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## Case Report

# Multiorgan metastatic invasive lobular Carcinoma initially presenting as diplopia <sup>☆</sup>

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## ABSTRACT

We present an interesting case of biopsy-proven multiorgan metastatic invasive lobular carcinoma to the orbits and kidney, initially presenting in a 76-year-old woman with diplopia. Invasive lobular carcinoma is a less common subtype of breast cancer and is often difficult to detect on imaging with an unusual metastatic pattern when compared to invasive ductal carcinoma. Metastatic invasive lobular carcinoma most frequently involves the orbits, ovaries, gastrointestinal tract, retroperitoneum and bone. Disease involving these organ systems detected on imaging should raise concern for metastatic disease when appropriate.

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## Introduction

We present an interesting case of biopsy-proven metastatic invasive lobular carcinoma to the orbits presenting initially with diplopia. Additional workup revealed a palpable breast mass upon which biopsy demonstrated invasive lobular carcinoma, similar to the orbital histology, as well as, histopathologic-proven metastatic disease to the kidney. Invasive lobular carcinoma is a less common subtype of breast cancer and is often difficult to detect on imaging with an unusual metastatic pattern when compared to invasive ductal carcinoma [1–4]. We emphasize the challenge in diagnosing

this malignancy on mammography and discuss the atypical metastatic disease pattern with an emphasis on the orbital and retroperitoneal findings.

## Case report

A 76-year-old woman presented to her physician, complaining of double vision and left eye droop. An magnetic resonance examination of the orbits was performed which demonstrated enophthalmos of the left globe with diffuse T2 hypointensity and infiltrative enhancement in the intraconal and extraconal

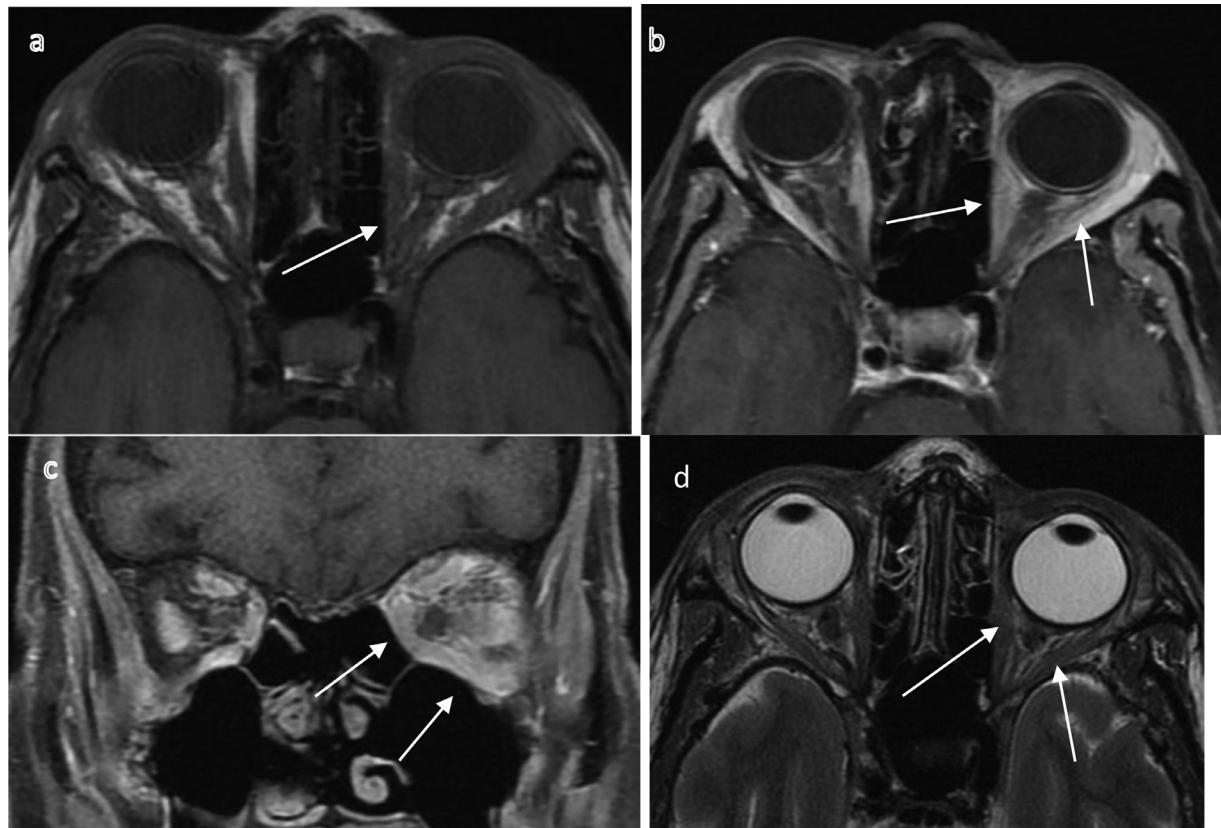
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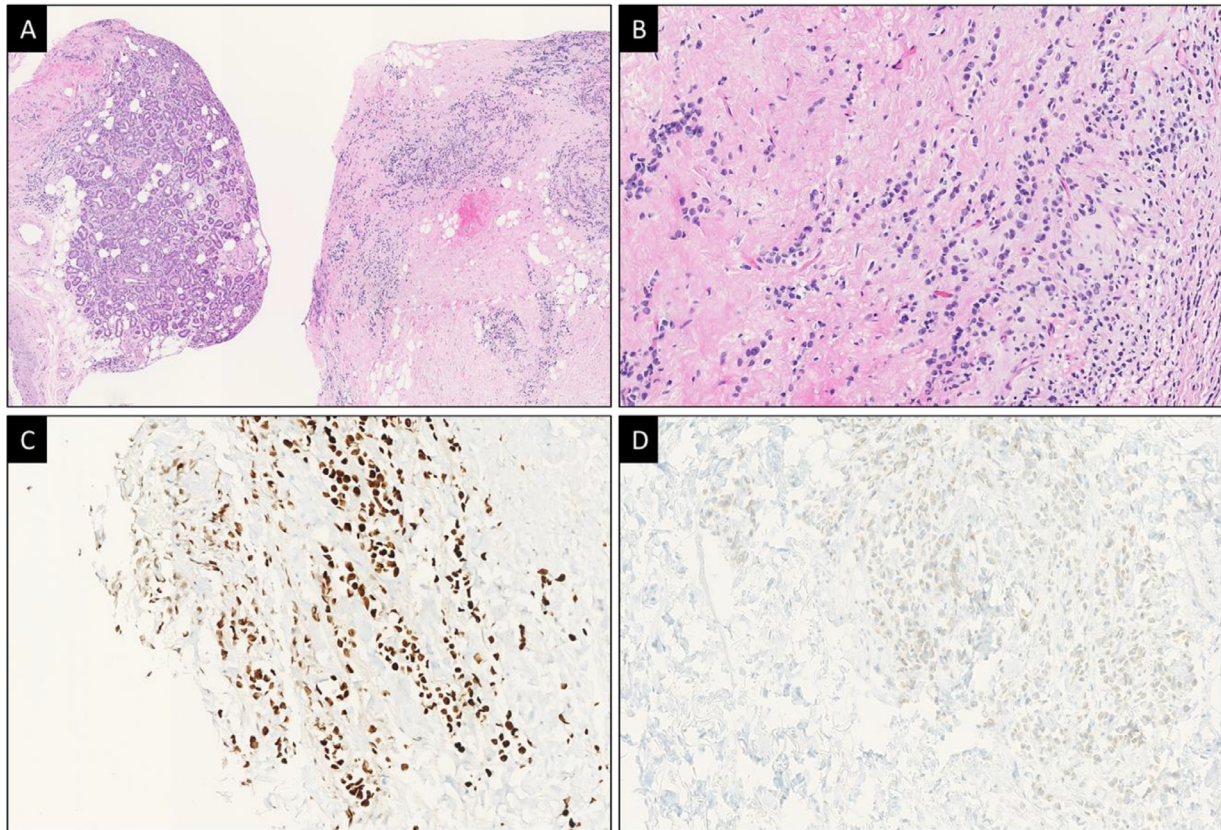
**Fig. 1 – MR examination of the orbit with and without IV contrast. (a) axial precontrast T1 weighted and (b) postcontrast T1-weighted images demonstrates diffuse infiltrative T1 hypointensity of the orbital fat predominately on the left with accompanying intraconal and extraconal enhancement. (c) Coronal postcontrast T1-weighted fat saturated image demonstrates an infiltrative pattern of enhancement of the left intraconal and extraconal orbit. (d) Axial T2-weighted image demonstrates left enophthalmos with diffuse infiltrative T2 hypointense signal changes of the left orbital retrobulbar fat (arrows).**

orbital fat bilaterally, with asymmetric involvement of the left orbit (Fig. 1). The patient was then seen at our institution's Ophthalmology department in which an orbitotomy was performed with biopsies taken for definitive diagnosis. Pathology demonstrated small fairly uniform infiltrative tumor cells involving fibrous connective tissue with characteristic single-file pattern of growth of lobular type mammary carcinoma in conjunction with loss of e-cadherin expression by immunohistochemistry, supporting lobular type of metastatic mammary carcinoma (Fig. 2). Subsequent mammographic workup revealed a subtle focal asymmetry in the upper outer quadrant of the left breast posteriorly, measuring approximately 2.9 cm (Fig. 3). After consultation with our institution's breast surgeon, it was noted on physical exam that the left breast was smaller than the right and demonstrated a palpable mass. A breast magnetic resonance imaging (MRI) was then completed to assess for extent and demonstrated mild asymmetric segmental heterogeneous nonmass enhancement in the central, slightly lateral left breast, involving the middle through the posterior thirds, measuring 5.2 cm in greatest dimension (Fig. 4). Since the palpable left breast abnormality was more suspicious than the subtle imaging findings, a palpation-guided core biopsy was performed. Pathology revealed small fairly uniform infiltrative tumor cells involving

fibrous stromal tissue and adipose tissue with characteristic single-file and concentric pattern of growth, typical of invasive mammary carcinoma, lobular type (Fig. 5). The patient then underwent a computed tomography (CT) examination of the chest, abdomen and pelvis to assess for metastatic disease. A heterogeneously enhancing mass was identified, arising from the inferior pole of the right kidney, measuring 5.6 × 6.1 × 6.3 cm (Fig. 6). A right nephrectomy was performed with pathology consistent with an oncocytoma with adjacent small fairly uniform infiltrative loosely cohesive tumor cells with areas demonstrating characteristic single-file pattern of growth, similar tumor morphology when compared to the previously biopsied breast tumor and consistent with metastatic mammary carcinoma, lobular type (Figs. 7 and 8). The patient is currently on systemic chemotherapy, given the presence of multiorgan metastatic disease.

## Discussion

Invasive lobular carcinoma (ILC) is a subtype of breast cancer, accounting for 10%–15% of all mammary carcinomas. ILC is historically difficult to detect on imaging due to multiple



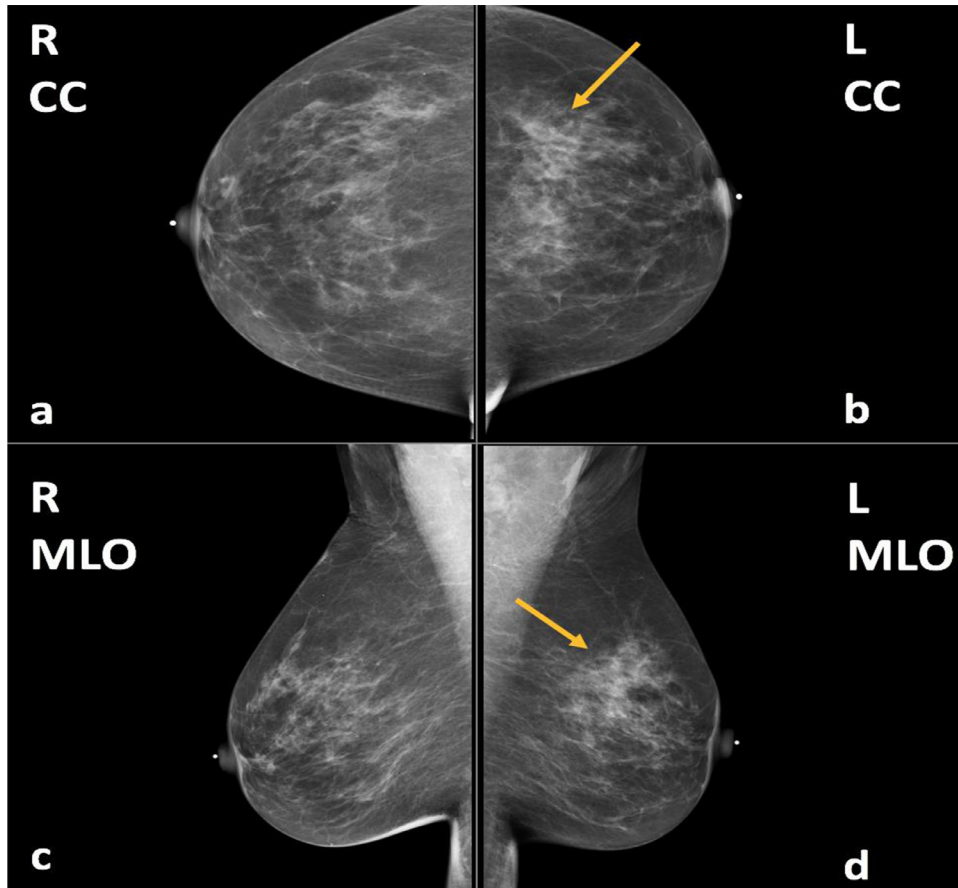
**Fig. 2** – Left orbital mass involved by metastatic mammary carcinoma (lobular type). (a) Patchy foci of irregular infiltrative tumor cells involving fibrous connective tissue, adipose tissue and portion of lacrimal gland (left) [low power, hematoxylin eosin, original magnification 50 x]. (b) small fairly uniform infiltrative tumor cells involving fibrous connective tissue with characteristic single-file pattern of growth of lobular type mammary carcinoma [intermediate power, hematoxylin eosin, original magnification 190 x]. (c) Estrogen receptor immunohistochemical stain demonstrating fairly strong diffuse nuclear staining in the tumor cells, supporting metastatic mammary carcinoma [intermediate power, original magnification 200 x]. (d) e-cadherin immunohistochemical stain demonstrating decreased to absent membranous staining in the tumor cells, supporting lobular type of metastatic mammary carcinoma [intermediate power, original magnification 200 x]. Additional immunohistochemical stains (not shown) demonstrated strong diffuse tumor cell staining with epithelial markers (AE1/3, Cam 5.2 and CK7), weak patchy tumor cell staining with BRST-2 (metastatic breast carcinoma marker) and the tumor cells were negative for CD45 (hematopoietic cell marker) and Melan-A (melanocytic maker), supporting the diagnosis of a metastatic mammary carcinoma.

factors, such as low density tumor cells, an infiltrative tumor growth pattern and the absence of typical microcalcifications. This results in overall low contrast differences between the tumor and normal fibroglandular tissue [5]. As a result, mammography has been found to have a low sensitivity in detecting ILC, reportedly ranging from 57% to 81% [6]. ILC characteristically demonstrates loss of cell membrane e-cadherin expression by immunohistochemistry, which is felt to be due to abnormalities and/or mutations in the *CDH1* gene, which normally encodes the e-cadherin membrane protein expressed by breast epithelial cells mediating cell to cell adhesion [7]. Therefore, this loss of e-cadherin expression is felt to give rise to the characteristic dyscohesive nature of ILC, which can be associated with a diffuse growth-pattern without well-defined margins, which is thought to be in part responsible for the difficulty in detecting ILC by mammography [7]. When compared to invasive ductal carcinomas, ILC more frequently

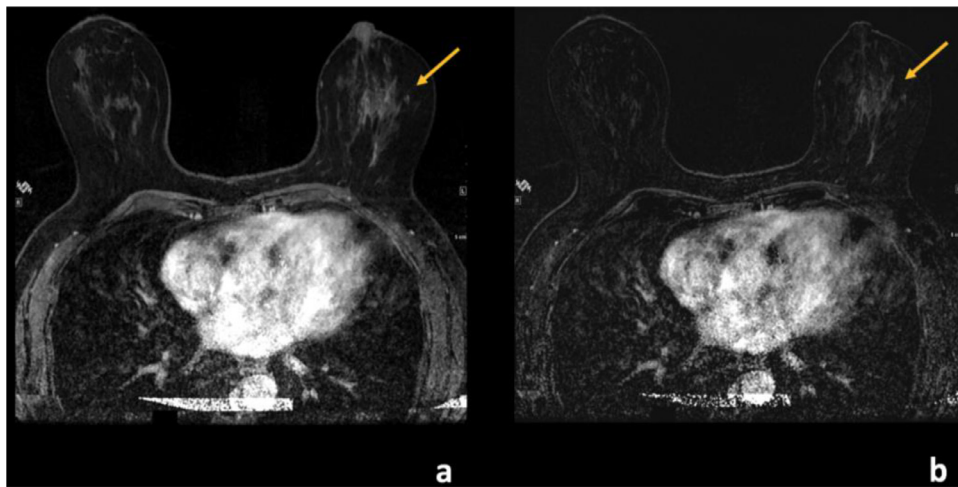
presents as multifocal tumor and with a higher incidence of bilateral breast disease [5]. ILC metastases overall tend to favor sites of estrogen production with preferential involvement of the ovaries, gastrointestinal tract, retroperitoneum, meninges, and bone [1,2,8,9]. Involvement of the orbits and retroperitoneum are further discussed below, as pertinent to our case.

Metastatic breast carcinoma to the orbit is responsible for 20%-50% of orbital metastasis cases [2,4]. The most common site of origin is the breast, most frequently being ILC [3]. Although there are no specific imaging findings on CT or MRI for orbital metastatic breast cancer, it is important to consider metastatic disease to the orbits in the setting of an infiltrative orbital process in the adult female. Variable appearances on MRI have been described in metastatic breast cancer to the orbit. Our case demonstrated paradoxical enophthalmos which is most often a sequela of scirrhous breast cancer, pro-

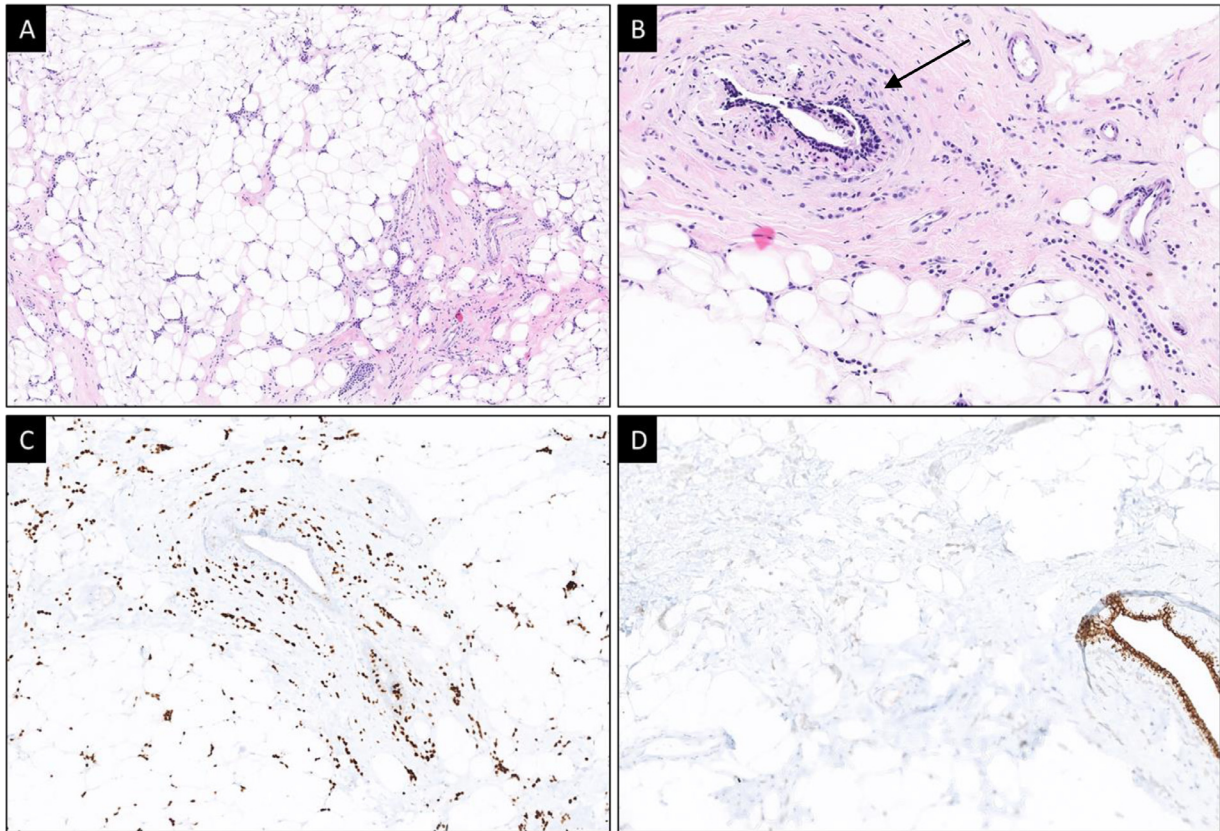




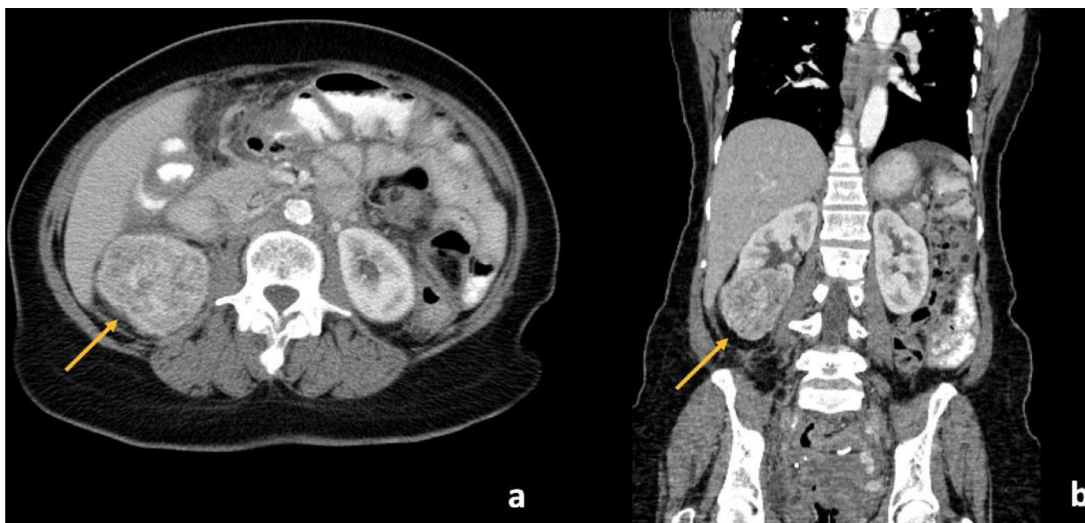
**Fig. 3** – Diagnostic bilateral mammogram. (a) Right breast craniocaudal (RCC), (b) Left breast craniocaudal (LCC), (c) Right breast mediolateral oblique (RMLO), and (d) Left breast mediolateral oblique (LMLO) views demonstrate a subtle focal asymmetry in the upper outer quadrant of the left breast posteriorly, measuring approximately 2.9 cm.



**Fig. 4** – Bilateral breast MRI with contrast. (a) First-pass postcontrast T1-weighted fat-suppressed and (b) First-pass postcontrast T1-weighted fat-saturated subtraction images demonstrate mild non-mass enhancement in the central, slightly lateral, left breast, extending from the middle through the posterior thirds, measuring 5.2 cm in greatest extent, in a somewhat segmental distribution.

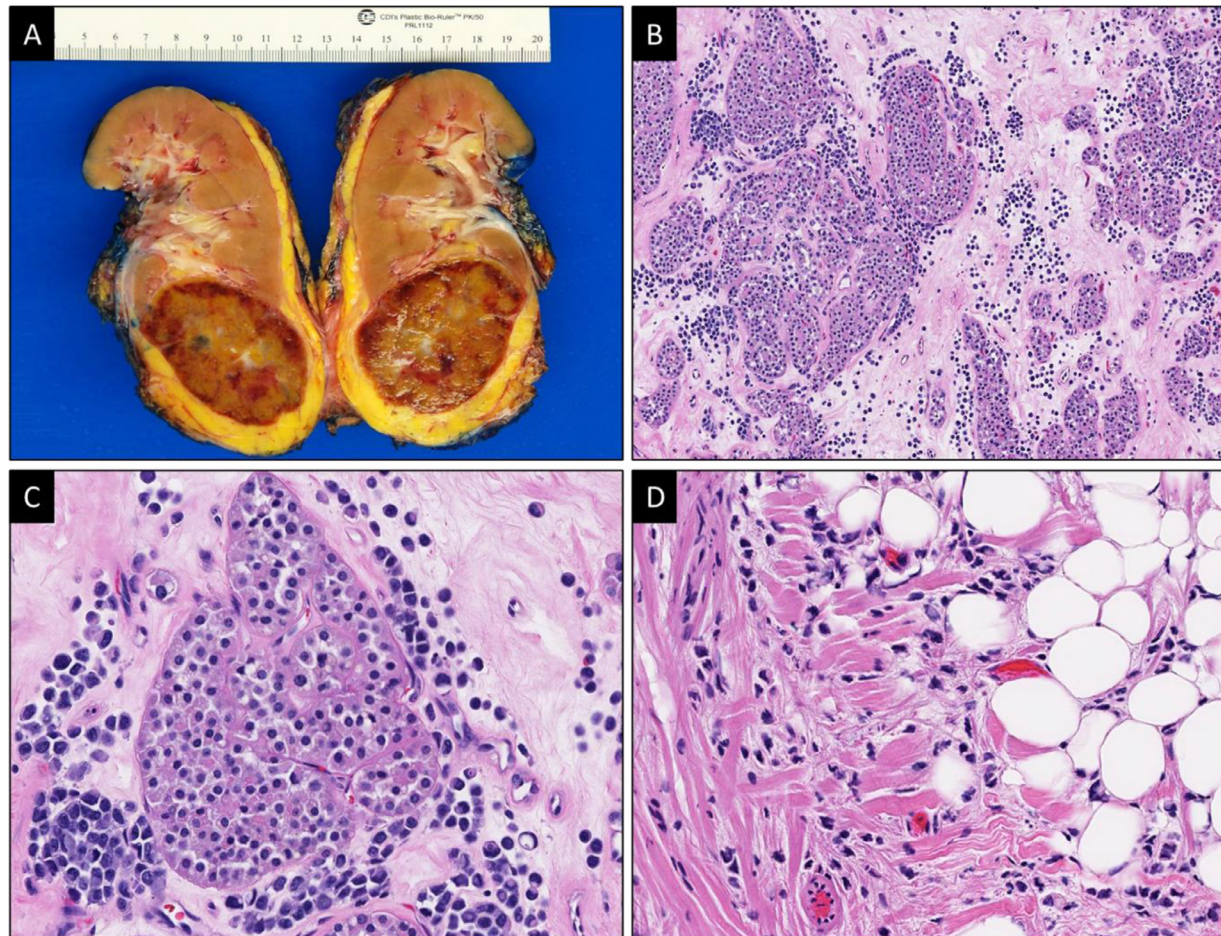


**Fig. 5** – Left breast mass involved by invasive mammary carcinoma (lobular type). (a) patchy foci of irregular infiltrative tumor cells involving adipose tissue and fibrous stromal tissue [low power, hematoxylin eosin, original magnification 90 $\times$ ]. (b) small fairly uniform infiltrative tumor cells involving fibrous stromal tissue and adipose tissue with characteristic single-file and concentric pattern of growth (arrow), typical of invasive mammary carcinoma (lobular type) [intermediate power, hematoxylin eosin, original magnification 200 $\times$ ]. (c) estrogen receptor immunohistochemical stain demonstrating fairly strong diffuse nuclear staining in the tumor cells, supporting primary mammary carcinoma [low power, original magnification 110 $\times$ ]. (d) e-cadherin immunohistochemical stain demonstrating decreased to absent membranous staining in the tumor cells (mid-left) with internal control staining of benign mammary duct (right), supporting lobular type of mammary carcinoma [intermediate power, original magnification 160 $\times$ ].



**Fig. 6** – (a) Axial and (b) Coronal contrast-enhanced computed tomography (CT) images demonstrate a cortical-based heterogeneously enhancing mass, arising from the inferior pole of the right kidney, measuring 6.3 cm.





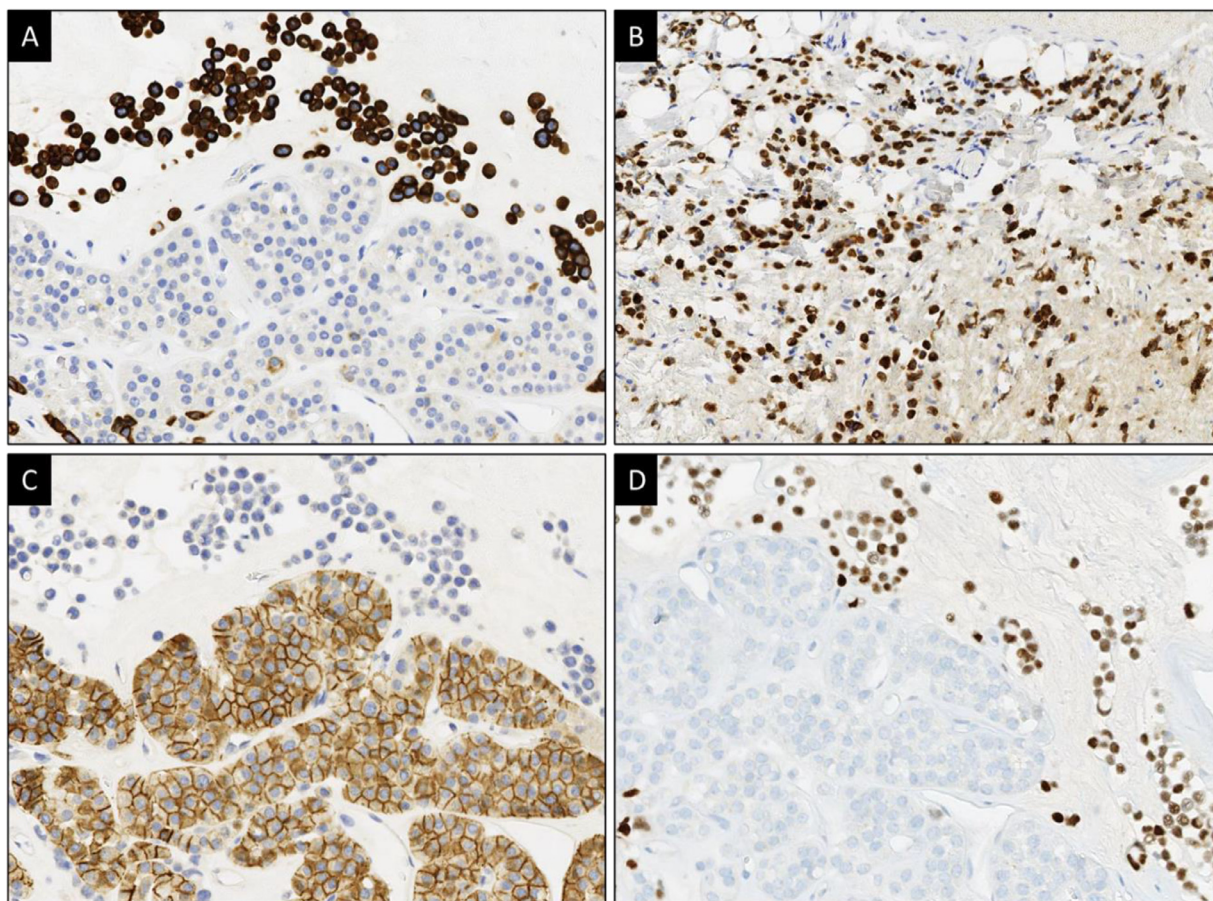
**Fig. 7 – Right kidney mass with oncocytoma involved by metastatic mammary carcinoma (lobular type) [tumor-to-tumor metastasis]. (a) gross photograph of right radical nephrectomy specimen (bisected in a coronal plane) demonstrating a fairly well-demarcated solid mahogany brown lower pole lesion (~ 5.9 cm) with central fibrous scar, an exophytic component abutting adjacent perirenal adipose tissue (eg, predominantly rounded pushing like lesional border) and was noted to have a rubbery to firm cut surface upon sectioning. (b and c) tumor cells with nested to alveolar pattern of growth and eosinophilic cytoplasm set in a fibrous myxoid hyalinized stroma, consistent with oncocytoma with adjacent small fairly uniform infiltrative loosely cohesive tumor cells with areas demonstrating characteristic single-file pattern of growth, consistent with metastatic mammary carcinoma (lobular type) [b: low power, hematoxylin eosin, original magnification 70 x; c: intermediate power, hematoxylin eosin, original magnification 200 x]. (d) metastatic mammary carcinoma (lobular type) involving perirenal fibroadipose tissue [intermediate power, hematoxylin eosin, original magnification 200 x].**

ducing infiltrative and fibrotic contraction of orbital fat [3,4]. This pattern manifests as heterogeneous hypointensity on T1- and T2-weighted sequences with diffuse enhancement of the retrobulbar fat, reflecting fibrotic infiltration. Additional differential considerations for an infiltrative orbital pattern on imaging includes infection, idiopathic orbital inflammation, and lymphoproliferative processes [4]. As such, a histological diagnosis should be sought in adult female patients to assess for metastatic disease.

Metastatic ILC to the peritoneal cavity and retroperitoneum is also not unusual for this entity. However, when ILC does metastasize to the abdomen or pelvis, it more frequently manifests as peritoneal or retroperitoneal serosal implants which are detected during metastatic workup or autopsy. Rarely ILC may present initially as a renal mass [8,9]. Patients can develop ureteral obstruction, secondary to

desmoplastic reaction and metastatic retroperitoneal fibrosis [9]. Desmoplastic reaction elicited by the tumor cells results in retroperitoneal fibrosis and is indistinguishable from idiopathic retroperitoneal fibrosis. CT imaging findings can include soft tissue encasement of the abdominal aorta and ureters and often hydronephrosis. Renal metastasis manifesting as a solid renal tumor is rare for ILC and has been reported in a few case reports [8,9]. In our patient, the renal mass was incidentally found on workup for metastatic disease and histologically confirmed as a renal oncocytoma involved by metastatic ILC (tumor-to-tumor metastasis) only upon nephrectomy. Tumor-to-tumor metastasis is considered to be quite rare and involves distinct metastatic disease to a second primary tumor (eg, metastatic ILC to renal oncocytoma as seen in our patient), where the most frequent recipient tumor has been found to be renal cell carcinoma and the most





**Fig. 8 – Right kidney mass with oncocytoma involved by metastatic mammary carcinoma (lobular type) [tumor-to-tumor metastasis] immunohistochemical stains. (a and b) cytokeratin 7 demonstrating strong diffuse cytoplasmic staining in the smaller infiltrative tumor cells and appears largely negative in the oncocytoma seen in a, supporting metastatic mammary carcinoma (b demonstrating perirenal fibroadipose tissue involvement by metastatic mammary carcinoma) [a: intermediate power, original magnification 200×; b: low power, original magnification 100×]. (c) e-cadherin demonstrating decreased to absent membranous staining in the smaller infiltrative tumor cells (top) and membranous staining of oncocytoma, supporting metastatic mammary carcinoma (lobular type) [intermediate power, original magnification 200×]. (d) estrogen receptor demonstrating moderate to strong diffuse nuclear staining in the smaller infiltrative tumor cells (top) and appears largely negative in the oncocytoma, supporting metastatic mammary carcinoma [intermediate power, original magnification 200×]. Additional immunohistochemical stain (not shown) for CD117 demonstrated strong diffuse staining in the oncocytoma and appeared largely negative in the metastatic mammary carcinoma.**

frequent donor tumor is noted to be lung cancer, followed by carcinomas of the breast, prostate, and thyroid [10,11]. In addition, renal oncocytoma has been previously reported to be a rare recipient tumor site for tumor-to-tumor metastasis, where reported donor tumors have included carcinomas of the breast (eg, as seen in our patient), prostate, and lung [10,12].

## Conclusion

We hope to bring awareness of the unusual metastatic pattern of ILC and emphasize the need for a comprehensive physical examination in these patients. It should also be noted that ILC can metastasize years after initial presentation and should be considered in patients with a remote history of breast cancer.

It is important for radiologists to be aware of this possibility and raise concern for metastatic disease when appropriate.

## Patient consent statement

The patient agrees to care at a university hospital with trainees. All personal health information has been removed and images de-identified.

## REFERENCES

- [1] Tomizawa Y, Ocque R, Ohori NP. Orbital metastasis as the initial presentation of invasive lobular carcinoma of breast. *Intern Med* 2012;51:1635–8. doi:10.2169/internalmedicine.51.7641.

- [2] Meltzer D, Chang A, Shatzkes D. Orbital metastatic disease from breast carcinoma. *Radiology* 2009;253(3):893–6.
- [3] Raap M, Antonopolous W, Dammrich M, Christgen H, Steinmann D, Langer F. High frequency of lobular breast cancer in distant metastases to the orbit. *Cancer Medicine* 2015;4(1):104–11.
- [4] Tailor T, Gupta D, Dalley R, Keen C, Anzai Y. Orbital neoplasms in adults: clinical, radiologic, and pathologic review. *Radiographics* 2013;33:6.
- [5] Johnson K, Sarma D, Hwang ES. Lobular breast cancer series: imaging. *Breast Cancer Res* 2015;17:94.
- [6] Hilleren DJ, Andersson IT, Lindholm K, Linnell FS. Invasive lobular carcinoma: mammographic findings in a 10-year experience. *Radiology* 1991;178:149–54.
- [7] Dabbs D, Oesterreich S. 'Lobular neoplasia and invasive lobular carcinoma' in Dabbs (2nd edition). In: *Breast Pathology*. Philadelphia, PA: Elsevier; 2017. p. 451–2. 460-462.
- [8] Al-Jarrah A, Taranikanti V, Sawhney S, Furrakh M, Al-Hosni M, Saparamadu P. Metastatic invasive lobular carcinoma of the breast masquerading as a primary renal malignancy. *Sultan Qaboos University Med J* 2013;13(3):460–2.
- [9] Yousef G, Gabril M, Al-Haddad S, Mulligan A, Honey J. "Invasive lobular carcinoma of the breast presenting as retroperitoneal fibrosis: a case report. *J Med Case Rep* 2010;4:175.
- [10] Bitner D, Clements M, Cathro H, Mithqal A, Schenkman N. Remote development of tumor-to-tumor metastasis of breast adenocarcinoma in a renal Oncocytoma. *Urology* 2017;107:e1–2.
- [11] Petraki C, Vaslamatzis M, Argyrakos T, Petraki K, Strakaki M, Alexopoulos C, et al. Tumor to tumor metastasis: report of two cases and review of the literature. *Int J Surg Path* 2003;11:127–35.
- [12] Horn AJ, Fritz BE, LaGrange CA, West WW, Lele SM. Clinically undiagnosed prostate carcinoma metastatic to renal oncocytoma. *Case Rep Urol* 2012;2012:307813.