombosis, which may have been a paraneoplastic phenomenon associated with the malignancy. This unique presentation has been highlighted as an important aspect of the case. Further imaging revealed an intrabdominal mass with raised CA 125, initially raising the suspicion of ovarian malignancy. An omental biopsy and the IHC profile revealed positive staining for CK7, calretinin, and WT1, while CK20, Ber-EP4, and PAX8 were negative, supporting a diagnosis of malignant mesothelioma. Genomic profiling with BAP1 mutation provides an additional approach to confirm the diagnosis.

This case has given an appropriate insight into the role of comprehensive IHC in differentiating the peritoneal mesothelioma from mimicking pathologies and guiding appropriate therapies.

Keywords: *Malignant peritoneal mesothelioma, ovarian cancer, immunohistochemistry, malignancy, diagnosis.*

INTRODUCTION

Malignant mesothelioma (MM) is a cancer originating from the mesothelial lining cells of the pleural, peritoneal, pericardial cavities, and the tunica vaginalis. Peritoneal mesotheliomas comprise 10-15% of all mesothelioma cases and are often associated with poor prognosis. These tumors present with non-specific clinical features and are frequently misdiagnosed due to their histological similarity with other ovarian neoplasm [1, 2]. Mesothelial neoplasms range from benign, localized tumors to aggressive, diffuse malignant types that infiltrate surrounding tissues and may metastasize to distant sites and carry a poor prognosis [3]. Additionally, malignant mesothelioma exhibits a broad range of histopathological patterns, which may mimic other tumors [4,5]. Histologically, malignant mesothelioma can be classified into epithelioid (60%), sarcomatoid (10-20%), and biphasic (20-30%) patterns [6, 7].

Differentiation from ovarian cancer is especially challenging when imaging and serum tumor markers (*e.g.*, elevated CA-125) suggest a gynecologic origin. Immunohistochemistry offers a powerful diagnostic tool by identifying tumor-specific antigen expression patterns [8, 9].

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Received: December 31, 2024; Revised: June 13, 2025; Accepted: August 12, 2025
DOI: https://doi.org/10.37184/lnjcc.2789-0112.7.2

- Prognosis. This condition almost inevitably results in a fatal outcome, unlike other mesothelial neoplasms, such as benign adenomatoid tumors and borderline malignant tumors like well-differentiated papillary mesothelioma and multicystic mesothelioma.
- Occupational compensation claims related to asbestos exposure. A review of the literature summarizes the etiology of asbestos-induced neoplasia, the potential mechanisms of tumor development, and diagnostic pitfalls [4].
  However, few immunostains have shown high specificity or sensitivity. For example, calretinin, WT-1, D2-40, and mesothelin are expressed in most mesotheliomas (high sensitivity); however, these markers are also found in a subset of epithelial ovarian cancers, which limits their diagnostic probability [10].

This case report presents a unique clinical scenario where peritoneal mesothelioma mimicked advanced-stage ovarian cancer. We emphasize the pivotal role of IHC and genomic profiling in achieving an accurate diagnosis, thereby preventing mismanagement.

CASE PRESENTATION

A 74-year-old woman, Para 2+0, with a past medical history of treated malignant melanoma and benign hemangioma, presented to the Emergency Department (ED) with left-sided upper limb and facial weakness, accompanied by seizures. She had no regular

  ISSN: 2789-0120 (Online) Liaquat National Journal of Cancer Care 2025; 7(1): 35-38

medication, completed her cervical screening program, and had no known asbestos exposure. She was a retired cleaner and a non-smoker, with no history of talcum powder use.

Initial head CT and MR Venography revealed extensive venous sinus thrombosis without infarcts. Given the unexpected thrombotic event, further investigations were conducted. A CT scan of the chest, abdomen, and pelvis identified an abdominal mass, followed by an MRI scan of the pelvis to further characterize the intra-abdominal mass.

Laboratory investigation showed markedly elevated CA 125 levels 1162 U/mL and 1106 U/mL on repeat testing at 2 weeks, while CEA and CA-19-9 were within normal limits (1.3 ug/L and 32 IU/mL respectively).

An ultrasound-guided biopsy of the omental mass was performed to achieve tissue diagnosis, which showed epithelioid cells infiltrating fibrous and adipose tissue, raising suspicion for mesothelioma. IHC supported by a genomic profiling was done to confirm the diagnosis, which revealed a mutation in the BAP1 gene.

