

Orbital Metastasis as The Initial Presentation of Breast Cancer

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Introduction

Breast cancer is the most common cancer among the female population of Malaysia, with an average lifetime risk of 31.1%.¹ Typical sites for metastasis of the breast carcinoma include the bones, liver, lungs, skin, and brain. In most cases, breast cancer is diagnosed first, but in 12–31% of the cases like in this case, the metastasis appear first as the initial presentation. In this case, we reported a case of a healthy young woman who presented with orbital metastasis as the initial presentation of breast cancer.

Methods

See case report.

Results

A 32-year-old married woman who was a passive smoker for the past six years presented at an ophthalmology clinic with a sudden onset of binocular horizontal diplopia for two days. This condition was associated with increased fullness of the right upper and lower eyelids and conjunctival redness for 3 months. She also complained of having had intermittent generalized headaches for the past three months. However, she denied any vomiting, seizures, limb weakness, or constitutional symptoms. Her other systemic symptoms

were unremarkable. She has 4 children and a significant positive family history of cancer; her grandfather and grandmother died of liver carcinoma and colon carcinoma, respectively.

Ocular examination showed visual acuity of 6/9 in each eye, with no relative afferent pupillary defect noted. There was a 2 cm x 4 cm x 3 cm non-tender mass with a firm, irregular border above the right lower eyelid and displaying fullness and erythematous medial canthal of the right upper eyelid. No proptosis or bruit was identified. Extraocular movement in the right eye was limited in all directions, while the left eye had limited abduction (**Figure 1**). Anterior segment examination showed nasally dilated episcleral vessels in both eyes. Intraocular pressure was high for both eyes. Dilated fundal examination showed bilateral optic disc swelling with normal macula and absence of retinitis, choroiditis, or vasculitis. The patient's treatment began with maximal topical antiglaucoma eyedrops.

A complete physical examination revealed peau d'orange skin changes in the breasts with an underlying 2-cm irregular mass in the retroareolar region of the left breast. An enlarged nontender Virchow's node was also palpable. The results of other systemic examinations were unremarkable.

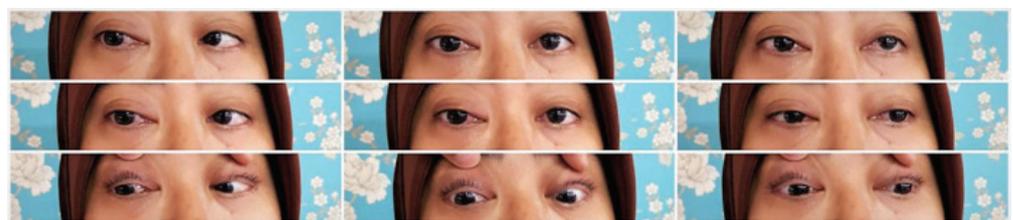


Figure 1: Images show there is a limitation of extraocular movements in all 9 cardinal gazes in the right eye with limitation of abduction in the left eye.

Mammography identified an irregular, high-density mass over the bilateral subareolar area. Contrast enhanced computed tomography (CECT) of the brain, orbit, thorax, abdomen, and pelvis showed bilateral infiltrative lesions within both the orbital floors and the brain, in keeping with metastases (**Figure 2**). In

addition, a bilateral heterogeneous mass was revealed within the breast parenchyma with thickening of the overlying skin, as well as an irregular heterogeneous lesion in segment IVa/VIII of the liver and periampullary region (**Figures 3 and 4**).

