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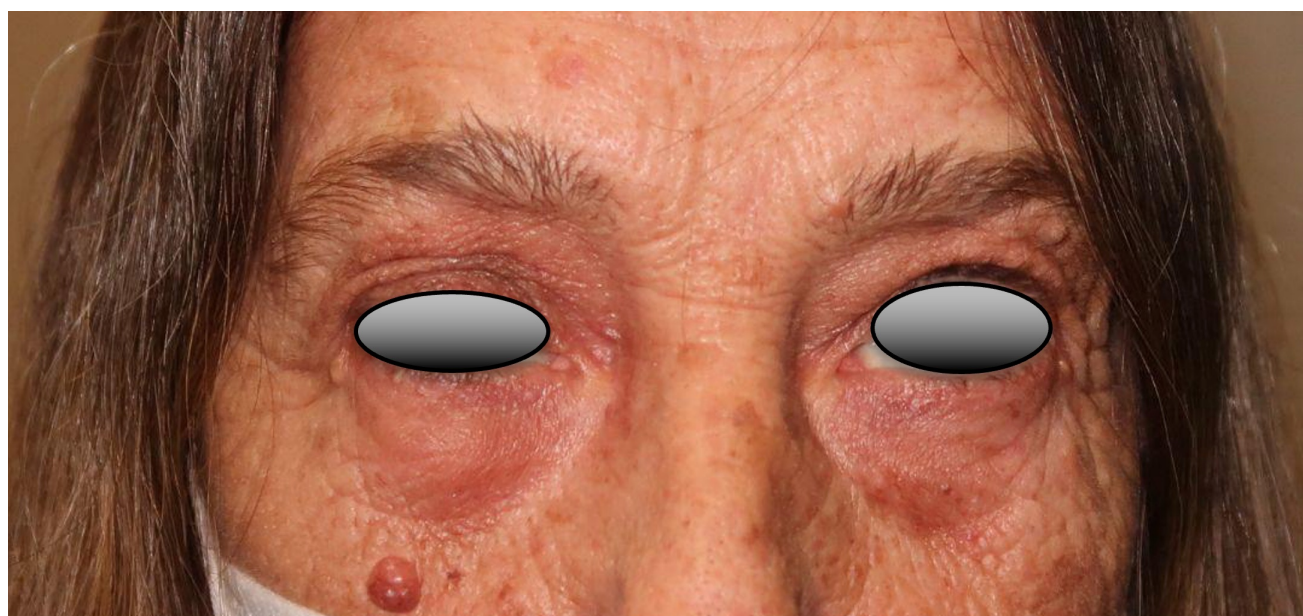
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## Background

- Orbital metastases account for 1-13% of all orbital neoplasms, with breast, melanoma, and prostate representing the most common primary tumors, respectively.
- Orbital metastases almost always occur in patients with a known primary
- Eyelid involvement was the initial presentation of this patient's breast cancer
- Isolated metastasis to the eyelid of any distant primary cancer is unusual
- Orbital metastasis from a breast primary carcinoma is typically of lobular phenotype; however in this case, invasive ductal adenocarcinoma was confirmed by immunohistochemistry.

