

Peritoneal Mesothelioma Presenting As Acute Abdominal Pain Secondary to Bowel Perforation

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Abstract

Peritoneal mesothelioma presents with nonspecific signs and symptoms usually in its terminal stage. The most common presentation is abdominal pain and ascites. Rarely, it may present as an acute abdomen with small bowel perforation. We present a rare case of a 67-year-old male with diffuse peritoneal mesothelioma and jejunal perforation.

Keywords: Peritoneal mesothelioma; Bowel perforation

Introduction

Peritoneal mesothelioma is a rare malignancy with a grim prognosis due to its insidious onset. It arises from mesothelial cells on serosal surfaces that line the pleural cavity, peritoneal cavity, pericardium, and tunica vaginalis. Numerous studies exist describing pleural mesotheliomas, while peritoneal mesotheliomas are a rarer occurrence [1-3].

Historically, malignant mesothelioma was solely a diagnosis of exclusion prior to 1960. As the use of immunohistochemistry and electron microscopy advanced, pathologic diagnostic criteria greatly improved [4,5].

Mesothelioma of peritoneal origin only accounts for about 10% to 15% of all mesothelioma cases [1]. The most common type is pleural mesothelioma, which has a strong association with asbestos exposure, chronic pleuritis, simian virus, and radiotherapy [1,2]. Peritoneal mesothelioma, on the other hand, is less associated with asbestos and exposure has only been documented in about 50% of all cases. Furthermore, peritoneal mesotheliomas usually present in the fifth decade versus the sixth decade for pleural mesotheliomas [1,2].

Peritoneal mesotheliomas usually present clinically with a diffuse growth pattern and metastasize late in the disease process, especially to the pleural cavity [6]. Unfortunately, most patients present in a later stage of their disease due to the nonspecific nature of signs and symptoms associated with peritoneal mesothelioma [1,6]. Thus, late presenting signs and symptoms make it clinically difficult for the early detection and treatment of peritoneal mesothelioma [6].

Case Presentation

A 67-year-old male presented to our institution with an acute onset of severe abdominal pain. The patient's wife reported that she was rubbing and massaging his abdomen in efforts to relieve the pain before he "passed out", and she called an ambulance. At the hospital, an initial physical exam was negative for guarding, but did show severe abdominal pain on palpation. Initial vital signs were body temperature of 99 Fahrenheit, respiratory rate of 16 breaths/min, heart rate of 102, and Blood pressure of 120/83. Initial pertinent laboratory findings in the emergency room were as follows: WBC 13.5×10^3 (4.8-10.8), RBC 2.05×10^6 (4.7-6.1), Hgb 5.2 g/dL (14-18), PT 16.1 s (9.5-11.5), INR 1.46 s (0.80-1.20), glucose 157 mg/dL (70-110), albumin 2.6 g/dL (3.5-5), total protein 5.4 g/dL (6-8), and calcium level of 7.5 mg/dL (8.5-10.6).

The emergency abdominal CT scan showed a 7.7 cm \times 6.8 cm \times 7.9 cm mass in the right upper quadrant, appearing to arise from a loop of

small bowel and exerting a mass effect on the duodenum. A similar round mass was seen in the right lower quadrant measuring 3.7 cm \times 4.0 cm \times 4.2 cm, in addition to a section of small bowel in the left and mid abdomen with circumferential thickening, inflammation, and signs of a small bowel perforation. At this point the patient was taken to the operating room for an emergency laparotomy. During surgery, a portion of the jejunum was submitted to pathology for gross evaluation and a frozen section diagnosis. The initial frozen section diagnosis was reported as "poorly differentiated malignant neoplasm." The tumor was resected, along with involved mesentery and lymph nodes, and sent to the pathology laboratory for final workup.

Post-surgery, a detailed history was obtained. The patient reported weight loss over the last two months prior to admission, with no fever, chills, or night sweats. He admitted to smoking 1.5 packs per day for 40 years. He denied any history of asbestos exposure. His previous occupations included rice farming in Taishan, China, adjacent to a coal-fired power station, and exposure to various pesticides but was unable to recall specific names.

Clinical course was complicated with cancer-related cachexia, diarrhea, melena, anemia, and venous thrombosis of both upper extremities. The patient expired 2 months post admission.

Pathology

The specimen consisted of a large loop of small bowel with serosal tumor masses (Figure 1). The small bowel was completely opened and showed numerous hemorrhagic tumor nodules on the mucosal surface (Figure 2) and part of the mesentery. On sectioning, the tumor nodules were found to be transmural.

Hematoxylin and Eosin (H&E) sections showed large, pleomorphic tumor cells on the bowel serosa, invading through the muscularis propria, and into lymphatic spaces of the serosal surface (Figures 3

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and 4). Within the mucosa the tumor cells were identified invading the lamina propria and lymphatic spaces (Figure 5). High power microscopy showed individual cells with high nuclear to cytoplasmic ratios, irregular nuclear borders, mitotic figures, and tumor cells showing one to multiple prominent nucleoli (Figure 6).

Immunohistochemical studies showed that the malignant cells were positive for pan-Cytokeratin and Mesothelin (Figures 7 and 8).



Figure 1: Loops of small bowel showing hemorrhagic tumor nodules on the serosal surface.



Figure 2: Small bowel mucosa with multiple hemorrhagic tumor nodules.

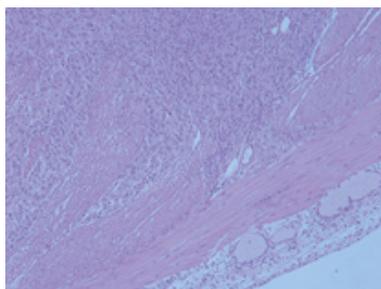


Figure 3: H&E section showing tumor cells invading muscularis propria (10x).

