Appendiceal Carcinoma Presenting as Adnexal Mass With Pseudomyxoma Peritonei—A Case Report and Review of Literature

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Clinical Practice Points

- Pseudomyxoma peritonei (PMP) is an uncommon tumor presenting with mucinous ascites and pressure symptoms. Females usually present with abdominal distension and ovarian mass. Cytoreductive surgery combined with hyperthermic intraperitoneal chemotherapy is the treatment of choice.
- Our patient had typical presentation of PMP who presented with ovarian mass. Left ovary showed a big tumor with mucinous ascites, and the appendix was normal looking. Histopathology revealed the primary appendiceal tumor, and mass in the ovary was metastatic.
- This case report highlights the importance of complete surgery including appendicectomy as most of the times primary tumor arises from the appendix.

Introduction

Pseudomyxoma peritonei (PMP) is an uncommon clinical condition characterized by a slow and progressive accumulation of peritoneal implants and mucinous ascites. Accumulation of mucin in peritoneal cavity results in massive symptomatic distension of abdomen. Twenty to thirty percent of female PMP patients present with an ovarian mass found during the evaluation for lower abdominal pain, a pelvic mass, menstruation problems, or infertility.¹ ² Although earlier there was controversy in nomenclature, it is now generally accepted that PMP arises as a result of neoplastic mucin-secreting cells with low-grade cytologic features disseminating within the peritoneal cavity. Appendicinal and ovarian neoplasms give rise to majority of the cases. We are presenting a case of adnexal (ovarian) mass with PMP resulting from appendiceal carcinoma.¹ ³

Case Report

A 45-year-old multiparous woman presented with gradually progressive abdominal distension and loss of appetite and weight for 6 months. She had bronchial asthma and uterovaginal prolapse for 10 years. There was no alteration in bowel or bladder function or awareness of mass. She attained menopause 6 years ago, and perimenopausal transition was smooth. She had 5-term vaginal deliveries and used barrier contraception.

On examination, patient’s general condition was good with pulse rate of 100/min, blood pressure of 140/80 mm Hg, and respiratory rate 30/min with mild pallor. Chest auscultation revealed bilateral rhonchi. Abdominal distention was present, with umbilicus everted, and small umbilical hernia was seen with moderate amount of free fluid but no palpable mass. On local examination, second-degree cervical descent with large rectocele and minimal cystocele was noticed. Uterus was normal sized, and there was no palpable adnexal mass. Paracentesis of approximately 30 mL revealed thick mucinous fluid. Preoperatively, she received salbutamol and ipratropium nebulation, intravenous hydrocortisone, and deriphyllin along with supportive treatment in consultation with pulmonologist for acute exacerbation of bronchial asthma. She was planned for laparotomy and taken up for surgery under high risk in view of bronchial asthma. Preoperative investigations revealed hemoglobin of 8.0 g/dL, renal and liver function tests were within normal limits, x-ray chest was normal, pulmonary function tests showed mild obstruction, arterial blood gas on room air (pH/pO₂/pCO₂/HCO₃⁻/Base excess/SaO₂)
was 7.41/145/32/20/−4/99%, and CA-125 = 29.6 U/mL. Peritoneal cytology was suggestive of PMP. The peritoneal cytology showed thick mucinous material with a few scattered mucinous epithelial cells having cytoplasmic vacuolation and eccentric nucleus with bland chromatin admixed with a few macrophages. There was no evidence of frank mucinous carcinoma. Ultrasonography revealed normal liver, spleen, gall bladder, and both kidneys; uterus normal size with thin endometrium; and large cystic mass in pelvis with internal septations and heterogenous foci. Mass showed coarse echotexture and was full of complex soft tissue echoes.

She underwent laparotomy under combined epidural and general anesthesia. Five kilograms of mucinous ascitic fluid was drained. Uterus, both tubes, and right ovary were normal. Left ovary was replaced by a tumor of 10 × 6 cm with capsule ruptured and mucinous material coating the whole of peritoneal cavity. Surface of liver, undersurface of diaphragm, and bilateral paracolic gutters were free of tumor, and there were no palpable retroperitoneal lymph nodes. Appendix was retrocecal 3 × 1 cm and buried in adhesions. Total abdominal hysterectomy with bilateral salpingo-oophorectomy and infracolic omentectomy and appendicectomy was done. Small paraumbilical hernia defect of 2 × 2 cm was present, which was repaired. Peritoneal wash was done with 5% dextrose. Pelvic floor repair was deferred because of high risk of anesthesia with prolongation of surgery. Postoperative period was uneventful, and she received intravenous amoxiclavulanic acid and metronidazole. She was discharged on the second postoperative day.

Histopathology revealed the following in the left ovary: mucinous tumor, borderline malignant, and metastatic. Tumor deposits were present on serosal aspect of left fallopian tube. Right ovary, right tube, endomyometrium, and cervix were unremarkable. No tumor deposits were seen on the omentum. Appendix showed mucinous tumor of borderline malignancy. Peritoneum revealed PMP. Overall features were suggestive of PMP, disseminated peritoneal adenomucinosis type (Figures 1–4).

