A Rare Presentation of a Clear Cell Variant of Peritoneal Mesothelioma

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ABSTRACT

Primary malignant peritoneal mesothelioma with clear cell subtype is a rare malignancy with few previously reported cases. We present a 63-year-old female who presented with abdominal distention and was diagnosed with clear cell mesothelioma of the peritoneum with an isolated metastasis to the liver. The patient underwent surgical resection of a greater than 50 cm mass with en-bloc partial liver and gastric resection with an uneventful post-operative course. There are established prognostic and treatment recommendations for peritoneal mesothelioma based on histological subtype and patient-specific factors, although they do not explicitly incorporate clear cell subtype. This case report describes the presentation, treatment and early outcome of a rare form of peritoneal mesothelioma.

INTRODUCTION

Primary malignant peritoneal mesothelioma is a rare malignancy. Clear cell subtype of the epithelioid variant is even rarer, with very few cases reported in the literature. In this case we present a 63 year-old female who presented with abdominal distention, who was found to have primary malignant peritoneal mesothelioma of clear cell subtype with hepatic metastases who ultimately underwent surgical resection with plan for adjuvant chemotherapy. Due to the lack of a well-defined presentation pattern or therapeutic strategy for this specific subtype, it is important to report this case and its outcomes.

CLINICAL SUMMARY

The patient is a 63 year-old female who presented with a 6-month history of gradually increasing abdominal girth, discomfort, and early satiety. She underwent esophagogastroduodenoscopy and colonoscopy, which were found to be normal. On abdominal computed tomography she was found to have an intra-abdominal mass 26 cm in size that appeared to be arising from the epigastrium and a 5cm centrally located hepatic mass consistent with solitary hepatic metastasis (Figure 1). The abdominal mass appeared to be encapsulated and there was no evidence of diffuse disease in the peritoneal cavity. The patient underwent a percutaneous biopsy of the mass with histopathology diagnosing as clear cell mesothelioma. On immunohistochemical staining, the tumor was positive for AE1/AE3 and CK7 suggesting an epithelial neoplasm and positive for calretinin, CK/CK6, and WT-1. It was negative for colorectal, GIST, hepatocellular, mullerian and renal tumor markers. The pathology was reviewed at two centers with concordant impressions. Given the histology, the patient was scheduled for a laparotomy and resection of her abdominal mass.

Figure 1. Axial (a) and coronal (b) abdominal computed tomography illustrating an intra-abdominal mass approximately 26cm in size that appeared to be arising from the epigastrium and a 5cm centrally located hepatic mass consistent with solitary hepatic metastasis.
On admission, she was noted to have leukocytosis to 16,100/μl and found to have a urinary tract infection, which was treated with a regimen of levofloxacin. She was anemic with a hemoglobin of 7.3g/dl, a platelet count of 830,000/ μl, a prothrombin time of 18.7 seconds, an albumin of 3.1g/dl, and prealbumin of 7.2mg/dl. On hospital day two, the patient underwent surgical resection. During the procedure, the mass was found to be greater than 50 cm in diameter, filling the entire abdomen and appeared to be arising from the greater omentum and distal stomach. The mass was densely adherent to and infiltrating the capsule of the left lateral segment of the liver and adherent to but not infiltrating the transverse colon (Figure 2). A distal gastrectomy and partial hepatectomy were performed en bloc with the mass and a Roux-en-Y gastrojejunostomy was performed. The liver lesion was left in situ given its central location and there was no evidence of any other peritoneal dissemination.

The patient required one unit of packed red blood cells with an adequate response and otherwise had an uncomplicated post-operative course with normalization of her leukocytosis. She was discharged on post-operative day seven. Pathology of the resected specimens confirmed clear cell malignant mesothelioma with negative surgical margins. Upon recovery, the liver metastasis will be restaged and treated with systemic or regional therapy.

DISCUSSION

Malignant mesothelioma is a rare malignancy of the serosal membranes of the pleura, peritoneum, pericardium, or tunica vaginalis testes. There are only 3300 cases of mesothelioma diagnosed in the United States every year, with only 10 to 15 percent peritoneal in etiology.4 Tumors derived from the serosal membranes often grow in a variety of histologic patterns. According to their light microscopic appearance, mesotheliomas have been subdivided into epithelioid, sarcomatoid, mixed epithelioid and sarcomatoid (biphasic), and desmoplastic subtypes. The most frequent histologic type of malignant mesothelioma is epithelioid. While epithelioid mesotheliomas usually have a tubulopapillary, adenomatoid, or solid pattern, on rare occasions they may also present with other histologic patterns including decidual, pleomorphic, small cell, signet-ring, as well as clear cell which is characterized by cells with cytoplasmic clearing usually caused by the accumulation of large amounts of intracytoplasmic glycogen.5,7

