

CASE REPORT

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# Breast metastasis as the first presentation of an anorectal melanoma diagnosed on fine needle aspiration cytology: a case report

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## Abstract

**Background** Primary anorectal melanoma is a rare and aggressive disease accounting for approximately 1–3% of all colorectal and anal cancers.

**Case report** We present a unique case of anorectal melanoma where the primary presentation was the metastatic breast lump which led to the detection of the primary tumor. A 70-year-old elderly postmenopausal female presented with complaint of left breast lump. On fine needle aspiration cytology, May Grunwald-Giemsa and Papanicolaou stained smears examined were highly cellular and showed sheets, clusters and singly scattered highly pleomorphic plasmacytoid cells having high nucleus to cytoplasmic ratio and scant to moderate cytoplasm with enlarged eccentric round to ovoid nuclei. Immunocytochemistry performed on cell block preparation showed tumor cells strongly positive for HMB-45, S-100 and negative for ER, PR, Her2neu, chromogranin, synaptophysin and Pan-CK. A thorough work up of the patient to look for the site of primary malignancy was done and radiological findings revealed presence of an ill-defined soft tissue mass in the anal canal. Biopsy from the anal mass confirmed the diagnosis of anal melanoma with metastasis to breast.

**Conclusion** The present case was reported to emphasize the importance of atypical presentation where the breast lump was the primary presentation of an anal melanoma. Therefore, we should have a strong index of suspicion for metastatic tumors in case of a breast lump especially when there is unusual morphology or unexpected immunophenotype, particularly if the neoplasm is triple-negative, in patients with a previous history of other malignancies.

**Keywords** Malignant melanoma, Breast lump, Metastatic, Anorectal

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## Introduction

In breast, primary malignancies are more common than a metastatic disease. Metastasis to breast most commonly occurs from a contralateral breast carcinoma followed by malignant melanoma, lymphoma, lung cancer, ovarian carcinoma, soft tissue sarcoma, gastrointestinal and genitourinary tumors [1].

Malignant melanoma (MM) which routinely occurs on the human skin and mucous membranes is a highly malignant tumor brought about by the excessive proliferation of atypical melanocytes [2]. More than 90% of the melanoma cases involve the skin tissues. Primary anorectal melanoma is relatively less common compared to the melanoma of other body parts [3]. Primary anorectal melanoma is a rare and aggressive disease accounting for approximately 1–3% of all colorectal and anal cancers. It is an uncommon site of primary melanoma with almost equal male to female preponderance and with an average age of presentation between the fifth and the sixth decades of life. Anorectal melanoma is associated with poor prognosis and high metastatic potential. In addition, breast metastasis from anorectal melanoma is even more uncommon. Very few cases have been reported in literature.

Here, we present a unique case of anorectal melanoma where the primary presentation was the metastatic breast lump which led to the detection of the primary tumor.

