



Pseudomyxoma Peritonei

Authors

Dr Nikita Gandotra¹, Dr Abhinav Sharma²

¹Resident, Government Medical College, Srinagar

²Senior Resident, MAMC, Delhi

Pseudomyxoma peritonei syndrome is characterized by mucinous ascites and mucinous tumor disseminated on peritoneal surfaces. The disease almost always originates from a perforated appendiceal epithelial tumor. Appendix tumors are unusual, accounting for 0.4% of all of the gastrointestinal tract malignancies. Although rare, the spectrum of malignant disease is complex and has led to confusion in accurate description of the natural history of these tumors. Consequently, many errors in diagnosis and treatment have occurred. Perhaps the most glaring error in management occurs in women who have ovarian tumors as a result of a perforated primary mucinous tumor of the appendix. Appendiceal tumors present with peritoneal seeding in a majority of patients. Dissemination to lymph nodes or to liver is extremely unusual. Advanced treatments of peritoneal carcinomatosis or peritoneal adenomucinosis have changed these survival rates from zero to approximately 80% for all patients. The term “mucocele” of the appendix refers to an accumulation of mucus within an abnormally distended appendiceal lumen, regardless of its cause. Mucoceles of the appendix are rare, appearing in 0.2-0.3 % of surgical specimens. A mucocele of the appendix can be caused by: obstruction of the appendiceal lumen, mucosal hyperplasia, mucinous cystadenoma,

mucinous cystadenocarcinoma⁽⁴⁾. Whatever the cause, obstruction of the lumen and accumulation of yellow mucous within the appendiceal lumen results. Majority of patients with mucocele are asymptomatic. Most mucoceles present with acute or chronic right lower quadrant pain (64%) but patients have presented with intussusception, gastrointestinal bleeding, intermittent colicky pain, abdominal masses, secondary infection and urologic symptoms.

Our patient presented with chronic abdominal pain and an abdominal mass.

○ **AT BARIUM ENEMA**, a smooth globular mass indenting the cecum may be seen, associated with non-filling of the appendix.

The combination of appendiceal non-filling and deformity of the inferomedial aspect of the cecum should always suggest the possibility of appendiceal disease, whether this be due to appendicitis (as is usually the case), appendiceal neoplasm or a mucocele.

○ Rupture of an appendiceal mucocele may give rise to pseudomyxoma peritonei in which the peritoneal cavity becomes filled with the gelatinous material either in the form of circumscribed collections or lying free. If this condition is discovered incidentally at laparotomy,

a careful search should be made for an underlying tumor, which is most commonly ovarian or appendiceal in origin. CT sometimes shows a characteristic appearance in pseudomyxoma peritonei, with septated fluid-density material in the peritoneal cavity and/or marked deformity and scalloping of the liver by the mucinous material. This condition is pathologically divided into 4 categories^[5]. A very rare type is secondary to occlusion of the lumen from post inflammatory scarring, progeric atrophy, congenital obstruction of Gerlach's valve or extramural compression. This type leads to atrophic mucosa. The other types are classified into a spectrum from mucous hyperplasia to mucinouscystadenoma to mucinous cystadenocarcinoma depending on the pathology of the mucosa. About 25% of mucocèles are from mucosal hyperplasia^[5]. These typically have minimal distension. Mucinous cystadenoma, which account for about 60% of mucocèles, are more markedly distended, however, they are typically asymptomatic. Mucocèles up to 40x24x20 cm have been reported. Mucinous cystadenocarcinomas (10-15% of cases) are more likely to be symptomatic and are believed to arise in cystadenomas. Thorough investigation of the colorectal tract is recommended after diagnosing an appendiceal mucocèle^[5]. Mucinous cystadenomas and cystadenocarcinomas may be indistinguishable grossly but histologically can be differentiated by two features:

- A. invasion of the appendiceal wall by atypical glands
- B. identification of epithelial cells in any intraperitoneal mucinous collection.

○ The distinction between mucinous cystadenomas and mucinous cystadenocarcinomas is important. Cystadenoma is cured by simple appendectomy, even in the presence of periappendiceal fluid collections right hemicolectomy is the best treatment for a malignant mucinous cystadenocarcinoma in a good risk patient. Rupture of appendiceal mucinous cystadenomas and mucinous cystadenocarcinomas may occur and

accounts for about 33 per cent of pseudomyxoma peritonei cases^[4]. The clinical presentation of a mucocèle is usually non-specific and up to fifty percent are discovered incidentally at surgery⁽²⁾. CT can play an important role in pre-operative diagnosis. The classical CT findings are:

- A cystic, well-encapsulated round or ovoid mass centered in the right iliac fossa.
- Mural calcification
- Absence of periappendiceal inflammation or abscess^(2,3)

Adequate opacification of the terminal ileum and cecum is essential for optimal examination. Pseudomyxoma peritonei is characterized on CT by the presence of low attenuation ascites with scalloping of liver contour due to peritoneal implants.

