Pseudomyxoma Peritonei from a Borderline Mucinous Tumor Arising in an Ovarian Mature Cystic Teratoma: A Rare Case Report

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Received date: April 06, 2016; Accepted date: June 10, 2016; Published date: June 17, 2016

Abstract

Pseudomyxoma peritonei (PMP) is a rare associated diagnosis of peritoneal carcinomatosis which, classically, has been characterized by a slowly progressive disease process. More recently, Ronnett et al., have histologically classified PMP into the slow growing disseminated peritoneal adenomucinosis (DPAM), the much more aggressive and invasive peritoneal mucinous carcinomatosis (PMCA) and an intermediate group (ID). Recent studies have shown that most cases of PMP arise from ruptured appendiceal tumors with dissemination of mucin producing epithelial cells into the peritoneal cavity. PMP, contrary to popular belief, almost never arises from a ruptured primary ovarian mucinous tumor, corroborated by two of the largest series on ruptured borderline mucinous ovarian neoplasms. A small number of cases have been reported, however, with peritoneal carcinomatosis secondary to rupture of an ovarian mucinous tumor associated with a mature cystic teratoma. These are usually CK7 negative and CK20 positive, and are immunohistochemically consistent with intestinal type of mucinous tumors that arise from intestinal elements of the teratoma. Other malignancies such as squamous cell carcinomas, malignant endodermal sinus tumors and chorio-carcinomas have been shown to arise from a mature teratoma. We present a case report describing one such rare case of DPAM arising from a ruptured borderline mucinous ovarian tumor in the background of a cystic teratoma.

Keywords: Tumor; Disease; Mucin; Carcinoma

Introduction

PMP is an uncommon entity with an incidence of 1-2 per million cases per year [1]. Many cases are found unexpectedly at laparotomy or laparoscopy, or may be suspected at cross sectional imaging during staging of another pathological entity. Werth in 1884 coined the term PMP, initially describing it in association with a mucinous tumor of the ovary. In 1901, Frankel described a case associated with a mucinous appendiceal cyst. Over the years, the term PMP has been used to describe almost every diffuse peritoneal mucinous tumor including those caused by lower GI tract and appendiceal mucinous primaries. The term PMP has been applied to carcinomatosis originating from the colon, rectum, gallbladder, small intestine, urinary bladder, lung, breast, fallopian tube and pancreas although the classic definition is from appendiceal or colonic tumors [2,3].

Controversy persists over the classification of mucinous epithelial neoplasms and their relation to PMP. Several recent studies, including those by Ronnett et al., have redefined PMP as a specific clinicopathologic syndrome in which mucinous ascites is associated with peritoneal lesions characterized by histologically bland to low grade adenomatous mucinous epithelium, along with pools of extracellular mucin and fibrosis originating from appendiceal tumors [4-6]. Ronnett and colleagues, coined new terminology forgoing PMP altogether and reported a pathologic system that has become widely accepted in the literature [6]. They classified low grade tumors with bland peritoneal mucinous neoplastic epithelium as DPAM/disseminated peritoneal adenomucinosis and high grade tumors with mucinous epithelial architecture similar to that of an invasive cancer, as PMCA/peritoneal mucinous carcinomatosis. They also included an intermediate group demonstrating a mixture of DPAM and PMCA that was termed PMCA-I. This classification is important from a prognostic standpoint, as patients with DPAM appear to obtain maximum survival benefit from cytoreductive surgery and heated intraperitoneal chemotherapy (CRS and HIPEC) while those with PMCA behave more like peritoneal carcinomatosis of lower GI origin.

Multiple studies have provided morphologic, immunohistochemical and molecular evidence that PMP/DPAM is almost always derived from ruptured low grade adenomatous mucinous tumors of the appendix in both males and females and those primary ovarian mucinous tumors are almost never a source of PMP/DPAM [7-11]. Similarly, studies looking at ruptured primary ovarian mucinous tumors have not shown any association with PMP [8,12-14]. This has led to the current conundrum: whether primary mucinous ovarian tumors are truly associated with PMP/DPAM.

Aside from primary mucinous ovarian tumors, mucinous epithelial neoplasms associated with ovarian mature cystic teratomas are well documented in the literature. Most information regarding these tumors, is based on individual case reports and case series. Ronnett and Siedeman in 2003 reported a subset of mucinous epithelial tumors arising in a background of mature teratomas with an immunophenotype more suggestive of a gastrointestinal lineage than ovarian epithelial origin, and described an association with PMP in some cases [15]. Since then, several new case reports have been described with similar pathology. This paper describes one such case encountered at Emory University.

