

CASE REPORT

Orbital metastasis from an occult breast carcinoma (T0, N1, M1)

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SUMMARY

The authors report a case of an orbital metastasis from an occult breast carcinoma. A 66-year-old woman presented with a growing left orbital tumour. Orbital CT scan was consistent with lymphoma. However, ocular pathology revealed small neoplastic cells showing an 'indian file pattern' suggestive of metastatic carcinoma and immunohistochemistry was positive for CK7, CK CAM5.2 and oestrogen receptor. A systemic evaluation was then performed with mammogram, breast ultrasound and MRI considered normal. An exhaustive systemic evaluation revealed multiple bone lesions, a right axillary lymph node lesion, which presented the same pattern on pathology and immunohistochemistry, with no evidence of a primary tumour. A diagnosis of a metastatic lobular carcinoma of the breast (T0, N1, M1) was made and the patient was started on chemotherapy and adjuvant hormonal therapy.

BACKGROUND

Orbital metastasis is uncommon and occurs in 2%–3% of patients with cancer.¹ It is rarely the initial manifestation of a systemic malignancy. Breast carcinoma is considered to be the most prevalent primary tumour, accounting for 29%–70% of all metastases to the orbit. Although uncommon, it can be the initial manifestation of breast carcinoma.²

This case demonstrates that orbital symptoms may be the primary presentation of this disease and that they can occur in the presence of a normal breast examination and negative mammogram, breast ultrasound and MRI. An orbital metastasis as first symptom of an occult breast cancer is a very rare occurrence but can be the initial and sole presenting feature of breast cancer.

CASE PRESENTATION

A 66-year-old woman was admitted to the ophthalmology department with a history of oedematous left lower eyelid. She referred a 2-month history of a slowly growing left lower eyelid mass with some ocular discomfort, but no pain, diplopia or visual impairment. The patient had no other ocular complaints, constitutional signs or symptoms. Her medical history was relevant for a thyroidectomy, appendectomy and a history of medically controlled arterial hypertension.

On admission, a tender tumefaction and a discrete erythema of the left lower eyelid were observed (figure 1). A palpable mass was noticed in the inferior quadrant of the left orbit. There was a minor

superior eye displacement without proptosis and a slight restriction of ocular vertical movements. There was no afferent pupillary defect and examination of the globes was unremarkable, with a normal Schirmer testing. Best corrected visual acuities were 20/20 in both eyes. There was no regional lymphadenopathy. Clinical and routine laboratory examinations did not reveal any abnormalities.

INVESTIGATIONS

Orbital CT demonstrated a circumscribed but not well-defined homogenous mass in the subcutaneous tissue of the inferior eyelid arising from the inferior portion of the left orbit. The mass was spontaneously enhanced without evidence of bone invasion or destruction (figure 2). Diagnostic impression of this lesion was of an orbital lymphoma.

The patient underwent an excisional biopsy through an anterior eyelid approach. The non-capsulated mass was growing in the subcutaneous tissue, arising from the orbit. A small excisional diagnostic biopsy was taken and submitted for conventional histopathological examination and immunohistochemistry. The biopsy revealed small neoplastic cells showing an 'indian file pattern' suggestive of a metastatic carcinoma, but the immunohistochemistry was inconclusive (figure 3). A second biopsy was then taken to excise as much as possible of the orbital tumour. In this second biopsy, immunohistochemistry revealed positivity for CK7, CK CAM5.2, progesterone and oestrogen receptors (figure 4). It was negative for CK20, E-cadherin, HER-2 and p63.

A systemic evaluation was then performed. Mammography, breast ultrasound and MRI were considered normal (figure 5). Gynaecologic examination revealed no alterations, as well as the endovaginal ultrasound and cervix cytology. A further survey was then performed including a whole-body CT scan. This revealed multiple lesions in the left femur, iliac, sacrum, and cervical and lumbar spines suggestive of metastasis, a right axillary enlarged lymph node, a nodular liver image and a gastric antral suspect image. An upper digestive endoscopy and a colonoscopy yielded negative results. A positron emission tomography (PET) scan revealed multiple bone and left orbital lesions, without images of a primary tumour (figure 6).

An axillary lymph node excision was then performed. This revealed the same histological (figure 7) and immunohistochemical pattern (figure 8) (positive for CK7, CK CAM5.2, progesterone and oestrogen receptors and negative for



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Figure 1 A tender tumefaction and a discrete erythema of the left lower eyelid.

CK20, E-cadherin, HER-2 and p63), compatible with a metastatic lobular carcinoma of the breast (T0, N1, M1).

TREATMENT

A diagnosis of occult breast carcinoma was made and the patient was started on chemotherapy and adjuvant hormonal therapy.

