Rapid Progression of Malignant Peritoneal Mesothelioma Mimicking a Postoperative Complication in a Young Woman: A Case Report

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Patient: Female, 35-year-old
Final Diagnosis: Malignant peritoneal mesothelioma
Symptoms: Abdominal pain • fevers • weight loss • fatigue • myalgia
Clinical Procedure: Biopsy • exploratory laparotomy • salpingo-oophorectomy
Specialty: Obstetrics and Gynecology • Oncology

Objective: Unusual clinical course
Background: Malignant peritoneal mesothelioma is a rare disease with a poor prognosis that often presents with vague symptoms and inconclusive laboratory test results. Causes include industrial pollutants, primarily asbestos, and certain genetic mutations, such as BAP1. Due to the nonspecific symptoms, it is often incidentally diagnosed during or after other surgical procedures.

Case Report: A 35-year-old healthy woman underwent an uncomplicated laparoscopic left salpingo-oophorectomy for a symptomatic large ovarian mature cystic teratoma. She subsequently presented with late-onset postoperative fever, leukocytosis, and multiple intra-abdominal masses. Following an exploratory laparotomy, extensive infectious disease evaluation, and multiple biopsies requiring interdisciplinary collaboration, malignant peritoneal mesothelioma was diagnosed by positive histologic staining of an omental biopsy for D2-40 and CK5/6. This first specimen was positive for BAP1, with the second, a liver biopsy, testing negative for BAP1. The tumor cell testing was also notable for mutations in NF2, MLL2, and ARID1A, and the hereditary cancer genetic testing was overall unremarkable. Her disease progressed rapidly, and she died 6 months after her initial procedure.

Conclusions: This case of rapidly developing malignant peritoneal mesothelioma following surgical management of an ovarian mature teratoma highlights the complexity in diagnosing a rare disease that presents with nonspecific symptoms in an otherwise young and healthy woman. The rapid disease course was likely accelerated by expansive intraperitoneal spread and multiple somatic oncogenic mutations in BAP1, NF2, MLL2, and ARID1A. Gynecologists should keep a broad differential for postoperative complications, as occult malignancies can present with symptoms that mimic postoperative complications.

Keywords: Mesothelioma, Malignant • Teratoma, Ovarian • BAP1 Protein, Human • NF2 Protein, Human

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Introduction

Malignant peritoneal mesothelioma is a rare disease with a poor prognosis. The incidence in industrialized countries is between 0.2 and 2 cases per million in women, with a mean age of presentation between 47 to 63 years old [1,2]. Patients typically present with nonspecific symptoms, such as abdominal pain, distension, weight loss, nausea, vomiting, dyspnea, or chest pain [2]. The leading cause of malignant peritoneal mesothelioma is industrial pollutants, specifically asbestos, although only 50% of patients report prior known asbestos exposure [3]. Additionally, the time between asbestos exposure and disease presentation can be long; thus, malignant peritoneal mesothelioma is often found incidentally during other procedures or, as in this case, as a suspected postoperative complication [4].

This is a case of an otherwise healthy woman that began with an uncomplicated laparoscopic left salpingo-oophorectomy for a large mature cystic teratoma. Her postoperative course was complicated by a late postoperative fever that led to multiple lengthy hospital admissions with extensive workups, additional procedures, and a final diagnosis of malignant peritoneal mesothelioma, ultimately culminating with her death.

Case Report

A 35-year-old gravida 2 para 2 Hispanic woman with an unremarkable obstetric, medical, and surgical history presented to an urban gynecology clinic for management of a left adnexal mass, diagnosed 3 years prior, and new-onset abdominal pain. She had immigrated from Mexico in her mid-20s and had completed childbearing. The physical examination was notable for a large, mobile left adnexal mass with diffuse abdominal tenderness. Transvaginal ultrasound detailed a large suspected cystic teratoma, and she was scheduled for surgical management (Figure 1).

One month after the appointment, she was evaluated in the Emergency Department for severe abdominal pain with guarding, but no cervical motion tenderness, on a bimanual examination. Laboratory studies were remarkable for a white blood cell (WBC) count of 14.5 k/uL and absolute neutrophil count of 12.0 k/uL, CA 19-9 of 69 U/mL, and normal CA 125 of 20.0 U/mL and CEA of 0.6 ng/mL. Transvaginal ultrasound and abdominopelvic computed tomography (CT) scan again confirmed the previously described left adnexal cyst with no other abdominal masses (Figure 2).

