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Male Breast Metastasis from Esophageal Adenocarcinoma Diagnosed by FNAC - A Case Report with Literature Review

Running Title: Diagnosis of metastasis to the male breast on FNAC

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Abstract: ***Metastasis to the male breast from extra-mammary sources is exceedingly rare, with only a few cases reported in medical literature, particularly from esophageal carcinomas. This article presents the rare case of a 59-year-old male who developed a breast lump and cervical lymphadenopathy without axillary involvement or nipple changes. Fine Needle Aspiration Cytology (FNAC) of both sites revealed similar malignant features, raising suspicion for metastasis rather than primary breast cancer. Subsequent endoscopic biopsy confirmed esophageal adenocarcinoma. Immunohistochemistry further supported the diagnosis, highlighting the value of CK7 positivity and GATA3/CK20 negativity. This case underscores the importance of clinical history, comprehensive examination, and targeted immunocytochemistry in distinguishing metastatic lesions from primary malignancies, thereby preventing misdiagnosis and unnecessary treatments.***

Keywords: Male breast metastasis, FNAC, Esophageal adenocarcinoma, Cytodiagnosis, Immunohistochemistry

1. Introduction

Metastasis to the breast from the extra-mammary origin is rare, accounting for only 1.7% to 6.6% [(1)]. Non-epithelial malignancies that metastasise to the breast are non-Hodgkin lymphoma and melanoma. In contrast, epithelial malignancies include contralateral breast cancer, renal cell carcinoma, ovarian malignancy, thyroid malignancy, and carcinoid tumour from the small intestine. Among all described sites, metastasis from the contralateral breast is the most common. Among sarcomas, alveolar rhabdomyosarcomas can metastasise to the breast [(2)]. Metastasis to the breast in males from extra-mammalian sites is very rare; primary malignancies that can metastasise to the breast in males include prostate, lung, stomach, colorectal cancer, melanoma, and sarcoma[(3)]. Only four female breast metastases (4 squamous cell carcinomas) and three male breast metastases (2 squamous cell carcinomas and one adenocarcinoma) from esophageal primary have been reported in the literature. This case report aims to present a rare instance of metastatic esophageal adenocarcinoma presenting as a male breast lump, highlighting the diagnostic importance of FNAC and immunocytochemistry in differentiating primary from secondary breast malignancies.

2. Case Report

A 59-year-old gentleman initially evaluated outside for a left breast lump with a trust biopsy being reported as triple negative invasive breast carcinoma, with Immunohistochemistry of ER, PR, and HER2 Neu being negative, was referred to our institution for further evaluation. The patient was referred from the surgery OPD to the FNAC clinic with a firm to hard eccentric (inferno-outer quadrant) mobile lump measuring 3 x 2 cm in the left breast for the past month. It was not associated with pain or nipple discharge/ ulceration. On clinical examination, no axillary nodes were palpable. However, the patient had palpable (2 x 2 cm) nodes in the left level II cervical region.

The Cervical lymph node enlargement in the absence of an axillary lymph node raised suspicion of a primary versus metastatic lesion of the breast. Further, when enquired, the

patient gave a history of dysphagia for eight weeks. We performed fine needle aspiration (FNAC) from the breast lump and cervical lymph node using a 25G needle using standard protocol. Ethanol-fixed and air-dried smears were made and stained with Papanicolaou and Giemsa stains. In addition, a cell block of the same was also processed.

Aspirate smears from the breast lump and cervical lymph node showed similar morphology. Smears were highly cellular, showing tumour cells arranged as clusters with vague glandular patterns. These tumour cells show moderately pleomorphic, enlarged vesicular nuclei, irregular nuclear membrane, conspicuous nucleoli, and abundant cytoplasm with lymphoid cells in a blood-mixed necrotic background **(Figure 1)**. Given the suspicion of metastasis, GATA3, CK7 & CK20 stains were attempted on the PAP-stained smear. While GATA3 & CK20 turned out to be negative, CK7 was positive. Hence, we reported the case as positive for malignancy, suspicious of metastasis to the breast and the same was communicated to the treating physician. In view of patient's dysphagia, endoscopy was performed and biopsy was taken from an ulcero-proliferative lesion in the lower end of the esophagus.