Radiological Findings

CT scan of abdomen and pelvis identified an enhancing solid mass within the pouch of Douglas (**Fig. 1**), mild abdominal ascites, and omental fat stranding. Further imaging with MRI of abdomen and pelvis illustrated ascites and indeterminate diffuse anterior omental thickening (**Figs. 2** and **3**), with right adnexal mass contiguous with a well-defined mass in the pouch of Douglas, shown in Fig. (**2a&b**)..

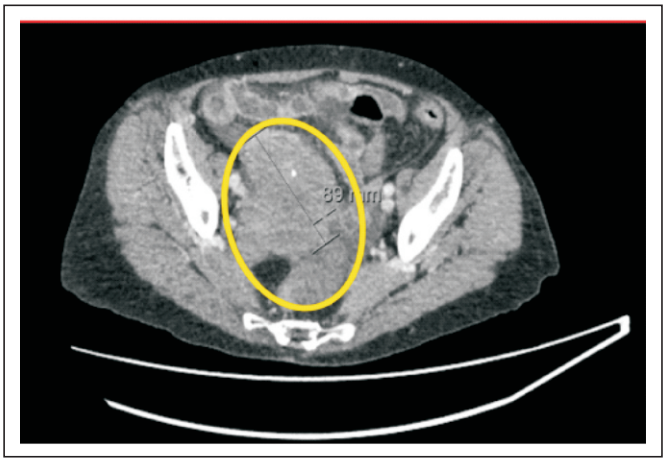

Fig. (1): Radiological image of a CT scan of the pelvis showing enhancing solid masses seen within the pouch of Douglas with adjacent pelvic free fluid. The right ovary was not separately visualized from these lesions.

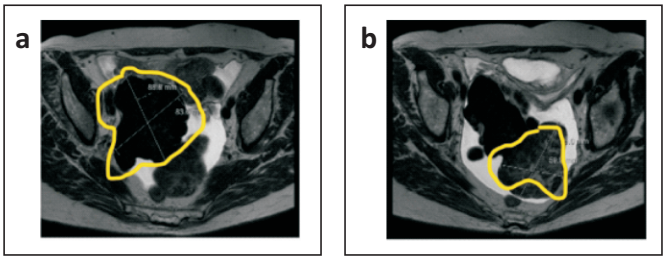

Fig. (2): Radiological image on an MRI scan of the pelvis. Right adnexal mass measuring 8.8 x 8.4 cm. Lobulated solid mass lesion in the Pouch of Douglas measuring 7.9x5.9 cm.

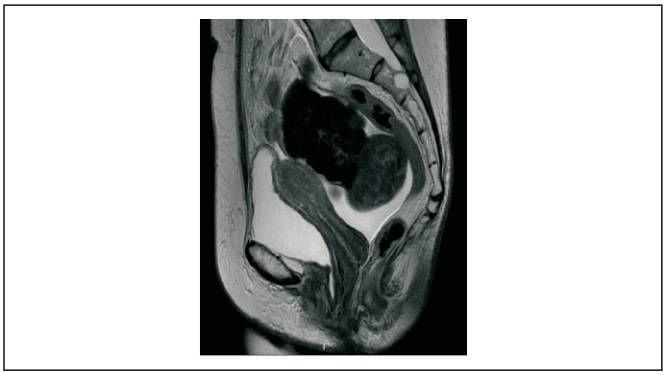

Fig. (3): MRI scan of abdomen and pelvis shows ascites and indeterminate diffuse anterior omental thickening.

Omental Biopsy and General Histopathological Findings

Following informed written consent, an ultrasound-guided (USG) approach was adopted under aseptic technique to obtain omental biopsies. Ten milliliters of 1% lidocaine were infiltrated in the subcutaneous tissues, followed by 4 x 16G USG biopsies from omental disease in the right iliac fossa. Samples were subjected to microscopy and immunohistochemistry.

Microscopy illustrated fragmented cores of adipose tissue, fibrous tissue, and striated muscle. Focally, there was a proliferation of epithelioid cells with moderate amounts of eosinophilic cytoplasm, ovoid nuclei, and prominent nucleoli. These epithelioid cells appeared to infiltrate fibrous and adipose tissue.