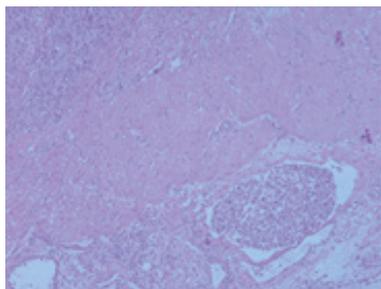


Figure 4: Tumor cells invading lymphatic spaces (10x).

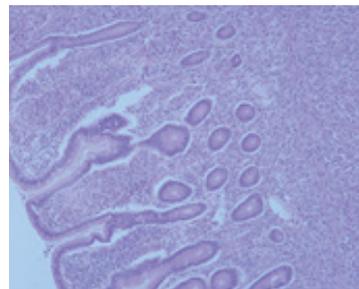


Figure 5: Tumor cells invading lamina propria and lymphatic spaces (10X).

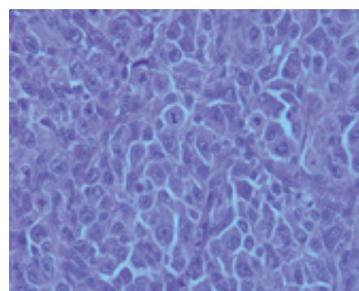


Figure 6: Pleomorphic tumor cells showing mitotic figures and nucleoli (40x).

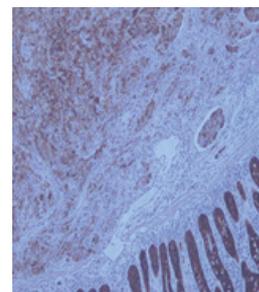


Figure 7: Keratin stain highlighting tumor cells and normal epithelium (10x).

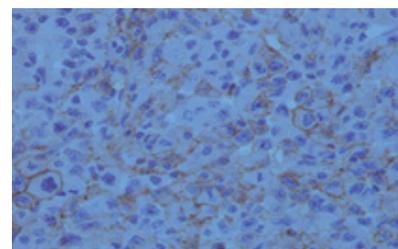


Figure 8: Tumor cells showing positive membrane expression of mesothelin (40x).

These positive tumor markers along with a number of other positive and negative markers confirmed the diagnosis of a diffuse malignant mesothelioma, epithelioid type.

Discussion

To the best of our knowledge this is one of a few case reports of a malignant peritoneal mesothelioma presenting with a small bowel perforation [1-3].

Patients with this type of malignancy usually survive an average

of 12 months from time of diagnosis; and commonly present with nonspecific abdominal pain and ascites. In contrast to pleural mesothelioma, a clinical history of asbestos exposure is only reported in 50% of the cases [1,2].

Histologically, peritoneal mesotheliomas can exhibit different histological patterns [4,5]. The most common is an epithelial pattern. However, a sarcomatous and biphasic pattern may also occur. Given the undifferentiated patterns of mesotheliomas, a tissue biopsy with immunohistochemical (IHC) stains remains the gold standard for definitive diagnosis [4,5].

Embryologically, mesothelium is composed of mesothelial cells that develop from mesoderm [7]. Mesothelial cells were initially believed to be a slippery layer that prevented adhesion between organs, however, recent findings indicate that mesothelial cells play a much more complex role [7]. Different studies have shown that they can modulate the inflammatory response by playing a role in leukocyte migration and synthesizing pro-inflammatory cytokines, growth factors, glycosaminoglycans, and other proteins [7]. All these factors, including lubricants, not only protect from abrasions, but may also play a role in tissue repair, response to infection, and possibly tumor dissemination [7].

Mesothelial cells have cell to cell complexes that allow for transport of molecules between cells. These include tight junctions, adherens junctions, gap junctions, desmosomes, cadherins, zonula occludens, and stomata [7]. It was proposed that stomata provide a direct link between pleural and peritoneal cavities, which explains how inhaled asbestos can enter the peritoneal cavity and cause asbestos-induced fibrosis in peritoneal mesothelioma.

Mesotheliomas may also present with paraneoplastic syndrome [1,6]. This includes secretion of Anti Diuretic Hormone (ADH), growth hormone, and corticotropic hormones. It can also predispose patients to thrombocytosis and increased fibrin degradation products, resulting in venous thrombosis, which occurred twice in our patient [1,2,6].

Conclusion

Treatment is difficult because many patients present at an advanced stage [6]. Median survival is less than a year in patients who receive different modes of treatment and less than 6 months in those untreated. Bowel perforation occurs late in the disease course and it is generally a result of increased tumor burden [1-3]. CT is the best initial diagnostic study, but definitive diagnosis should be made from

a tissue biopsy followed by IHC studies [4,5]. Numerous national and international interest groups have issued guidelines for the diagnosis of mesothelioma, with IHC becoming the gold standard for definite diagnosis [4,5].

While current treatment has prolonged survival, the prognosis for peritoneal mesothelioma is still poor. Because it is a rare malignancy, there is currently not enough evidence from scientific studies to support one treatment over another.

A generally accepted first line treatment is cytoreductive surgery (CRS) with hyperthermic intraperitoneal chemotherapy (HIPEC) [6]. HIPEC is advantageous in that use of heat allows greater penetration as well as greater drug concentration than systemic chemotherapy. Other treatment options may also include early postoperative intraperitoneal chemotherapy (EPIC) and radiation [6].

Diffuse malignant peritoneal mesothelioma is a rare neoplasm with a poor prognosis. Although most patients present late in their disease, early detection with tissue biopsy and IHC's may provide better opportunities for patients and clinicians for better clinical outcomes.

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