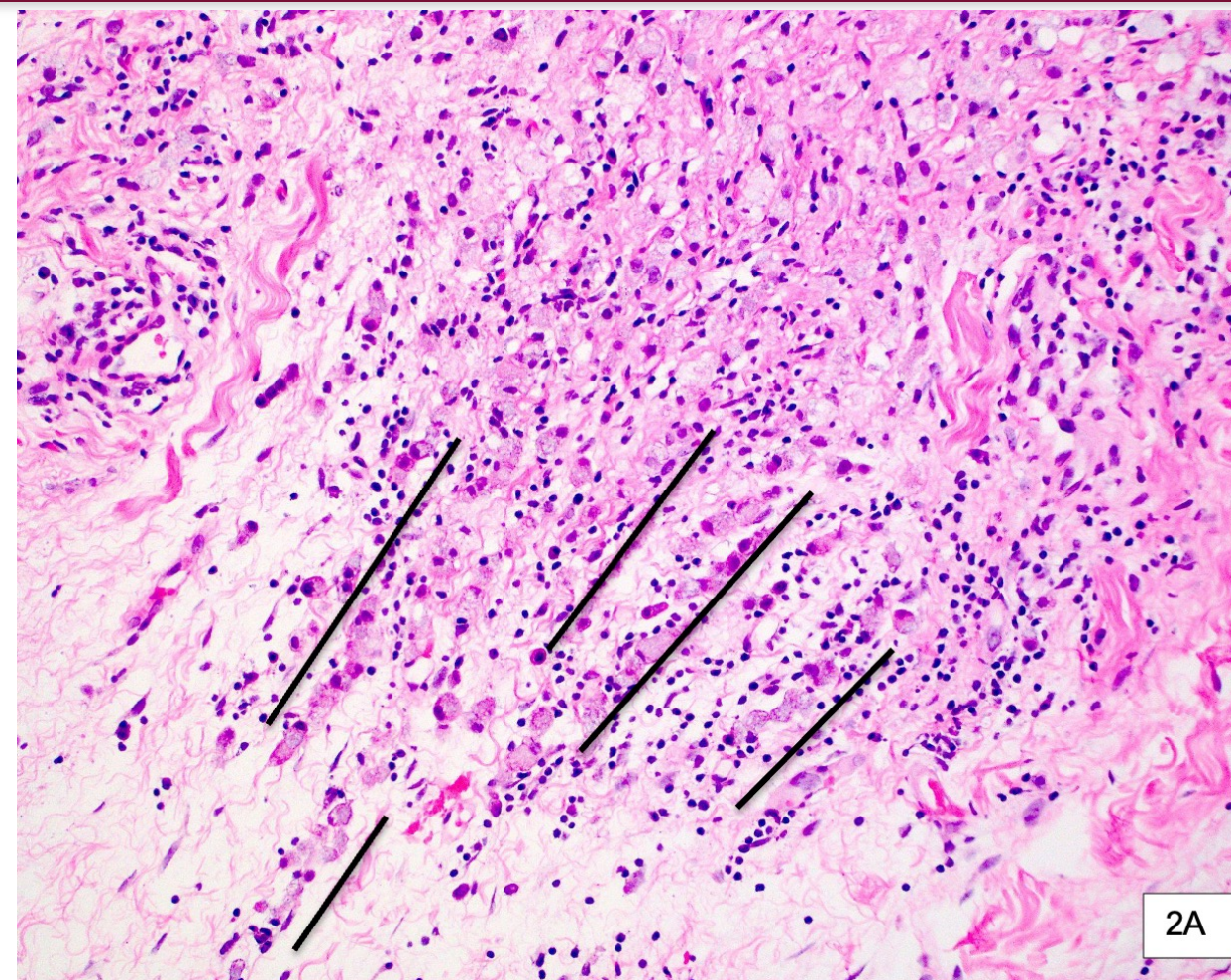
## Case Presentation

- 66 year-old female presented with 2.5 weeks of a bump on her right lower eyelid (RLL). She also noted right upper eyelid (RUL) drooping seven months prior, which had gradually worsened.
- Physical exam revealed mild nontender soft tissue thickening along the right superior orbital rim, RUL and RLL (Figure 1). The remainder of the ophthalmic examination was intact
- MRI of orbits revealed abnormal enhancing pre-septal soft tissue superior and inferior to the globe involving the lids, with no post-septal extension.
- Biopsy of the RLL soft tissue mass revealed a poorly cohesive carcinoma with signet ring cell forms, positive for keratin CAM5.2, CK7, GATA3, BRST-2, mammaglobin, ER, and E-cadherin, confirming an ER positive breast adenocarcinoma. Even though the histopathology showed a poorly cohesive carcinoma, including signet ring cell forms, the positive E-cadherin stain supported a ductal breast phenotype.
- CDX-2 by immunohistochemistry was negative, excluding a gastrointestinal primary carcinoma.

