Original Article

Primary Breast Cancer with Orbital and Rectal Metastasis: A Case Report

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ABSTRACT

Background: Breast cancer is known to metastasize to many sites. Orbital metastasis is a rare occurrence, along with rectal metastasis. Currently, there are no published case reports of primary breast cancer with synchronous orbital and rectal metastasis.
Case Description: We report a 58-year-old menopausal female who presented a right orbital mass, causing eventual blindness of the affected eye. A biopsy of the orbital mass showed a poorly differentiated carcinoma. Further work-up revealed a right breast mass with a biopsy consistent with invasive ductal carcinoma, with estrogen-receptor and progesterone-receptor being positive. The metastatic evaluation showed multiple lung and bone metastasis and a rectal mass with histopathology consistent with metastatic carcinoma. Immunohistochemical staining showed substantial estrogen and progesterone receptor positivity for both rectal and orbital masses consistent with primary breast carcinoma. The patient underwent palliative chemotherapy with six cycles of Docetaxel and Cyclophosphamide followed by CDK4/6 inhibitor with Aromatase inhibitor. The patient has been well on follow-up with good clinical and radiologic response and stable disease as of this reporting.
Conclusion: Our case demonstrates an exceptional presentation of a primary breast malignancy with synchronous orbital and rectal metastasis. This case report attests to the broad clinical presentation of breast carcinoma and the need for extensive work-up via imaging and pathological review in its recognition and eventual diagnosis of a once thought to be double primary that will undergo further investigation as a single entity.

Keywords: Breast cancer, orbital metastasis, rectal metastasis, case report

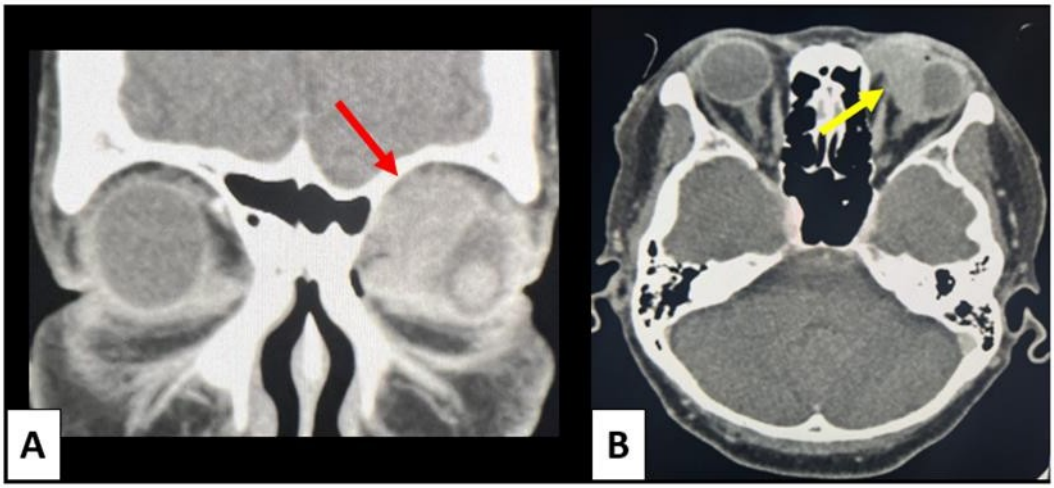
INTRODUCTION

Breast cancer is one of the most common malignancies worldwide. Common sites of metastasis involve the bones, liver, and lungs.[1] Orbital metastases, in general, are relatively uncommon, representing 1-13 % of reported orbital tumors, and are seen in 2-5 % of patients with systemic malignancies. These metastasize via the hematogenous route, with the most significant portion coming from breast and lung carcinoma. [2] Common presenting symptoms include diplopia, ocular pain, visual impairment, and eventual vision loss, which may significantly impact the functional status of the oncological patient. [3] More so, gastrointestinal tract involvement from primary breast cancer is an even rarer phenomenon, with one study showing the rates of metastasis to be 4.5 and 0.2 percent for invasive lobular carcinoma and invasive ductal carcinoma, respectively. [4] The

finding further underscores the unusual metastatic presentation of breast carcinoma.

