Pseudomyxoma Peritonei with Progressive Abdominal Distention

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Abstract
Pseudomyxoma peritonei is a rare condition, and poorly understood which characterized by mucinous implants diffusely involving the peritoneal surfaces. Most cases originate from ruptured appendiceal mucocles or ovarian cysts. This report describes a case of massive gelatinous ascites which was diagnosed with pseudomyxoma peritonei. The diagnosis processes need multidisciplinary approaches to use. In addition, literature on the clinical presentation, diagnostic procedures, and treatment options have been briefly reviewed.

Key words: pseudomyxoma peritonei, gelatinous ascites
Introduction

Pseudomyxoma peritonei, a progressive disease within the peritoneum, is characterized by the production of large amounts of mucinous fluid that gradually fills the peritoneal cavity, resulting in the characteristic “jelly belly”. The incidence is approximately one per million per year or 2 per 10,000 laparotomies, and two to three times more common in female than males.

There is a considerable debate regarding the appropriate classification and type of tumor to be included in this syndrome. The main controversy is related to the inclusion or exclusion of the more “malignant” forms of the disease and to the site of origin of the tumor. Commonly, it arises from mucinous tumor of the appendix and occasionally from the ovary, colon, rectum, stomach, gall bladder, bile duct, small intestine, urinary bladder, lung, breast, pancreas, and fallopian tube. Sometimes it arises from retroperitoneal tissues which are known as pseudomyxoma extraperitoneal.

We demonstrated one patient who has clinical diagnosis with disseminated peritoneal adenomucinosis (DPAM) and progression of the disease. The diagnosis is difficult to diagnose.

Case Report

A 78-year-old woman presented with slowly progressive abdominal distention without other complaints for more than a year. She visited our hospital in May 2009. She had diabetes mellitus and hypertension with medical control. She does not smoke cigarettes or drinking alcohol. She was healthy and had no serious medical illness before. She was pallor but jaundice and cyanosis were absent. Abdominal examination revealed large abdominal distention (Fig. 1) with massive ascites but no stigmata of chronic liver disease, tenderness or intra-abdominal mass. Pelvic examination revealed only cysto-rectocele with no significant abnormality. Examinations of respiratory, cardiovascular and nervous systems were also normal.

Laboratory testing showed elevated serum concentrations of CEA and CA19-9 (Table 1). Abdominal ultrasonography (USG) showed large amount of ascites with irregular echogenic density, 6.0 cm. subcapsular fluid pocket at superolateral aspect of liver. Others visceral organs appeared normal (Fig. 2). A computed tomography (CT) scan after oral and intravenous contrast showed massive septate ascites with compression of intra-abdominal organ, pattern of scallop liver, invasion of parenchyma of liver, and calcification. There was no any intra-abdominal mass that can be seen. (Fig. 3)

Figure 1 Abdominal distention pattern (jelly belly)
Table 1  Laboratory Findings on Admission

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>White Blood Cell</td>
<td>4300/ul</td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>9.4 g/dl</td>
</tr>
<tr>
<td>Hematocrit</td>
<td>27.5%</td>
</tr>
<tr>
<td>Platelet</td>
<td>450 x 10^3/ul</td>
</tr>
<tr>
<td>Total protein</td>
<td>8.5 g/dL</td>
</tr>
<tr>
<td>Albumin</td>
<td>3.4 g/dL</td>
</tr>
<tr>
<td>Aspartate aminotransferase</td>
<td>30 U/L</td>
</tr>
<tr>
<td>Alanine aminotransferase</td>
<td>11 U/L</td>
</tr>
<tr>
<td>Alkaline phosphatase</td>
<td>95 U/L</td>
</tr>
<tr>
<td>Total bilirubin</td>
<td>0.61 mg/dl</td>
</tr>
<tr>
<td>Direct bilirubin</td>
<td>0.27 mg/dl</td>
</tr>
<tr>
<td>Blood urea nitrogen</td>
<td>12 mg/dl</td>
</tr>
<tr>
<td>Creatinine</td>
<td>0.9 mg/dl</td>
</tr>
<tr>
<td>Blood sugar</td>
<td>102 mg/dl</td>
</tr>
<tr>
<td>CEA</td>
<td>272.2 ng/ml</td>
</tr>
<tr>
<td>CA 19-9</td>
<td>241.7 U/ml</td>
</tr>
<tr>
<td>CA12-5</td>
<td>15.5 U/ml</td>
</tr>
<tr>
<td>AFP</td>
<td>1.87 ng/ml</td>
</tr>
<tr>
<td>HBsAg</td>
<td>negative</td>
</tr>
<tr>
<td>Anti-HBs</td>
<td>negative</td>
</tr>
<tr>
<td>Anti-HCV</td>
<td>negative</td>
</tr>
</tbody>
</table>

An abdominal paracentesis was performed. The aspiration contained a large amount of red jelly-like mucus (Fig. 4). Polymerase chain reaction (PCR) of ascitis fluid was negative for Mycobacterium tuberculosis. Cytological study showed reactive mesothelial cells, lymphocyte and histiocyte. To confirm the diagnosis, peritoneoscope was performed with biopsy. Intra-abdominal cavity showed a but not any mass found. The peritoneal biopsy revealed mucinous lake with fibrous stroma and few lymphocytes in the wall, and the picture was consistent with PMP (Fig. 5).