Arch Surg Oncol
ISSN:2471-2671 ASO an open access journal

Volume 2 • Issue 3 • 1000114
Case Presentation

The patient is a 61 year old female who presented to an outside hospital in February 2014 with progressive shortness of breath and abdominal distension for 3 months. A CT scan of her abdomen and pelvis showed massive ascites along with a left ovarian/pelvic complex cystic mass and an incidental 3.3 cm left adrenal adenoma. Tumor markers were drawn as part of her workup, and these showed an elevated CEA of 80.55 and CA 125 of 75 with normal CA19-9 and LDH levels.

She underwent a paracentesis with aspiration of thick mucin concerning for PMP. An esophagogastroduodenoscopy (EGD) and colonoscopy were normal other than 15-20 shallow antral erosions. She was referred to Gynecologic and Surgical oncology at Emory where a repeat CT scan in 09/2014 showed reaccumulation of large volume ascites and a 20 × 16 cm multiloculated complex cystic pelvic mass which was concerning for an immature teratoma. She was taken to the OR on 07/31/2014 and underwent an exploratory laparotomy with drainage of 15 liters of mucinous ascites and a left partial oophorectomy for biopsy. Pathology revealed pools of mucin with low cellularity and a mucinous cystadenoma of the ovary.

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Her final pathology report showed a mucinous borderline tumor of the ovary with intestinal differentiation arising in association with a mature cystic teratoma. Ascitic fluid analysis showed extra-ovarian mucin with scant epithelium consistent with DPAM (Figure 1). There was no evidence of an invasive carcinoma, and a sclerosed and rudimentary appendix was identified with no evidence of an appendiceal tumor.

Her post-operative course was uneventful and she was discharged in 2 weeks, tolerating a regular diet. Follow up imaging has demonstrated no recurrence, with most recent CT scan in January 2016 showing no evidence of recurrent disease or ascites.

Discussion

Numerous cases involving PMP/DPAM have been published where an appendiceal mucinous tumor has not been identified, and some of these have occurred in women with mucinous tumors involving the ovaries, leading to a questionable conclusion of the ovary being the primary site of origin. However, morphologic, immunohistochemical and molecular genetic studies provide compelling evidence that the clinical syndrome of PMP is derived from ruptured low grade adenomatous mucinous tumors of the appendix even in women. Interestingly, studies of the more aggressive PMCA also showed no primary ovarian origin [4-6].

There are outliers to the above dogma. Ronnett et al. published three cases of mucinous tumors arising in an ovarian mature cystic teratoma that were associated with PMP. Two of these ovarian mucinous tumors had the same histologic features as those encountered in typical cases of PMP/DPAM derived from ruptured appendiceal mucinous tumors, with irregularly distributed bland to low-grade adenomatous mucinous epithelium associated with pseudomyxoma ovarii. The third tumor had histologic features of an adenoma combined with carcinoma, similar to cases of PMCA-I. In all three cases, the appendices were entirely normal microscopically, hence it was clear that the primary source was the mucinous tumor arising from a mature teratoma. Upon further examination with immuno-histochemical analysis, all three tumors displayed a lower GI tract phenotype rather than a primary ovarian mucinous tumor phenotype. This pathologic finding suggested that these tumors were derived from a gastrointestinal type mucinous epithelial component of the teratoma. Typical GI mucinous tumors...
stain for CK 20 with focal or absence of staining for CK 7 markers. Primary non-teratomatous ovarian mucinous tumors stain for CK 7 with focal or absence of staining for CK 20. Interestingly, teratomatous ovarian mucinous tumors associated with PMP have been found to stain for CK 20 similar to their lower GI counterparts, hence supporting the above findings.

In contrast to these cases, ruptured non-teratomatous ovarian mucinous tumors may result in a localized accumulation of extracellular mucin that is invariably devoid of mucinous epithelium and associated with an inflammatory infiltrate, containing histiocytes and giant cells. Multiple reports have not shown these tumors to be differentiated from their teratomatous counterparts due to evenly distributed cystic structures lined by proliferative mucinous epithelium, with minimal pseudomyxoma ovarii and no involvement of the ovarian surface.