OUTCOME AND FOLLOW-UP

Orbital metastasis reduced with therapy and systemic disease was controlled under hormonal therapy. Patient was followed up by clinical visits for 5 years. Follow-up included life status, orbital recurrence and distant metastasis. Follow-up examinations were

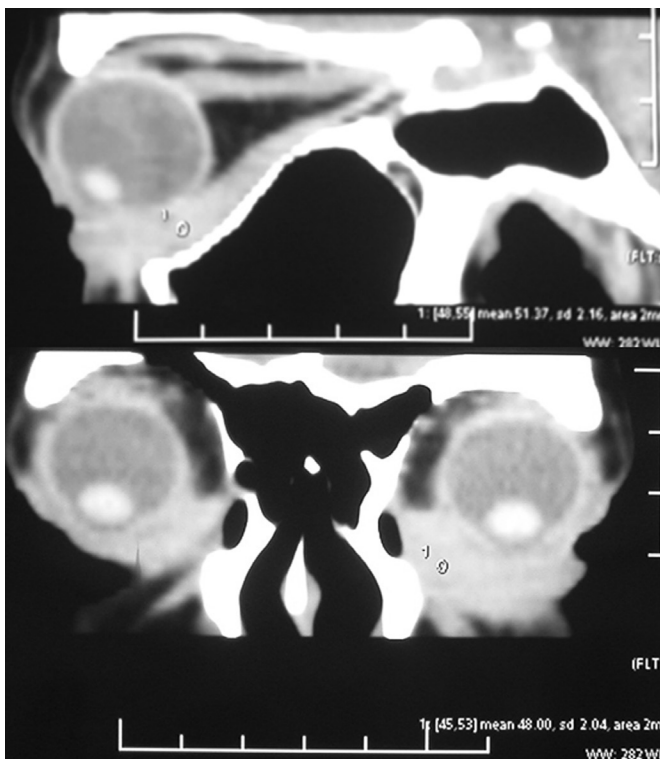


Figure 2 Orbital CT scan showing a circumscribed but not well-defined mass in subcutaneous tissue of the inferior eyelid arising from the inferior portion of the left orbit.

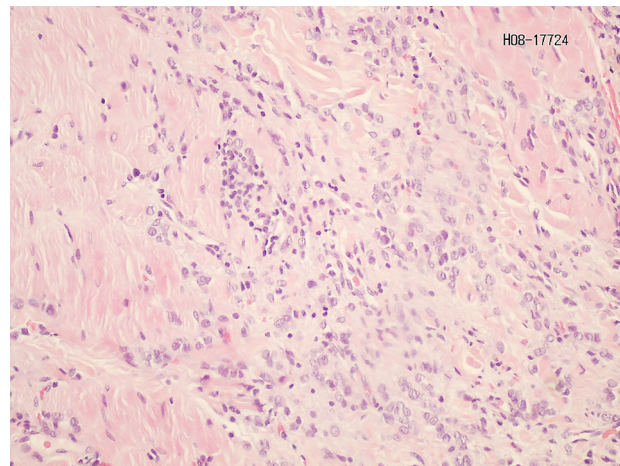


Figure 3 Small neoplastic cells showing an 'indian file pattern' suggestive of a metastatic carcinoma.

conducted every 6 months and included breast ultrasound; mammography; breast MRI; head, chest and abdominal CT; and PET scan.

DISCUSSION

Metastatic tumours to the orbit represent approximately 7% of all orbital lesions in the older adult population, and 29%–70% have its origin in a breast carcinoma.^{1 3} Breast lobular carcinoma has its origin in the terminal duct apparatus and has a diffuse distribution throughout the breast which explains its lack of consistent features on breast imaging. It is most often an incidental finding in a breast biopsy performed for an unrelated mammographic abnormality. The detection of invasive lobular carcinoma in mammography is known to be a difficult task. False-negative rates have been reported to range from 8% to 19%. This is most likely related to the fact that lobular carcinomas spread through the breast parenchyma by means of diffuse infiltration of single rows of malignant cells in a linear fashion around non-neoplastic ducts.^{4 5}

The addition of ultrasonography and MRI to mammography results in a significant increase in breast cancer detection rate.⁶ When used with gadolinium-diethylenetriamine penta-acetic acid, breast MRI has been shown to be sensitive to 83%–100% of