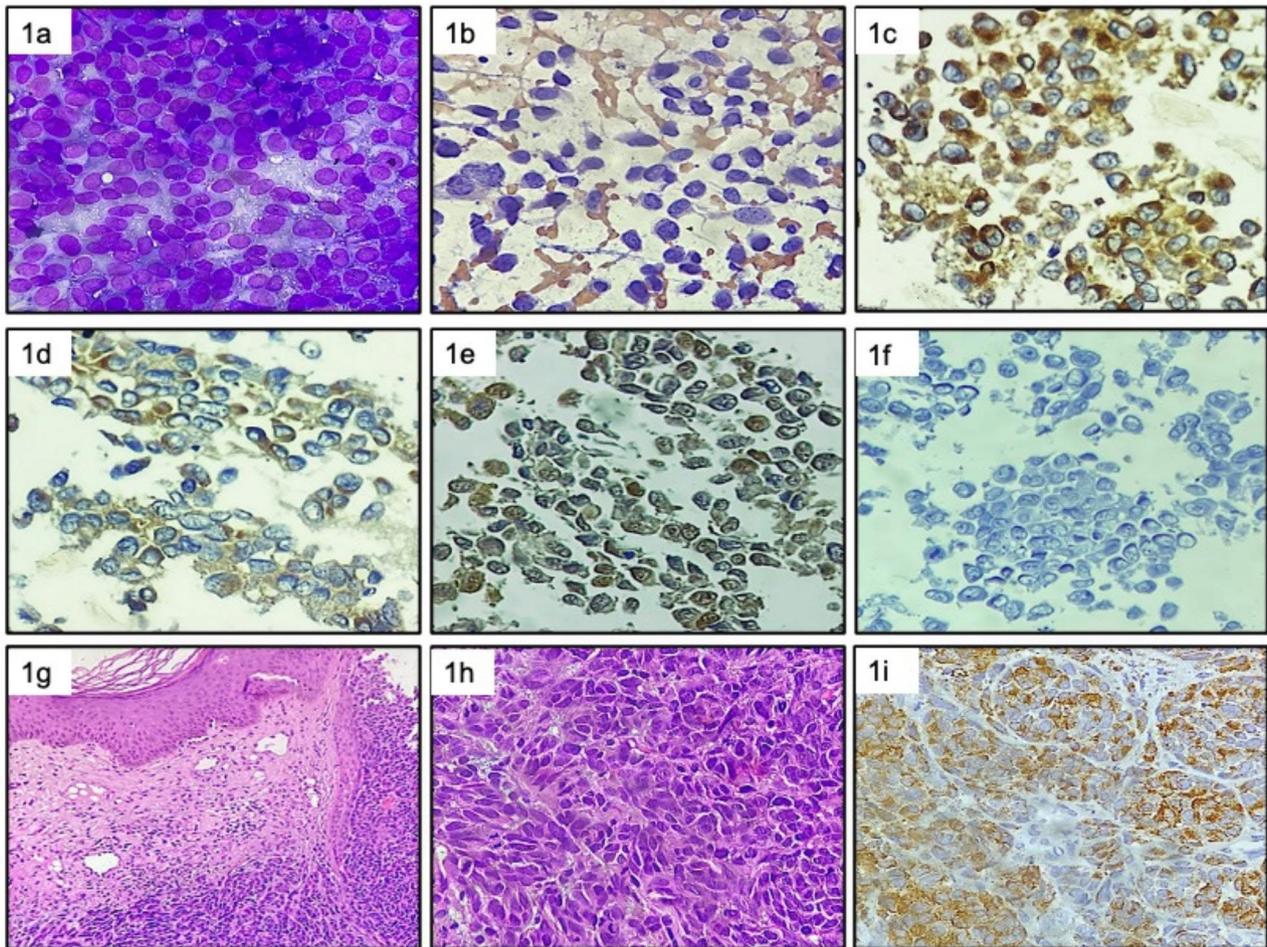
## Case report

A 70-year-old elderly postmenopausal female presented with complaint of left breast lump in surgical OPD of a tertiary care hospital. It was a solitary painless lump in lower inner quadrant of breast noticed by the patient 1 month back. On palpation, it was 2×2 cm in dimension, firm, mobile and non-tender. She had no prior history of any malignancy or history of breast carcinoma in family. On fine needle aspiration cytology, May Grunwald-Giemsa and Papanicolaou stained smears examined were highly cellular and showed sheets, clusters and singly scattered highly pleomorphic plasmacytoid cells having high nucleus to cytoplasmic ratio and scant to moderate cytoplasm. They had large sized eccentric round to ovoid nuclei with irregular nuclear membrane and opened up chromatin with single prominent nucleoli. The first differential diagnosis was a high grade Invasive ductal carcinoma. Immunocytochemistry panel comprising of ER, PR and Her2neu was ordered on the cell block which turned out to be negative. Thus, the next possibility was a triple negative breast cancer versus a metastatic tumor. Considering the morphological findings of plasmacytoid cells with prominent nucleoli, further immunocytochemistry was ordered which showed tumor cells to be strongly positive for HMB-45, S-100 and negative for chromogranin, synaptophysin and Pan-CK. The findings

were suggestive of a melanoma. There was no breast imaging done prior to the FNAC. However, breast being an unusual presentation for melanoma, this was followed up by a thorough work up of the patient to look for the site of primary malignancy. Contrast Enhanced Computed Tomography (CECT) – Whole Abdomen revealed a large ill-defined soft tissue mass in anal canal and distal rectum with heterogeneous enhancement. It was 6.5×6 cm in size involving the bilateral ischioanal fossa laterally, posterior vaginal wall anteriorly, anal verge inferiorly and distal rectum superiorly. Also, enlarged perirectal lymph nodes were present. Further, an edge biopsy was taken from the anal mass. The tissue piece was fixed with 10% formalin, paraffin embedded and routinely stained with Hematoxylin and eosin. Sections examined showed a submucosal tumor with clear cut zone of demarcation from the overlying stratified squamous epithelium. The tumor cells were arranged in nests of varying sizes. Individual tumor cells were epithelioid in shape, had high nucleus to cytoplasmic ratio and scant to moderate amount of eosinophilic cytoplasm. They had pleomorphic enlarged nuclei with irregular nuclear membrane, nuclear hyperchromasia with coarse irregularly distributed chromatin and occasional prominent eosinophilic nucleoli. High mitotic activity including atypical mitoses was also seen. Immunohistochemistry performed showed tumor cells with strong positivity for HMB-45, S-100 and negative for Pan-CK, synaptophysin and chromogranin. Ki 67 index was nearly 70%. Features were confirmative of melanoma arising in the anal canal with metastasis to left breast (Fig. 1). Positron emission computed tomography scan revealed metastatic lesions in the liver and lumbar spine. The primary tumor resection was done followed by adjuvant chemotherapy for the multiple metastatic lesions. She tolerated the treatment well and is currently on follow-up.