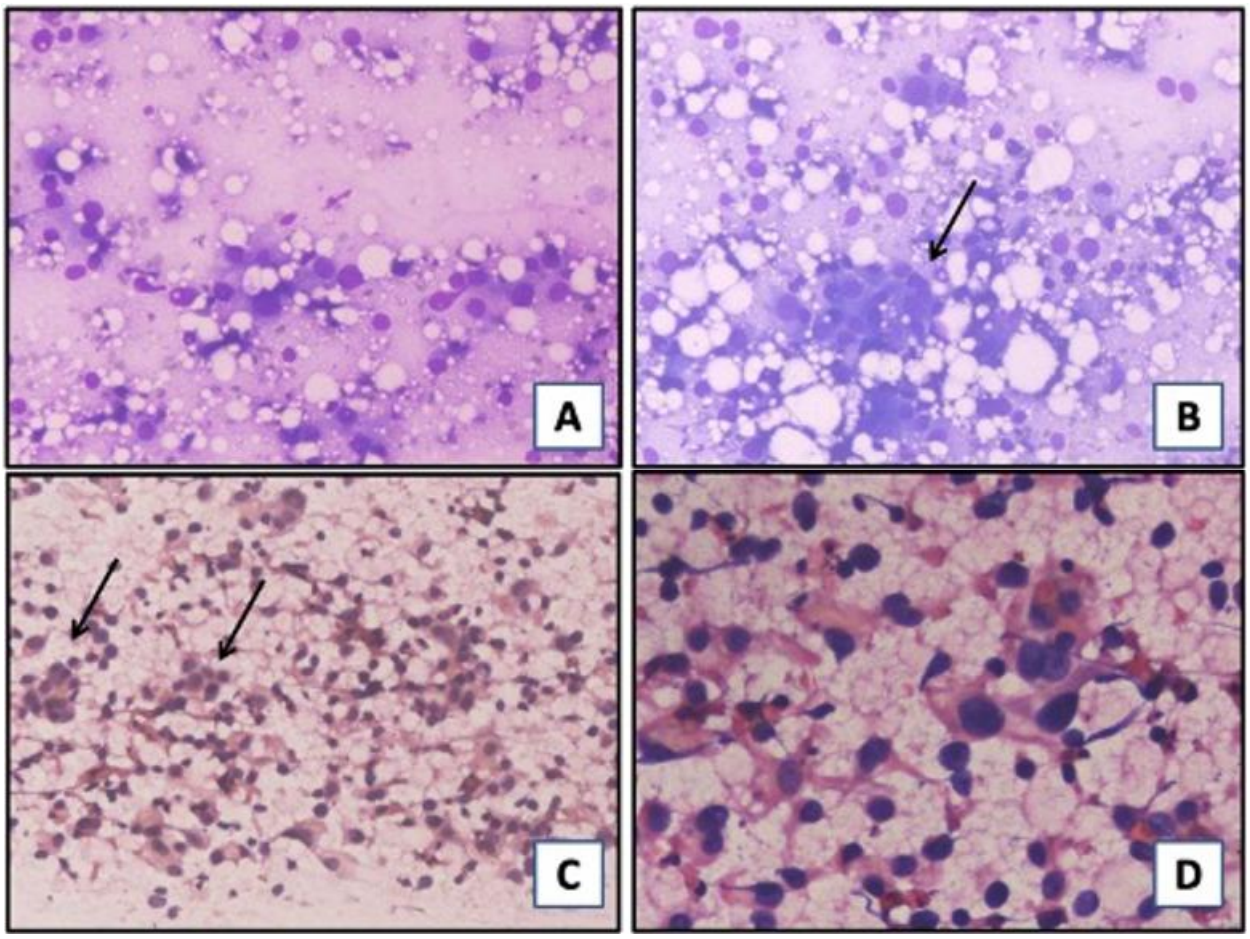

Figure 1: A-D are images from the breast FNAC (Arrow shows glandular differentiation).

