Schwannoma of the Appendix Mimicking a Metastatic Breast Cancer

A case report

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Abstract

Metastatic breast cancer (MBC) represents 5-10% of newly diagnosed breast cancer cases, referred to as de novo stage IV MBC. Distinguishing a distant lesion in breast cancer patients can be challenging. Therefore, obtaining a histopathological confirmation of a metastasis is advisable, as a suspicious metastatic lesion may turn out to be benign or exhibit different immunohistochemistry compared to the primary site. In this case, we describe a woman undergoing staging scans for newly diagnosed breast cancer, where radiological findings suggested appendix metastasis. However, subsequent laparoscopic appendicectomy revealed an appendicular schwannoma, confirmed through immunohistochemistry. The patient then received curative-intent breast cancer treatment. With the increasing use of advanced staging
scans in breast cancer, clinicians should thoroughly investigate and confirm metastatic disease, especially in uncommon metastatic sites, before initiating treatment.

Keywords: Schwannoma, metastasis, breast cancer, appendix.

Introduction

Metastatic breast cancer (MBC), also known as de novo stage IV MBC, represents 5-10% of newly diagnosed breast cancer (BC) cases in Western countries and 13% in Oman.\textsuperscript{1,2} Gastrointestinal (GI) tract metastases from BC are infrequent, reported in autopsy series with varying incidence (8-35%).\textsuperscript{3} Distinguishing distant lesions in breast cancer patients can be challenging,\textsuperscript{4} impacting treatment decisions reliant on disease stage.\textsuperscript{5} Hence, histopathological confirmation is advisable as suspicious metastatic lesions may prove benign or exhibit different immunohistochemistry compared to the primary site.\textsuperscript{6} This case report describes an appendicular schwannoma mimicking metastatic breast cancer. Schwannomas are the most common type of peripheral nerve tumors and can rarely affect the GI system, often being diagnosed incidentally. Diagnosis is confirmed through histopathology and immunohistochemistry. Total surgical excision is the recommended treatment for GI schwannoma.

Case Report:

A 55-year-old woman presented at a one-stop breast clinic with a one-month history of a left breast lump, with no other symptoms. The patient had a medical history of type 2 diabetes mellitus and hypertension, managed with regular medication, with no relevant family history. On examination, a 3 cm ill-defined, hard, mobile lump was noted in the upper outer quadrant of the left breast. Breast Ultrasonography revealed an irregular hypoechoic lesion measuring 2.9 x 1.7 cm in the left breast at 3 o'clock position, with microcalcifications within. Left axillary ultrasound indicated a suspicious lymph node measuring 6.6 mm. Mammogram showed asymmetric density in the left breast classified as BIRADS 5. True cut biopsy confirmed invasive Ductal carcinoma (IDC) with negative estrogen and progesterone receptors, positive HER2, and a Ki67 of 45%. Fine needle aspiration cytology from the left axillary lymph node was negative for metastasis.

During staging workup, Contrast-enhanced Computed Tomography (CE-CT) scans revealed two subserosal nodules in the appendix (figure 1. A-C) and prominent mesenteric lymph nodes in the right iliac fossa (figure 1. C). A Positron Emission Tomography scan (PET)
indicated a hypermetabolic left breast mass (SUV max 17.8) (figure 2. A&B) and suspicious metastatic lesion in the appendix (SUV max 21.5) (figure 2. C-D).

In a Multidisciplinary Meeting, consensus favored evaluating the appendicular lesion before initiating breast cancer treatment. Diagnostic colonoscopy showed no abnormality. Subsequently, the patient underwent laparoscopic appendectomy to determine the exact nature of the appendicular lesion.

Pathological examination revealed a well-demarcated tumor at the appendix tip, composed of spindle-shaped cells proliferating in a bundle from the muscularis externa (figure 3.a). The tumor displayed classic schwannoma features, including spindle cell morphology, nuclear palisading, and Verocay bodies (figure 3.b). Vascular invasion and lymph duct invasion were absent. Immunohistochemical studies confirmed S-100 protein positivity (figure 3.c) and negativity for CD117, DOG-1, CD34, SMA, Desmin, AE1/3, CAM5.2, B-Catenin, ALK-1, c-KIT and CD34(figure 3.d), confirming the appendicular schwannoma diagnosis.

Following the exclusion of metastatic disease, the patient commenced neoadjuvant chemotherapy based on anthracycline, taxane and dual Her2 blockades. Subsequent left breast image-guided wide local excision and sentinel lymph node biopsy revealed a pathological complete response (pCR). Adjuvant radiotherapy and 18 cycles of trastuzumab every 3 weeks were administered. The patient also received Alendronate and Calcium with Vitamin D for osteopenia, alongside regular medications. It's worth noting that the patient underwent comprehensive panel of gene testing, including NF1 and NF2, but no responsible gene was detected. The patient consent was obtained for publication purposes.

