



Appendiceal Adenocarcinoma Presenting as Palpable Breast Masses

Muhammed Yaman Swied, MBBS¹, Yahia Al Turk, MD¹, and Michael Maitar, MD¹

¹Department of Medicine, Southern Illinois University School of Medicine, Springfield, IL

ABSTRACT

Appendiceal tumors are rare and are most commonly diagnosed incidentally during surgical removal of the appendix for acute appendicitis. Appendiceal adenocarcinomas are the most common appendiceal cancers, and their metastasis to the breast is extremely uncommon. We report a case of mucinous appendiceal adenocarcinoma presenting with breast metastasis. To the best of our knowledge, there has been only one case published in the literature about appendiceal cancer with metastasis to the breast. Interestingly, our patient's initial presentation was palpable breast masses rather than gastrointestinal symptoms.

KEYWORDS: appendiceal cancer; breast metastasis; mucinous adenocarcinoma

INTRODUCTION

Appendiceal tumors are rare, representing 0.5% of all gastrointestinal tumors.¹ Over the past years, the number of appendectomies performed in the United States has been steadily increasing, as has the incidence of appendiceal cancer.² Although appendiceal cancers are most commonly found incidentally at the time of appendectomy, they might be discovered incidentally during colonoscopy, as in our case.³ In more than 50% of cases, appendiceal cancers are asymptomatic and often detected incidentally.⁴ However, most symptomatic patients present with acute appendicitis because of appendiceal lumen obstruction.⁴ Although appendiceal cancers may be capable of distant metastasis, only one case of breast metastasis originating from a primary appendiceal cancer has been reported.⁵ We report a case of an appendiceal mucinous adenocarcinoma with metastasis to the breasts.

CASE REPORT

A 95-year-old woman presented to her primary care physician for evaluation of palpable bilateral breast masses. She underwent a diagnostic mammogram, which revealed a 4.1-cm mass at the 3 o'clock position in the left breast and a 2.4-cm mass at the 9 o'clock position in the right breast. Given that, she underwent an ultrasound-guided core needle biopsy. Immunohistochemical stains from the biopsy showed neoplastic cells positive for CDX2 and CK20 and negative for CK7, estrogen receptor, progesterone receptor, GATA3, PAX8, and TTF-1. This immunohistochemical profile (CDX2+, CK20+, and CK7-) suggested the diagnosis of metastatic invasive adenocarcinoma corroborative with coloappendiceal primary and excluded other primary sites, including ovarian mucinous adenocarcinoma, which is positive for CK7. In addition, the primary origin was likely appendiceal, given the extensive mucinous features seen on histopathological examination (Figure 1). Soon after her diagnosis of metastatic breast cancer, she presented to the emergency department because of one episode of dark red blood per rectum. Laboratory data showed a hemoglobin of 8.4 g/dL. Iron panel showed an iron level of 65, high ferritin of 1,866, low total iron binding capacity of 179, and percent saturation of 31.3, consistent with anemia of chronic disease. Chest, abdominal, and pelvic computed tomography (CT) scans showed bilateral breast masses with numerous pulmonary nodules throughout the lungs and a hypoenhancing lesion in the right hepatic lobe along with supraclavicular and mediastinal lymphadenopathy concerning for metastatic disease (Figure 2). Given the patient's history of chronic kidney disease, the appendix was not evaluated well on the CT scan because of the lack of intravenous contrast, and therefore, no appendiceal or colorectal pathology was seen on the CT scan. The patient eventually underwent a colonoscopy that showed an appendiceal orifice villous mass (Figure 3). Multiple biopsies with cold forceps were taken from the appendiceal mass for pathology. Esophagogastroduodenoscopy was also performed and showed a 2-cm hiatal

