

Malignant peritoneal mesothelioma without asbestos exposure: An ovarian cancer imitator



Kassondra S. Grzankowski^{a,*}, Rachel M. Brightwell^a, John M. Kasznica^b, Kunle O. Odusi^a

^a Department of Gynecologic Oncology, Roswell Park Cancer Institute, Buffalo, NY, USA

^b Department of Pathology, Roswell Park Cancer Institute, Buffalo, NY, USA

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Introduction

Malignant peritoneal mesothelioma (MPM) is a rare, aggressive tumor. 15% of mesotheliomas arise from the peritoneum as opposed to the pleura. MPM's prevalence in the United States is 1–2/1,000,000. With an estimated 400 new cases, MPM accounts for 0.024% of all new cancers diagnosed annually (Howlader et al., 1975–2011; Bridda et al., 2007). MPM is rapidly fatal with a median survival of 6–12 months and mean symptom-to-survival time of 345 days. Untreated, survival is approximately six months. The principal risk factor for acquiring the disease, history of asbestos exposure is evident in only 50% of patients with peritoneal mesothelioma (Bridda et al., 2007).

Case report

We present a 67 year old postmenopausal female with worsening abdominal bloating, distension and early satiety for one month.

The patient's history included stage I (pT1N0) infiltrating ductal carcinoma of the left breast treated with lumpectomy in 1997 followed by adjuvant chemoradiation, iron deficiency anemia, depression, and hiatal hernia. She is a nonsmoking, retired teacher of Ashkenazi Jewish decent with negative BRCA testing, and no known asbestos exposure. Family history was significant for breast cancer in a paternal aunt.

Worsening pain and shortness of breath prompted computed tomography (CT) revealing ascites and omental caking. She underwent paracentesis with removal of 1000 mL of ascites but needed an additional paracentesis two weeks later removing an additional 4100 mL. She was referred to a gynecologic oncologist.

Physical examination

The patient's condition was fair and she appeared to be in no distress. Other than tachycardia, vital signs were normal. Abdominal exam revealed distension and tenderness on palpation, but no mass. Pelvic exam revealed normal female genitalia with no masses noted on bimanual rectovaginal exam.

Laboratory data

Her CA-125 was 188 U/mL; CA 27–29 was 91 U/mL; and CEA was 1.1 ng/mL.

Histological findings

Histocytological assessment of collected ascites was read as “atypical epithelioid cells mixed with mesothelial cells, cannot exclude adenocarcinoma or mesothelioma”, although no purely malignant cells were identified. Singly dispersed cells with vacuolated cytoplasm with targetoid appearance suspicious for breast carcinoma were identified. Immunohistochemical (IHC) reactivity was not seen for ER or MOC-31, markers for breast cancer distinguishing between mesothelioma and adenocarcinoma. These cells were positive for calretinin found in both benign mesothelial cells and mesothelioma (Fig. 1A–B).

Treatment and follow-up

The findings of ascites, omental caking, and elevated CA-125 in conjunction with her symptomatology that included pain, weight loss, bloating, nausea, poor appetite, and weakness, suggested primary peritoneal cancer versus recurrent metastatic breast cancer thus the patient underwent exploratory laparotomy. Omental tumor frozen section assessment was reported as serous adenocarcinoma, consistent with primary peritoneal origin. At this point the decision was made to perform debulking surgery with total abdominal hysterectomy, bilateral salpingo-oophorectomy, infracolic omentectomy, and resection of

* Corresponding author at: Roswell Park Cancer Institute, Department of Gynecologic Oncology, Elm and Carlton Streets, Buffalo, NY 14263, USA. Fax: +1 716 845 7608.

E-mail address: Kassondra.Grzankowski@roswellpark.org (K.S. Grzankowski).