CASE PRESENTATION

A 58-year-old menopausal Filipino female with controlled essential hypertension presented, five months before consultation, with a right orbital mass causing pain, amaurosis (blindness), and proptosis (eye bulging). This presentation ultimately led to blindness in her right eye. The patient also complained of occasional dyspnea at rest. A computed tomography (CT) scan of the orbit with contrast revealed a lobulated enhancing mass along the superior aspect of the right orbit. The mass compressed the ocular globe, obscuring the fascial plane. The right ocular lobe showed thickening. The mass measured approximately 3.4 x 1.9 x 2.9 cm with erosion and mild remodeling at the roof of the right orbit **(Figure 1).**



Sagittal **Coronal**

FIGURE 1 CT scan of the orbits with contrast, lobulated enhancing mass 3.4 x 1.9 x 2.9 cm of the right orbit with thickening obscuring the fascial plane.

A core needle biopsy of the orbital mass showed a Poorly differentiated Adenosquamous carcinoma. Further physical examination showed a 10 cm fixed right breast mass on the right upper quadrant at the ten-clock position, which the patient did not disclose at the time. Metastatic work-up with computed tomography scan of the chest and whole abdomen with contrast showed an irregular right breast mass measuring 10.1 x 4 x 8.9 cm with suspicious infiltration to the right pectoralis muscle. (Figure 2). There was a suspicious mass lesion in the dextrolateral aspect of the distal rectum extending to the anorectal junction, measuring approximately 3.1 x 1.3 x 3.6 cm with enlarged para-aortic and inter-aortocaval lymph nodes. These findings were suspicious for a Primary breast malignancy with a possible second primary rectal carcinoma with lymph node metastasis. However, the patient currently does not have any gastrointestinal-related complaints. Whole body PET (Positron Emission Tomography) CT scan confirmed the presence of a hypermetabolic stable enhancing lobulated right breast mass infiltrating the pectoralis muscle with thickening of the overlying skin and nipple retraction findings consistent with breast carcinoma. There were findings of hypermetabolic mediastinal, bilateral axillary, and abdominal lymph nodes consistent with metastases and multiple hypermetabolic varisized solid pulmonary nodules

scattered in both lung fields compatible with pulmonary metastases. PET CT scan showed hypermetabolic eccentric wall thickening in the distal rectum with prominent mildly FDG avid mesorectal lymph node suspicious with a primary malignancy. (Figure 6, B). FDG avid lesions in the parietal bone, left scapula, right 7th,8th, and left 4th, 7th ribs, C3, C6, T4, T8, and L3 vertebrae consistent with bone metastasis.

