CASE REPORT

Hyperthermic Intraperitoneal Chemoperfusion in The Treatment of a Patient with Pseudomyxoma Peritonei from Mucinous Appendiceal Neoplasm 32 Years After Appendectomy for Perforated Appendicitis

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ABSTRACT
The ideal treatment for pseudomyxoma peritonei is an active area of investigation with mounting evidence for the benefit of complete cytoreduction and hyperthermic intraperitoneal chemoperfusion (HIPEC). The unusual nature of this disease was demonstrated with a report of a patient with pseudomyxoma peritonei of appendiceal origin discovered thirty-two years after appendectomy. The recurrence was discovered during exploration for possible recurrence of perforated GIST that was operated upon six years prior.

Key words: Delayed appendiceal cancer, Cytoreduction, Appendiceal remnant cancer

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ÖZET
Müsinöz Apendiks Tümörüne Bağlı Perfore Apendiks Olgusundan 32 Yıla Sonra Gelişen Psödomiksoma Peritonei İçin Yapılan Hipertermik Kemoterapi
Psödomiksoma peritonei tedavisi aktif araştırmaların yapıldığı bir alandır ve tam sitoredüksiyon ile hipertermik intraperitoneal kemoterapinin (HIPEK) faydalarını gösteren çalışmalar bildirilmiştir. Bu çalışmada apendiks müsinöz kist adenokarsinomdan 32 yıl sonra normalden farklı olarak bildirilmiş bir psödomiksoma peritonei oğusu bildirilmiştir. Bu nüks oğlu 6 yıl önce gastrointestinal stromal tümör perforasyonu (GIST) nedeniyle operede edilmiş olup tesadüfen GIST nüksü düşünülen opereye edildiğinde saptanmıştır.

Anahtar kelimeler: Geçikmiş apendiks kanseri, Sitoredüksiyon, Apendiks remnant kanseri

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INTRODUCTION
Pseudomyxoma peritonei (PMP) is characterized by the seeding of the peritoneal cavity with mucinous ascites and mucin-secreting epithelial cells, most commonly caused by neoplasms of appendiceal origin with non-invasive histology. There is a wide variety of invasiveness, often leading to an insidious onset of symptoms. Mucinous appendiceal neoplasms are often discovered at appendectomy for appendicitis or presumed appendicitis. These cases can also be discovered at exploration for other abdominal or gastrointestinal symptoms. This study reported a case of an extremely delayed diagnosis of appendiceal mucinous neoplasm thirty-two years after appendectomy for perforated appendicitis. Diagnosis in this patient was made at exploration for follow-up of presumed recurrent small bowel gastrointestinal stromal tumor (GIST).

CASE REPORT
The patient was a 70-year-old male with a history dating back to 1980 at which time he underwent an emergent open appendectomy through a right lower quadrant incision for perforated appendicitis. After the appendectomy, the patient had been in good health with only hyperlipidemia and glaucoma. While on vacation in 2006, the patient presented to the emergency department of a local hospital with peritonitis, and on exploration was found to have a ruptured 8.5 cm gastrointestinal stromal tumor (GIST) of the proximal jejunum. The GIST was resected along with approximately 20 cm of jejunum. A sigmoid mesenteric implant was also resected. While the histology was low-grade (no mitotic figures in 50 high power fields), given its location in the small bowel, size, and rupture, the patient was at high-risk of recurrence. He underwent adjuvant therapy with imatinib 400 mg daily for four years and 600 mg daily for one year. Serial imaging demonstrated hepatic subcapsular lesions which were initially stable in size. These were presumed GIST implants. There was also a cystic lesion near the cecal wall, stable in size (Figure 1).

The patient underwent elective exploratory laparotomy for presumed recurrent GIST after the liver lesion was noted to grow slightly. At exploration, lakes of mucin were discovered in the right lower quadrant, which were removed. A wedge resection from segment 7 was performed to excise the subcapsular lesion, and two abdominal wall nodules were resected. There was no other evidence of gross disease. Pathology revealed a well-differentiated mucinous adenocarcinoma in one of the abdominal wall lesions, and the liver lesions. There was no evidence of recurrent GIST.

Figure 1. CT showing cystic lesion in right lower quadrant.

Figure 2. Intra-operative photograph of appendiceal remnant.