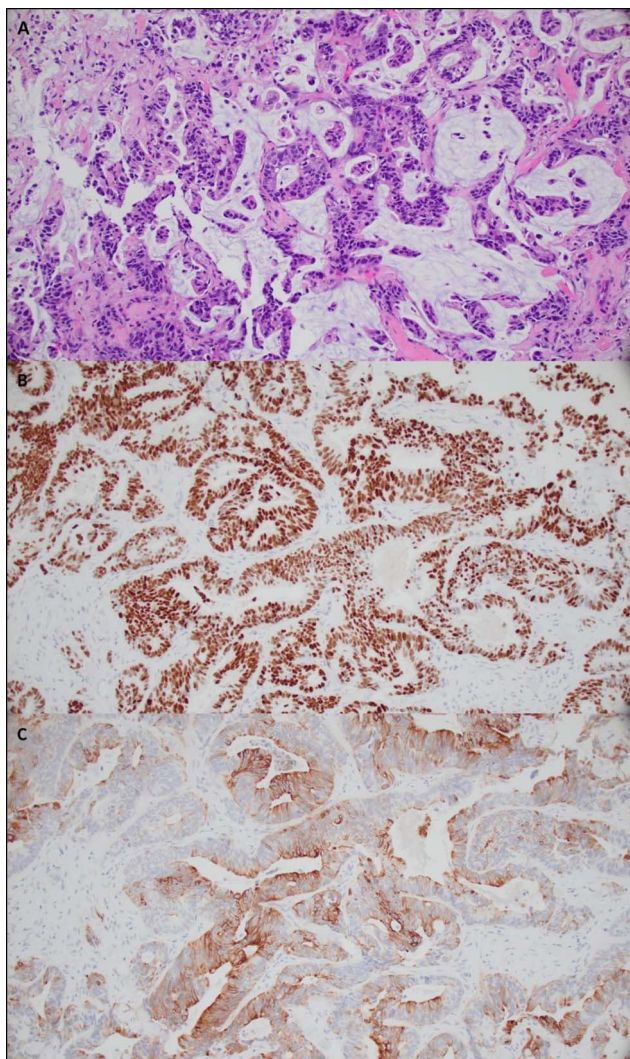


Figure 1. (A) Hematoxylin and eosin stain showing adenocarcinoma with enteric and mucinous features (20× magnification). Immunohistochemical stains showing neoplastic cells positive for CDX2 (B) and CK20 (C).

hernia and 5-mm benign nodule with reactive changes at the gastroesophageal junction. Immunohistochemical staining from the appendiceal mass biopsy supported the diagnosis of invasive mucinous adenocarcinoma (Figure 4). The patient and her family decided to proceed with hospice care and died peacefully one week later.

DISCUSSION

Appendiceal tumors can be divided based on their histology into 5 main subtypes: mucinous neoplasms, colonic-type nonmucinous adenocarcinoma, signet ring cell adenocarcinoma, goblet cell adenocarcinoma, and neuroendocrine tumors.⁴ Appendiceal mucinous tumors are rare, with approximately 3,500 cases diagnosed annually in the United States.⁶ Appendiceal mucinous neoplasms are classified based on the extent of mucosal involvement into mucinous adenomas, low-grade appendiceal

mucinous neoplasms, high-grade appendiceal mucinous neoplasms, and mucinous adenocarcinoma.⁴

Appendiceal mucinous adenocarcinomas are the most common subtype of primary appendiceal adenocarcinomas, with an incidence rate of 37% of all appendiceal cancers.⁷ Mucinous adenocarcinomas are invasive glands with high-grade cytologic atypia and extracellular mucin that compromise more than 50% of the lesion's cross-sectional area.⁸ Like other types of appendiceal cancers, patients with mucinous appendiceal adenocarcinoma can present with nonspecific symptoms such as abdominal pain, right lower-quadrant pain, weight loss, fatigue, anorexia, fever, vomiting, and features of intestinal obstruction. Mucinous appendiceal adenocarcinoma can also present with anemia and lower gastrointestinal bleeding.⁹ In our case, the patient presented initially with palpable breast masses and presented later with one episode of blood per rectum. Although appendiceal cancers are often discovered incidentally during radiologic evaluation for unrelated complaints or in pathologic specimens after an appendectomy, they may be found incidentally on colonoscopy.³ In our case, the appendiceal orifice mass was found on colonoscopy while searching for the source of breast adenocarcinoma and lower gastrointestinal bleeding.

Primary breast cancers are the most common cancers in females worldwide, but extramammary metastasis to the breasts is rare. Immunohistochemistry is essential to differentiate primary breast cancers from metastatic ones. Most breast adenocarcinomas are positive for CK7 and negative for CK20 and CDX2, whereas lower gastrointestinal tract adenocarcinomas are positive for CK20 and CDX2 and negative for CK7.^{10,11} In our case, immunohistochemical stains from the breast biopsies were positive for CK20 and CDX2 and negative for CK7. The endoscopic findings along with the histological features seen on the routine and specialized staining confirmed that the breast masses were metastatic from the appendix. Although there have been abundant case reports of colonic adenocarcinoma with breast metastasis in the literature, only one case of appendiceal adenocarcinoma with breast metastasis has been reported.⁵ Patients with metastatic colonic adenocarcinoma to the breasts have a poor prognosis and often require palliative care, so the management should be individualized according to the patient's functional status, comorbidities, and presence of metastasis in another site.^{12,13} Similarly, in our case of metastatic appendiceal adenocarcinoma to the breasts, the patient had a poor prognosis and was not a candidate for treatment because of her poor functional status, multiple comorbidities, and the presence of metastasis.