Predominately clear cell mesothelioma is an especially rare finding with fewer than 30 cases reported in the literature, and even rarer to present specifically in the peritoneum, with only one previous case reported in the peritoneum of a female patient.1-3,5-7 While the tumor can occur in children and young adults, it is usually found in older adults. Males and females are equally affected, however males are at a higher risk due to increased occupational exposure.4 While the etiology of malignant clear cell mesothelioma is unknown, it has been associated with asbestos exposure, radiation treatment, and mutations in the BAP1 gene.8 The symptoms can often be unspecific and depend on the size and location of the tumor. Small sized tumors may be asymptomatic during the initial stages of tumor growth while large-sized tumors can present with pain, obstructive symptoms, fatigue, and weight loss. Our patient presented with relatively mild symptoms that appeared to be caused by compression rather than infiltrative effects and she continued to maintain an excellent performance scale with an ECOG score of 1 despite the size of the mass in her abdomen.

In order to diagnose clear cell mesothelioma in our patient, an initial diagnosis was made after a complete evaluation of the patient’s history and physical along with an abdominal CT scan. While imaging tools such as CT, MRI, and PET scan may reveal the presence of a tumor, a tissue biopsy is necessary to make a definitive diagnosis. The differential diagnosis for malignant mesothelioma depends on the predominant histologic category. Most tumors are a mixture of more than one cell type; therefore, due to the rarity of clear cell mesothelioma this diagnosis can often be missed. While immunohistochemical staining plays an important role
in the workup of malignant mesothelioma, IHC varies depending on the histological type of mesothelioma, the location of the tumor, and the type of tumor being considered in the differential diagnosis. These variants can often be confused with a variety of other neoplastic conditions with a similar clear cell morphology. In our case this patient’s diagnosis was confirmed by immunohistochemical studies which demonstrated reactivity for calretinin, keratin 5/6, and WT1, an important pattern that is characteristic of mesothelioma. Calretinin is demonstrated in nearly all epithelioid mesotheliomas, keratin 5/6 is expressed in 75%-100% of mesotheliomas, and approximately 70%-95% of mesotheliomas show nuclear positivity for WT1. In addition, we were careful to rule out other causes of clear cell tumors. The diagnosis of epithelioid mesothelioma with clear cell morphology can often be difficult as it must be differentiated from clear cell renal cell carcinomas, clear cell carcinomas of the lung, clear cell melanoma, and other clear cell tumors that can metastasize to the pleura or peritoneum. Therefore, immunohistochemical panels should contain both positive and negative markers for mesothelial differentiation and for neoplasms considered in the differential diagnosis.9

Clear cell mesothelioma is a highly aggressive cancer that requires a multidisciplinary approach. The prognosis for malignant peritoneal mesothelioma is relatively poor due to organ dysfunction, local invasion and metastasis, and the high rate of recurrence. Stage and histology are the strongest prognostic factors among patients with mesothelioma, with sarcomatoid and biphasic histologic subtypes having worse outcomes compared with epithelioid mesothelioma. In addition to size, stage, and grade of the tumor, prognosis generally depends on a combination of factors including age, overall health of the patient, cell growth rate, and response to treatment.10

The European Organization for Research and Treatment of Cancer (EORTC) has developed prognostic scoring systems for peritoneal mesothelioma. They reviewed data from 204 adults with malignant peritoneal mesothelioma and when five factors were taken into consideration (poor performance status, high white blood cell count, male gender, sarcomatous subtype, and the certainty of the diagnosis), a low risk group with a prognostic score of 0-2 poor prognostic factors and a high risk group with >3 prognostic factors were found to have a one-year survival rates of 40 and 12 percent, respectively.11 Median survival from the date of study entry was 8.4 months. Similarly, the Cancer and Leukemia Group B (CALGB) evaluated 337 patients with malignant mesothelioma and found that pleural involvement, increased serum LDH, poor performance status, chest pain, increased platelet count, non-epithelial histology, and age older than 75 years predicted poor survival. These factors were differentiated into six prognostic subgroups with median survival times ranging from 1.4 to 13.9 months with a median survival overall of seven months.12 Using these scoring systems our patient fell into the low risk subgroup with a 40% survival rate of one year and a mean survival rate of 9 months. Though our patient was older with a high-grade, bulky tumor, due to her previous good health and the resectability of her tumor given the encapsulated nature of the tumor, we determined that she was a good candidate for surgery. We hope that this case demonstrates the importance of recognizing clear cell variant mesothelioma early and understanding predictive prognosis given individual patient characteristics. Through early detection, we can avoid complications and help increase positive outcomes.

REFERENCES