Malignant Biphasic Peritoneal Mesothelioma in a Reproductive Age Woman

Sanaz Ghafouri, MD and Parvin Peddi, MD

Introduction

Malignant mesothelioma is a rare and aggressive disease that affects the serosal membranes of the pleura, peritoneum, pericardium or tunica vaginalis testis. The peritoneum is the second most common site of origin after the pleura, and therefore, much of the data for malignant peritoneal mesothelioma (MPM) has been extrapolated from what is known for pleural mesothelioma. The median age at diagnosis is approximately 68 years. It is often an incidental finding on imaging, and vague presenting symptoms, such as abdominal distention, pain, nausea and weight loss, that makes this disease a diagnostic challenge. Therapeutic options include either cytoreductive surgery (CRS) with hyperthermic intraperitoneal chemotherapy (HIPEC) or systemic chemotherapy, depending on patient and disease-specific factors. While MPM rarely becomes metastatic, it carries a poor prognosis which is correlated to disease extensiveness within the peritoneal cavity. Additionally, “biphasic” and sarcomatoid subtype are associated with higher morbidity and mortality.

We report a young woman who was found to have an adnexal mass on imaging after presentation with amenorrhea, which was later biopsy proven to be biphasic MPM. Though she was diagnosed with a diffuse disease with the histologic subtype associated with worse prognosis, she responded well to systemic chemotherapy alone several years from diagnosis.

A 33-year-old female with a complex congenital cardiac history, including heterotaxy, unbalanced AV canal, univentricular heart, pulmonary atresia, and bilateral superior vena cava, presented to her gynecologist for evaluation of amenorrhea. She had a pelvic ultrasound at an outside hospital that showed a possible uterine mass, along with CA-125 elevated at 285 U/ml. The CEA, CA 19-9, AFP, hCG and LDH were within normal limits. CT of the chest, abdomen and pelvis showed a normal uterus and ovaries, without evidence of the reported mass, but significant for a nutmeg liver and moderate ascites. She underwent paracentesis with cytology that was negative for malignancy. The ascites was suspected to be secondary to congestive hepatopathy due to her cardiac condition, which was eventually confirmed by liver biopsy.

Six months later, repeat pelvic ultrasound showed normal uterus, and no evidence for the previously seen uterine mass. However, the right ovary contained a 2 cm partially exophytic and complex cystic structure, suspected to be a functional cyst with internal hemorrhage. CT of the chest, abdomen and pelvis was yet again unremarkable for malignancy, but showed the previously noted ascites. However, the CA-125 continued to rise to 315 U/ml, and then to 548 U/ml six months later. Along with the rising CA-125, she developed night sweats, heavy vaginal bleeding lasting up to 3 weeks at a time, dysmenorrhea and weight gain.

Given her persistent ascites and rising CA-125, she underwent exploratory laparoscopy with peritoneal and ovarian biopsies showing biphasic mesothelioma, 40% sarcomatoid type with lymphohistiocytoid features. Endometrial curettage and ascites fluid were negative for malignancy.

She completed six cycles of Cisplatin and Pemetrexed, with repeat exploratory laparoscopy and biopsies that were negative for residual disease. Initially, she was planned for cytoreductive surgery with hyperthermic intraperitoneal chemotherapy (HIPEC) during the exploratory laparoscopy. However, she was high risk given her underlying cardiac and liver disease, and anticoagulation. As there was no evidence of gross disease during the procedure, HIPEC was deferred in favor of observation after systemic chemotherapy. She has had repeat PET-CT every six months which have not shown evidence for recurrence. She continues to have outpatient therapeutic paracentesis every two weeks. She has been doing impressively well four years from diagnosis, and her CA-125 remains stable. Unfortunately, she was denied cardiac transplant due to the malignancy. From an oncologic standpoint has no contraindications to transplant given her remarkable improvement and may eventually, be reconsidered.

Discussion

Malignant mesothelioma is rare, with 3,330 new cases diagnosed annually, with about 400 cases (10-15%) of peritoneal origin. Up to 50% of individuals with MPM have no known history of exposure to asbestos, and this percentage may be even greater among children and women. Other predisposing risk factors for MPM include SMV virus 40, radiation exposure, genetics, heavy metals, chronic inflammation and non-asbestos fibers.

According to the National Center for Health Statistics, the median age is 74 years and 68 years for pleural and peritoneal
mesotheliomas, respectively. The SEER database shows only about 2% of US mesothelioma cases are diagnosed in patients younger than 40, like the patient in this case. To our knowledge, Anish et al were the first to comprehensively evaluate and distinguish characteristics of MPM in this younger age subgroup. They concluded that within this young cohort, women were more commonly diagnosed, peritoneal mesotheliomas were comparable in prevalence to pleural mesothelioma, and those diagnosed were more likely to be treated surgically. Additionally, though biphasic and sarcomatoid MPM have worse overall prognosis overall, the young cohort had significantly improved overall survival compared to the older patients, regardless of histologic subtypes. Favorable prognosis factors included young age, female gender, having primary peritoneal mesotheliomas, and undergoing surgery and radiation. Younger patients with MPM were also less likely to have had asbestos exposure, and more likely to have been predisposed based on genetics or exposure to non-asbestos fibers.

While rare to find MPM in a young person, the diagnosis remains challenging in all age groups. The symptoms are relatively nonspecific, including abdominal distention, abdominal pain, nausea, weight loss and malaise. CT of the abdomen, is usually the first diagnostic test and cytology of ascitic fluid is of limited value, and oftentimes inconclusive. The diagnosis is established by biopsy, which establishes the subtypes: either epithelioid, which is the more common, sarcomatoid, or biphasic tumor, a combination of epithelioid and sarcomatoid. One study showed overall survival was 55 months for epithelioid subtype, compared to 13 months for the sarcomatoid and biphasic subtypes.

Tumor markers have not been helpful for diagnosis of peritoneal mesothelioma, but CA-125, AFP and CEA can sometimes be elevated. Xu et al, reported serum CA-125 with clinical significance in MPM, with a baseline value less than 280 U/mL associated with more favorable prognosis. IFCA-125 levels significantly decreased after patients received systemic chemotherapy, it correlated with disease control. They concluded that the serum CA-125 could be prognostic for overall survival for MPM patients receiving systemic chemotherapy, like our patient in the case.

Therapeutic options for MPM include CRS and HIPEC versus systemic chemotherapy. The decision is based on patient and disease specific factors. CRS and HIPEC are promising for those without extraperitoneal disease, who have good performance status, and who are predicted to have complete response to the treatment. However, those who are not candidates, can benefit from systemic chemotherapy with Pemetrexed and Cisplatin combination, like our patient.

MPM remains a diagnostic challenge, and oftentimes carries a poor prognosis given delay in identifying this rare disease. However, while even more rare in younger populations, it is important for clinicians to recognize MPM as a potential cause for non-specific symptoms such as abdominal distention, weight loss or malaise, and to continue evaluating these inci-

dental findings, so patients can be treated in a timely manner and hopefully respond as well as the patient in this report.

REFERENCES

10. Yan TD, Haveric N, Carmignani CP, Chang D, Sugarbaker PH. Abdominal computed tomography scans in the selection of patients with malignant peritoneal mesothelioma for comprehensive treatment with cytoreductive surgery and perioperative intraperitoneal...


Submitted March 18, 2019