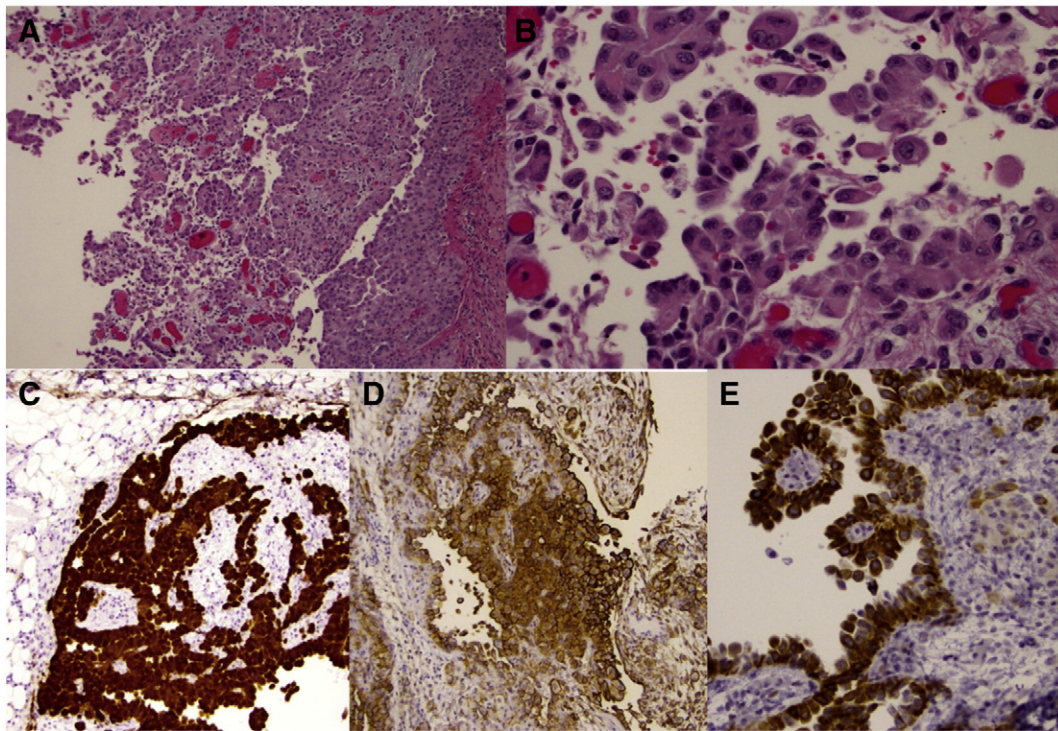


Fig. 1. A) Mid-power view showing the mainly papillary architecture of this primary peritoneal mesothelioma. Note the proliferation of malignant epithelioid type mesothelial cells. Hematoxylin–eosin (H&E) stain. Original magnification 100 \times . B) Higher power view of the tumor showing the classic malignant mesothelial cell features. H&E stain. Original magnification 400 \times . Supporting the diagnosis of malignant mesothelioma: C) strong calretinin positivity. Original magnification 100 \times . D) Strong D2–40 positivity. Original magnification 100 \times . E) Strong CK5/6 positivity. Original magnification 200 \times .

gastrocolic ligament tumor. 95% of tumor was removed; however, there were 1 cm nodules and plaques in the small and large bowel mesentery, posterior surface of the stomach, and gastro-hepatic ligament towards the porta hepatis that were left.

Final pathology revealed MPM in the omentum and uterus. There was surface involvement of bilateral ovaries and tumor involving the para-tubal soft tissues. IHC was positive for WT-1, calretinin, D2-40, and cytokeratin (CK) 5/6, and negative for CK7, ER, mammaglobin, PAX-8, and CK20. Although IHC can assist in identifying mesothelial cells, none are specific for mesothelioma. CK5/6, calretinin and WT-1 are used collectively for mesothelioma (Fig. 1C–E).

