

An Unexpected Destination of Breast Cancer: Appendiceal Metastasis

Meme Kanserinin Beklenmedik İstasyonu: Appendiks Metastazı

İ Zülfi Zahidli¹, İ Burak Yavuz², İ Yunus Kaycı³, İ İshak Aydın⁴, İ İsmail Cem Yurtçu⁴, İ Gökberk Sevük⁴, İ Arbil Açıkalmı⁵, İ İsmail Cem Eray⁴

¹Hilvan Şehit Halit Şiltak State Hospital, Clinic of General Surgery, Şanlıurfa, Türkiye

²Koç University Hospital, Department of General Surgery, İstanbul, Türkiye

³University of Health Sciences Türkiye, Adana City Training and Research Hospital, Department of General Surgery, Division of Gastroenterological Surgery, Adana, Türkiye

⁴Çukurova University Faculty of Medicine, Department of General Surgery, Adana, Türkiye

⁵Çukurova University Faculty of Medicine, Department of Pathology, Adana, Türkiye

Abstract

Appendiceal metastasis from breast cancer is rare and most commonly encountered in patients with advanced-stage disease. Such metastases typically occur in the setting of intra-abdominal dissemination. Appendiceal involvement may remain clinically silent and may not present with specific symptoms. In cases of asymptomatic appendiceal enlargement, a primary appendiceal tumor is often suspected, which may impede consideration of metastatic lesions, particularly those originating from breast cancer. However, some patients may present with gastrointestinal symptoms such as abdominal pain, nausea, and vomiting. The diagnosis is typically established using imaging modalities, including ultrasonography, computed tomography, and magnetic resonance imaging, in conjunction with histopathological confirmation by biopsy. Metastatic lesions should not be misinterpreted as primary appendiceal malignancies. Treatment strategies depend on the patient's overall condition, the extent of metastatic disease, and other clinical factors; they may include surgical intervention, chemotherapy, or targeted therapies. Overall, the prognosis of metastatic breast cancer remains poor. The treatability of appendiceal metastasis and the patient's overall health status are important factors influencing prognosis. In this report, we present the case of a 49-year-old woman diagnosed with estrogen receptor-positive and progesterone receptor-positive breast cancer who was evaluated for abdominal pain and subsequently found to have acute appendicitis secondary to metastatic breast carcinoma, and we review the relevant literature.

Keywords: Appendiceal metastasis, breast cancer, colon, ileum

Öz

Meme kanserinin appendiks metastazı, nadir görülen bir durumdur. Genellikle ileri evre meme kanseri olan hastalarda ortaya çıkar. Appendiks metastazı, genellikle karın içi yayılım sırasında gerçekleşir. Appendiks metastazı genellikle belirgin semptomlar göstermeyebilir. Asemptomatik appendiks büyümesinde genellikle birincil apendiks tümörü olduğunda şüphelenilir ve bu da metastatik tümörlerden, özellikle de meme kanserinden kaynaklanan metastazlardan şüphelenmeyi zorlaştırır. Ancak bazı hastalarda karın ağrısı, bulantı, kusma veya sindirim problemleri gibi belirtiler ortaya çıkabilir. Tanı genellikle görüntüleme yöntemleri (ultrason, bilgisayarlı tomografi, manyetik rezonans görüntüleme) ve biyopsi ile konur. Metastatik lezyonlar, primer appendiks kanseri ile karıştırılmamalıdır. Tedavi, hastanın genel durumu, metastazın yaygınlığı ve diğer faktörlere bağlıdır. Cerrahi müdahale, kemoterapi veya hedefe yönelik tedaviler içerebilir. Genel olarak, metastatik meme kanseri prognozu daha kötüdür. Appendiks metastazının tedavi edilebilirliği ve hastanın genel sağlık durumu, prognozu etkileyen önemli faktörlerdir. Bu olguda östrojen reseptörü ve progesteron reseptörü pozitif, meme kanseri tanısı almış 49 yaşındaki bir kadın hastanın karın ağrısı nedeniyle değerlendirildiği ve sonrasında meme karsinom metastazlarına bağlı akut apandisit olan vakayı ve ilgili literatürün bir incelemesini sunuyoruz.