The possibilities of gastric and intestine cancers have been rule out. Gastroendoscopy showed mild gastritis but colonoscopy was not performed due to patient’s condition.

After many investigations were performed; the conclusion of diagnosis was compatible with

Figure 2  Ultrasoundography showed large amount of irregularity echoic density of ascites and 6.0 cm subcapsular fluid pocket at superolateral aspect of liver (black arrow)
Computed tomographic scan of abdomen A. CT showed typical scalloping of liver (black arrow) and low-attenuation implants in liver, indicating parenchymal invasion (white arrow). B. Massive amounts of septated ascites and small calcification (arrow). C. Soft tissue infiltration (arrow) in left upper quadrant surrounding the stomach and spleen, indicating interstitial reticular infiltration of the peritoneum. D. Large amount of ascites with displacement of small bowel.

Red jelly-like mucinous ascites

Disseminated peritoneal adenomucinosis by clinical progression, cytological, and imaging patterns. Patient and her relatives were advised to undertake laparotomy, intra and postoperative intraperitoneal chemotherapy, but they denied. Five months later, she died from complications of gut obstruction and peritonitis.

Discussion

The term pseudomyxoma peritonei (PMP)
has been used in reference to any condition, benign or malignant, in which the peritoneal cavity is filled with gelatinous substance. A clinical case consistent with this diagnosis was first described by Rokitansky in 1842, but R. Werth, gynecologist, first described PMP in 1884 as a peculiar reaction of peritoneum produced by ovarian neoplasm. In 1901 Frankel described it in association with appendiceal cyst. The mean patient age is about 58 years. PMP consists of neoplastic mucin producing cells in the peritoneal cavity. Mucin usually is secreted from ruptured mucinous neoplasm. Recent morphologic, immunohistochemical, and molecular genetic studies have suggested that the appendix is most likely the originate site of PMP, which sometimes involves other visceral organs. The ovary, colon, uterus, common bile duct, pancreas, and stomach have been documented as rare sites of PMP origin. Many case report series showed that primary tumor causing PMP are associated with appendiceal tumors such as appendiceal mucinous adenoma, appendiceal adenocystadenoma, or adenocarcinoma.

After the wall of the appendix ruptures, symptoms and signs of PMP can progress for months or even years within the abdomen and pelvis without causing any symptoms. As the disease progresses, the peritoneal cavity is filled in a characteristic pattern with mucinous neoplasm and mucinous ascites. The greater omentum is thickened (omental cake) and infiltrated extensively by the tumor. The most common symptom with PMP is a gradually increasing abdominal girth. The Second most common symptom is ovarian mass, usually on right side, in women and new-onset of hernia in men. The Yhird most common symptom is presenting with appendicitis, a clinical manifestation of ruptured appendiceal mucocele with local inflammation.

PMP has been classified into three pathological subtypes with different pathological characteristics (including malignant features) and associated with a different prognosis: disseminated peritoneal adenomucinosis (DPAM), peritoneal mucinous carcinomatosis with intermediate or discordant features (PMCA–I/D), and peritoneal mucinous carcinomatosis (PMCA). Histopathologically, DPAM is characterized by an abundance of extracellular mucus with focally adenomucinous

Figure 5 Histological examination of the omental biopsy specimen revealed areas of fibrotic fatty tissue with mucous lake without identifiable neoplastic cell, suggesting that it would have been difficult to acquire the cells in a biopsy sample.
epithelium with hardly any atypia or mitotic activity which has a good prognosis. PMCA, in contrast, is characterized by peritoneal tumor which is composed of more abundant mucinous tumor cells with the architectural and cytological features of carcinoma. Finally, the intermediate subtype PMCA-I is characterized by an abundance of DPAM lesions, not focal areas with PMCA lesions. The behavior and prognosis of PMCA-I subtypes is between DPAM and PMCA. Many studies implied that cytomorphologic features are an important prognostic indicator, such as in the study by Ronett et al.\textsuperscript{19}, which reported 5-year survival rates as 75\% for DPAM, 50\% for PMCA-I, and 14\% for PMCA. In the study by Jackson et al.\textsuperscript{22}, they reviewed cytology from peritoneal washing and classified histological subtype. Analysis of follow-up data showed that DPAM had better prognosis than PMCA. Moreover, study by Gupta S. et al, reported median survival for patients with DPAM, PACA-I, and PMCA were 7.7, 1.2, 0.7 years, respectively.\textsuperscript{23} Beside, there are some serologic markers that may also be a survival predictor, CEA and CA 19-9, but there is only a small number of patients. CA 19-9 is may be a prognostic factor for predicting recurrent disease\textsuperscript{24} and CEA elevation is possible in poor prognosis recurrence of diseases.\textsuperscript{25}