Postoperatively, she received 6 cycles of oxalplatinum and 5-flourouracil and under regular follow-up.

Discussion

PMP is an enigmatic syndrome characterized by copious production of mucinous ascites that, over time, fills the peritoneal cavity. It is a rare condition, incidence being 1 per million per year. Classically, it presents at laparotomy as “jelly belly.” The term was coined by Werth in 1884 when he described the condition in association with mucinous carcinoma of the ovary. In 1901, Frankel described a case of PMP in association with a cyst of the appendix. Definition, origin, etiology, and treatment of this peculiar condition are controversial. There is a spectrum of disease varying from mucinous cystadenomas of appendix to mucinous cystadenocarcinoma arising anywhere in abdominal cavity. Recently, it has been proposed that the term PMP syndrome be strictly applied to a pathologically and prognostically homogeneous group of cases characterized by histologically benign peritoneal tumors that are frequently associated with an appendiceal mucinous adenoma and have a unique natural history. Pathologically, the peritoneal mucinous lesions are termed “disseminated peritoneal adenomucinosis” or simply adenomucinosis. Cases of peritoneal
carcinomatosis, regardless of the presence of abundant extracellular mucin, are excluded from this definition. In addition to appendiceal and ovarian tumor, PMP has been found to originate from other intra-abdominal organs such as colon and rectum, stomach, gall bladder and bile ducts, small intestine and urinary bladder, lungs, breast, fallopian tube, and pancreas. Synchronous disease is found in ovary and appendix in most females, and the disease is reported to be more prevalent in females.

PMP is not considered to be biologically aggressive as it does not invade or metastasize, but disease is invariably fatal as space required in abdomen is eventually replaced by mucinous tumor, resulting in death unless the disease is definitely treated. Clinical presentation is varied, and most patients present with abdominal distension. In women, most cases are diagnosed while being investigated for an ovarian mass as happened in the present case. In a study by Sugarbaker et al., 27% cases presented with suspected acute appendicitis, 23% with increasing abdominal distension, and 14% as new-onset hernia. In women, 39% cases were diagnosed while being evaluated for an ovarian mass. A delay in diagnosis is common, and many patients are labeled as irritable bowel syndrome for number of years before definitive diagnosis.

It has been shown that although PMP usually manifests with a synchronous primary tumor (or an unknown primary), the interval between the discovery of the primary (appendical) tumor and the clinical diagnosis of PMP can vary significantly.

With the availability of imaging techniques, diagnosis can be suspected pre-operatively. Ultrasound has been reported to be useful for the diagnosis of an appendiceal mucocoele or PMP, however, usually in combination with computerized tomography. Contrast-enhanced computerized tomography (CECT) and magnetic resonance imaging are the main modalities used. Computed tomography with oral, rectal, and intravenous contrast remains the gold standard for diagnostic imaging in PMP. CECT findings in PMP are pathognomonic with appropriate radiologic techniques. It demonstrates the characteristic distribution pattern of mucinous ascites which can be differentiated from normal (watery) ascites by analyzing density properties (Hounsfield units [HU]). Mucinous ascites has a significantly higher density image (5-20 HU) than normal ascites (± 0 HU). Furthermore, it shows low attenuation of soft tissue masses with internal mottled densities, distinctive rim-like calcifications, and characteristic septae. Striking feature is the relative sparing of small bowel and mesentery with small bowel compartmentalization in the center of abdominal cavity by large omental cake. There is a characteristic layer of tumor surrounding and scalloping the diaphragmatic surface of the liver. Radiologic findings which can point toward tumor inoperability include segmental obstruction of small bowel and tumor masses greater than 5 cm on small bowel and mesentery of jejunum and ileum.

Tumor markers are not of much use; both CA-125 and CEA levels may be elevated. Many patients are erroneously interpreted as advanced ovarian cancer or advanced metastatic intestinal carcinoma. Current opinion regarding the pathophysiology of PMP suggests that it usually originates as an adenoma in submucosa of the appendix which eventually ruptures releasing mucus-containing epithelial cells into peritoneal cavity. Over the years, primary tumor grows little in size, but epithelial cells within the peritoneal cavity continue to proliferate and produce large quantities of mucin. These cells get redistributed in peritoneal cavity along the direction of movement of fluid and by gravity and concentrate at the normal sites of peritoneal fluid absorption. There is complete or near complete absence of mucinous tumors on the intestinal surfaces because of active movement during peristalsis, exceptions to this being antrum of stomach and pylorus, the ileocecal region, and rectosigmoid sites which are relatively fixed.