Anahtar Kelimeler: Apandiks metastazı, meme kanseri, kolon, ileum



Address for Correspondence: Yunus Kaycı, MD, University of Health Sciences Türkiye, Adana City Training and Research Hospital, Department of General Surgery, Division of Gastroenterological Surgery, Adana, Türkiye

E-mail: ykayci@hotmail.com **ORCID ID:** orcid.org/0000-0001-8502-4367

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Introduction

Breast cancer is the most common malignancy among women worldwide, accounting for approximately 25% of all cancer cases, with an estimated 2.3 million new diagnoses annually (1). The reported five-year survival rate for breast cancer reached 92% during the 2013-2017 period, representing a substantial improvement compared with the 76% rate reported for 1988-1992. This progress largely reflects earlier detection through effective screening programs, as well as advances in surgical, radiological, and systemic treatment strategies (2). The most common metastatic sites of primary breast cancer include regional lymph nodes, bone, liver, lung, brain, and skin (3). Appendiceal tumors are often detected incidentally during radiological examinations or abdominal surgery, most commonly initiated for tumor-related acute appendicitis.

Case Presentation

A 49-year-old woman presented to the emergency department with a one-day history of abdominal pain. Her medical history revealed that she had undergone a left modified radical mastectomy in 2014 for invasive lobular carcinoma (ILC) of the breast. Immunohistochemical analysis demonstrated estrogen receptor (ER) positivity in 80% of tumor cells, progesterone receptor positivity in 40% of tumor cells, HER2 (c-erbB2) negativity, and a Ki-67 proliferation index of 5%. Following surgery, the patient received chemotherapy and attended regular breast cancer follow-up visits; however, she had discontinued routine follow-up approximately one year prior to presentation. Physical examination revealed diffuse abdominal pain with more pronounced tenderness in the right lower quadrant, accompanied by guarding, abdominal rigidity, and rebound tenderness. Contrast-enhanced computed tomography (CT) showed areas of air-fluid levels and inflammatory changes in the mesenteric fat consistent with possible peritonitis, along with increased appendiceal wall thickness. These findings were interpreted as indicating possible appendicitis secondary to colonic inflammation (Figure 1). Preoperative laboratory investigations demonstrated elevated tumor markers, with a CA-125 level of 45.3 U/mL and a CA 15-3 level of 32.7 U/mL. In addition, inflammatory and biochemical parameters were elevated, including C-reactive protein at 30.7 mg/L and total bilirubin at 1.36 mg/dL.

Written informed consent was obtained from the patient for publication of this case report and accompanying images.

The patient was taken for emergency surgery. Intraoperative exploration revealed widespread peritoneal implants. A perforation was identified at the site of tumor implantation in the appendix and was partially contained by the omentum. Adhesions were present within the bowel. Adhesiolysis and

appendectomy were performed, and multiple biopsies were obtained from the peritoneum. Postoperatively, the patient received antibiotic therapy and intravenous fluid replacement. Enteral nutrition was initiated on postoperative day 2, and the patient was discharged on postoperative day 4. Histopathological examination revealed metastases consistent with metastatic breast carcinoma involving the appendiceal wall (appendectomy specimen), small-bowel mesentery, peritoneum, and omentum (excisional biopsies). Immunohistochemical analysis demonstrated CK7 and GATA-3 positivity, ER positivity in 100% of tumor cells, CK20 negativity, and HER2 (c-erbB2)1+ positivity (Figure 2). For restaging purposes, an F-18 FDG positron emission tomography (PET)/CT scan was performed and showed focally low-to-moderate hypermetabolic lymph nodes in both cervical lymphatic chains (reactive?); right axillary lymph nodes with fatty hila and thin cortices without increased metabolic