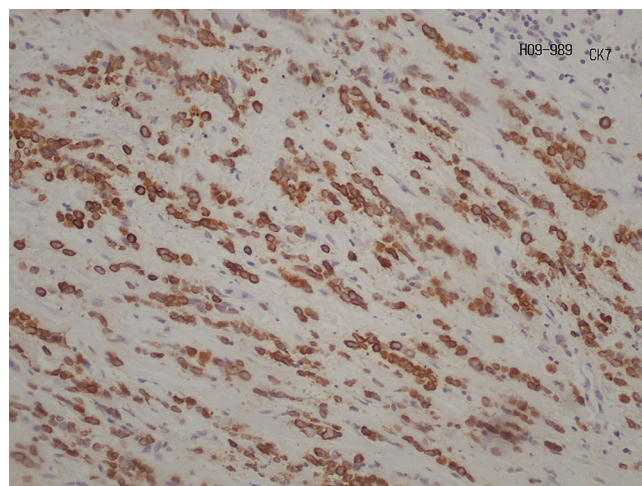


Figure 4 Immunohistochemistry—positive results for CK7 (and also for CK CAM5.2 and oestrogen receptor).

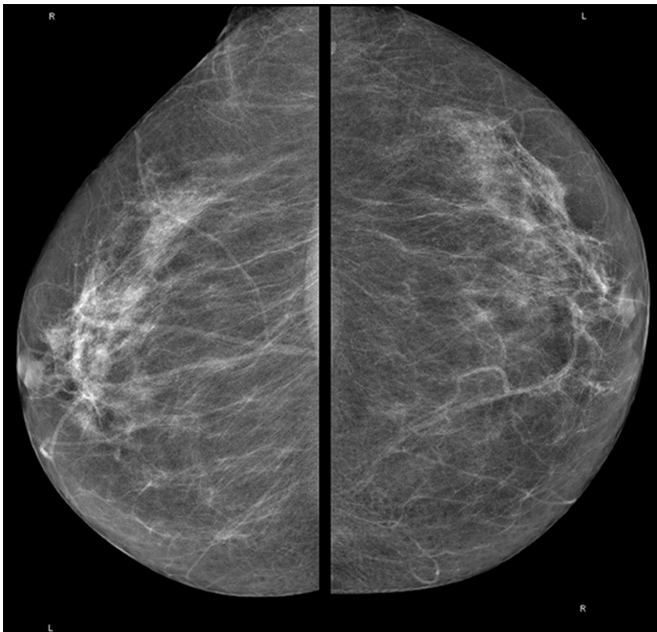


Figure 5 Mammography was considered normal.

breast cancers exceeding a few millimetres in size. Nevertheless, there are cases of imaging occult carcinomas leading to systemic disease. Histologic characteristics may explain why primary invasive lobular carcinomas cannot be found with different imaging techniques, even in advanced stages. These characteristics include a diffuse invasive pattern and a poor desmoplastic reaction. In their course, occult tumour cells spreading is frequent and could be an early event, related to the lobular histological type, but independent of classical histoprosthetic parameters. The locoregional metastatic spread of occult tumour cells seems to be not a prerequisite for systemic involvement.⁷

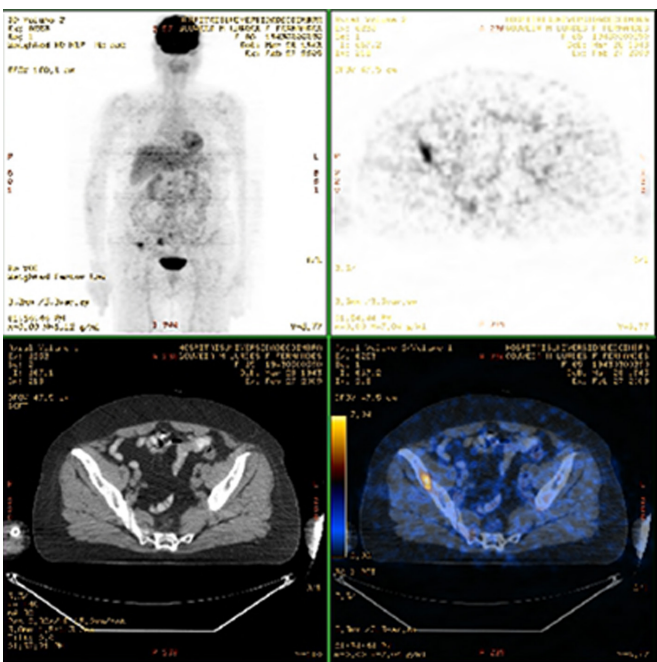


Figure 6 Positron emission tomography (PET) scan with multiple bone and left orbital lesions, but without suggestive images of a primitive tumour.