In support of the findings of Ronnett, McKenney et al., evaluated the morphologic, immunohistochemical and clinical features of 42 patients with mucinous epithelial tumors of the ovary arising in association with mature ovarian teratomas [17]. The age range of these patients was 17-66 years and tumor size ranged from 5.5 to more than 200 cm. Using the 2003 WHO classification description which breaks down the mucinous tumors based on histology types, 17 (40%) were mucinous cystadenomas, 16 (38%) were intestinal type mucinous epithelial neoplasm of low malignant potential (IM-LMP), 4 (10%) were IEC and 5 (12%) were invasive carcinomas. Of the 42 cases, 10 (24%) had classic PMP and 2 (5%) had more localized accumulation of peritoneal mucin. Evaluation of all 12 cases revealed 6 with acellular pseudomyxoma ovarii and 6 with acellular mucinous epithelium, with minimal pseudomyxoma ovarii and no involvement of the ovarian surface. The morphologic, immunohistochemical and clinical features of 42 patients with mucinous epithelial tumors of the ovary arising in association with mature ovarian teratomas [17]. The age range of these patients was 17-66 years and tumor size ranged from 5.5 to more than 200 cm. Using the 2003 WHO classification description which breaks down the mucinous tumors based on histology types, 17 (40%) were mucinous cystadenomas, 16 (38%) were intestinal type mucinous epithelial neoplasm of low malignant potential (IM-LMP), 4 (10%) were IEC and 5 (12%) were invasive carcinomas. Of the 42 cases, 10 (24%) had classic PMP and 2 (5%) had more localized accumulation of peritoneal mucin. Evaluation of all 12 cases revealed 6 with acellular pseudomyxoma ovarii and 6 with acellular mucinous epithelium, with minimal pseudomyxoma ovarii and no involvement of the ovarian surface. The morphologic, immunohistochemical and clinical features of 42 patients with mucinous epithelial tumors of the ovary arising in association with mature ovarian teratomas [17]. The age range of these patients was 17-66 years and tumor size ranged from 5.5 to more than 200 cm. Using the 2003 WHO classification description which breaks down the mucinous tumors based on histology types, 17 (40%) were mucinous cystadenomas, 16 (38%) were intestinal type mucinous epithelial neoplasm of low malignant potential (IM-LMP), 4 (10%) were IEC and 5 (12%) were invasive carcinomas. Of the 42 cases, 10 (24%) had classic PMP and 2 (5%) had more localized accumulation of peritoneal mucin. Evaluation of all 12 cases revealed 6 with acellular pseudomyxoma ovarii and 6 with acellular mucinous epithelium, with minimal pseudomyxoma ovarii and no involvement of the ovarian surface. The morphologic, immunohistochemical and clinical features of 42 patients with mucinous epithelial tumors of the ovary arising in association with mature ovarian teratomas [17]. The age range of these patients was 17-66 years and tumor size ranged from 5.5 to more than 200 cm. Using the 2003 WHO classification description which breaks down the mucinous tumors based on histology types, 17 (40%) were mucinous cystadenomas, 16 (38%) were intestinal type mucinous epithelial neoplasm of low malignant potential (IM-LMP), 4 (10%) were IEC and 5 (12%) were invasive carcinomas. Of the 42 cases, 10 (24%) had classic PMP and 2 (5%) had more localized accumulation of peritoneal mucin. Evaluation of all 12 cases revealed 6 with acellular pseudomyxoma ovarii and 6 with acellular mucinous epithelium, with minimal pseudomyxoma ovarii and no involvement of the ovarian surface. The morphologic, immunohistochemical and clinical features of 42 patients with mucinous epithelial tumors of the ovary arising in association with mature ovarian teratomas [17]. The age range of these patients was 17-66 years and tumor size ranged from 5.5 to more than 200 cm. Using the 2003 WHO classification description which breaks down the mucinous tumors based on histology types, 17 (40%) were mucinous cystadenomas, 16 (38%) were intestinal type mucinous epithelial neoplasm of low malignant potential (IM-LMP), 4 (10%) were IEC and 5 (12%) were invasive carcinomas. Of the 42 cases, 10 (24%) had classic PMP and 2 (5%) had more localized accumulation of peritoneal mucin. Evaluation of all 12 cases revealed 6 with acellular pseudomyxoma ovarii and 6 with acellular mucinous epithelium, with minimal pseudomyxoma ovarii and no involvement of the ovarian surface.

In summary, mucinous epithelial neoplasms associated with ovarian mature teratomas exhibit a histologic and immune-phenotypic spectrum. While the IM-LMP/borderline and carcinoma subtypes resemble mucinous tumors arising in the lower GI tract, the cystadenoma subtype exhibits a non-enteric phenotype. Such resemblance to a GI tumor may be mistaken for a metastasis if the teratomatous component is not identified on histologic examination. The presence of a normal appendix after complete microscopic examination however, in a majority of cases with and without PMP, provides a compelling argument against an appendiceal primary. Ovarian teratoma associated benign and IM-LMP mucinous neoplasms with peritoneal low grade mucinous epithelium, seem to be at low risk for intra-abdominal recurrence, however numbers are few and follow up is limited. At present, teratomatous ovarian mucinous tumors represent the only cases of ovarian origin of PMP and much is still to be learned about survival and patterns of recurrence in comparison to their lower GI counterparts.

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