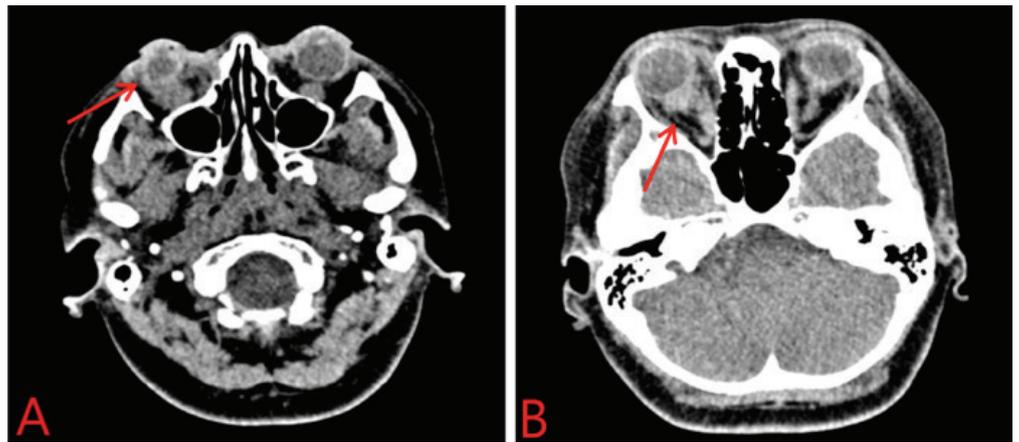


Figure 2: CT scan imaging of the orbit: Axial view A) and B) images showed retro-orbital mass bilaterally, which was worse on the right side. The right extraocular area is filled up with an enhancing soft tissue mass (red arrow).

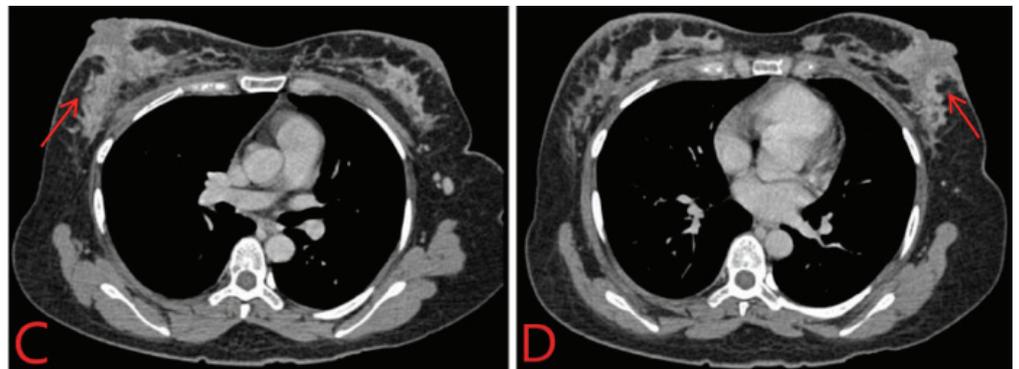


Figure 3: . CT imaging of thorax: Axial view C) and D) images demonstrated bilateral mass at the retroareolar areas of the breast with subcutaneous thickening at the periareolar area (Red arrows).

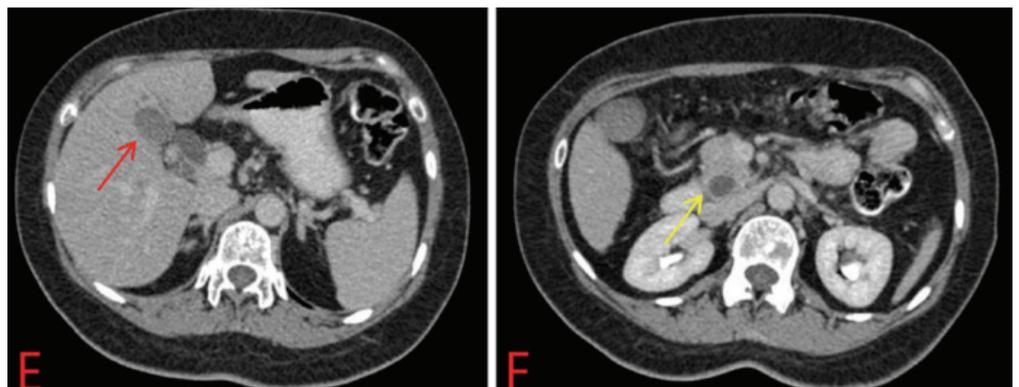


Figure 4: CT imaging of abdomen: Axial view E) Images showed an irregular heterogenous hypodense metastatic lesion in segment IVa/VIII (red arrow) and F) periampullary region (yellow arrow).