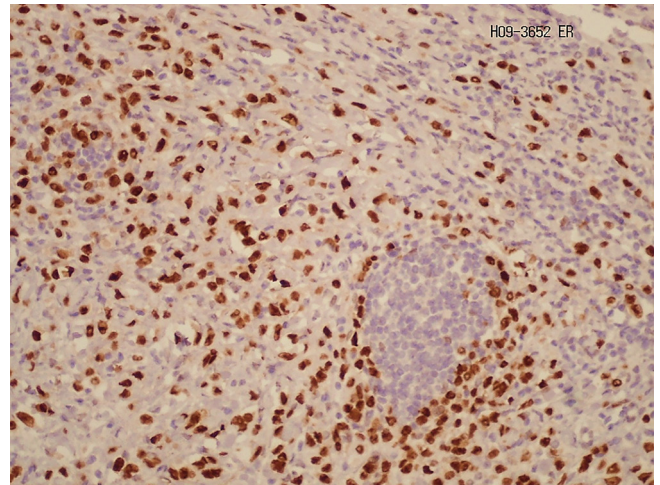


Figure 7 Axillary lymph node excisional biopsy revealed the same histological pattern suggestive of metastatic carcinoma.

In this case, no breast mass was clinically evident and mammography, ultrasonography and MRI yielded no pathological findings. Previous cases report that orbital manifestation is usually discovered secondary to breast cancer.^{1 2 8-10} This case demonstrates that orbital symptoms may be the primary presentation of the disease and it can occur in the presence of normal breast examination or negative mammogram.

Occult primary breast carcinoma represents less than 1% of breast carcinoma cases. Most patients have ipsilateral axillary lymphadenopathy and distant metastases at the time of presentation. However, the distant metastatic pattern of invasive lobular carcinoma differs significantly from that of invasive ductal carcinoma. Whereas ductal carcinoma often metastasises to the lung, liver, bone and brain, lobular carcinoma tends to spread to the gastrointestinal tract, genitourinary tract, peritoneum, retroperitoneum, leptomeninges and eventually orbit.¹¹⁻¹³ Some investigators have suggested that invasive lobular carcinoma has a higher distant metastasis rate,^{12 13} likely because of its infiltrative nature. It has been postulated that loss of E-cadherin, the cell-to-cell adhesion molecule, facilitates the metastasis process. Like in the breast, metastatic invasive lobular carcinoma tends to

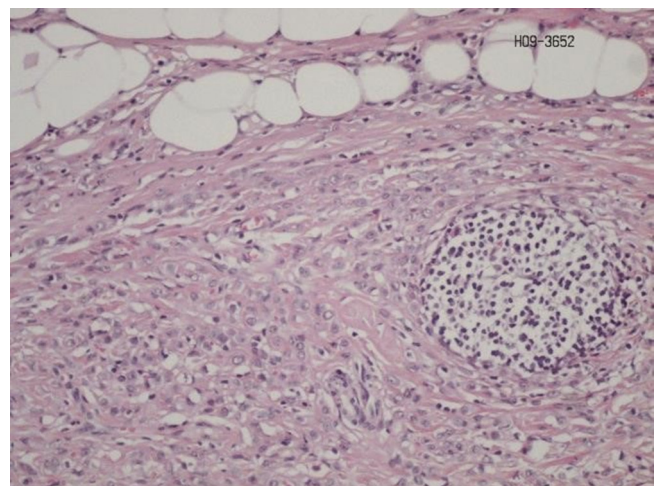


Figure 8 Lymph node biopsy showed positive results for oestrogen receptor (and also for CK7, CK CAM5.2).

Learning points

- ▶ An orbital metastasis as first symptom of breast cancer is a rare occurrence.
- ▶ There are cases of imaging occult breast carcinomas leading to systemic disease.
- ▶ Orbital metastasis can occur in the presence of normal breast examination and negative mammography, ultrasonography and MRI.
- ▶ An orbital metastasis can be the initial and sole presenting feature of an occult invasive lobular breast carcinoma.
- ▶ Only an accurate pathological and immunohistochemical biopsy study can lead to a correct diagnosis.

infiltrate the affected organs in a diffuse process, as in our case, instead of forming a tumour nodule.

The incidence of invasive lobular carcinoma metastasis to the orbit is unknown, although a few cases have been reported^{14–18} and could represent the cancer subtype with the highest prevalence among orbital metastases.¹⁸ In all reported cases, the tumour involved the extraocular muscles with a diffuse thickening, and a diffuse infiltration of orbital soft tissues, causing proptosis. Usually, orbital metastasis is diagnosed after a known invasive lobular carcinoma. In rare cases, orbital metastatic disease manifests prior to the primary malignancy, and the ophthalmologist is the first to make the diagnosis after breast imaging. Nevertheless, an orbital metastasis as the initial and sole presenting feature of an occult invasive lobular breast carcinoma cancer is an extremely rare occurrence and only an accurate pathological and immunohistochemical study can lead to a correct diagnosis.

Contributors RPP planned, conducted and wrote the manuscript. JF helped with data acquisition and analysis. MNB reviewed and edited the manuscript. RP helped with the writing and revision of the manuscript.

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