Shortly thereafter, the patient presented to our institution for the option of cytoreductive surgery with HIPEC, which was performed after institutional review of pathology and discussion in our multidisciplinary tumor board. At exploration, there was no mucin, but an appendiceal remnant was noted-likely retained tip of appendix (Figure 2). The liver and peritoneal surfaces were clear of the disease, but there were a few cystic lesions at the hilum of the spleen in close proximity to the tail of the pancreas. A right hemicolectomy was performed. In addition, distal pancreatectomy with splenectomy, and excision of two small mesenteric implants were performed. Minimal adhesions were completely lysed, and the abdominal cavity was perfused with mitomycin C (40 mg total for ninety minutes at 43°C at a flow rate of 2 L/min). A stapled ileocolic anastomosis was com-
pleted after perfusion, and the abdomen was closed. Pathology demonstrated a low-grade mucinous cystic tumor in the appendiceal remnant, which most likely represented a well-differentiated mucinous adenocarcinoma (Figure 3). There was no nodal involvement, and no tumor in any other specimens. This was classified as a CC-0 resection (completeness of cytoreduction-0 - no visible disease remaining). The patient was discharged on the seventh post-operative day without any complications.

DISCUSSION

This case represents an atypical presentation of a rare malignancy. Aggressive follow-up and surveillance for recurrence of GIST (another rare malignancy) failed to accurately identify the true clinical entity thirty-two years after removal of the usual source of malignancy. Retained appendiceal material is most frequently reported in the form of an appendiceal stump. In a review of the literature by Subramanian and Liang, they have found one hundred and ninety-eight articles regarding retained appendix and stump appendicitis [1]. In this body of the literature, there have been fifty-seven cases of stump appendicitis particularly. Only one has been described as inflammation of a retained appendiceal tip located near the gallbladder. 26% of these cases have been after perforated or phlegmonous appendices. There has been no mention of malignancy in the retained appendiceal material. There are scattered reports of appendiceal PMP after prior appendectomy, one of them thirty-five and the other twenty-three years after initial appendectomy [2-5].

Despite being a rare clinical entity, PMP is an active area of clinical investigation and the optimal treatment is not agreed upon. A part of this therapeutic debate stems from the variable histology seen in this disease. The most frequently referenced histological classification is that outlined by Ronnett et al. This scheme breaks PMP into 3 basic categories [6]. Disseminated peritoneal adenomucinosis (DPAM) is a low-grade lesion with a better prognosis, characterized by extracellular mucin, and a lack of atypia or mitoses. DPAM is usually associated with appendiceal origin. Peritoneal mucinous adenocarcinoma (PMAC) is a high-grade adenocarcinoma, usually derived from appendix or colonic primary, associated with atypia and mitoses, and with a poor prognosis. A third, or intermediate histology is also identified (PMAC-I) with features mainly of DPAM, but with some features of PMAC. Accordingly, this histology carries an intermediate prognosis. Another histopathologic classification by Misdraji et al. describes the classification of appendiceal mucinous tumors into low-grade appendiceal mucinous neoplasm (LAMN) or mucinous adenocarcinoma (MACA) [7]. Other authors have argued for the high-grade versus low-grade description as well but the most widely quoted system is that of Ronnett et al. [8].

Sugarbaker et al. have proposed complete cytoreduction and heated intraperitoneal chemoperfusion for attempted cure, which has been adopted by many centers, including ours, and has demonstrated improved survival in the hands of experienced surgeons [9,10]. The rationale is that mucinous disease is a local extension as opposed to hematogenous spread and the ideal time to treat any residual microscopic disease is immediately after resection of all disease and lysis of all adhesions. Sugarbaker has demonstrated five and ten year survival rates of 75-100% and 68% with cytoreduction and HIPEC for DPAM. The more invasive pathologies were less successfully treated, with 50% and 21% five and ten year survivals for PMAC-I, and 14% and 3% for PMAC [6-11]. Survival was also dependent on completeness of cytoreduction [12]. Patients with CC-0 resections of DPAM had a five year survival of 86% [12].
The other side of the argument is from those who feel the increased risk of the extensive cytoreduction and HIPEC are not worth the benefit. They also argue that these results are not widely reproducible by surgeons who are not at these specialized centers with varying protocols and surgeon skill. Miner et al. have reported their experience with PMP and selective intraperitoneal chemotherapy in both high-grade and low-grade disease with an overall 21% ten year survival[2]. Given the inconsistencies in histopathologic classification between institutions and the variability in surgeon skill, it is difficult to compare retrospective series of patients. Prospective trials have been difficult to initiate and maintain.

Pseudomyxoma peritonei is a rare clinical entity. Even rarer is a delay in presentation greater than thirty years after appendectomy. The patient in the present study had an even more complex presentation given his vigilant surveillance for recurrent GIST. When detected, aggressive therapy can extend survival, especially for appropriately selected patients. In our patient, his low-grade histology and slow progression are likely to portend a better outcome. It is unclear what impact his surveillance and treatment for GIST had on his presentation or course.

REFERENCES


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