Meanwhile, the patient also submitted the slides and blocks of the true-cut biopsy of the breast lump performed elsewhere for review. Both slides were evaluated, and the esophageal biopsy was reported as adenocarcinoma with a papillary pattern **(Figure 2A & B)**. In contrast, the breast biopsy was reported as a metastatic lesion **(Figure 2C & D)**. On immunohistochemistry, these tumour cells in the breast lesion were positive for CK7 and negative for GATA-3 & CK20(confirming esophageal primary). Later, a PET-CT workup revealed a well-defined soft tissue density nodule in the breast. In addition, the thoracic esophagus showed circumferential thickening, and lung, liver, and cervical lymph nodes showed metastatic deposits.

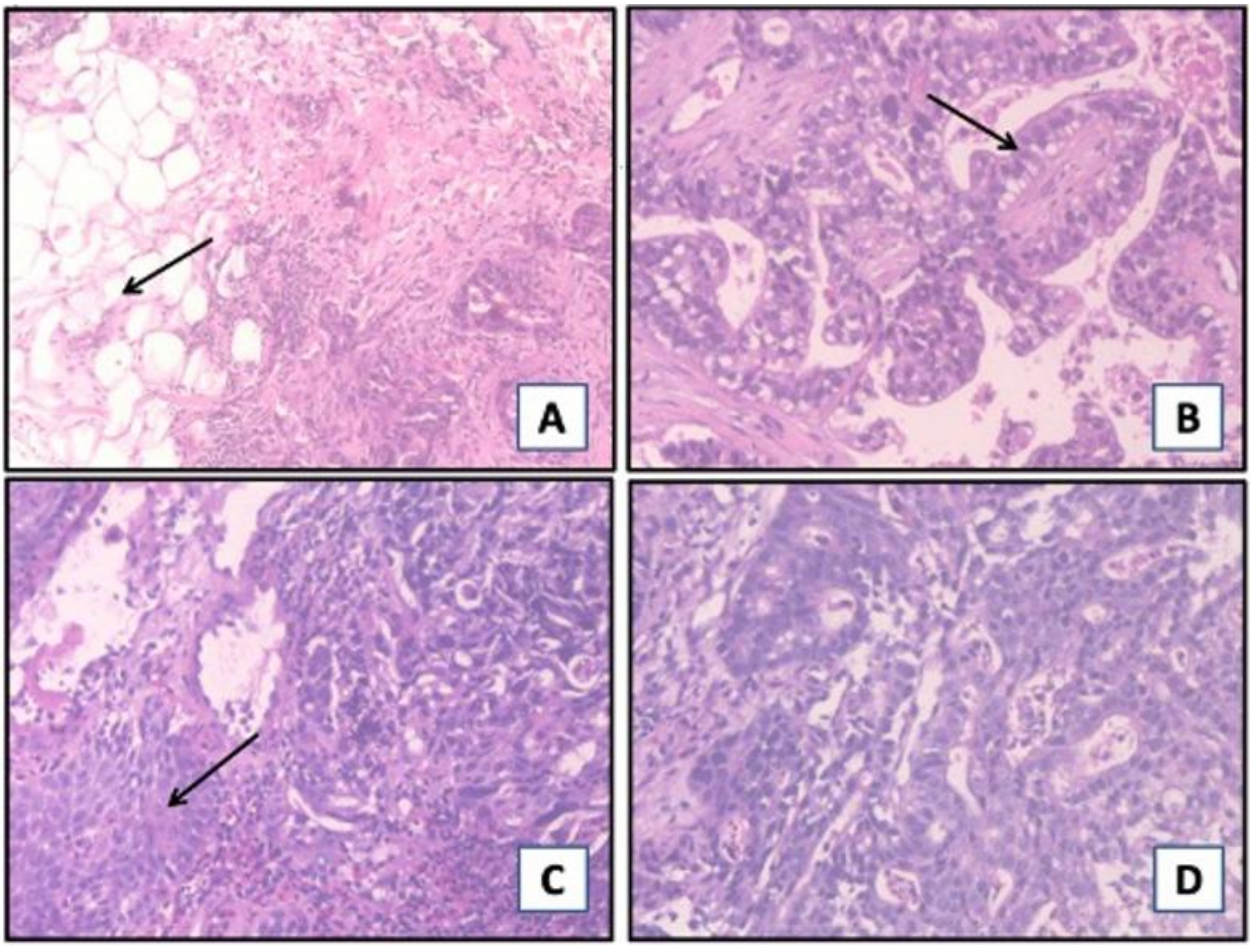

Figure 2: A and B are biopsies from the breast (in A, the Arrow shows the fibrofatty stroma); C and D are biopsies from the esophagus (in C, the Arrow shows the squamous epithelium of the esophagus & in D, the Arrow highlights the papillary architecture).

3. Discussion

Esophageal cancer is a fatal malignancy that can rapidly spread anywhere in the body. Common metastatic sites of esophageal cancer are the regional lymph nodes, liver, lungs, and bones [4]. Almost 40 to 60% of esophageal cancers are not resectable at the time of diagnosis, and 26% of locally advanced esophageal cancers show distant metastasis in the first two years of therapy. Distant metastatic sites include the lung, liver, and bones. There are very few cases in the literature regarding breast metastasis from the esophagus, as summarised in **Table 1.** In all the cases in the literature, breast lump presentation was preceded by primary esophageal malignancy tissue diagnosis and treatment. However, in our case, the patient was evaluated for a breast lump, which further led to the discovery of an esophageal lesion.