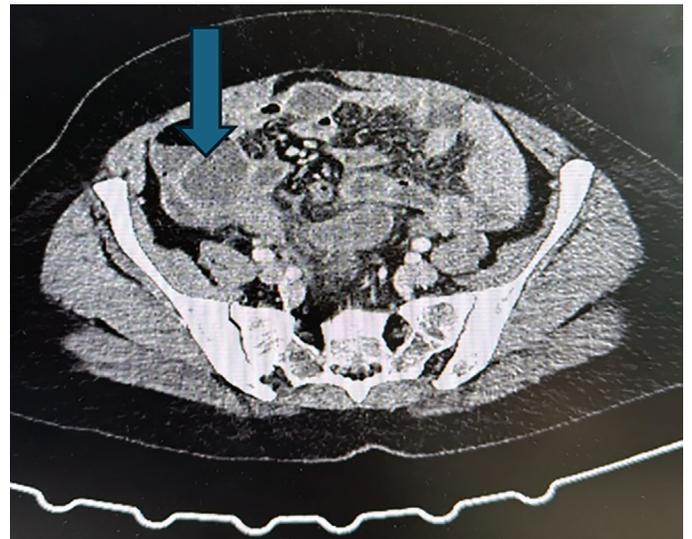


Figure 1. CT image demonstrating the appendix and surrounding tissues (900×512)

CT: Computed tomography

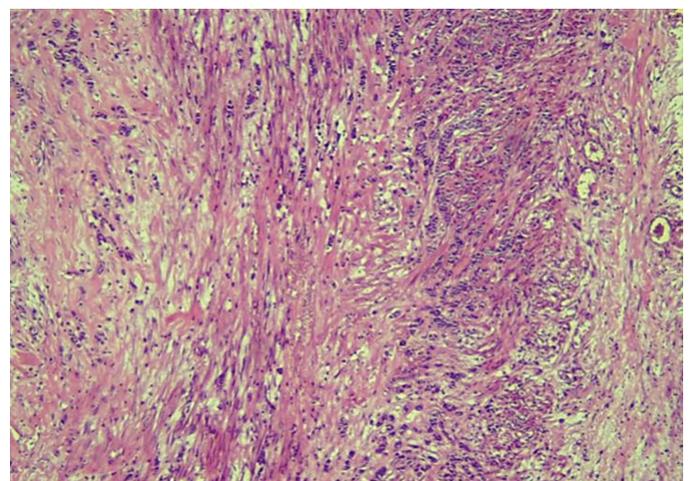


Figure 2. Tumor cells infiltrating the appendiceal wall

activity (reactive?); hepatomegaly; paraaortic and mesenteric lymph nodes without increased metabolic activity; and a fluid collection along the midline of the anterior abdominal wall, both infra- and supraumbilical, suggestive of postoperative changes. The patient was subsequently referred to the medical oncology department.

Discussion

The most common site of distant metastasis in breast cancer is the bone (3). Isolated metastasis to the appendix is rare, and most cases are presumed to result from peritoneal seeding. ILC demonstrates a distinct metastatic pattern compared with invasive ductal carcinoma, largely due to the loss of E-cadherin expression, a transmembrane adhesion molecule encoded by the *CDH1* gene. Loss of E-cadherin disrupts intercellular adhesion and promotes a discohesive growth pattern, allowing tumor cells to infiltrate tissues in a diffuse manner and disseminate more easily to distant sites. This molecular alteration is considered a key factor underlying the increased tendency of ILC to metastasize to the gastrointestinal tract (GIT), peritoneum, retroperitoneum, and gynecological organs (4). Previous studies have shown that the metastatic pattern of breast cancer is influenced by two major factors. The first is ER status, because ER-negative tumors are more likely to metastasize to the GIT. The second is histopathological subtype, with lobular carcinomas demonstrating a greater propensity for GIT metastasis (5,6). While ER-positive tumors typically show a predilection for bone metastasis, gastrointestinal and peritoneal metastases may still occur, particularly in ILC. Despite ER positivity, the biological behavior of lobular carcinoma, especially the loss of E-cadherin and its diffuse infiltrative growth pattern, facilitates dissemination to the peritoneal cavity and gastrointestinal organs. Therefore, ER positivity does not exclude the possibility of gastrointestinal metastasis, particularly in patients with lobular histology, as observed in the present case (7-9). ILC has a higher tendency to metastasize to the GIT, gynecological organs, peritoneum, and retroperitoneum, whereas ductal carcinoma more frequently spreads to the liver, lungs, and brain (10). ILC accounts for approximately 14% of all breast cancer cases (11). Our case involved peritoneal carcinomatosis and appendiceal metastasis arising in the setting of invasive lobular breast carcinoma, thereby supporting the majority of findings reported in the literature. Peritoneal involvement is thought to occur primarily through transcoelomic spread. Tumor cells with reduced intercellular adhesion may detach from the primary tumor or metastatic deposits and disseminate within the peritoneal cavity. These free tumor cells can subsequently implant on peritoneal surfaces, proliferate, and form metastatic nodules. In cases of peritoneal carcinomatosis, metastatic implants may directly involve adjacent intra-abdominal organs,