Following this, immunostaining was performed with findings as illustrated below in Table **1**.

With the pictorial presentation of IHC markers illustrated in Fig. (**4a-4h**)

Immunohistochemistry

Table 1: Immunohistochemical staining revealed the following results. (Seegene, Korea).

Immunohistochemistry	Patient's Result	Explanation
CK7	Positive	Expressed in epithelial tumors; positive in both ovarian serous carcinoma and mesothelioma
Calretinin	Positive	Strong marker for mesothelioma; typically, negative in ovarian cancer
WT1	Positive	Seen in both mesothelioma and serous ovarian carcinoma
E-cadherin	Positive	Adhesion marker; favors epithelial tumors like ovarian carcinoma
GATA3	Weak Positive	More common in breast/urothelial cancers; rarely seen in mesothelioma
CK20	Negative	Excludes GI and urothelial carcinomas
Ber-EP4	Negative	Helps rule out adenocarcinoma; usually negative in mesothelioma
CDX2	Negative	Rules out GI origin; not typical for mesothelioma or ovarian cancer
PAX8	Negative	Strong Müllerian marker; negative result excludes ovarian origin

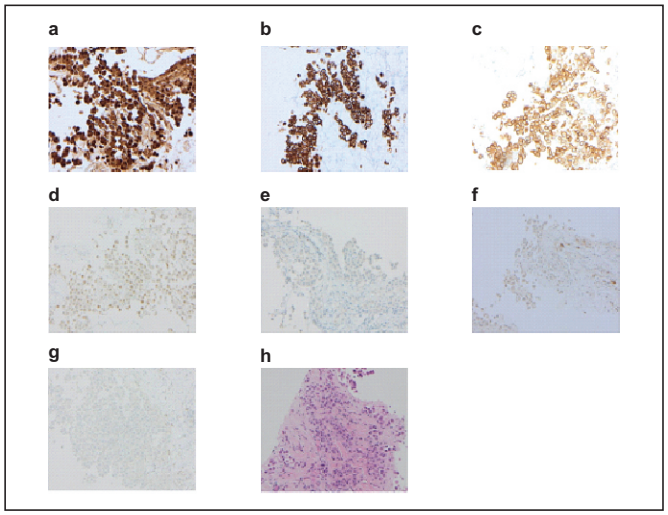

Fig. (4): a) Comprehensive immunohistochemistry panel illustrating the immunostaining pattern calretinin positive **b)** Cytokeratin 7 positive **c)** E-Cadherin positive **d)** GATA3 weak positive **e)** PAX8 negative **f)** BerP4 negative **g)** Oestrogen receptor negative **h)** Haematoxylin + eosin stain, which revealed proliferating mesothelial cells, with focal extension into surrounding fibrous and adipose tissue, displaying features consistent with malignant mesothelioma.

Treatment and Outcome

The patient was referred to the Peritoneal Malignancy Unit in Basingstoke and commenced on palliative first-line immunotherapy with nivolumab (360 mg intravenously every 3 weeks) and ipilimumab (1 mg/kg intravenously every 6 weeks), for a duration of up to 2 years, depending on treatment response.

Her treatment response and disease progression were monitored through routine blood tests and CT scans of the abdomen and pelvis every three months. She responded to the immunotherapy, completing one year of treatment. During this time, she experienced mild symptoms of diarrhea and vomiting, which were managed conservatively.

The first CT scan following immunotherapy showed some ascites, which was attributed to an immune response to the treatment and managed conservatively. Subsequent CT scans showed stable ascites and omental disease, along with evidence of disease regression as shown in Fig. (**5**). This supports the previous explanation of a possible immune reaction to immunotherapy concerning the first CT scan findings following initiation of treatment.

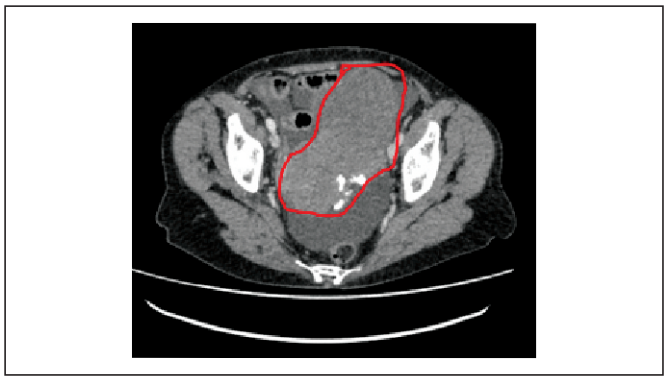

Fig. (5): CT scan after a year of immunotherapy (Post treatment) showed a broadly stable omental disease and ascites with a mild decrease in size of the pelvic lesion.