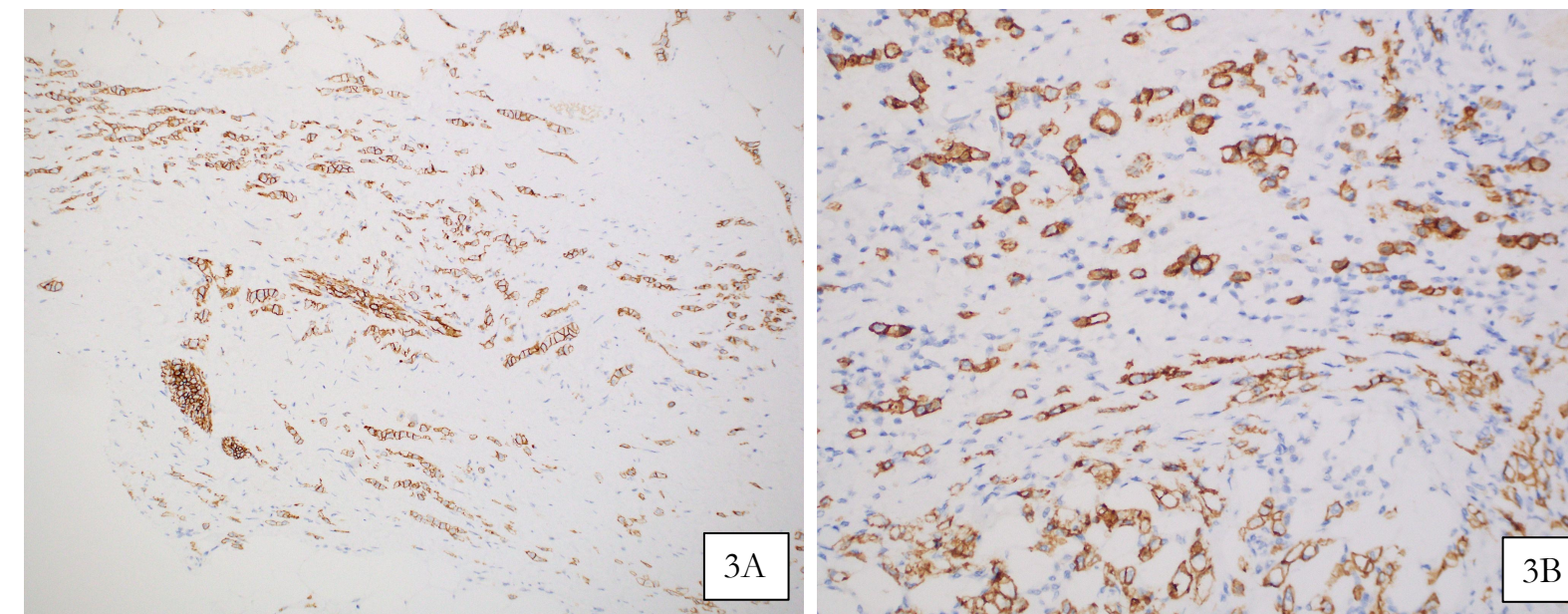
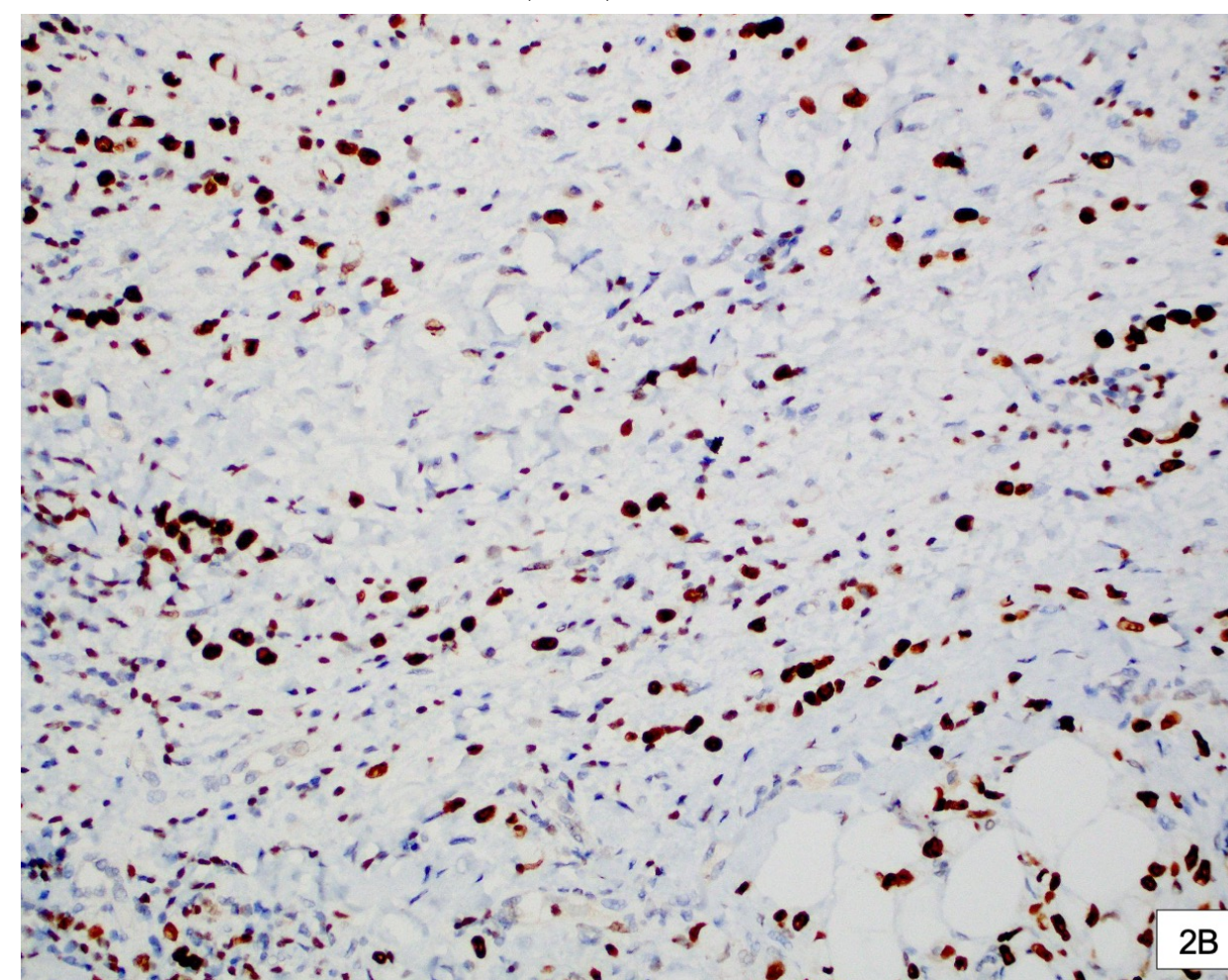