Pathologically, there is a spectrum of disease ranging from adenomucinosis to adenocarcinoma or there may be an adenoma—carcinoma sequence such that the tumor may at some stage undergo malignant transformation to a more aggressive variant. From a clinical/pathologic point of view, PMP should always be regarded as borderline malignant. Regarding the origin of concomitant mucinous tumors of appendix and ovary, two theories has been proposed: they either (1) arise as independent primaries or (2) represent an appendiceal primary tumor with metastasis to the ovaries. The appendiceal mucinous tumors are always CK-7 positive. William and Hart studied CK-7 expression in primary appendiceal mucinous tumor and simultaneous tumor of appendix and ovary and PMP and concluded that appendiceal cystadenomas are CK-7 negative, whereas borderline mucinous ovarian tumors are always CK-7 positive. William and Hart in review of mucinous tumors of the ovary revealed that PMP almost never results from a ruptured primary ovarian mucinous neoplasm. In a clinicopathologic study of 22 cases of mucinous tumors of ovary and appendix by Young et al., it was seen that both tumors were synchronous in 21 cases, and in 7 cases ovarian tumors were bilateral. In 20 cases, appendix was considered abnormal at operation, and in 2 cases, it appeared normal. Twenty-one patients had PMP. Microscopically, ovarian and appendiceal tumors were of benign/borderline malignancy. There were a number of features to suggest that ovarian tumor in these cases was secondary to appendiceal tumor frequency of
bilaterality of ovarian tumors, their right-sided predominance, histologic similarity, presence of mucin, and atypical mucinous cells on the ovarian surface. Jaffrey et al. supported an independent origin of the ovarian and appendiceal tumors in clinicopathologic study of 25 cases. Majority of them had either a pelvic mass or abdominal/pelvic pain. High frequency of bilateral ovarian tumors (11 of 25) and right-sided predominance for unilateral ovarian tumors were found.

The proper treatment for PMP remains uncertain because data with a high level of evidence are lacking, but the combination of (aggressive) surgical debulking with peritonectomy and hyperthermic intraperitoneal chemotherapy seems to improve the outcome. Surgery is the mainstay of treatment for PMP. Radiotherapy has little role because of unacceptable side effects from such a wide-field tumor. Systemic chemotherapy is not reliably effective because of borderline malignancy of the cells and relatively poor blood supply. Miner et al. reported a 10-year survival of 21% (12% disease free) in 97 patients treated by serial debulking, systemic chemotherapy, and/or delayed intermittent intraperitoneal 5-fluorouracil over a 22-year period in Memorial Sloan Kettering. Traditional and still practiced surgical approach is debulking surgery whereby, at laparotomy, as much as possible of tumor is removed. Procedure involves appendicectomy, omentectomy, and total hysterectomy with bilateral salpingo-oophorectomy in females as was done in the present case. Disease eventually recurs, and symptomatic recurrence is treated by further laparotomy and debulking. But each repeated procedure becomes ineffective and dangerous because of risk of bowel injury and peritonitis. Alternative surgical approach is complete tumor removal, stripping of parietal peritoneum, and resecting intra-abdominal structures at fixed sites that contain tumor laden visceral peritoneum to accomplish complete cytoreduction but morbidity and mortality from complete cyto-reduction is high. Surgery is combined with intraperitoneal intraoperative heated chemotherapy (HIIC) using agents like 5-fluorouracil/mitomycin. In a multi-institutional study of 2298 patients of PMP, Chua et al. had shown better progression-free survival in patients who received hyperthermic intraperitoneal chemotherapy (HIPEC). In a 12-year follow-up of 53 consecutive patients of PMP, Vaira et al. described overall 5- and 10-year survival of 94% and 84.6%, respectively, in patients treated with cytoreductive surgery and HIPEC with acceptable morbidity. Owing to high morbidity and mortality of surgery, proper selection of patients is important. Radiologic findings which can point toward tumor inoperability include segmental obstruction of small bowel and tumor masses greater than 5 cm on small bowel and mesentry of jejunum and ileum.

Median survival of patients varies from months to years. The estimated 1-, 2-, 5-, and 10-year survival rates have been shown to be 98%, 86%, 53%, and 32% in one study, and outcome of tumor is strongly associated with tumor biology. Various factors which were shown to adversely affect patients’ survival were diffuse disease, presence of abdominal distension, history of weight loss, invasion of other organs, and use of systemic chemotherapy. Biological behavior of the tumor (low-grade mucinous adenocarcinoma) and history of complete cytoreduction were independently associated with prolonged survival. The natural history of PMP creates the potential risk for recurrence or progression after macroscopic complete or incomplete tumor removal. PMP patients who have been treated by surgery, with or without (intraperitoneal) chemotherapy, should therefore be monitored for progression or recurrence of disease.

To conclude, PMP is a rare condition which, though of borderline malignancy, is invariably fatal and it follows an unremitting and prolonged clinical course. There may be a diagnostic dilemma regarding site of primary tumor especially in females who present with ovarian masses. In most of the cases, ovarian mass is the result of metastasis from some other primary, mostly appendiceal. CECT scan is the best modality of diagnosis, and in many cases, diagnosis and tumor operability can be assessed with close certainty on the basis of CECT findings. Optimal treatment involves complete cytoreduction combined with HIIC.

References