Table 1: Breast metastasis from esophageal carcinoma

S.no	Study	Patient sex & age	Tumor location	Diagnosis	Metastasis location
1	Nielsen et al., 1981[10]	84 y/o female	Middle esophagus	Squamous cell carcinoma	5 cm central mass located on the right breast
2	Miyoshi et al., 1999[6]	44 y/o male	Upper middle esophagus	Squamous cell carcinoma	Painful mobile hard mass beneath the left nipple
3	Shiraishi et al., 2001[11]	57 y/o female	Middle esophagus	Squamous cell carcinoma	2.5 cm mobile painless hard mass in the upper outer quadrant of the left breast
4	Santeufemia et al., 2006[9]	51 y/o male	Middle esophagus	Squamous cell carcinoma	3 cm× 3 cm hard mobile nodule in the upper lateral quadrant of the left breast
5	Norooz et al., 2009[12]	35 y/o female	Middle & Lower esophagus	Squamous cell carcinoma	4 cm× 4.5 cm mobile, painful, hard mass just below the right nipple
6	Jena et al., 2014[4]	32 y/o male	Lower esophagus	Adenocarcinoma	2 cm× 2 cm mobile, hard lump in the upper outer quadrant of the left breast
7	A Ghibour et al.,2016[13]	57 y/o female	Middle lower esophagus	Squamous cell carcinoma	10 cm × 9.5 cm painful hard mass involving the left breast
8	Our case	59 y/o male	Lower esophagus	Adenocarcinoma	3 x 2 cm lump in the infero-outer quadrant of the left breast

Metastasis to the breast from extra-mammary origin is very rare, accounting for only 0.5 to 3% of all breast malignancies[5]. The breast has a large amount of fibrous tissue with poor blood supply, which makes it an unusual site for metastasis. Usually, breast metastasis is identified easily in already known extramammary malignancies with widespread metastasis. However, if the patient presents with a metastatic breast lump as the initial complaint, a metastatic breast lump can mimic primary benign or malignant lesions of the breast, leading to a wrong diagnosis, which will result in unnecessary surgical resections[6].

