Mucinous Tumor of Uncertain Malignant Potential in a Perforated Appendectomy Specimen. A Case Report

Gulgun Tahan[1], Irfan Koc[2], Umit Seza Tetikkurt[3], Osman Yucel[2]

1) Unit of Surgery, Marmara University Institute of Gastroenterology. 2) Department of General Surgery II.
3) Taksim Education and Research Hospital

Abstract

Mucinous tumors of uncertain malignant potential are rare; there are only occasional reports. We report the first case where the tumor was identified incidentally following resection of a perforated appendicitis. There was no previous history to suggest for a mucinous tumor. No other abnormalities were found at surgery. Treatment included right hemicolectomy, considering the risk of residual or metastatic disease of about 10%. The patient is alive and well twelve months after resection of the tumor.

Key words

Appendix - mucinous tumor

Introduction

Fewer than 1% of all patients with suspected appendicitis are found to have an association with a malignant process (1,2). Generally the diagnosis is made at the time of appendectomy or at pathological examination. Even less commonly, acute appendicitis may be the first presentation of a cecal neoplasm (3,4).

The classification of appendiceal mucinous tumors is controversial and terminology is inconsistent, particularly when a mucinous tumor lacks overtly malignant features but is associated with extra-appendiceal spread. Morphologically, identical tumors that are associated with appendiceal rupture and peritoneal seeding have been designated as ruptured adenomas. The presence of invasion is required for the diagnosis of adenocarcinoma (5). It is appropriate to use the term mucinous tumor of uncertain malignant potential (UMP) for neoplasms in which the histological features do not allow distinction between a lesion that is benign from the one that has the potential to cause metastases (6). There is loss of the normal complement of lymphoid tissue in the wall adjacent to the neoplastic epithelium accompanied by fibrosis of submucosa and muscularis propria. The appendix may be transformed into a cystic structure composed of a thin fibrous wall lined by neoplastic mucinous epithelium. It is difficult to exclude invasion in these cases and it is useful to designate the lesion as "a mucinous tumor of uncertain malignant poten-tial". Calcification in the fibrous wall may also occur (7). Because of a different therapeutic management, confirming the diagnosis of mucinous tumor of UMP is important.

We present a case of mucinous appendix tumor with uncertain malignant potential. Clinical and morphological features are discussed.

J Gastrointestin Liver Dis
June 2007 Vol.16 No 2, 197-200
Address for correspondence: Dr. Gulgun Tahan
Cavusdere Cad.
Huzur Camii Sokak
Akman Apt. No:1/1 D: 9
Uskudar 34672, Istanbul, Turkey
E-mail: veytahan@yahoo.com

Case report

A 42-year-old man presented with a 2-day history of right lower quadrant abdominal pain, fever, and nausea. Laboratory studies revealed Hb 13.3 g/dl, Hct 42.3%, leukocyte 15,400/mm^3, platelet count 270,000/mm^3. At radiological examination, small bowel gas patterns were seen in the right lower quadrant. On ultrasonographic examination, the appendix was not clearly identified but there was diffuse intraperitoneal free fluid. The presumed diagnosis was acute appendicitis and an open appendectomy was performed. The appendix was found to be perforated into the abdominal cavity. There was also diffuse seropurulent fluid throughout the abdomen and localized mucinous fluid around the periappendicular region. Cytological examination of the mucinous fluid was performed. The incision was widened and following intraabdominal mechanical cleaning, appendectomy was performed but due to the fragile nature of the ruptured appendiceal tissue, the specimen was not intact. The postoperative cause was uneventful.