## Discussion and conclusion

According to WHO (2019), metastatic solid neoplasms to the breast represent 0.2 to 1.1% of all breast malignancies, and 0.02–0.4% are due to systemic involvement by hematological malignancies [4]. Hematopoietic neoplasms are one of the most common neoplasms with which secondary involvement of the mammary parenchyma is known [5]. Metastasis to breast most commonly occurs from a contralateral breast carcinoma followed by lymphoma/ leukemia, malignant melanoma, lung cancer, ovarian carcinoma, gastric carcinoma, prostatic carcinoma, renal cell carcinoma, colorectal carcinoma, soft tissue sarcoma (rhabdomyosarcoma), malignant mesothelioma, neuroendocrine tumors and cervical squamous cell carcinoma [6]. Zhou et al. in their study on tumors metastatic to breast reported 28.6% lung adenocarcinomas, 17.8% high grade serous ovarian carcinomas, 14.3%



**Fig. 1** Cytochemical and histopathological photomicrographs of the metastatic and primary tumor

**a, b)** May Grunwald-Giemsa and Papanicolaou stained smears show clusters of plasmacytoid cells with eccentric nuclei and scant to moderate cytoplasm. [200x magnification]

**c-f)** Immunocytochemistry in cell block preparation shows positive expression for Melan-A (**c**), HMB-45 (**d**), S-100 (**e**) and negative expression for ER (**f**). [200x magnification]

**g-h)** Hematoxylin and eosin-stained sections show a submucosal tumor comprising of tumor cells arranged in nests. Individual tumor cells were epithelioid in shape, with high nucleus to cytoplasmic ratio and scant to moderate cytoplasm with high mitotic activity. [100x, 200x magnification]

**i)** Immunohistochemistry shows positive expression of HMB-45 in the tumor cells. [200x magnification]

melanomas, 14.3% malignant mesenchymal tumors, 10.7% gastric adenocarcinomas, 7.1% rectal adenocarcinomas, 3.6% pancreatic neuroendocrine tumors and 3.6% prostatic carcinomas [7]. DeLair et al. in their study on non-mammary metastasis to breast reported 58% carcinomas, 22% melanomas and 20% sarcomas. The most common tumors among carcinomas and sarcomas were ovarian high grade serous carcinoma and uterine leiomyosarcoma respectively [8]. A solitary lesion is the most frequent clinical presentation. However, metastatic lesions may produce changes similar to those of primary breast cancer on mammography, but they are more likely to be multiple, are frequently bilateral and form a nidus of tumor cells that are usually round with

fairly well-defined margins. Microcalcifications are not a distinguishing feature between primary and metastatic tumors [1]. Due to the rarity of breast metastasis as well as unusual clinicopathological features, it may be difficult to make the diagnosis specially when the breast lesion is the first presentation of unknown extramammary primary cancer [9].

Anorectal malignant melanoma is an aggressive malignant tumor. Most patients with such melanomas complain for bleeding, pain, or an anal mass. Anorectal MM frequently occurs near the dentate line. As the tumor is highly invasive and lymphatic vessels are abundant near the dentate line, local spread and distant metastases may occur in the early phase of the disease and it has been

reported that 38% of patients already have metastatic disease at the time of diagnosis [10]. Lymphatic spread to mesenteric nodes is more common than to inguinal nodes while lungs, liver and bones are the most frequent sites of distant metastases. Breast is a very unusual and rare site of metastasis in anorectal melanoma with a 1.2% metastatic rate to the breast, resulting in a 5-year overall survival of 20% [11, 12]. Breast metastases classically lie in the subcutaneous plane and are easily palpable. In contrast, primary breast carcinomas are usually deep-seated but also often palpable [13, 14]. Radiological findings may aid in the diagnosis of metastatic breast disease. On mammography, metastatic lesions usually present as solitary or multiple well-circumscribed masses mostly located in the upper outer quadrants without any calcifications, spiculations and desmoplastic reaction that are observed in majority of primary breast carcinomas [15, 16]. However, mucinous adenocarcinomas of the rectum and metastatic ovarian carcinomas are exceptions where, metastatic lesions to the breast may exhibit calcifications [17]. Metastatic tumors may rarely cause diffuse parenchymal involvement similar to that seen in inflammatory carcinoma of breast, which may be seen in metastatic stomach cancer [15, 18].