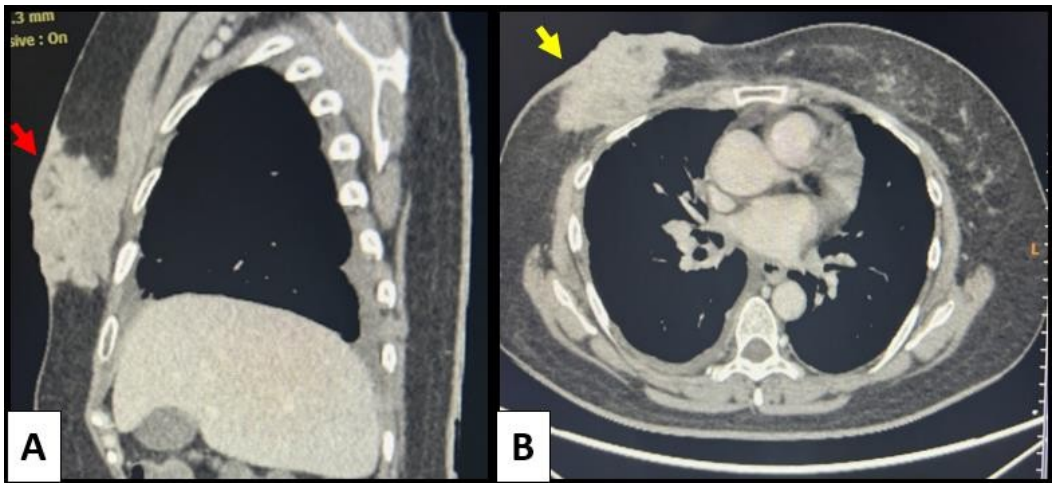


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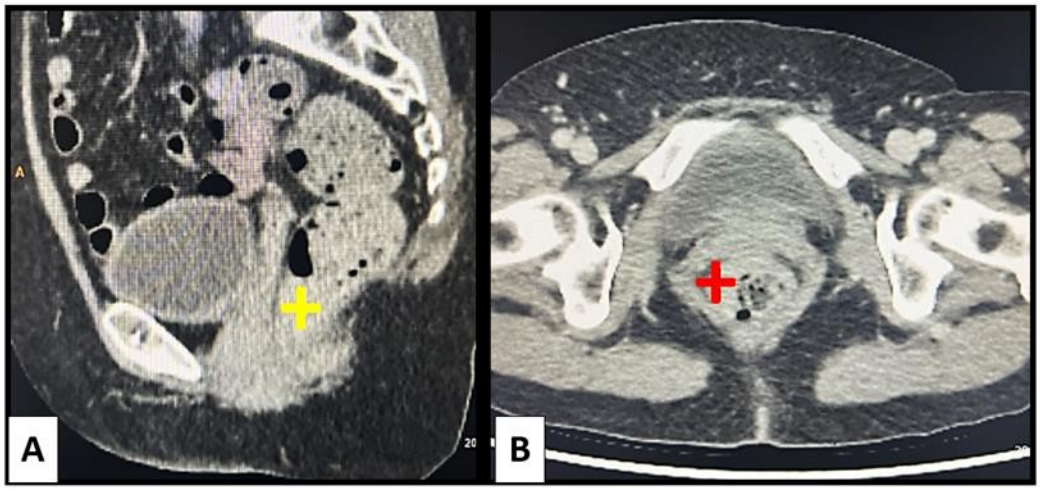
Figure 2 CT scan of the chest with contrast shows an irregular enhancing mass (arrow) in the right breast with distortion of the breast architecture.



Sagittal **Coronal**

FIGURE 3 CT scan of the whole abdomen with contrast showing a suspicious mass (cross) at the distal rectum extending to the anorectal region.

The patient underwent a core needle biopsy of the right breast mass. Biopsy showed Invasive ductal Carcinoma, Grade 1-2. The Breast Panel showed estrogen receptor-positive 100 %, progesterone receptor-positive 90%, and human epidermal growth factor receptor (Her 2) negative. (Figure 4 and 4.1). Colonoscopy showed a rectal mass 5cm from the anal verge. A biopsy was then

performed. Histopathologic examination showed small round cells. Initially, a neuroendocrine tumor was considered. Immunohistochemical staining showed that chromogranin and synaptophysin were negative but showed both Estrogen 100% and Progesterone 100% receptor-positive, with a low Ki67 of 10% (Figure 6). CEA was expected at 35 ng/ml (Normal value: 0.14-6.5 ng/ml), and CA 15-3 elevated at 204 U/ml (Normal value: 32 U/ml). Consequently, the right orbital mass showed intense nuclear staining for estrogen receptors at 90% and progesterone at 80 %. (Figure 5). Comparing the biopsy specimens, the poorly differentiated areas of the orbital and rectal biopsy showed a similar morphology to the tumor in the breast.

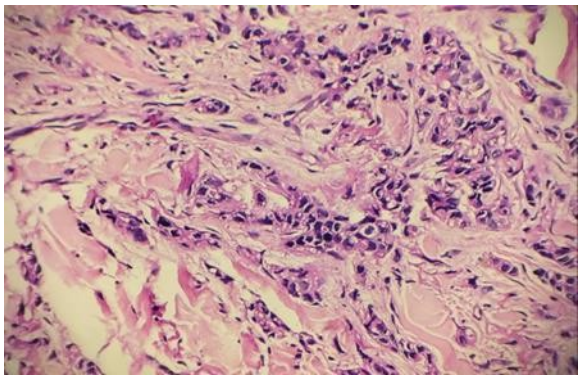


FIGURE 4 Hematoxylin and eosin stain of the right breast mass reveals infiltrating cords and nests of ductal cells within a desmoplastic stroma. Increased mitotic activity is also present.