Appendiceal cancer can spread to other parts of the abdomen directly from the appendix, typically when it ruptures. The most common way for appendiceal cancers to spread inside the abdomen is through the peritoneal cavity, resulting in significant mucinous dissemination and peritoneal metastases.¹⁴ Less frequently, appendiceal cancer can metastasize

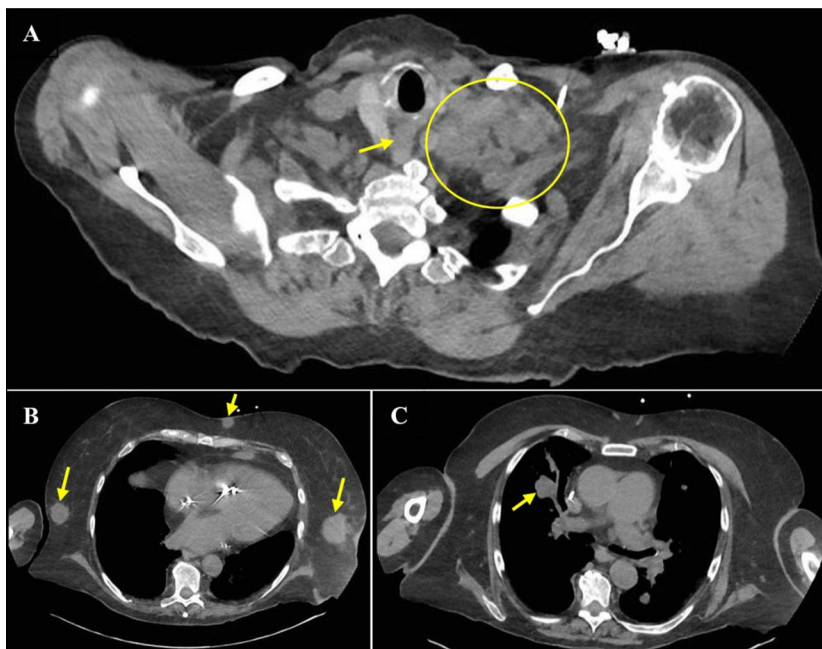


Figure 2. (A) Axial section of the chest CT showing mediastinal (yellow arrow) and left supraclavicular lymphadenopathy (yellow circle). (B) Axial section of the chest CT showing bilateral breast masses (yellow arrows). (C) Axial section of the chest CT showing numerous pulmonary nodules throughout the lungs, with the largest measuring 2.6 cm (yellow arrow). CT, computed tomography.

outside the peritoneal cavity to distal sites, including regional lymph nodes, liver, lung, brain, and bone.^{14,15}

In conclusion, we report a case of breast masses secondary to appendiceal adenocarcinoma. Our case highlights the importance of considering the possibility of metastatic disease in patients presenting with breast masses. Appendiceal adenocarcinoma should be considered in the differential diagnosis of metastatic breast cancer, particularly in patients with gastrointestinal symptoms or histology suggestive of gastrointestinal origin. Accurate diagnosis is essential for appropriate management and improved patient outcomes.

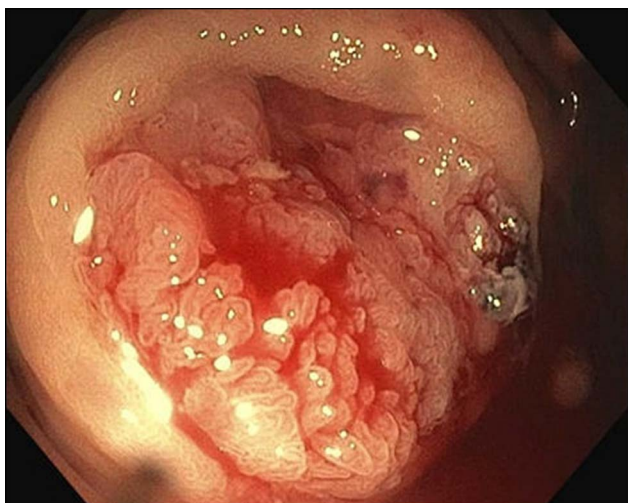


Figure 3. Bulging villous mass occupying and protruding from the appendiceal orifice.

DISCLOSURES

Author contributions: MY Swied was involved in the care of the patient, wrote the first draft of the manuscript, and wrote the final version after receiving input from the other authors. Y. Al Turk was involved in the care of the patient and reviewed and edited the first draft of the manuscript. M. Maitar performed diagnostic esophagogastroduodenoscopy and colonoscopy on the patient, provided pictures and captions of colonoscopy images, and approved the final draft of the manuscript. Y. Al Turk is the article guarantor.