She was referred to the oculoplastic team for an orbital biopsy. Histopathological examination of the right orbital floor (**Figure 5**) lesion and the breast tissue biopsy yielded results compatible with breast cancer metastasis in the orbit. Immunohistochemistry analysis confirmed that the primary tumor originated in the breast. Therefore, this discovery was followed by a definitive diagnosis of infiltrative lobular breast carcinoma with disseminated metastases.

The patient's care was subsequently co-managed by both the oncology and surgical teams. Palliative chemotherapy and radiation therapy were commenced before planned surgery. Unfortunately, however, the patient died three months after the diagnosis was made.

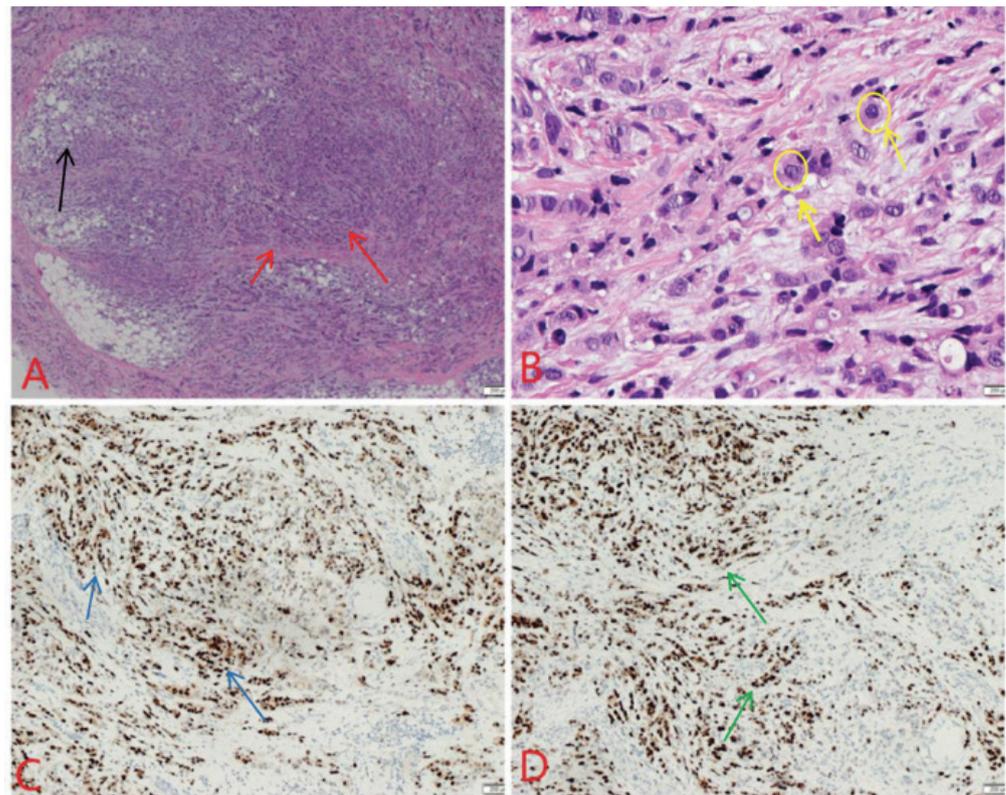


Figure 5: Left orbital tissue biopsy specimen: A) demonstrated malignant cells arranged predominantly in cords, infiltrated the fatty tissue (red arrow). B) Malignant cells are moderately pleomorphic, having hyperchromatic to vesicular nucleus, inconspicuous nucleoli and moderate amount of cytoplasm. (yellow arrow) C) 60% of tumour cells PR positive. D) (green arrow) 70% of tumour cells ER positive. (blue arrow)

Discussion

The incidence of metastasis of the orbit in a patient with systemic malignancy has been reported to vary between 2 and 3%.^{2,3} Metastatic breast carcinoma is considered the most common primary tumor to metastasize in the orbital region, accounting for 55–60% of cases, followed by lung carcinoma (16%–20%), cutaneous melanoma (4.5%), prostate carcinoma (3.6%), and gastrointestinal carcinoma (3.6%).^{4,6}

Orbital metastases can display a variety of clinical presentations. Based on a case series by Ahmad et al., diplopia (48%), proptosis (26%), pain (19%), decreased vision (16%), ptosis (10%), and palpable orbital mass were among this condition's most common symptoms.⁷ In our case, the patient presented with subacute onset of diplopia with underlying gradual onset of a right orbital mass.