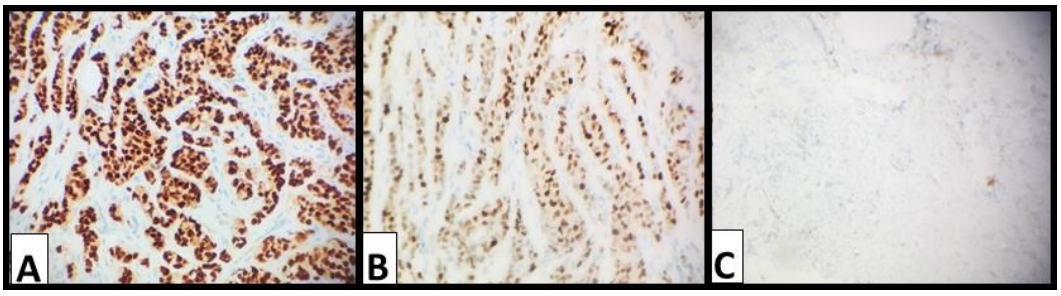


FIGURE 4.1 Breast Panel: Estrogen receptor showing intense positive staining of 100%, B. Progesterone receptor staining showing 90% positivity C. Her 2-receptor staining negative.

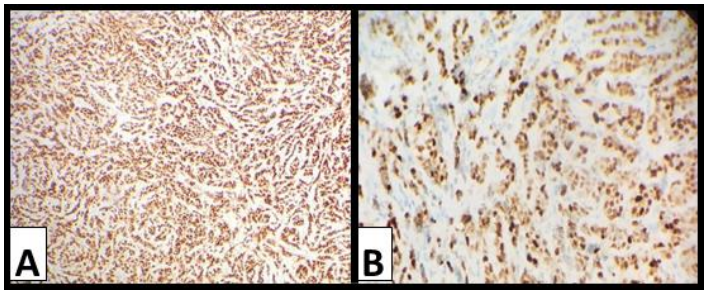


FIGURE 5 Immunohistochemical staining of Right orbital mass**, A.** Estrogen receptor showing intense positive staining of 90%, **B**. Progesterone receptor staining showing 80% positivity.

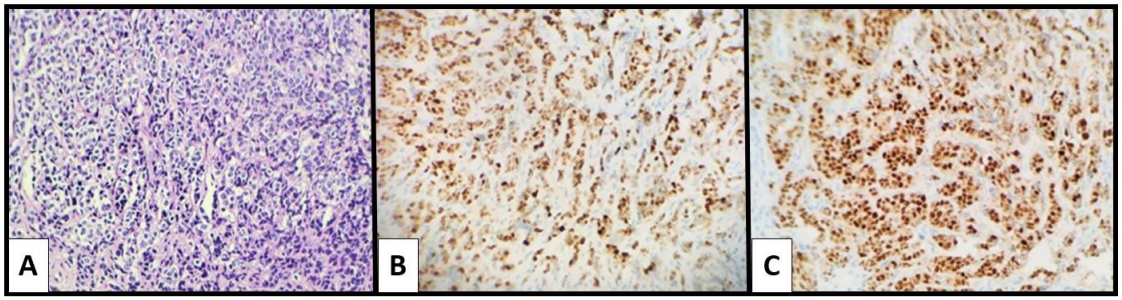
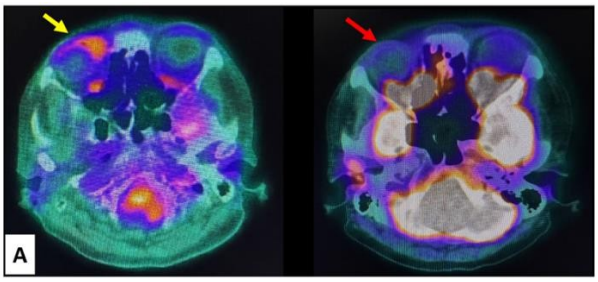


FIGURE 6 A. Hematoxylin and eosin stain of the rectal mass show sheets and prominent nests of small round tumor cells with fine nuclear chromatin and inconspicuous nucleoli. **B** Estrogen receptor showing intense positive staining of 100%, **C**. Progesterone receptor staining showing 100% positivity.