Breast metastases are usually seen in young patients as they have high blood flow in the breast [7]. Clinically and microscopically, metastatic lesions may not differ from primary breast lesions; thus, differentiating metastasis from primary lesions is crucial in avoiding unwanted radical surgical procedures[8]. However, there are subtle clinical differences between primary lesions and metastatic lesions. Metastatic lesions are well-circumscribed, painless, mobile lumps and are not associated with any nipple discharge/Paget's disease or axillary lymphadenopathy. On mammography, metastatic lesions are well-circumscribed lesions with high density and regular margins without skin thickening, which can mimic benign lesions like fibroadenoma. Further metastatic lesions lack spicules/microcalcifications and desmoplastic reactions in primary breast malignancies[8]. Even though there are some subtle differences in imaging findings of primary and metastatic breast carcinoma, at times, they might look indistinguishable [5]. A mammogram was not performed given the patient's male gender.

Cyto-morphologically aspirating smears of malignancy cannot ascertain the site of origin. Hence, a proper clinical evaluation can provide important clues for diagnosis. In our experience, male breast carcinoma very frequently presents with nipple ulceration (Paget's disease) or is fixed to the underlying muscle in the presence of axillary lymphadenopathy. The absence of an axillary node, a mobile lump, no nipple areola involvement, and the presence of a cervical lymph node with mild dysphagia have raised suspicion of metastasis in the breast, which led to further work on the upper GI endoscopy and biopsy from the esophagus. Had there been an axillary node, the patient would have been diagnosed as a primary breast malignancy by mistake. The breast biopsy elsewhere was reported as triple-negative breast carcinoma, possibly because of the lack of availability of clinical details. This case emphasises the necessity of proper history-taking and clinical examination of patients in the FNAC clinic. A breast lump in the presence of widespread metastasis should always alarm the pathologist about the possibility of a secondary lesion.

This case also emphasizes the importance of algorithmic approach using preliminary IHCs such as CK7 & CK20 in adenocarcinoma presenting at rare sites. Skipping these IHCs lead to an incorrect diagnosis of the primary malignancy. Further site specific IHCs such as GATA-3, mammaglobin & GCDFP-15 are also useful markers in primary breast malignancy. In our case negative GATA-3 and positive CK7 signified a foregut primary rather than a breast primary.

Categorizing the primary is very important in this case as the median survival time of metastatic esophageal cancer patients is only six months. Treatment with chemotherapy can provide an overall survival of 12 months. The prognosis of breast metastasis is generally poor, and patients hardly survive 12 months[9]. In our case, the patient was lost to follow-up after the FNAC and biopsy review.

The significance of this report lies in its potential to improve diagnostic precision and reduce misdiagnosis in cases where breast lumps may actually be secondary lesions, especially in male patients with atypical clinical presentations.

4. Conclusion

This case report presents an unusual manifestation of esophageal adenocarcinoma metastasizing to the male breast, initially misdiagnosed as a primary breast carcinoma. It reinforces the importance of thorough clinical evaluation, detailed patient history, and the strategic application of FNAC and immunohistochemistry in differentiating metastatic lesions from primary tumors. Prompt identification of such rare presentations is crucial to avoid unnecessary surgical interventions and to guide appropriate systemic management.

Declarations:
All authors declare that there is no conflict of interest.
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Data is not shared in this manuscript.

Author Contribution:
1) Dr Lumen - Manuscript preparation and cytodiagnosis
2) Dr K.C. Sharan – Data collection and cytodiagnosis
3) Dr Swetha Param – Procedure and cytodiagnosis
4) Dr Debasis – Concept, cytodiagnosis and manuscript preparation
5) Dr Nachiappa Ganesh Rajesh - Concept, cytodiagnosis and manuscript preparation

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