Implants can also be seen on the visceral surfaces and as nodules within cavities. These nodules may show calcification usually in a rim like fashion. The absence of scalloping does not rule out pseudomyxoma peritonei. Loculation of ascitic fluid with associated mass effect should also lead to a consideration of pseudomyxoma peritonei. Pseudomyxoma peritonei is also known to develop from ovarian cystadenocarcinoma. In these patients a mucinous neoplasm of the appendix is also nearly always present. Whether the ovarian and appendiceal tumors represent independent primary tumors whether the ovarian tumors are secondary to appendiceal tumors remains a controversy.

Both tumors are actually synchronous, but one may appear many years after the removal of the other. Mucinous cystadenocarcinomas arising from the urachus, uterus, or omphalomesenteric duct are also known to cause pseudomyxoma peritonei. The differential diagnosis of mucocèle of the appendix includes mesenteric cyst, duplicatiocyst, right ovarian cyst and hydrosalpinx.

PATHOGENESIS: MUC GENES

Pseudomyxoma peritonei is a disease of MUC2-expressing goblet cells

Pseudomyxoma peritonei, a syndrome first described by Karl F. Rokitsansky in 1842, is an enigmatic, often fatal intra-abdominal disease characterized by dissecting gelatinous ascites and multifocal peritoneal epithelial implants secreting copious globules of extracellular mucin. Our studies revealed that pseudomyxoma peritonei is a disease of MUC2-expressing goblet cells. MUC2 expression accounts for the voluminous deposits of extracellular mucin (mucin: cell ratios exceeding 10:1) and distinguishes pseudomyxoma peritonei secondarily involving the ovary from primary ovarian mucinous tumors with peritoneal implants.

Because mucinous tumors of the appendix similarly express MUC2, the MUC2 expression profile also supports an appendiceal rather than ovarian origin for pseudomyxoma peritonei. Increased steady-state mRNA is observed in pooled cases of pseudomyxoma peritonei. Extracellular mucin accumulates dramatically in pseudomyxoma peritonei because the number of MUC2-secreting cells dramatically increase and because this MUC2 has no place to drain. These studies suggest that pseudomyxoma peritonei should be regarded as a disease of MUC2-expressing goblet cells whose MUC2 expression might be susceptible to pharmacological targeting.

LABORATORY AND RADIOLOGY

Prognostic value of baseline and serial carcinoembryonic antigen and carbohydrate antigen 19.9 measurements in patients with pseudomyxoma peritonei treated with cytoreduction and hyperthermic intraperitoneal chemotherapy.

- **BACKGROUND:** Tumor markers are useful for diagnosis and follow-up. We studied the prognostic value of baseline and serial carcinoembryonic antigen (CEA) and carbohydrate antigen 19.9 (CA19.9) measurements in patients with pseudomyxoma peritonei treated with

cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (HIPEC).

- **METHODS:** Sixty-three patients with pseudomyxoma peritonei were treated with cytoreductive surgery and HIPEC. The tumor markers CEA and CA 19.9 were collected before therapy and at 3-month intervals during follow-up.
- **RESULTS:** Preoperative CEA and CA19.9 levels were increased in, respectively, 75% and 58% of the patients. Baseline tumor marker values were related to the extent of tumor. Immediately after HIPEC, both tumor markers decreased markedly ($P < .0001$). CA19.9 was shown to be a more useful tumor marker than CEA for follow-up. Patients who never attained a normal CA 19.9 level showed a higher recurrence rate at 1 year (53%), in comparison to patients who did so (6%). The median lead time of increased CA19.9 to recurrence was 9 months.
- **CONCLUSIONS:** The measurement of the tumor marker CA19.9 is useful in evaluating therapy in patients with pseudomyxoma peritonei treated with cytoreductive surgery and HIPEC. CA19.9 is a prognostic factor for predicting recurrent disease.

PROGNOSIS AND TREATMENT

Histopathologic Analysis in 46 Patients with Pseudomyxoma Peritonei Syndrome: Failure versus Success with a Second-Look Operation. Hui Yan, et al. *Mod Pathol* 2001; 14:164-171.

- Histopathologic assessment of aggressive versus noninvasive character of the mucinous tumor has been shown to have an impact on survival in patients treated with cytoreductive surgery and intraperitoneal chemotherapy.
- Unsuccessful second-look surgery for patients with a clinical diagnosis of pseudomyxoma peritonei tumor was often related to an inaccurate initial histologic classification of appendiceal mucinous tumor. Also, a transition from less to

more aggressive histology was frequently seen in patients dying of this disease. Assessment of tumor histology can predict the outcome if a uniform surgical treatment is used in patients with peritoneal dissemination of mucinous epithelial tumors of the appendix.

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