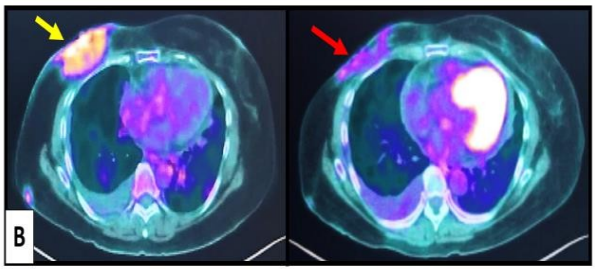
These findings were consistent with a Primary Right Breast carcinoma stage IV (c T4aN1M1) with orbital, rectal, bone, and lung metastasis, ER and PR positive, HER two negative. Initial work-up showed 2D echo results of concentric left ventricular hypertrophy with segmental wall motion abnormality, normal global systolic function, and an Ejection fraction of 63%. 12-lead ECG showed paroxysmal Atrial fibrillation. Due to the high burden of the disease and symptomatic lung metastasis, the patient was started with palliative chemotherapy with Docetaxel at 75 mg/m2 and Cyclophosphamide at 600 mg/m2 every 21 days for six cycles with monthly zoledronic infusion and showed overall good clinical response. The right orbital mass decreased in size; however, her vision did not recover. After six chemotherapy cycles, a whole-body PET CT scan revealed a significant decrease in size and metabolic activity in the right orbital and breast mass, lymph nodes, bone, and multiple pulmonary nodules. (Figure 7).
Further testing for germline BRCA1/2 mutation results showed to have no mutations present. The patient received palliative radiotherapy to the right breast, right supraclavicular area, posterior axilla, and T1-T8 region. The patient was then started on CDK4/6 (Cyclin-dependent kinase 4 and 6 inhibitor) using Abemaciclib with Aromatase inhibitor- Anastrozole in the background of the patient's cardiac status. The patient shows remarkable improvement in exertional dyspnea with a resolution of bone pain and overall improvement in her functional status. She is currently continuing her Abemaciclib with Anastrozole with no adverse effects and is continuing follow-up.

DISCUSSION

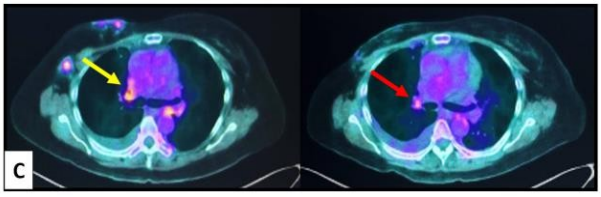
Breast cancer metastatic presentations are likely to increase owing to a more significant number of survivors.[4] This case report details the initial presentation of a patient with an orbital mass. Subsequent imaging revealed additional masses in the breast and rectum. These were initially misdiagnosed as separate primary tumors (double primary). However, further immunohistochemical investigation revealed synchronous metastases to the rectum and orbit originating from the primary breast carcinoma. Orbital metastasis from a primary breast malignancy is relatively uncommon, more so with rectal metastasis. No published local and international literature report describes synchronous orbital and rectal metastasis from a breast primary. Advancements in diagnostic imaging and improved survival rates in patients with



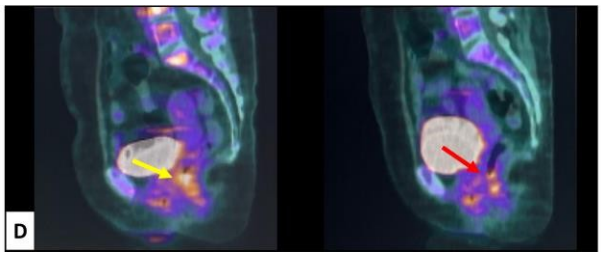
There is a significant decrease in the size of the right Orbital mass lesion, from 3.1 × 1.6 x 2.3 cm to 1.8 x 0.8 x 1.2 cm (previously). This mass lesion is no longer FDG-avid. (RECIST v1.1 -84% Partial response with complete metabolic response)



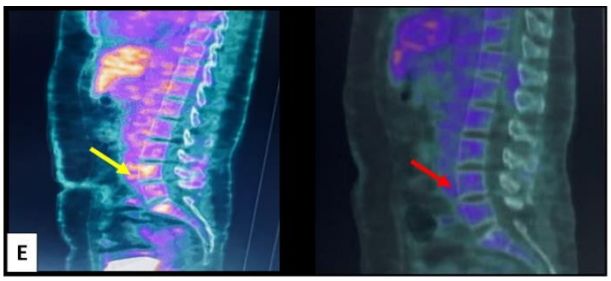
The FDG-PET scan demonstrates a significant reduction in the activity of the right breast mass (SUVmax 2.8, previously 5.6). This coincides with a decrease in the mass's size, which now measures 7.3 × 1.4 × 6.9 cm compared to the prior measurement of 7.8 × 4.1 x 7.0 cm. RECIST v1.1 criteria indicate 20% stable disease.