The patient was referred to thoracic medical oncology who initiated chemotherapy with cisplatin 60 mg/m² and pemetrexed 500 mg/m² every 21 days for 4 cycles. CT after completion of treatment showed mesenteric stranding, but overall improvement of disease. She has been continued on maintenance pemetrexed every 3 weeks. The most recent abdominopelvic CT scan a year from diagnosis revealed no interval change with stable mesenteric stranding and nodularity.

Discussion

The histological diagnosis of MPM can often be challenging. For this patient ascites was examined for MOC-31 and ER to try to differentiate mesothelioma and adenocarcinoma. MOC-31 has good sensitivity and specificity for generic adenocarcinoma of 92% and 87%, respectively. MOC-31 is seen in approximately 7% of malignant mesotheliomas. ER is positive in most breast cancers; ~70% in the well-moderately differentiated types, and ~20% in poorly differentiated types. ER positivity is low in mesotheliomas at around 10%. ER is included in IHC panels to distinguish peritoneal serous carcinoma from malignant peritoneal mesothelioma, where ER positivity favors serous cancer (Ordóñez, 2005, 2006). Although frozen section can accurately diagnose malignancy in

the majority of cases, they are often called serous in the setting of MPM. This is especially true in the low grade papillary subtypes of mesothelioma as this pathology often tops the differential in women of post-reproductive age with the clinical findings of ascites, peritoneal involvement, and omental caking. They can be distinguished readily on permanent section and with the addition of the IHC as described in the figure caption. This tumor on permanent fixation showed predominantly a surface/encasing type growth with papillae. On higher power the cells in this tumor were globally blander as compared to a typical serous carcinoma and had features of classic mesothelial cells. The IHC panel with positive CK5/6, calretinin, and D2-40 supported the diagnosis of MPM.

There is no consensus on the optimal treatment for MPM, and most available clinical data is derived from retrospective studies and case reports. Treatment entails a combination of palliative cytoreductive surgery, chemotherapy, and rarely, radiation (Vogelzang et al., 2003). Over the last decade cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (HIPEC) among centers with expertise in this form of therapy, resulted in median survival approaching five years for appropriately selected patients and is considered a first line recommendation (Haslinger et al., 2013). A multi-institutional registry study evaluated cytoreductive surgery combined with HIPEC for diffuse, malignant, peritoneal mesothelioma. Among 401 patients enrolled, 187 (46%) had complete or near-complete cytoreduction, and 372 (92%) received HIPEC. Of the HIPEC patients, 311 (83%) received cisplatin and doxorubicin. The median follow-up period was 33 months. The overall median survival was 53 months (1–235 months), and 3- and 5-year survival rates were 60% and 47%, respectively. Four prognostic factors were independently and significantly associated with improved survival in a multivariate analysis: epithelial subtype, absence of lymph node metastasis, completeness of cytoreduction, and use of HIPEC (Yan et al., 2009).

The patient in this case report had residual tumor up to 1 cm, making HIPEC a poor choice for treatment, as the upper limit for this modality is 2.5 mm. Therefore systemic chemotherapy was indicated. Most clinical trials for chemotherapy in mesothelioma have excluded MPM, and data has been extrapolated from patients with pleural mesothelioma. The addition of pemetrexed to cisplatin, the single most active agent against malignant mesothelioma, was associated with significantly improved survival with greater antitumor activity compared with cisplatin alone. Median survival in the pemetrexed/cisplatin arm was 12.1 versus 9.3 months in the control arm. Median time to progression was significantly longer in the pemetrexed/cisplatin arm: 5.7 versus 3.9 months. Response rates were 41.3% in the pemetrexed/cisplatin arm versus 16.7% in the control arm (Vogelzang et al., 2003). One analysis on MPM, specifically pemetrexed with or without cisplatin had a favorable safety profile, and a 25% response rate in chemotherapy-naïve patients indicated activity in this patient population (Janne et al., 2005). Ongoing trials are investigating the efficacy of maintenance pemetrexed in MPM. Prolonged progression free survival has been seen in pleural mesothelioma with this treatment.

Conflict of interest statement

The authors declare no conflicts.

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

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