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7 Schwannoma of the Appendix Mimicking a Metastatic Breast Cancer

8 *A case report*

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18 **Abstract**

19 Metastatic breast cancer (MBC) represents 5-10% of newly diagnosed breast cancer cases,
20 referred to as de novo stage IV MBC. Distinguishing a distant lesion in breast cancer patients
21 can be challenging. Therefore, obtaining a histopathological confirmation of a metastasis is
22 advisable, as a suspicious metastatic lesion may turn out to be benign or exhibit different
23 immunohistochemistry compared to the primary site. In this case, we describe a woman
24 undergoing staging scans for newly diagnosed breast cancer, where radiological findings
25 suggested appendix metastasis. However, subsequent laparoscopic appendectomy revealed
26 an appendicular schwannoma, confirmed through immunohistochemistry. The patient then
27 received curative-intent breast cancer treatment. With the increasing use of advanced staging

28 scans in breast cancer, clinicians should thoroughly investigate and confirm metastatic
29 disease, especially in uncommon metastatic sites, before initiating treatment.

30 **Keywords:** Schwannoma, metastasis, breast cancer, appendix.

31

32 **Introduction**

33 Metastatic breast cancer (MBC), also known as de novo stage IV MBC, represents 5-10% of
34 newly diagnosed breast cancer (BC) cases in Western countries and 13% in Oman.^{1,2}

35 Gastrointestinal (GI) tract metastases from BC are infrequent, reported in autopsy series with
36 varying incidence (8-35%).³ Distinguishing distant lesions in breast cancer patients can be
37 challenging,⁴ impacting treatment decisions reliant on disease stage.⁵ Hence,
38 histopathological confirmation is advisable as suspicious metastatic lesions may prove benign
39 or exhibit different immunohistochemistry compared to the primary site.⁶ This case report
40 describes an appendicular schwannoma mimicking metastatic breast cancer. Schwannomas
41 are the most common type of peripheral nerve tumors and can rarely affect the GI system,
42 often being diagnosed incidentally. Diagnosis is confirmed through histopathology and
43 immunohistochemistry. Total surgical excision is the recommended treatment for GI
44 schwannoma.

45

46 **Case Report:**

47 A 55-year-old woman presented at a one-stop breast clinic with a one-month history of a left
48 breast lump, with no other symptoms. The patient had a medical history of type 2 diabetes
49 mellitus and hypertension, managed with regular medication, with no relevant family history.
50 On examination, a 3 cm ill-defined, hard, mobile lump was noted in the upper outer quadrant
51 of the left breast. Breast Ultrasonography revealed an irregular hypoechoic lesion measuring
52 2.9 x 1.7 cm in the left breast at 3 o'clock position, with microcalcifications within. Left
53 axillary ultrasound indicated a suspicious lymph node measuring 6.6 mm. Mammogram
54 showed asymmetric density in the left breast classified as BIRADS 5. True cut biopsy
55 confirmed invasive Ductal carcinoma (IDC) with negative estrogen and progesterone
56 receptors, positive HER2, and a Ki67 of 45%. Fine needle aspiration cytology from the left
57 axillary lymph node was negative for metastasis.

58

59 During staging workup, Contrast-enhanced Computed Tomography (CE-CT) scans revealed
60 two subserosal nodules in the appendix (figure 1. A-C) and prominent mesenteric lymph
61 nodes in the right iliac fossa (figure 1. C). A Positron Emission Tomography scan (PET)

62 indicated a hypermetabolic left breast mass (SUV max 17.8) (figure 2. A&B) and suspicious
63 metastatic lesion in the appendix (SUV max 21.5) (figure 2. C-D).

64

65 In a Multidisciplinary Meeting, consensus favored evaluating the appendicular lesion before
66 initiating breast cancer treatment. Diagnostic colonoscopy showed no abnormality.

67 Subsequently, the patient underwent laparoscopic appendectomy to determine the exact
68 nature of the appendicular lesion.

69

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

77

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

86

87 **Discussion:**

88 Metastatic breast cancer (MBC) represents 5-10% of newly diagnosed cases, referred to as de
89 novo stage IV MBC.¹ GI tract metastases from BC are rare, occurring in 8-35% of cases.³
90 Identifying distant lesions during staging scans in newly diagnosed breast cancer patients
91 presents challenges, ascertaining whether these lesions represent distant metastases or
92 primary lesions within the organ.