The previously seen FDG-avid perivascular. Paratracheal, bilateral hilar, and subcarinal lymph nodes are now normal in size and exhibit a significant decrease in FDG activity (SUVmax up to 3.2, previously 4.9). The previously seen FDG-avid left axillary lymph node now has low-grade FDG activity (SUVmax 0.8, previously 2.7).



Re-evaluation shows a decrease in the thickness of the previously described eccentric wall thickening in the distal rectum, now measuring 4 mm compared to 10 mm. It also demonstrates an interval decrease in FDG activity (SUVmax 3.5, previously 5.0). The mildly FDG-avid prominent right mesorectal lymph node has resolved.



There is a significant interval decrease in FDG activity in the lesions along T4, T8, L3 vertebrae, and right acetabulum (SUVmax up to 2.5, previously 5.3)

FIGURE 7 PET CT Side-by-side comparison before (left; November 24, 2022) and after six cycles of chemotherapy Docetaxel and Cyclophosphamide (right; May 9, 2023).

metastatic disease have led to the detection of orbital metastasis with an incidence of 1% to 13%. Of all cancers that affect the orbit, breast cancer is the primary source in 28.5% to 58.8% of cases.[5] Case reports and case series reporting on orbital metastasis from a breast carcinoma primary yielded a few reports in the local setting. One case report discussed a 45-year-old woman presenting with progressive right eye proptosis with a right breast mass biopsied to be an invasive carcinoma with mucinous features. This patient underwent right pterional craniotomy and excision of the sphenoorbital mass with immediate resolution of the proptosis.[6] In one retrospective analysis, the most frequent symptoms included decreased visual acuity (64.2%), pain (57.1%), amaurosis (28.5%), changes in mobility (28.5%), and edema (21.4%).[7] Our patient presented with proptosis with a visible enlarging mass of the right eye, which eventually led to visual loss. A study conducted by *Parrozzani et al*. reported that patients with choroidal orbital metastases are more likely to have ER-positive and PR-positive primary breast cancer than patients with breast cancer metastasizing to any other location.[8]

In our patient, a biopsy of the orbital mass showed estrogen at 90% and progesterone at 80 % receptor positivity. Estrogen production by periorbital fat likely promotes orbital metastasis from primary breast cancer through cellular tropism. This aligns with the observation that most cases involve hormone-sensitive tumors. Estrogen receptor positivity has been found in conjunctiva, tear glands, and tarsal conjunctiva, which could explain predilection in these sites.[9] The widespread nature of orbital metastasis at diagnosis, coupled with its limited chance of cure, necessitates orbital surgery primarily for diagnostic purposes rather than therapeutic ones.[10] Extensive surgical excision is usually not indicated unless the tumor is small, well-circumscribed, and easily accessible or if the tumor is causing extreme proptosis and pain**.**[11] External beam radiation therapy (EBRT) aims to control the tumor's size and preserve visual function. The recommended dosage is 35–40 Gy to the affected orbit in divided doses over 3 to 5 weeks. However, dosage depends on the proximity of the tumor's radiation sensitivity, standard tissue tolerance, and the patient's overall prognosis. Complications of ocular radiotherapy are either acute or chronic. Acute complications include self-resolved radiation blepharoconjunctivitis with a risk of infection.

In contrast, chronic complications may be cutaneous and conjunctival telangiectasias, eyelash loss, cataracts, dry eye, radiation retinopathy, and optic neuropathy.[12] Since most patients with breast cancer and ocular metastases will also have metastases in other locations, palliative systemic treatment is the preferred approach in most cases. Surgical intervention is only recommended for uncontrollable local symptoms.[13,14]

As for rectal metastasis from a breast primary, the gastrointestinal tract (GI tract) is not commonly involved in breast cancer, which accounts for only less than 1% of all breast carcinoma cases.[15] In an extensive review of 206 patients with GI tract metastases originating from breast cancer, only 7% had metastases to the rectum**.** Notably, despite accounting for only less than 15% of all histologic breast cancer subtypes, invasive lobular carcinoma (ILC) is much more frequently encountered in metastasizing to the GI tract than the more common invasive ductal carcinoma (IDC).[16] Infiltrating lobular carcinoma (ILC) was shown to have a particular affinity for the gastrointestinal tract, with a reported rate of metastasis to this tract of 4.5% vs. 0.2% for IDC (which involves the esophagus, stomach, small bowel, extrahepatic bile duct).[4] The reasons behind the specific attraction (tropism) of invasive lobular carcinoma (ILC) to the gastrointestinal tract are still unclear.