On ultrasonography, metastatic lesions may be solitary or multiple, round to oval, with hypoechoic and solid echo patterns and well-defined posterior margins. Hematogenous metastases usually have circumscribed margins with absence of spiculations, calcifications, architectural distortion, or posterior acoustic shadowing while lymphangitic metastases present as diffuse trabecular thickening due to lymphatic channel obstruction [19, 20].

Ravdel et al. found that metastatic melanoma usually presents as well circumscribed and hypoechogenic masses on ultrasonography in contrast to primary breast cancers which appeared to be hyperechogenic [21].

The suspicion of a secondary tumor metastatic to breast should arise especially when there is unusual morphology or unexpected immunophenotype, particularly if the neoplasm is triple-negative, in patients with a previous history of other malignancies. The histological features which should raise the suspicion of a metastatic tumor include a well circumscribed unencapsulated tumor with periductal or perilobular distribution, absence of in-situ carcinoma, multiple microscopic foci of tumor in addition to the grossly evident masses and many lymphatic tumor emboli. Metastatic tumors tend to replace the breast tissue rather than arising from it [22, 23].

Axillary lymph node involvement was less common in metastases than in primary breast cancers. On mammogram, lesions are usually dense and rounded, not causing distortion of the surrounding parenchyma, neither showing calcifications, however, lesions from ovarian, thyroid,

or mucin-producing gastrointestinal tract carcinoma may appear ill-defined, with parenchymal distortion and sporadic calcifications [24, 25].

An extended immunohistochemical panel comprising HMB-45, S-100, LCA, CD3, CD20, TTF-1, CK7, CK20, WT1, p53, CDX2 may be needed to exclude the possibility of a metastatic tumor. Additionally, imaging should be done to search for a possible primary if metastasis is suspected.

The present case was unique as the first presentation of the anorectal melanoma was in the form of a metastatic breast lump which later led to diagnosis of the primary tumor. Metastatic melanoma possess a diagnostic challenge because morphologically it used to mimic primary breast malignancies. Ravdel et al. studied 16 cases of malignant melanoma and they found only single case with spindled morphology. Another previous study showed only two cases out of 20 had melanin pigments and rest all were amelanotic melanoma [21]. Due to the broad morphological spectrum of this disease, FNAC alone could not provide sufficient information and diagnosis requires further studies including immunohistochemical studies.

Surgical therapy for metastatic tumors should be as conservative as possible and usually includes wide local excision.

Treatment for a solitary foci of metastatic disease may be surgical resection. Large tumors may be treated with mastectomy along with chemotherapy for tumors like carcinoid, lymphomas and choriocarcinomas which respond well to chemotherapy [26].

The therapeutic principle used for the treatment of melanoma metastatic to the breast tissue does not differ from that of melanoma metastatic to other sites [27]. The standard therapeutic approach remains surgery supplemented with radiotherapy, chemotherapy and immunotherapy. Advanced melanoma, though usually refractory to systemic therapy, may occasionally respond to treatment with biologic response modifiers and cytotoxic agents [26].

In case, a metastatic tumor is misdiagnosed as a primary invasive breast carcinoma and treated, the actual primary tumor may be missed and may present at a much more advanced stage leading to adverse outcome and worse prognosis for the patient.

Metastasis to the breast is an indicator of poor prognosis with overall survival ranging from 4.7 to 11 months only [28].

Therefore, in conclusion, metastasis of tumors to the breast is a very rare phenomenon. The finding of anorectal melanoma that has metastasized to the breast requires complete evaluation for diffuse metastatic disease, because in most cases it is associated with wide dissemination, in particular to the brain, lung, and liver, as

it might directly influence the prognostic assessment and the establishment of effective therapeutic approaches. It is also essential to recognize that malignant tumors in the breast might be metastatic melanomas, so as to avoid unnecessary mutilating surgery. Fine needle aspiration cytology is very important in diagnosis of both primary and metastatic breast tumors. The diagnosis in the present case was based on cytomorphological features as well as the immunocytochemistry on cellblock obtained from FNAC.

#### Author contribution

SM and AAK conceived the idea and were the main contributor to writing of the manuscript. SA and MS diagnosed the case and were responsible for critically revising the manuscript. The authors read and approved the manuscript.

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#### Declarations

##### Ethics approval and consent to participate

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##### Consent for publication

Not applicable (no identifying information is present in the case report).

##### Competing Interest

None.

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