Due to concern for ovarian torsion, she underwent an urgent diagnostic laparoscopy. Since the mass extended above the umbilicus, a supraumbilical Hassan entry was performed. Abdominal-pelvic survey confirmed a large, benign-appearing cyst arising from the left ovary, with no gross intraperitoneal lesions. Pelvic washings were obtained due to the size of the mass. For improved laparoscopic visualization, approximately 1 L of fluid was drained from the cyst via laparoscopic aspiration needle. An Endoloop was placed around the puncture site to avoid intraperitoneal spillage. The surgeons then performed a salpingo-oophorectomy, after shared decision making, given the patient’s completed family status. The specimen was removed in

Figure 1. Transvaginal ultrasound, with large suspected cystic teratoma measuring 19.9×13.3×14 cm with a volume of 1373 cm³.

Figure 2. Coronal computed tomography scan with large cystic teratoma measuring 10.1×13.2×15.9 cm and fat stranding along the superior right aspect of the dermoid at the level of the umbilicus. Normal appendix shown. Arrow points to pelvic mass.
an endoscopic bag, without intra-abdominal spillage, and the patient was discharged the same day. Pathological analysis confirmed a mature cystic teratoma and was negative for malignant tissue in the pelvic washings sample, fallopian tube, and ovary. She was evaluated in the clinic on postoperative days 5 and 15 for nausea with vomiting and “tugging” at her supraumbilical port site. During both visits, she had normal vital signs with a benign abdominal examination. Therefore, further workup was not recommended. On postoperative day 28, she presented to the Emergency Department with fever, abdominal pain, and myalgias. Initial vital signs were normal, but laboratory test results showed WBC count of 25 k/uL with absolute neutrophil count of 21 k/uL. Abdominopelvic CT scan showed two 5-cm anterior mid-abdominal peripherally enhancing fluid collections, suggestive of abscesses (Figure 3).

She was admitted to the hospital, and intravenous piperacillin/tazobactam was initiated. Overnight, she was febrile to 39 °C and had tachycardia with leukocytosis with a WBC count of 27 k/uL and a maximum lactate of 1.8 mmol/L. Interventional Radiology was consulted to drain the masses, but only 1 drain was successfully placed and had minimal fluid output. Antibiotics were broadened to ceftaroline and metronidazole. As she had no clinical improvement by day 3, the decision was made to proceed with surgery. She underwent a diagnostic laparoscopy via Palmer’s point entry with the benign gynecology team. Laparoscopy was remarkable for normal pelvic anatomy and a thick omental adhesion to the anterior abdominal wall circumferentially surrounding the umbilicus, with concern for bowel involvement (Figure 4). General Surgery was consulted, and the procedure was converted to an exploratory laparotomy, with removal of the suspected infected hematomas. Only a small area of the rind adhered to the transverse colon was left unresected. An intraperitoneal drain was placed, and cultures of the specimen later returned negative. A histopathological specimen was not sent by the surgical team due to gross appearance consistent with the suspected infectious hematoma and low suspicion for other etiology. By postoperative day 4, she had clinically improved with a WBC count of 12 k/uL and decreased drain output. She was discharged in stable condition.

Approximately 7 weeks after her initial surgery, she presented to an outside hospital with worsening abdominal pain and fever. She had leukocytosis, peaking at a WBC count of 31 k/uL, and an abdominopelvic CT scan showed multiple ring-enhancing lesions. She was started on ceftriaxone and metronidazole. The Infectious Disease and Oncology departments were consulted. The following tests returned negative: urinalysis, blood

![Figure 3](image1.png)  
**Figure 3.** Coronal computed tomography scan with bilobed midline anterior abdominal wall masses both measuring 5×4×4 cm. Arrow points to bilobed masses.

![Figure 4](image2.png)  
**Figure 4.** Diagnostic laparoscopy via Palmer’s point. (A) Normal pelvic anatomy with surgically absent left fallopian tube, as detailed by the arrow, and ovary and no gross intraperitoneal lesions. (B) Large omental adhesion, highlighted by the arrow, to the anterior abdominal wall containing transverse colon and suspected abscesses.
was extremely broad and included intraabdominal abscesses, pathologic evaluation. At this time, the differential diagnosis was narrowed to lymphoma, leukemia, lymphoma, disseminated tuberculosis, and an exaggerated inflammatory response in the postoperative period. Tumor markers such as AFP, CEA, and LDH were normal, with a mildly elevated CA 125 at 38u/mL. The initial pathology slides from the mature teratoma were reviewed by a specialized gynecologic pathologist, and were again found to be negative for malignant disease or thyroid tissue.