Discussion:
Metastatic breast cancer (MBC) represents 5-10% of newly diagnosed cases, referred to as de novo stage IV MBC. GI tract metastases from BC are rare, occurring in 8-35% of cases. Identifying distant lesions during staging scans in newly diagnosed breast cancer patients presents challenges, ascertaining whether these lesions represent distant metastases or primary lesions within the organ.

In our case, a staging contrast enhanced computed tomography (CE-CT) scan revealed an appendicular lesion confirmed as suspicious for metastasis on PET scan. However,
differential diagnoses include gastrointestinal stromal tumors (GISTs) and solitary
neuroendocrine tumors. Occasionally, lymphomas and GI adenocarcinomas may mimic
mesenchymal tumors.7

Fluorodeoxyglucose (FDG)-positron emission tomography is effective in detecting malignant
tumors. However, FDG accumulation has been noted in schwannomas,8 making it
challenging to differentiate them from distant metastases through imaging alone.
Furthermore, the discordance rates in biomarkers between primary tumors and metastatic
disease emphasize the importance of histopathological assessment. Studies have reported
hormone receptor discordance rates ranging from 30% to 40% and HER-2/neu discordance
rates ranging from 10% to 30%.9 These findings highlight the importance of histopathological
confirmation of suspicious appendicular lesions before starting treatment. This approach led
to the consideration of laparoscopic appendectomy, resulting in the diagnosis of appendicular
schwannoma., and the breast cancer was treated with curative intent.

Schwannoma is a rare mesenchymal tumor affecting the gastrointestinal tract, primarily
observed in the stomach and often diagnosed incidentally.10 Appendiceal schwannoma, an
exceptionally rare variant, has been documented in only 15 reported cases in the existing
literature, and definitive characteristic findings are yet to be established.11 Clinical
presentations vary, ranging from asymptomatic cases to appendicitis-like abdominal pain.
Notably, perforation is an exceedingly rare occurrence.12

On histology, schwannomas are typically composed of spindle cells that stain strongly
positive for S100 and focally for GFAP and CD57 on Immunohistochemistry. These findings
are sufficient to confirm the diagnosis in the absence of KIT positivity and smooth muscle
markers.10 While schwannoma andon GIST have similar histological findings in that they
both demonstrate a spindle-like proliferation, they have distinct immunohistochemistry
staining. Greater than 95% of GISTs express c-Kit (CD117), CD34 (70%), and H-caldesmon
(80%).10

Levy et al. described the radiological features of histopathologically proven schwannomas as
well-defined homogeneously attenuating mural masses on CT. They lack the poor prognostic
factors seen typically in gastrointestinal stromal tumors such as low attenuating haemorrhage,
necrosis, or degradation within the tumor.13 Furthermore, Suzuki et al highlighted the
radiological findings of peritumoral lymph node swelling as a potential differentiator for
Schwannoma compared to other appendicular tumors, serving as a valuable diagnostic clue.
This lymphadenopathy may be linked to cytokine release from tumor cells, inducing
chemokinesis of lymphocytes. Coincidentally, our radiological findings align with known
patterns as described by Suzuki et al. Nonetheless, additional research on the diagnostic
characteristics of schwannoma is warranted.

For confirmed gastrointestinal schwannomas, complete surgical excision is the recommended
approach, while partial excision may be considered for large tumors posing a risk of nerve
damage. It is noteworthy that even with partial excision, the occurrence of malignant
transformation remains extremely rare.

**Conclusion**

Our case highlights the importance of maintaining a broad spectrum of differential diagnoses
and obtaining histopathological confirmation when identifying lesions during staging scans in
patients with breast cancer. This approach not only confirms the diagnosis but also ascertain
immunophenotypes to enable the selection of the most suitable subsequent therapy.

**Author Contributions**

ZA, AA-S, BSA, FA and JZM contributed to writing the initial draft of the manuscript and
critical review. KAB and AA contributed to the critical review All authors approved the final
version of the manuscript.

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Figure 1 (A-C): Selected contract enhanced CT images of the abdomen showing contract filled appendix with two eccentric nodular wall thickening. The thick blue arrow is pointing to the largest one. There are prominent adjacent regional mesenteric lymph nodes (blue stars).

Figure 2: FDG-18 PET-CT scan, showing the primary left breast cancer (A & B), SUVmax 17.8 (white arrow) with an FDG avid left appendix mass (C & D), SUVmax 21.5 (blue arrow).
Figure 3 (A-D): Pathological findings in Hemotoxylin and Eosin staining showing spindle-shaped heterotypic cells proliferating in a bundle (A). Tumor showed features of a schwannoma including spindle cell morphology, nuclear palisading and Verocay bodies (B). In immunohistochemical studies, tumor cells were diffusely positive S-100 protein (C) and were negative for CD117 (D).