including the appendix (12). In 1946, Oldfield (8) reported the first case of metastatic breast cancer presenting as acute appendicitis (13). McLemore et al. (9) performed a retrospective analysis of histopathological findings from appendectomy specimens and emphasized the rarity of metastatic tumors involving the appendix. Among 7,970 analyzed specimens, 0.9% contained tumors, the most common of which were carcinoid tumors. Only 15% of all identified tumors were secondary malignancies, the majority of which were metastatic colorectal cancers (14). Yoon et al. (15) also reported 139 cases of secondary appendiceal tumors, with the ovary being the most common primary site (56 cases). According to a comprehensive literature review by Ng et al., (16) among 15 reported cases of breast cancer with appendiceal metastasis, appendiceal perforation occurred in seven cases. Histopathological evaluation revealed ductal carcinoma in 10 cases, lobular carcinoma in four cases, and an undifferentiated tumor in one case. Hormone receptor status was reported in only four cases, with ER positivity in three cases, progesterone receptor positivity in three cases, and HER2 positivity in two cases. Regarding treatment, nine patients were managed with appendectomy alone, while six underwent right hemicolectomy (16).

Appendiceal metastasis may occur through hematogenous spread, lymphatic dissemination, or peritoneal seeding. In the presence of peritoneal carcinomatosis, peritoneal implantation is considered the most likely mechanism. Tumor infiltration of the appendiceal wall may lead to luminal obstruction, impaired vascular supply, inflammation, and eventual perforation, clinically mimicking acute appendicitis, as observed in the present case (14).

Although current clinical findings are often non-specific, CT remains the gold standard for the diagnosis of appendiceal tumors (17). PET may be useful in the evaluation of stage IV patients without abdominal pain. Non-neoplastic perforated appendicitis and perforated appendiceal tumors are often difficult to distinguish from one another (18).

Conclusion

Metastasis of breast cancer to the GIT is rare, and appendicitis resulting from metastatic breast cancer is exceedingly uncommon. With advances in systemic therapies that have improved survival in patients with advanced-stage breast cancer, unusual sites of distant metastases have been increasingly recognized. The diagnosis of atypical metastatic sites is challenging and requires a combination of clinical, laboratory, and radiological findings for confirmation. Nevertheless, gastrointestinal involvement can be anticipated and observed, particularly in patients with a history of advanced (stage IV) breast cancer. Although appendicitis is primarily regarded as an inflammatory condition, oncologic

etiologies should be considered in patients with a known history of advanced breast cancer to ensure appropriate therapeutic decision-making. In most reported cases of appendicitis secondary to metastatic breast cancer, appendiceal perforation is observed. Treatment is generally managed by appendectomy, although right hemicolectomy may be required in selected cases. Early intervention in such patients helps prevent serious complications such as sepsis. While this management approach may not directly influence overall survival from the primary malignancy, multidisciplinary management may lead to improved clinical outcomes.

Ethics

Informed Consent: Written informed consent was obtained from the patient for publication of this case report and accompanying images.

Footnotes

Authorship Contributions

Concept/Design: Z.Z., Data Collection or Processing: Z.Z., Y.K., İ.A., G.S., Analysis or Interpretation: Z.Z., Y.K., İ.C.Y., A.A., İ.C.E., Literature Review: B.Y., Writing, Reviewing and Editing: Z.Z., B.Y., İ.C.E.

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