She tolerated treatment well with manageable side effects. Imaging after one year showed stable disease and mild regression of the pelvic lesion, consistent with treatment response (**Fig. 5**).

Follow-up imaging was assessed using RECIST 1.1 criteria (Response Evaluation Criteria in Solid Tumors), demonstrating stable disease with a mild reduction in lesion size, consistent with partial treatment response.

At the time of last follow-up, the patient had achieved a progression-free survival (PFS) of over 12 months, and overall survival (OS) continues to be monitored.

DISCUSSION

Distinguishing between malignant peritoneal mesotheliomas and epithelial ovarian carcinoma can be challenging due to the overlapping morphological features of these malignancies [11]. This case was no exception. Adding to the diagnostic complexity, MRI had identified an adnexal mass, and the CA-125 level was elevated at 1162. These findings initially painted the picture of a possible ovarian malignancy. The general histopathological and immunohistochemical findings were critical for accurately diagnosing malignant peritoneal mesothelioma. The biopsy findings in this case, which included epithelioid and papillary cell morphology with stromal invasion, which is usually present in both mesothelial and ovarian neoplasms, added to the diagnostic challenge. As seen in this case, the accuracy of diagnosis can be significantly improved using immunohistochemical marker panels. The panel explores the presence of markers commonly expressed in mesotheliomas (positive mesothelioma markers) and those typically absent in mesotheliomas but frequently found in epithelial ovarian carcinomas [8].

In this patient, a comprehensive panel of markers clarified the diagnosis. Cytokeratin 7 (CK7), a common epithelial marker often expressed in both epithelial ovarian tumors and mesotheliomas, was positive in this case. The positive findings of CK7 initially left the differential diagnosis open between the two possibilities. However, the presence of both calretinin and WT-1 indicated a strong likelihood of peritoneal mesothelioma. Although markers such as E-cadherin and GATA3 may have introduced some uncertainty to the diagnosis of mesothelioma, the presence of significant negatives, such as the absence of PAX8- a transcription factor involved in Müllerian system development, and Ber-EP4- an epithelial cell adhesion molecule, potentially ruled out the possibility of an ovarian carcinoma. The absence of CK20 and CDX2 helped rule out the possibility of the neoplasm originating from a gastrointestinal or urothelial

source. In addition to immunohistochemistry, genomic profiling identified a mutation in the BAP1 gene. This mutation has been shown in literature to be linked to a high proportion of peritoneal mesothelioma cases [12]. Further supporting this diagnosis.

The combination of immunohistochemical markers was essential for differentiating peritoneal mesothelioma from epithelial ovarian carcinoma in this case. The positive expression of CK7, WT1, and calretinin strongly supported the diagnosis of peritoneal mesothelioma, while the negative results for PAX8, Ber-EP4, CK20, and CDX2 ruled out other differential diagnoses [13].

CONCLUSION

The diagnosis of peritoneal mesothelioma is often challenging, as its clinic-pathological features may mimic other intrabdominal neoplasia, such as ovarian malignancies. Therefore, it is crucial to adopt the use of immunohistochemistry during the diagnostic process. Immunohistochemistry provides the opportunity to assess a host of markers, which, in combination, can rule out potential differential diagnoses and help in the accurate diagnosis of peritoneal mesothelioma. This case demonstrates the overlapping immunohistochemical profiles of malignant mesothelioma and epithelial ovarian carcinoma and underscores the importance of a comprehensive IHC panel in distinguishing between the two malignancies. Although there may be significant overlap in marker expression, careful interpretation of results can provide clarity. A combination of IHC with genomic profiling further enhances the chances of making an accurate diagnosis of peritoneal mesothelioma.

CONSENT FOR PUBLICATION

Written informed consent was obtained from the patient for the publication of this case report and any accompanying images.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

ACKNOWLEDGEMENTS

We thank the Department of Pathology, Radiology, and Medical Oncology for their contribution to the diagnostic process.

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