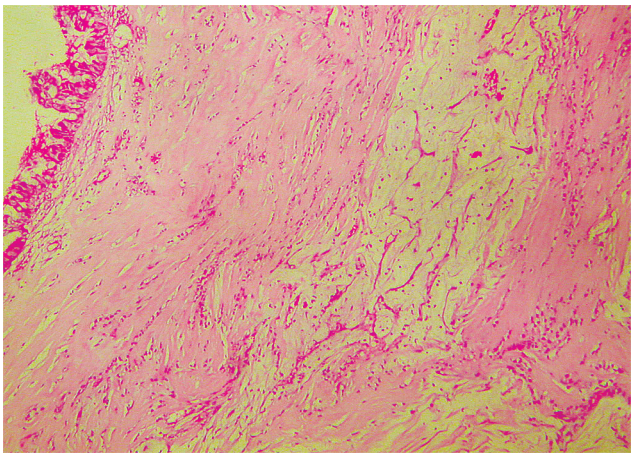

Fig.1 Villous projections are covered by a single layer of mucus rich columnar cells on a surface of mucinous neoplastic epithelium. Muscularis mucosa is not intact and lymphoid tissue is absent. Mural hyalinization and mucin extravasation are prominent (HE, x40).

The appendix had a cystic appearance on gross examination. The specimen was in multiple pieces with the greatest measuring 5x3x1 cm. The appendiceal diameter was 2.1 cm. The wall was thick, fibrotic and had a granular mucoid lining. Mucin exudated from the rupture site of the appendix. Microscopic examination showed circumferential replacement of the normal appendiceal epithelium by proliferative mucinous epithelium. The tumor had a single layer of neoplastic mucinous cells with occasional small epithelial tufts overlying a fibrotic and atrophic lamina propria and submucosa. Villous projections were covered by a single layer of mucus rich columnar cells on a surface of mucinous neoplastic epithelium. The nuclei of the neoplastic cells were typically elongated, hyperchromatic and lacked prominent nucleoli. Mitotic figures were scarce and usually limited to basal regions. Diffuse acellular mucin pools were present on the appendiceal serosa. The muscularis mucosa was not intact and lymphoid tissue was absent. Mural hyalinization and mucin extravasation were prominent (Fig.1).

The abdominal ultrasonographic findings on the 15th postoperative day were normal. Carcinoembryonic antigen (CEA) and alpha fetoprotein values were within normal limits. The colonoscopy performed at the end of the first postoperative month, was normal. Since the diagnosis of mucinous tumor of UMP was established, right hemicolectomy, end-to-end ileocolostomy and partial distal omentectomy were performed. Mucinous material was not found around the appendiceal stump or in other parts of the abdomen at the time of the operation. No other abdominal pathological findings were noted. Ascending colon, cecum and omentum specimens were evaluated. Reactive changes were noted in all of 13 lymph nodes found in mesentery with the largest being 1 cm in diameter. A residual mucinous tumor was detected in the stump of the appendix, but the remainder of the colon was free of any pathological changes. Chronic inflammation together with acellular mucinous fluid was found in the omentum and mesentery biopsies. The patient has been followed for 12 months, and is doing well.

Discussion

If during conventional appendectomy a significant mass is palpated in the cecum and the appendix, the surgical approach may need to be modified. However if such a tumor is detected in the pathologic specimens only, a second approach is required.

Appendiceal adenomas, which include cystic mucinous adenomas, generally are villous adenomas and they are seen rarely, except in the cases of familial adenomatous polyposis. Adenomas generally are encountered coincidentally. Appendiceal and colonic adenomas share similar characteristics and development stages. Appendiceal cystic adenomas are frequently found together with colorectal adenomas and adenocarcinomas (8).

Mucinous neoplasia of the appendix was formerly defined as mucocele, however today this terminology is used only for a dilated appendix with mucin. Mucocele is seen in 0.3% of appendectomies (9). In earlier classifications of appendiceal neoplasms, high grade appendiceal mucinous tumors were designated as “malignant mucoceles” or “grade 1 noninvasive, papillary adenocarcinoma of the appendix”, which unlike colonic types of adenocarcinoma, occasionally spread as pseudomyxoma peritonei (5). Later, these lesions were reclassified as benign neoplasms and the term cystadenoma was applied to denote their resemblance to colonic adenomas and to reflect their low grade cytologic features, lack of destructive invasion and benign clinical course. Adenoma can be diagnosed in the presence of mucin within the wall, if the muscularis mucosa is intact. Some authors proposed an intermediate category of mucinous borderline tumor of the appendix to reflect the uncertain biologic behavior of these lesions as well as their morphologic similarities to mucinous tumors of the ovary (5). The “borderline” terminology is best not applied to the appendix as it may suggest a similar favorable prognosis to that seen in the ovary. Finally, some authors have proposed the term “appendiceal mucinous neoplasm of uncertain malignant potential”, to describe mucinous tumors that break through the muscularis mucosa (5). It may be suitable for any mucinous tumor of the appendix that shows low grade epithelial tongues pushing deeply into the underlying tissue on a broad front but without infiltrative invasion or desmoplasia. Alternatively, the designation “low grade mucinous cystic tumor” or “low grade appendiceal mucinous neoplasm” has been suggested. This terminology is suitable for any such neoplasm that is not frankly malignant histologically (5,7,10).