Financial disclosure: None to report.

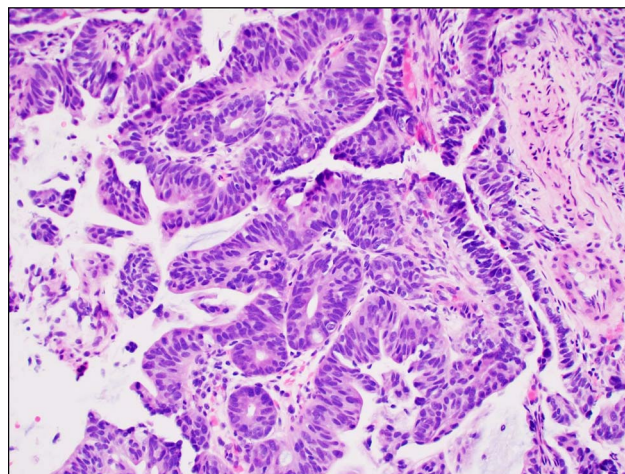


Figure 4. Hematoxylin and eosin stain showing appendiceal adenocarcinoma with mucinous features (20× magnification).

Previous presentation: This case has been presented at the American College of Gastroenterology Annual Scientific Meeting; October 20-25, 2023; Vancouver, Canada.

Informed consent could not be obtained for this case report. All identifying information has been removed from this case report to protect patient privacy.

Received February 11, 2024; Accepted May 7, 2024

REFERENCES

- Köhler F, Matthes N, Rosenfeldt M, Kunzmann V, Germer CT, Wiegering A. Neoplasms of the appendix. *Dtsch Arztebl Int* 2023;120(31-32):519–25.
- van den Heuvel MG, Lemmens VE, Verhoeven RH, de Hingh IH. The incidence of mucinous appendiceal malignancies: A population-based study. *Int J Colorectal Dis* 2013;28(9):1307–10.
- Kozacek K, Reese R, Laczek J, Voorhees P. Taking caution at road's end: Incidental finding of appendiceal goblet cell tumor on colonoscopy. *ACG Case Rep J* 2023;10(11):e01211.
- Osueni A, Chowdhury YS. Appendix cancer. In: *StatPearls*. StatPearls Publishing: Treasure Island (FL), 2023.
- Davies T, Chouari T, Ray C, Elgammal S. Appendiceal adenocarcinoma with breast metastases. *BMJ Case Rep* 2021;14(5):e240808.
- Choudry HA, Pai RK. Management of mucinous appendiceal tumors. *Ann Surg Oncol* 2018;25(8):2135–44.
- Roma K, Baldwin M, Sedmak D, Silva M, Stellar W, Many G. Late stage diagnosis of mucinous adenocarcinoma of the appendix: A case report of an unusual tumor with a rare presentation. *BMC Gastroenterol* 2020;20(1):281.
- Nagtegaal ID, Odze RD, Klimstra D, et al. The 2019 WHO classification of tumours of the digestive system. *Histopathology* 2020;76(2):182–8.
- Soto Llanes JO, Dosal Limón SK, Iberri Jaime AJ, Zambrano Lara M, Jiménez Bobadilla B. Lower gastrointestinal bleeding secondary to appendiceal mucinous neoplasm: A report of two cases and a review of the literature. *Cureus* 2024;16(1):e52908.
- Arnaut K, Hawa N, Agha S, Kadoura L, Aloulou M, Ayoub K. A case report of multiple bilateral breast metastases after colorectal cancer. *Int J Surg Case Rep* 2021;81:105759.
- Fleming M, Ravula S, Tatishchev SF, Wang HL. Colorectal carcinoma: Pathologic aspects. *J Gastrointest Oncol* 2012;3(3):153–73.
- Hsieh TC, Hsu CW. Breast metastasis from colorectal cancer treated by multimodal therapy: Case report and literature review. *Medicine (Baltimore)* 2019;98(51):e18016.
- Taccogna S, Gozzi E, Rossi L, et al. Colorectal cancer metastatic to the breast: A case report. *World J Gastrointest Oncol* 2020;12(9):1073–9.
- Hoehn RS, Rieser CJ, Choudry MH, Melnitchouk N, Hechtman J, Bahary N. Current management of appendiceal neoplasms. *Am Soc Clin Oncol Educ Book* 2021;41:1–15.
- Minhas A, Hendrickson J, Minhas SA. Frequency and risk factors for metastasis in newly diagnosed appendiceal carcinoma. *Cureus* 2021;13(7):e16341.

Copyright: © 2024 The Author(s). Published by Wolters Kluwer Health, Inc. on behalf of The American College of Gastroenterology. This is an open access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.