The diagnosis of PMP is often difficult because it usually has an insidious presentation, while radiological feature is an important tool for diagnosis PMP. Ultrasonography is the first imaging technique to use for further establishment of the diagnosis. Typical findings are nonmobile echogenic ascites with multiple semisolid masses and scalloping of the hepatic and splenic margins due to extrinsic pressure of adjacent peritoneal implants.\textsuperscript{26,27}

Computer tomography (CT) of the abdomen and pelvis are the most widely applied technology which has been used with great success in the diagnosis of the PMP syndrome. CT findings are often highly suggestive of PMP, and sometimes these are pathognomonic.\textsuperscript{2} The most common finding is a large volume of mucinous ascites, which has the density properties (Hounsfield Units [H.U.]) higher than normal (5-20 H.U. vs. +/- 0 H.U.)\textsuperscript{28} and displaces the small bowel. Other characteristic findings are omental thickenings, multiseptated lesions, scalloping of organs, and curvilinear calcifications.\textsuperscript{26,29} Bechtold et al. have revealed the pattern of CT for classified histological characteristics of the disease. DPAM was characterized by larger amount of ascites, no omental cake, typical hepatic scalloping, no lymphadenopathy, some calcified mass, and no primary lesion is present. However, PMCA were commonly found in the presence of omental cake, coexistent disease in the chest, lymphadenopathy and visualization of a primary mass.\textsuperscript{30}

There is currently no accepted standard treatment for PMP. The choice of treatment strategy has varied much in the past. Only one report suggested observation\textsuperscript{31}, but survival data was not supported from large studies. Untreated PMP patients would eventually suffer death through intestinal obstruction by massive mucinous ascites and large tumor deposits.\textsuperscript{32} Traditional surgical treatment is repeated interval debulking procedures for relief of symptoms, but with limited expectation of long-term survival and no prospect of cure.\textsuperscript{2}

Currently a cytoreductive surgery (CRS) and
perioperative loco–regional chemotherapy (PLC) regimen have been shown in multiple studies to improve survival, as compared with historical controls. Aggressive cytoreductive surgery including parietal peritonectomy and resection of involved viscera are used to reduce macroscopic tumor masses. Technique for PLC is usually hyperthermic intra–peritoneal chemotherapy (HIPEC) with mitomycin-C or 5-fluorouracil for eradication residual microscopic tumors. In study by Smeek RM, et al. report survival analysis in patients who received cytoreductive surgery with hyperthermic intra–peritoneal chemotherapy show survival benefit in DPAM subgroup than PMCA–I and PMCA with statistical significantly, hazard ratio 1.9 (1.0–3.5) and 4.1 (1.5–11.1), respectively. On the other hand, combined treatment has relatively high morbidity and mortality rates due to complications from extensive surgery. Treatment related morbidity and mortality seem to be related to age, tumor load, extent of cytoreductive surgery, and associated operative factors.

In this patient, clinical presentation was an abdominal distention like jelly belly pattern, and with large amounts of gelatinous ascites. She did not have any previous surgical treatment such as appendectomy or Cesarean section. Radiographic showed typical patterns of scallop liver, and parenchymal invasion. No lymph node involvement or no primary lesion was presented. Peritoneal biopsy was done under peritoneoscope. Histopathology is compatible with DPAM, due to its abundance of extracellular mucus without cellular atypia. However, tissue sampling may not be sufficient, because it was found only fibrotic fatty tissue with mucous lake, and without adequate cellularity. Histopathology classification may be under diagnosis that reflects to the prognosis. The primary tumor may be raised from both appendix and ovary because it is the most common organ causing of this disease, but it is suggestively originated from appendix. She had normal gynecologic examination and tumor marker of the ovary is in normal range. There were many limitations to diagnose and definite treatments in this case especially she did not received cytoreductive surgery that was a major indicator to the survival.

She seemed to have good prognosis or slow progression. She had some bad indications such as old age, inadequate tissue sampling, cytoreductive incomplete, serum CEA, and CA19–9 elevation. All of this factors effect to prognosis and survival of her disease.

Conclusion

Even though clinical diagnostic modalities like USG, CT and MRI can provide supportive evidence in favor of PMP, but the definitive diagnosis can only be made by explorative laparotomy. It is useful for diagnosis especially histological pattern and it may identify primary site of the origin. Prognosis of this disease majority depends on histological pattern. There is evidence that treatment should be more aggressive for improving survival. In the present, combination of CRS–PLC is possibly becoming the new standard of care.

References