Histopathologic evaluation of the omental biopsy stained positive for CAM 5.2, D2-40, CK5/6, BAP1 (retained), Baf47 (retained), and p53 (mostly positive). The second biopsy from the liver 2 weeks later showed fragments of a poorly differentiated epithelioid malignant neoplasm, with extensive necrosis. The tumor cells had copious amorphophilic cytoplasm and plump atypical vesicular nuclei. In areas, there was a dis cohesive pseudovascular appearance, likely reflecting tumor friability in the setting of prominent necrosis. The tumor cells stained positive for pancytokeratin, D2-40, CK5/6, CAM 5.2, and were mostly positive for p53, and stained negative for BAP1, CD31, CD34, TFF1, ER, claudin-4, PAX8, SALL4, WT-1, GATA3, ER, ARG-1, CK7, CK20, CDX2, calretinin, mucin, CD68, SOX10, Melan A, and CD45. Due to its rarity, and to confirm the diagnosis of malignant peritoneal mesothelioma, the pathology was sent for consultation to one of the top academic centers in the United States.

She received the diagnosis of stage IV malignant peritoneal mesothelioma, epithelioid subtype, given the positive staining for D2-40 and CK5/6. She underwent chemotherapy treatment with intravenous cisplatin and pemetrexed. Biomarker testing showed a tumor mutational burden of 27 mutations with stable microsatellite status. The following mutations were reported: NF2, MLL2, ARID1A, PIK3CA, EP300, NFE2L2, and TERT. An expanded 8-gene hereditary cancer genetic testing returned with no clinically significant mutations, gross deletions, or duplications, including for the BAP1 gene. A variant of uncertain clinical significance was identified in ATM, c.8716G>A (p.V2906I). She denied prior known asbestos exposure.

Five months after the initial surgery, she was admitted to the primary hospital for management of a small bowel obstruction. She remained inpatient for a month before choosing full comfort care, after which she died in the presence of her family members.

**Discussion**

To the best of our knowledge, this is the first case of rapidly developing malignant peritoneal mesothelioma following malignant transformation of the mature teratoma, chemical peritonitis with granuloma formation, thyroid storm from previously undiagnosed struma ovarii, paraneoplastic syndrome from an undiagnosed malignancy, autoimmune reaction, leukemia, lymphoma, disseminated tuberculosis, and an exaggerated inflammatory response in the postoperative period.
surgical management of an ovarian mature teratoma. It is plausible that our patient’s initial abdominal pain was secondary to malignant peritoneal mesothelioma, as the ovarian dermoid had been stable in size for years, during which she had remained asymptomatic. Malignant peritoneal mesothelioma undergoes expansive rather than infiltrative intraperitoneal spread [5] and has been found to seed port or biopsy sites, where the peritoneum has been violated [6]. We suspect the first postoperative intra-abdominal masses adjacent to the supraumbilical port site were from malignant peritoneal mesothelioma seeding the trocar site and then proceeding to spread throughout the abdomen. As a result, the multiple procedures and biopsies during her extensive evaluation may have accelerated the disease course.

Malignant peritoneal mesothelioma is a rare condition, even more so than pleural mesothelioma, but risk factors include asbestos or other industrial mining pollutant exposure, which can account for up to 50% of cases [7]. More recent findings have identified a link between BAP1, a tumor suppressor located on chromosome 3p21.3, and familial cancer syndromes, including mesothelioma, melanoma, and clear-cell renal carcinoma, with many affected individuals having one or more malignancies during their lifetime [8]. As our patient’s neoplastic cells stained entirely negative for BAP1 in the second biopsy, this indicates a loss of function mutation. Since the hereditary cancer genetic testing was negative for BAP1, it can be presumed to be a de novo somatic mutation. For patients with a germline wild-type BAP1 mutation, mesothelioma tends to progress more rapidly than for those with germline BAP1-mutant mesothelioma. Additionally, the NF2, MLL2, and ARID1A mutations likely heightened her tumorigenesis and accelerated the disease process, as mutations in NF2 and MLL2, tumor suppressors, increase genomic instability [9]. Lastly, the ARID1A mutation, which can be found in 20% of cancers, likely further promoted oncogenesis [10]. Unfortunately, our patient died prior to additional genetic testing.

This case of malignant peritoneal mesothelioma highlights the complexity in diagnosing a rare disease that presents with nonspecific symptoms. It is unique in that it was discovered during workup of a suspected postoperative complication a young, otherwise healthy woman following a minimally invasive gynecologic surgery for a benign ovarian cyst. Additionally, our patient’s rapid disease course was likely accelerated by the expansive intraperitoneal spread and seeding of trocar sites from her various procedures along with the multiple somatic oncogenic mutations in BAP1, NF2, MLL2, and ARID1A, as she had no significant germline mutations.

Conclusions

Gynecologic surgeons should keep a broad differential for postoperative complications in otherwise young and healthy-appearing women, as occult malignancies can present with a variety of nonspecific symptoms.

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Declaration of Figures’ Authenticity

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References: