

## Rare Presentation of Metastatic Lobular Mammary Carcinoma to the Orbit

F Rhana Mousavi<sup>1</sup>, Mina Bekheit<sup>2</sup>, Nick A Hirad<sup>3</sup>, Nicki Hirad<sup>4</sup> and Abanoub Gabra<sup>1\*</sup>

<sup>1</sup>Department of Pathology and Laboratory Medicine, HCA East Florida, USA

<sup>2</sup>Dr Kiran C Patel School of Medicine, NOVA Southeastern University, USA

<sup>3</sup>Florida Atlantic University, Florida, USA

<sup>4</sup>Halmos College of Arts and Sciences, NOVA Southeastern University, USA

**\*Corresponding Author:** Abanoub Gabra, Department of Pathology and Laboratory Medicine, HCA East Florida, USA.

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### Abstract

While orbital metastases may be the first manifestation of occult breast cancer metastases, they may also be discovered in patients who have already undergone chemotherapy and hormone therapy and may instead represent recurrence of breast cancer. It is reasonable to caution clinicians of new-onset eye symptoms especially in patients with a previous history of breast cancer, metastatic or localized, and that these complaints ought to be worked up fully. This is a case of 58-year-old female, who noticed a small nodular lesion in upper eyelid (orbital area) while on vacation in Italy. The lesion appears to her as a mosquito bite with minimal itching. However, the lesion grew in a few weeks and became irritated. The patient was found to have a one cm hard and non-mobile nodular lesion by physical exam. A biopsy was performed and sent to the pathology department with metastatic lobular carcinoma, breast primary confirmed by immunohistochemistry studies.

**Keywords:** Metastatic Lobular Carcinoma; Lobular Carcinoma In Situ (LCIS); Breast Cancer; Orbital Metastases

### Introduction

Lobular carcinoma commonly arises from the precursor lesion Lobular carcinoma *in situ* (LCIS). The relative risk of invasive lobular carcinoma ILC is 9 to 10 times greater in patients with LCIS than the general population. LCIS was first described by Foote and Stewart in 1941 in a report that characterized its morphology as loose cells without polarity; with varying shapes; but of homogenous size. It is also widely accepted that LCIS commonly presents with multiple foci and that it is an incidental finding on microscopy since it is difficult to detect clinically. While classic LCIS is a known risk factor and nonobligate precursor for invasive lobular carcinoma, it is largely treated as a benign lesion [1]. Because classic LCIS is an incidental finding in biopsy, the true incidence is likely underestimated. Nevertheless, its incidence on biopsy is 1.8% to 2.5%. Notably, LCIS incidence has more than tripled (3.5x) from 1978 to 1998, with the highest uptick in incidence among women older than 50 years, likely due to increased breast cancer screening with incidental findings [1].

While orbital metastases may be the first manifestation of occult breast cancer metastases, they may also be discovered in patients who have already undergone chemotherapy and hormone therapy and may instead represent recurrence of breast cancer as seen in the case report by Eckardt. This patient presented with 3 weeks of left orbital pain with slight exophthalmos three years after completion of chemotherapy for invasive ductal cancer of the breast. Staging revealed multifocal metastases to the orbital bones, the orbits, cervical

spine, right femur, left ilium and ribs. With a mean survival after discovery of 31 months, orbital metastases of breast cancer portend a poor prognosis; the probability of other metastases is high in these patients [7]. Thus, it is reasonable to caution clinicians of new-onset eye symptoms especially in patients with a previous history of breast cancer, metastatic or localized, and that these complaints ought to be worked up fully.

### Case Presentation

This is a case of 58-year-old female, who noticed a small nodular lesion in upper eyelid (orbital area) while on vacation in Italy. The lesion appears to her as a mosquito bite with minimal itching. However, the lesion grew in a few weeks and became irritated. She had her annual mammogram studies done regularly, reported normal consecutively. She presented in an Ophthalmologist office for her evaluation and found to have a one cm hard and non-mobile nodular lesion by physical exam. A biopsy was performed and sent to the pathology department with metastatic lobular carcinoma, breast primary confirmed by immunohistochemistry studies. Thereafter, a PET scan was ordered showing metastatic carcinoma to brain and L3. She underwent chemotherapy based on her immune-profile (ER +, PR+, and Her2 -) and genetic testing.

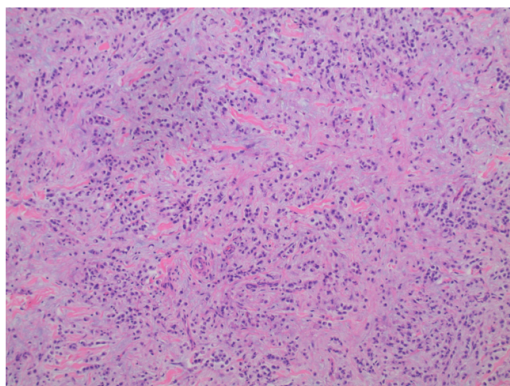


Figure A: Hematoxylin and eosin stain 20x power.

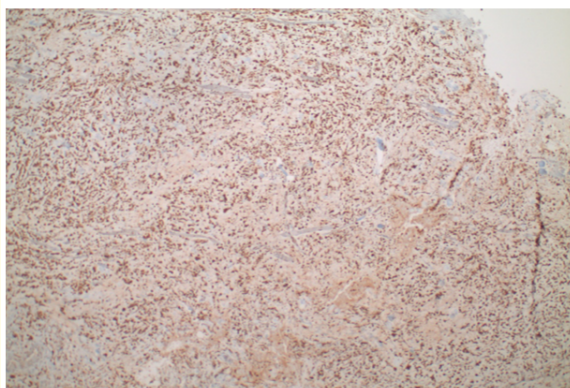
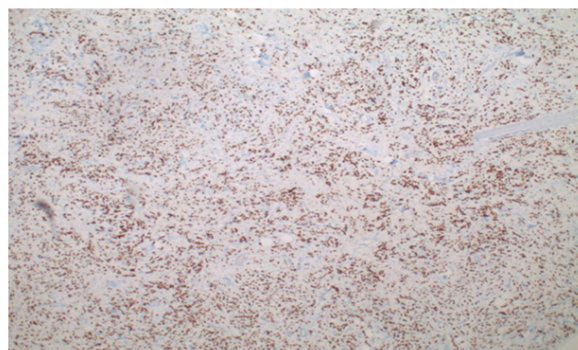
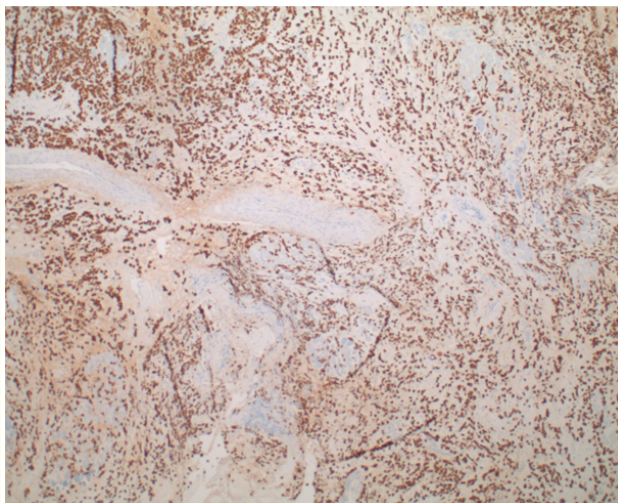


Figure B: GATA 3 IHC, 20x power.



**Figure C:** GCDFP15 IHC, 20x power.



**Figure D:** Pan-cytokeratin IHC, 20x power.

### Discussion

Invasive lobular carcinoma ILC has unique features including: loss of cell-to-cell adhesion molecule E-cadherin; positivity for estrogen receptor ER and progesterone receptor PR; and, negativity for human epidermal growth factor receptor HER-2 negativity. ILC typically shows single-file strands of small discohesive cells. Histological, clinical, and radiographic identification of ILC are difficult although MRI has the highest reported sensitivity in its detection even compared to mammography. ILC does not typically present with a palpable mass like other types of breast cancer [2]. ILC is usually multicentric and does not cause significant damage to surrounding tissue that would be readily observed on radiography. Lastly, while microcalcifications on mammography commonly suggest presence of breast cancer, rarely does ILC contain microcalcifications [3]. It was found that chemotherapy often leads to low rates of complete pathological response later requiring mastectomy; this may be explained by ILC's low proliferative index. Non-surgical treatment options include endocrine therapy

with letrozole being the more promising choice as compared to tamoxifen due to increased resistance observed with tamoxifen use to treat ILC [3].

Much like its precursor, ILC also saw an uptick in incidence in women over the age of 50 likely due to widespread breast cancer screening as well as increased use of hormone replacement therapy, since ILC is ER positive. ILC represents a minority of all breast cancer cases, approximately 5 - 15% of the total, but patients typically present at later stages and tend to be older than those with other forms of breast cancer. Some well-known risk factors for ILC include alcohol, early menarche, late menopause, nulliparity/low parity, family history of hereditary diffuse gastric cancer syndrome, and positivity of germlines mutation CHD1 [3].

Most deaths from breast cancer occur due to metastases [4]. ILC has a proclivity to metastasize in unusual sites namely the serosa, meninges, ovaries, the luminal gastrointestinal tract, CSF and the orbits as in the case of our patient [2]. The incidence of breast cancer metastases to unusual sites is rising due to prolonged survival with modern treatments and the availability of more sensitive imaging modalities [4]. While the breast is commonly the source of metastases to the orbits (29 - 70%) [5], such a finding is usually made well after a primary cancer has been identified [6]. However, in a case by Reeves, a 61-year-old female with a history of hysterectomy and BSO due to metastatic disease (without identification of a primary cancer) presented with left upper eyelid ptosis as well as left enophthalmos and decreased visual acuity. Four years later she again presented with worsening symptoms but a brain CT showed infiltrating homogenous mass in the left orbit. Upon histological review, infiltrating adenocarcinoma reminiscent of breast cancer was found, though breast examination was unremarkable. However, mammography showed a spiculated opacity in the left breast which, when explored with needle biopsy, showed infiltrating lobular carcinoma identical to that from the orbit. These findings were compared with the histological findings from the uterine metastases and matched. The patient was treated with radiation and tamoxifen. Eight years later, the patient required a bowel resection due to a rectal obstruction which showed, interestingly enough, adenocarcinoma with focal signet features on pathology-consistent with another ILC metastasis [6].

In another case by Proenca, a 66-year-old female presented with edematous left lower eyelid with a 2-month history of growing left lower eyelid mass that was otherwise asymptomatic. Biopsy demonstrated 'Indian file' pattern consistent with metastatic carcinoma and immunohistochemistry staining pattern suggestive of ILC. Subsequent studies including MRI, US, and mammography as well as gynecologic examinations returned without abnormalities. Whole-body CT survey showed multiple lesions in the bones, an enlarged axillary lymph node as well as suspicious masses in the GI tract. The patient was then started on chemotherapy and hormonal therapy [5]. This case represents occult breast carcinomas on both breast imaging and physical examination. Virtually all case reports of ILC metastases to the orbits describe involvement of the extraocular muscles with induration as well as infiltration of orbital soft tissues responsible for proptosis.

Another case study by Spraker demonstrated metastatic ILC 35 years after diagnosis and subsequent excision of LCIS discovered in the right breast upon palpation of a lump. This patient was treated with anastrozole and then proton radiotherapy with a favorable response. Because LCIS is considered a benign disease, it is unusual that the patient then went on to develop orbital metastases. It is possible that ILC was present at the time but went unnoticed or that the patient later developed ILC in the remaining breast tissue post-mastectomy [8]. In a study at the university of Virginia, of the 2,743 new cases of breast cancer just 20 involved symptomatic orbital metastases, representing 0.7% of the total. The presentations included unilateral orbital pain, proptosis, diplopia with decreased visual acuity as the most common [9].

### Conclusion

This is a case of 58-year-old female, who noticed a small nodular lesion in upper eyelid (orbital area). The lesion appears to her as a mosquito bite with minimal itching. However, the lesion grew in a few weeks and became irritated. The patient was found to have a one cm hard and non-mobile nodular lesion by physical exam. A biopsy was performed and sent to the pathology department with metastatic lobular carcinoma. Patient had normal mammogram screenings. Awareness of this condition raises the possibility of lobular carcinoma to metastasize before being clinically or radiologically detectable.

### Disclaimer

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