Although the majority of orbital metastasis have been found in patients with known diagnoses of breast cancer, a small percentage of cases (12–31%), including our case, this same metastasis

was found before breast cancer had been diagnosed. Thus, with the absence of a primary carcinoma diagnosis, finding metastatic diseases presents a challenge. Furthermore, Ferry et al. found that the latency period between primary carcinoma and orbital metastasis may range from 4 to 6.5 years.¹⁰

Diagnosing metastatic disease requires a high index of clinical suspicion. In our case, the patient presented with an orbital mass, and the etiology varied from non-infective to infective causes. Possible differential diagnoses could include thyroid eye disease, carotid–cavernous fistula, orbital cellulitis, lymphoproliferative disorder (lymphoma), and idiopathic orbital inflammatory disease. Most orbital metastases will produce a motility deficit, pain, and/or impaired vision in comparison with benign lesions, which are usually asymptomatic or progress slowly.¹¹ Differentiating orbital metastasis from other differential diagnosis can be made by doing a thorough history taking and physical examination. In our case, the presence of a strong family history of cancer, in addition to the detection of a palpable retro-areolar mass in the patient's left breast, strongly pointed

to malignancy as the primary source of her complaints.

Imaging of the orbital lesion will also aid in determining whether a mass is malignant or benign. Metastatic lesions are more likely to involve the anterior orbital rather than the posterior orbit, as well as bone or extraocular muscles.³ Our patient's imaging of the orbit revealed the presence of an ill-defined mass arising from the right retroconal region, with involvement of the right medial and inferior rectus, which are associated with left extraocular muscle involvement.

The majority of metastases to the orbit do not need to be biopsied, especially in patients known to have metastatic disease. However, in instances of solitary metastasis to the orbit in patients with no identifiable metastatic disease elsewhere, tissue biopsy is crucial for definitive diagnosis only if it accessible.¹¹

Following the diagnosis of infiltrative lobular breast carcinoma stage IV with metastases to the brain, our patient was subjected to palliative care treatment. The aims of palliative care are to improve quality of life, to provide comfort, and to help preserve vision. Palliative care treatment for metastatic breast cancer includes radiotherapy, chemotherapy, and hormonal therapy. Radiotherapy has become the primary treatment for orbital metastases,

showing a high objective response rate with symptoms improvement in 80% of cases and vision restoration in some cases.¹²⁻¹³ However, chemotherapy is needed in cases of systemic disease.¹⁴

Extensive orbital surgery such as enucleation is not recommended, since is not curative and is related to high ocular morbidity. However, such procedures may be used in cases involving intractable ocular pain or unmanageable local hygiene. The prognosis for this condition is rather poor, with a median survival rate of 22–31 months following the diagnosis of orbital metastasis.^{7,14} Unfortunately, our patient succumbed to the disease three months after the diagnosis, which was much sooner than deaths reported in existing literature.

Conclusion

Despite increased breast cancer awareness and advancement in technology for early breast cancer diagnosis, a small percentage of patients still present with metastatic signs and symptoms of advanced stages of breast cancer. This case illustrated that undiagnosed metastatic breast carcinoma can initially present with orbital symptoms. Hence, in the presence of slow-growing orbital pathology and a strong family history of cancer in a female patient, a detailed systemic examination of the breasts especially is necessary for establishing the diagnosis.

How does this paper recommend changes to general practitioners (GPs)?

- Painless orbital swelling in a patient should prompt the GPs to collect a detailed medical history and to perform a physical examination.
- GPs have a key role in cancer detection, since they are the first point of contact for patients with possible cancer symptoms or signs. Once malignancy is suspected, an early referral to an ophthalmologist should be made.
- GPs should emphasize the importance of regular surveillance of breast cancer symptoms or signs in patients with risk factors at a primary level (e.g., yearly mammograms and breast self-examinations).

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