93

94 In our case, a staging contrast enhanced computed tomography (CE-CT) scan revealed an
95 appendicular lesion confirmed as suspicious for metastasis on PET scan. However,

96 differential diagnoses include gastrointestinal stromal tumors (GISTs) and solitary
97 neuroendocrine tumors. Occasionally, lymphomas and GI adenocarcinomas may mimic
98 mesenchymal tumors.⁷

99
100 Fluorodeoxyglucose (FDG)-positron emission tomography is effective in detecting malignant
101 tumors. However, FDG accumulation has been noted in schwannomas,⁸ making it
102 challenging to differentiate them from distant metastases through imaging alone.

103 Furthermore, the discordance rates in biomarkers between primary tumors and metastatic
104 disease emphasize the importance of histopathological assessment. Studies have reported
105 hormone receptor discordance rates ranging from 30% to 40% and HER-2/neu discordance
106 rates ranging from 10% to 30%.⁹ These findings highlight the importance of histopathological
107 confirmation of suspicious appendicular lesions before starting treatment. This approach led
108 to the consideration of laparoscopic appendectomy, resulting in the diagnosis of appendicular
109 schwannoma., and the breast cancer was treated with curative intent.

110
111 Schwannoma is a rare mesenchymal tumor affecting the gastrointestinal tract, primarily
112 observed in the stomach and often diagnosed incidentally.¹⁰ Appendiceal schwannoma, an
113 exceptionally rare variant, has been documented in only 15 reported cases in the existing
114 literature, and definitive characteristic findings are yet to be established.¹¹ Clinical
115 presentations vary, ranging from asymptomatic cases to appendicitis-like abdominal pain.
116 Notably, perforation is an exceedingly rare occurrence.¹²

117
118 On histology, schwannomas are typically composed of spindle cells that stain strongly
119 positive for S100 and focally for GFAP and CD57 on Immunohistochemistry. These findings
120 are sufficient to confirm the diagnosis in the absence of KIT positivity and smooth muscle
121 markers.¹⁰ While schwannoma and GIST have similar histological findings in that they
122 both demonstrate a spindle-like proliferation, they have distinct immunohistochemistry
123 staining. Greater than 95% of GISTs express c-Kit (CD117), CD34 (70%), and H-caldesmon
124 (80%).¹⁰

125
126 Levy et al. described the radiological features of histopathologically proven schwannomas as
127 well-defined homogeneously attenuating mural masses on CT. They lack the poor prognostic
128 factors seen typically in gastrointestinal stromal tumors such as low attenuating haemorrhage,
129 necrosis, or degradation within the tumor.¹³ Furthermore, Suzuki et al highlighted the

130 radiological findings of peritumoral lymph node swelling as a potential differentiator for
131 Schwannoma compared to other appendicular tumors, serving as a valuable diagnostic clue.
132 This lymphadenopathy may be linked to cytokine release from tumor cells, inducing
133 chemokinesis of lymphocytes.¹⁴ Coincidentally, our radiological findings align with known
134 patterns as described by Suzuki et al. Nonetheless, additional research on the diagnostic
135 characteristics of schwannoma is warranted.

136

137 For confirmed gastrointestinal schwannomas, complete surgical excision is the recommended
138 approach, while partial excision may be considered for large tumors posing a risk of nerve
139 damage. It is noteworthy that even with partial excision, the occurrence of malignant
140 transformation remains extremely rare.¹⁰