**Fig. 1 Clinical presentation of eyelid ptosis and nodular growth RLL**  
*Clinical findings*  
On the physical exam, mild nontender soft tissue thickening was present along the right superior orbital rim, RUL, and throughout most of the RLL

## Histopathologic Findings



**Fig. 2**  
(A) Biopsy right lower eyelid showing infiltrating carcinoma in a "single-file" pattern, denoted by black lines (H&E 20X)  
(B) GATA3 with nuclear positivity in the malignant cells, helping to confirm breast carcinoma (20X)



**Fig. 3** Comparison of biopsies from the eyelid and subsequent breast core proved to be the same invasive ductal breast adenocarcinoma with lobular features  
(A) E Cadherin 10X breast  
(B) (E Cadherin 20X eyelid)

## Clinical Course

- After diagnosis of breast cancer via eyelid biopsy, the patient was evaluated by oncology, where a palpable right breast mass was found. Estrogen receptor PET scan showed disease in her breast, right axilla, left cervical nodes, calvarium, and right periocular area. Biopsy of right breast lesion confirmed the ER positive, low-grade breast ductal adenocarcinoma.
- The patient was treated with endocrine therapy and CDK4/6 inhibitors. She is well at one year with remission of the eyelid disease and stability of her metastatic lesions, maintained on exemestane.

## Discussion

- Rare is the initial presentation of breast carcinoma to be orbital involvement. Presented is a case of eyelid ptosis as the initial presentation of breast carcinoma, with eyelid biopsy confirming invasive ductal adenocarcinoma.
- Biopsy revealed poorly cohesive carcinoma with signet ring cell forms. The histopathologic differential diagnosis for malignancies with signet ring cells includes lymphoma, gastrointestinal, breast, eccrine sweat gland, salivary gland and primary signet ring cell carcinoma of the eyelid.
- CDX-2 negativity excluded a gastrointestinal primary.
- Primary breast carcinoma was confirmed in this case on the basis of positivity for keratin CAM5.2, CK7, GATA3, BRST-2, mammaglobin, ER, and E-cadherin. The positive E-cadherin excluded lobular carcinoma even though the carcinoma was poorly cohesive and had signet ring cell forms. Thus, a metastatic ductal adenocarcinoma with lobular features, as the initial presentation of breast carcinoma, was diagnosed.
- While metastases of distant primary cancers to the eyelid are rare, maintaining a high level of suspicion in any patient with atypical eyelid thickening will help assure timely diagnosis and management.

## References

- Togashi, Keita, et al. "Metastatic Orbital Tumor from Breast Ductal Carcinoma with Neuroendocrine Differentiation Initially Presenting as Ocular Symptoms: A Case Report and Literature Review." *Frontiers*, 6 Jan. 2021
- Raap M, Antonopoulos W, Dämmrich M, et al. High frequency of lobular breast cancer in distant metastases to the orbit. *Cancer Med*. 2015;4(1):104-111. doi:10.1002/cam4.331
- Palmisciano P, Ferini G, Ogasawara C, et al. Orbital Metastases: A Systematic Review of Clinical Characteristics, Management Strategies, and Treatment Outcomes. *Cancers (Basel)*. 2021;14(1):94. Published 2021 Dec 24. doi:10.3390/cancers14010094
- Ahmad SM, Esmaili B. Metastatic tumors of the orbit and ocular adnexa. *Curr Opin Ophthalmol*. 2007;18(5):405-413. doi:10.1097/ICU.0b013e3282c5077c
- Bianciotto C, Demirci H, Shields CL, Eagle RC Jr, Shields JA. Metastatic tumors to the eyelid: review of the literature. *Arch Ophthalmol*. 2009;127(8):999-1005. doi:10.1001/archophtho

The authors have no significant relationships with, or financial interests in, any commercial companies pertaining to this poster.