CLINICAL VIGNETTE

A 31-Year-Old Male with Mucinous Adenocarcinoma of the Appendix

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Case Presentation

A 31-year-old male presented with intermittent RLQ abdominal discomfort and bulging sensation for 3 months. He denied systemic symptoms and had an unremarkable physical exam. Laboratory testing including CBC and CMP were normal. Ultrasound (US) was negative for hernia. One year later he re-presented with right upper quadrant pain. RUQ US showed gallstones and he was given the presumptive diagnosis of biliary colic and referred for laparoscopic cholecystectomy. Intraoperatively peritoneal metastatic implants were noted and cholecystectomy was aborted. Laparoscopy revealed a 4 cm appendiceal mass, diffuse omental and peritoneal metastatic implants and a single implant along the medial aspect of the gallbladder. There was little-to-no ascitic fluid. A peritoneal implant fragment and enlarged internal mammary lymph nodes were biopsied. He was referred for advanced imaging and tumor markers. CEA level was elevated at 21.5 ng/mL (≤3.0). CT chest, abdomen and pelvis confirmed an appendiceal tumor with metastasis to the liver and sigmoid colon, as well as enlarged right cardiophrenic and internal mammary lymph nodes.

Biopsy of the peritoneal implant revealed a moderately differentiated, low-grade mucinous adenocarcinoma with focal areas of architectural complexity and luminal necrosis. Histology was supportive of lower gastrointestinal or appendiceal primary. Biopsy was positive for CK20, CDX-2, and Ber/EP4 markers. Sanger sequencing was positive for KRAS mutation and FISH Her2 was negative for Her2 amplification. Biopsy of the right internal mammary lymph node revealed necrosis, but was otherwise unremarkable.

Due to the aggressive extensive adenocarcinoma with poor prognosis, goal of treatment was palliative systemic chemotherapy via PICC line. Hyperthermic intraperitoneal chemotherapy (HIPEC) was also considered, but due to high mortality and the enlarged right cardiophrenic lymph node, systemic chemo was favored. He was started on CAPEOX (capecitabine 1000 mg/m^2 on days 1-15 and oxaliplatin 130 mg/m^2 IV on day 1. The regimen was continued for 2 months but was complicated by diarrhea, enteritis, and hand-and-foot syndrome, and progression of disease. Regimen was switched to irinotecan and bevacizumab, which was for six cycles over three months. He sought a second opinion and underwent diagnostic laparoscopy, cytoreductive surgery (CRS) seven months after diagnosis. CRS included HIPEC with mitomycin-C, omentectomy, splenectomy, cholecystectomy, right diaphragm resection, right colon low anterior resection, diverting ileostomy, and peritonectomy. His post-operative course was complicated by focal perforation of the small intestine near the ileostomy site with peritonitis requiring exploratory surgery, cleaning, and creation of new ileostomy. He also developed high ileostomy output, requiring daily IVFs despite maximum fiber, imodium, and lomotil. Ostomy output decreased and the patient underwent ostomy reversal five months after creation.

Discussion

Mucinous appendiceal tumors are quite rare, with 1000-2000 annual cases in the United States.[1] These tumors have a slight female predominance and most commonly affect Caucasians between 50-70 years.[2] Our patient did not fit the typical demographic profile.

Patients are often asymptomatic or have vague symptoms, which is why these tumors are frequently diagnosed incidentally while undergoing evaluation or treatment for another condition. Due to the insidious nature of appendiceal adenocarcinoma, patients frequently have peritoneal dissemination at the time of diagnosis. Occasionally peritoneal dissemination results in pseudomyxoma peritonei (PMP), a clinical syndrome with diffuse mucinous peritoneal ascites due to dissemination of mucin-producing cells in the peritoneum.

Due to the rare incidence of mucinous appendiceal carcinomas, there is limited knowledge, and they are often treated as colorectal cancer.[3] Treatment is commonly surgical– CRS or appendectomy for localized lesions and more extensive surgical management for metastatic appendiceal mucinous neoplasms such as in our patient– followed by chemotherapy.[3] However, most chemotherapy drugs have little effect on these tumors, which show intrinsic resistance to cytotoxic drugs because of slow mitotic rates.[3] HIPEC may be considered an option, but has varying efficacy, though there is some evidence of reduced incidence of peritoneal metastasis.[4,5] Prognosis is related to the presence of KRAS mutations, with KRAS-mutated tumors having far worse prognosis than KRAS-wild-type tumors.[6]

Conclusion

Early diagnosis of appendiceal adenocarcinoma is challenging due to the insidious presentation of these tumors, and many have metastatic disease at the time of diagnosis.[1] Imaging

should be considered in patients who present with chronic nonspecific abdominal complaints. Although appendiceal adenocarcinomas are treated similarly to colorectal adenocarcinomas, they are distinct clinical entities and more studies are needed to further define optimal of treatment.

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