When a mucinous tumor of UMP is detected in an appendectomy specimen, right hemicolectomy can be suggested considering the risk of 10% of residual disease and metastases (8). Hesketh suggested right hemicolectomy to appendectomy alone, and traditionally epithelial malignancies of the appendix have been treated by right hemicolectomy to steer clear of peritoneal spreading (11).

In a recent prospective study, Gonzalez-Moreno and Sugarbaker revealed their data on 501 patients with epithelial malignancy of the appendix. The patients’ median follow-

up was 4 years. Two surgical procedures were evaluated and a right hemicolectomy did not confer a survival advantage to appendectomy alone. Even in univariate analysis a survival advantage was shown for the patients treated by appendectomy alone compared with those who underwent right hemicolectomy. It was hypothesized that patients more likely to be harmed by right hemicolectomy were those in whom tumor cell entrapment was possible within the right hemicolectomy site (12).

There is little consensus on whether pseudomyxoma peritonei should be classified as malignant or not, and on the point of separation between pseudomyxoma peritonei and carcinomatosis peritonei due to high-grade mucinous carcinoma. The treatment for pseudomyxoma peritonei remains controversial with continually evolving surgical procedures. Recently, Bryant et al. evaluated a cohort of 1,000 treated pseuomyxoma peritonei patients in a systematic review and economic evaluation to examine the clinical effectiveness and cost of the Sugarbaker procedure (13) for treating pseudomyxoma peritonei in the UK up to April 2004. Survival after operation was approximately 95% at 2 years and 60-68% at 10 years, with 41-52% of patients having no evidence of disease at the end of follow-up. The marginal cost for one patient over a maximum of 5 years was about £ 9,700. They found evidence for the effectiveness of the Sugarbaker procedure is limited in quantity and quality, but suggests partial benefit for the patients (14).

Taking these data together a right hemicolectomy should be only performed if it is necessary to clear the primary tumor or achieve complete cytoreduction or appendiceal or ileocolic lymph node involvement is demonstrated or if a non-mucinous histological type is identified by histo-pathological examination (12). In accordance with better understanding with recent data in the literature, an appendectomy first was applied in one case. However, the surgery was extended to right hemicolectomy to clear the residual primary tumor for complete cytoreduction.

Surgical resection alone has been demonstrated to be ineffective for the treatment of peritoneal implant and pseudomyxoma peritonei. Cytoreductive surgery and intraperitoneal hyperthermic chemotherapy have been reported as anecdotally efficacious in patients with disseminated mucinous tumors of the appendix. Hyperthermic chemotherapy can extend survival for only selected patients with peritoneal implant and pseudomyxoma peritonei (15-17).

In the present case, no postoperative chemotherapy or hyperthermic chemotherapy were performed because of curable surgery without node metastasis (9). No signs of recurrence have been observed for 12 months since the last operation.

Follow-up colonoscopy and pelvic examination are also warranted for the high association with another colon malignancy (18). Recently, the use of CEA and carbohydrate antigen 19-9 (CA 19-9) tumor markers were shown to have practical value in the management and follow-up of patients with mucinous appendiceal malignancy (19).

This case is a rare observation of a mucinous tumor of UMP. Neoplasia should be considered in the differential diagnosis of appendicitis even if they are not suspected preoperatively or during the operation, since they may only be found during pathological examination. When a mucinous tumor of UMP has been evidenced into an appendectomy specimen, a wider resection, as right hemicolectomy may be a more appropriate surgical procedure with the right indications.

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