141

142 **Conclusion**

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

147

148 **Author Contributions**

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

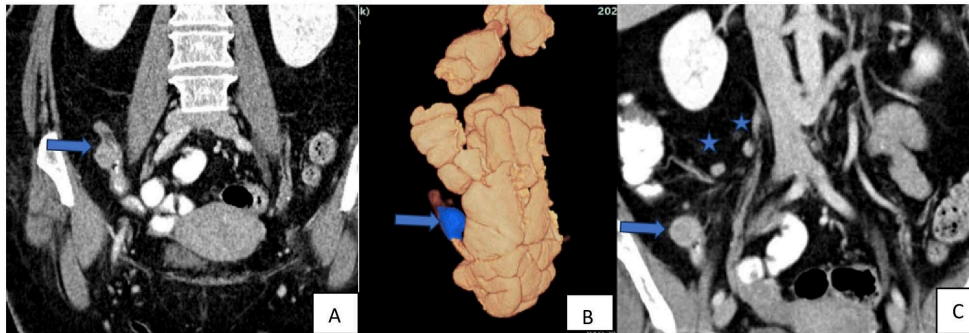
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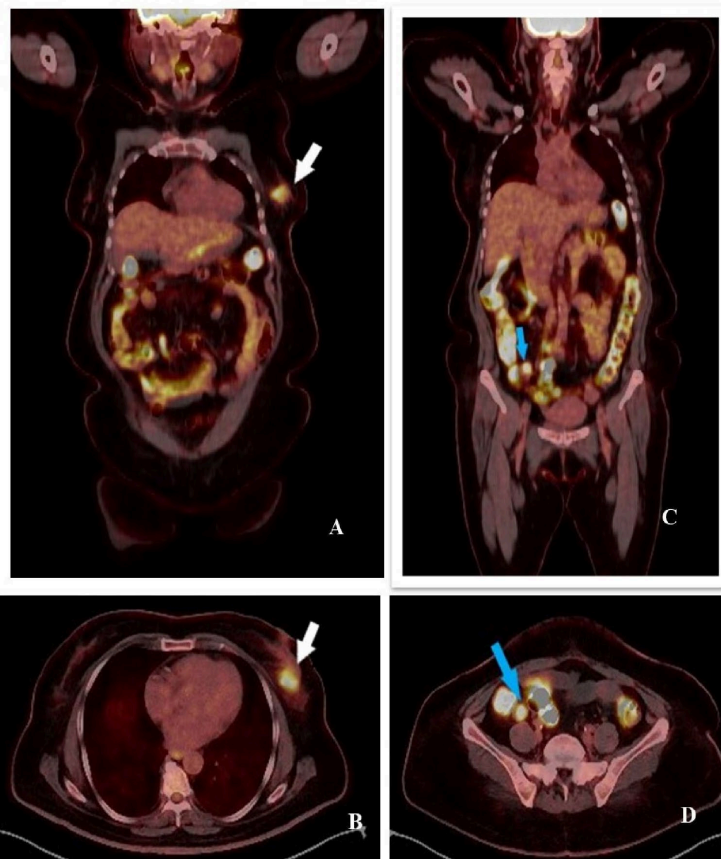
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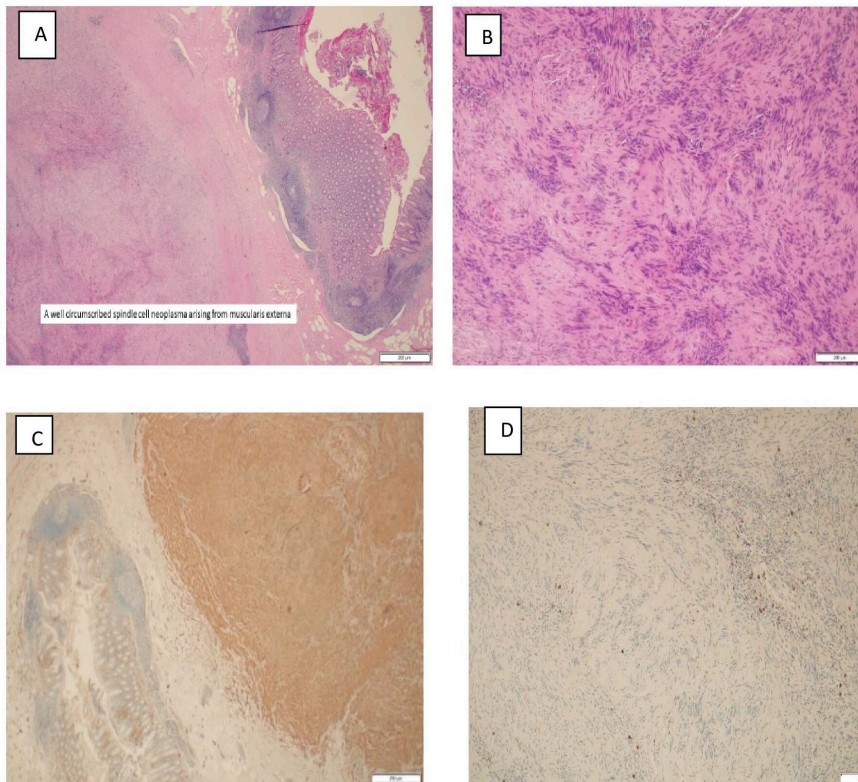
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Figure 1 (A-C): Selected contrast enhanced CT images of the abdomen showing contract filled appendix with two eccentric nodular wall thickening. The thick blue arrow is pointing to the largest one. There are prominent adjacent regional mesenteric lymph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



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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).



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Figure 3 (A-D): Pathological findings in Hematoxylin 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).