Researchers propose that the loss of E-cadherin, a cell-to-cell adhesion molecule specific to epithelial cells, in breast ILC might be a contributing factor. This loss is associated with the formation of tumors with irregular borders and diffuse infiltration, unlike those typically seen in

the invasive ductal carcinoma (IDC) subtype.[17] Thus, in our patient with an IDC subtype, metastasizing to the rectum is rarely encountered and reported, which makes this case all the more rare. Immunohistochemistry staining is the most critical result needed to identify the origin of rectal lesions. Our patient's rectal mass and small round tumor cells suspicious for a neuroendocrine tumor were synaptophysin and chromogranin negative with a positive Estrogen and progesterone receptor status reminiscent of the primary breast mass, which confirms a metastatic location**.**

In metastatic breast cancer patients, the goals of treatment include prolonging survival and enhancing the quality of life (QOL). Therefore, treatments associated with minimal toxicity are preferred. Preferred first-line therapy for metastatic HR- HR-positive, HER2-negative breast cancer includes aromatase inhibitor in combination with CDK 4/6 inhibitor -Palbociclib, Ribociclib Abemaciclib has been shown to have improved progression-free survival compared to giving hormonal therapy alone.[18] Treatment for orbital metastases is inevitably palliative, given that the hematogenous spread of cancer to the orbit is a sign of systemic disease and the involvement of other sites.[10] Because most patients have concomitant progressive systemic disease, chemotherapy followed by hormone therapy in cases of hormone-sensitive tumors is indicated in patients with good performance status. Systemic treatment, when combined with radiotherapy, can significantly improve palliative outcomes.[19] Due to our patient presenting visceral crisis with symptomatic lung metastasis with evidence of cardiac dysfunction, she underwent palliative chemotherapy with 6 cycles of Docetaxel and Cyclophosphamide. The patient also showed good clinical and radiographic response, as evidenced by her interim whole- body PET CT scan. The prognosis of patients with metastatic orbital tumors is relatively poor, with median survival ranging from 22 to 31 months for breast cancer.[20] A study by *Ferry et al*. found that 92% of patients with ocular metastasis died from metastatic breast cancer.[21] The same study also showed that the invasive lobular histological subtype is more likely to cause orbital metastasis than invasive ductal carcinoma.[22] Nevertheless, rare cases of long-term survival after the diagnosis of breast cancer presenting as an orbital mass have been reported.[23]

As in our case, the patient presented with rectal and lung metastases simultaneously. Exhaustive investigation revealed that this was a case of primary breast carcinoma with orbital, lung, and rectal metastases rather than a double primary tumor.

CONCLUSION

Our case demonstrates an exceptional presentation of a primary breast malignancy with synchronous orbital and rectal metastasis. This case report highlights the broad clinical presentation of breast carcinoma. It emphasizes the importance of extensive work-up, including imaging and pathological review, for accurate diagnosis. Initially suspected to be a double primary cancer, further investigation revealed it to be a single entity.

DATA AVAILABILITY STATEMENTS

Not publicly available. The authors will make the raw data underpinning this article's conclusions accessible upon request without unnecessary restriction. To protect ethical considerations and participant privacy, the authors cannot publicly share the data. However, they can make it available upon reasonable request with approval from the institutional ethics committee.

ETHICS STATEMENT

The Ethics Review Board/Committee of Chong Hua Hospital approved the study. Written informed consent was obtained from the patient for the publication of this case report.

AUTHORS CONTRIBUTION

HMG, writing – original draft, review & editing; AJU, resources, review & editing.

FUNDING

This research received no external funding.

CONFLICT OF INTEREST

The authors declare no conflicts of interest related to commercial or financial relationships.

PUBLISHER'S NOTE

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DECLARATION OF USE OF GENERATIVE ARTIFICIAL INTELLIGENCE

No generative AI technologies were used in the writing of this manuscript.

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Received: 2023 Nov 15 **Received in revised form:** 2024 Mar 08 **Accepted:** 2024 Jun 11

CITATION
Garmino HM, Uson AJB. Primary breast cancer with orbital and rectal metastasis: a case report. *Philipp J Oncol* [Internet]. 2025 [cited 2025 Jun 15];1(1):e001. Available from: https://www.philsoconc.org/post/primary-breast-cancer-with-orbital-and-rectal-metastasis-a-case-report