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Compressive optic neuropathy caused by sinonasal adenosquamous carcinoma with orbital extension: A case report

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ABSTRACT

Purpose: Adenosquamous carcinoma (ASC) of the head and neck, specifically sinonasal ASC, is a rare and aggressive malignancy with metastasis occurring in 80% of patients in its initial reporting; sinonasal ASC with orbital extension has rarely been reported in literature. Despite treatment, ASC carries a poor prognosis with a 5-year survival of approximately 22%, with 50% dying within 23 months.[10] Mucoepidermoid carcinoma (MEC) and ASC have similar morphologic features. It is imperative to distinguish these two entities apart as the biologic behavior and prognosis of ASC is much worse than that of poorly differentiated MEC and squamous cell carcinoma. This case provides a rare presentation of a secondary orbital tumor, ASC with orbital extension, that manifests with ocular symptoms and is therefore relevant to practitioners in the field of ophthalmology while reviewing the histology of ASC with the goal of distinguishing the entity from its differential diagnoses.

Observation: To further understand the natural history of this unusual tumor, we report a case of adenosquamous carcinoma in a 76-year-old female who presented with a three-day history of left-sided: vision loss (worse centrally and nasally), afferent pupillary defect, esotropia and abduction deficit, cervical lymphadenopathy and an extraconal mass on MRI producing a compressive optic neuropathy. We provide photography that demonstrates the patient's presentation, histologic slides provided via biopsy of the malignancy, and radiologic findings on magnetic resonance imaging, all of which support the diagnosis.

Conclusions/Importance: This case adds to the limited literature of sinonasal adenosquamous carcinoma while exploring orbitotomy techniques for adequate extraconal mass biopsies of the entity. Our manuscript reviews key histological findings of ASC provided by the patient's biopsies and details how to differentiate the cancer from other pathologies, like MEC; A differentiation that proves vital for practitioners due to the widely differing prognosis of the two pathologies. We present the first case of sinonasal ASC with orbital extension causing ophthalmologic symptoms.

1. Introduction

Adenosquamous carcinoma of the head and neck is a rare malignancy, with fewer than 100 cases reported in English literature as of 2013.[1] Some researchers consider ASC controversial, as it was formerly considered the same entity as salivary gland mucoepidermoid carcinoma (MEC). The term "adenosquamous carcinoma" was first proposed in 1960 by Gerughty et al. in a series of 10 cases involving the nose, oral cavity, and larynx, where it was shown to be extremely aggressive, with 80% of the patients developing metastases. Due to the presence of unequivocal separate components of squamous cell carcinoma and adenocarcinoma, Gerughty et al. considered ASC to be distinct from mucoepidermoid carcinoma.[2] In 1984, Evans highlighted the worse prognosis of ASC of the head and neck in comparison with MEC, even high-grade MEC, and proposed that ASC should be considered a distinctive neoplasm.[3] Separating these two neoplasms proves crucial when one examines a patient's prognosis. Metastases and death from MEC is uncommon, whereas is frequent in cases of ASC.[2] ASC is histologically characterized by mixed differentiations and distinct areas of both squamous cell carcinoma (SCC) and adenocarcinoma, as defined by the World Health Organization.[4] In ASC, SCC usually predominates, can be in situ or invasive, and can range from well to poorly differentiated.

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The adenocarcinomatous component can have a tubular, alveolar, and/or glandular morphology.[5]

Collection and evaluation of protected patient health information were compliant with the Health Insurance Portability and Accountability Act (HIPAA). Informed consent to publish an identifiable photograph was obtained from the study participant. This study was in accordance with the ethical standards of the 1964 Helsinki declaration and its later amendments.

1.1. Case presentation

A 76-year-old female with no smoking history was referred to the Baylor Scott & White Ophthalmology Clinic from an outside emergency department with a history of painless vision loss in the left eye and painless right sided cervical lymphadenopathy. She reported that when she awoke three days prior, her vision was dark centrally and nasally; however, she reported relatively preserved temporal visual fields. The patient denied any significant past ocular or medical history and was not taking any prescription medications. She indicated that she had not seen a primary care physician for many years but had recently made an appointment, that was upcoming, for right sided neck swelling that was noticed three months prior and was slowly enlarging. On the physical exam, her best corrected visual acuity was significant for light perception in the left eye. Examinations of her pupils revealed a left 3+ relative afferent pupillary defect with sluggish reactivity. Her intraocular pressures were 13 mmHg in the right eye and 14 mmHg in the left eye. Her motility and alignment testing was notable for a left abduction deficit, left esotropia, and left hypertropia by Hirshberg (Fig. 1). Right sided cervical lymphadenopathy was present. Optical coherence tomography of the patient's macula revealed no evidence of chorioretinal folds or retinal ischemia.

Computed tomography and magnetic resonance imaging of her head, neck, and orbits demonstrated enlarged and necrotic cervical lymphadenopathy suspicious for squamous cell carcinoma and a left intraorbital extraconal lesion measuring 27 mm anteroposterior, 10 mm transversely, and 20 mm craniocaudally along the medial orbital wall extending back toward the orbital apex resulting in lateral deviation of the medial rectus and optic nerve sheath (Fig. 2A & 2B). Additionally, there was sinonasal opacification within the sphenoid sinuses and ethmoid air cells, and a few enlarged right submandibular lymph nodes, indicating the likely sinonasal source of the lesion.

The patient was referred to Interventional Radiology for an ultrasound guided biopsy of her right level IIb lymph node. The Biopsy revealed metastatic keratinizing moderately differentiated squamous cell carcinoma, invading the soft tissue. p16 was negative and PD-L1 5–10%. Perineural invasion was identified. Hematology/Oncology recommended that the patient undergo orbital mass biopsy and debulking. An oculoplastics surgeon performed a left anterior orbitotomy, transcaruncular approach, with exploration of the left medial orbit with debulking and biopsy of the left medial orbital mass. The gross specimen was divided into two fragments, 1A and 1B. Microscopic evaluation revealed dense fibrovascular connective tissue with areas of adipose tissue and skeletal muscle containing lobules and cords of moderately to poorly differentiated cells with squamous and glandular differentiation (Fig. 3). Individual cell keratinization and occasional signet ring-like cells were present. PAS-alcian blue stain disclosed focal stromal staining with alcian blue and focal-alcian blue-PAS staining within tumor cells in both specimens indicating the presence of acid mucopolysaccharide (Fig. 4). The mucicarmine stains exhibited stromal/extracellular staining as well as intracytoplasmic staining in both specimens (Fig. 4). The immunohistochemical stains of specimens 1A and 1B disclosed staining of the tumor cells with BER-EP4, CK5/6, CEA (glandular more than squamous component), P40 (squamous more than glandular component), p63 (squamous more than glandular component), and CK7 (glandular component only) (Fig. 5). The tumor cells disclosed no staining for CK20, p53, TTF-1, and p16 in both specimens. The tumor

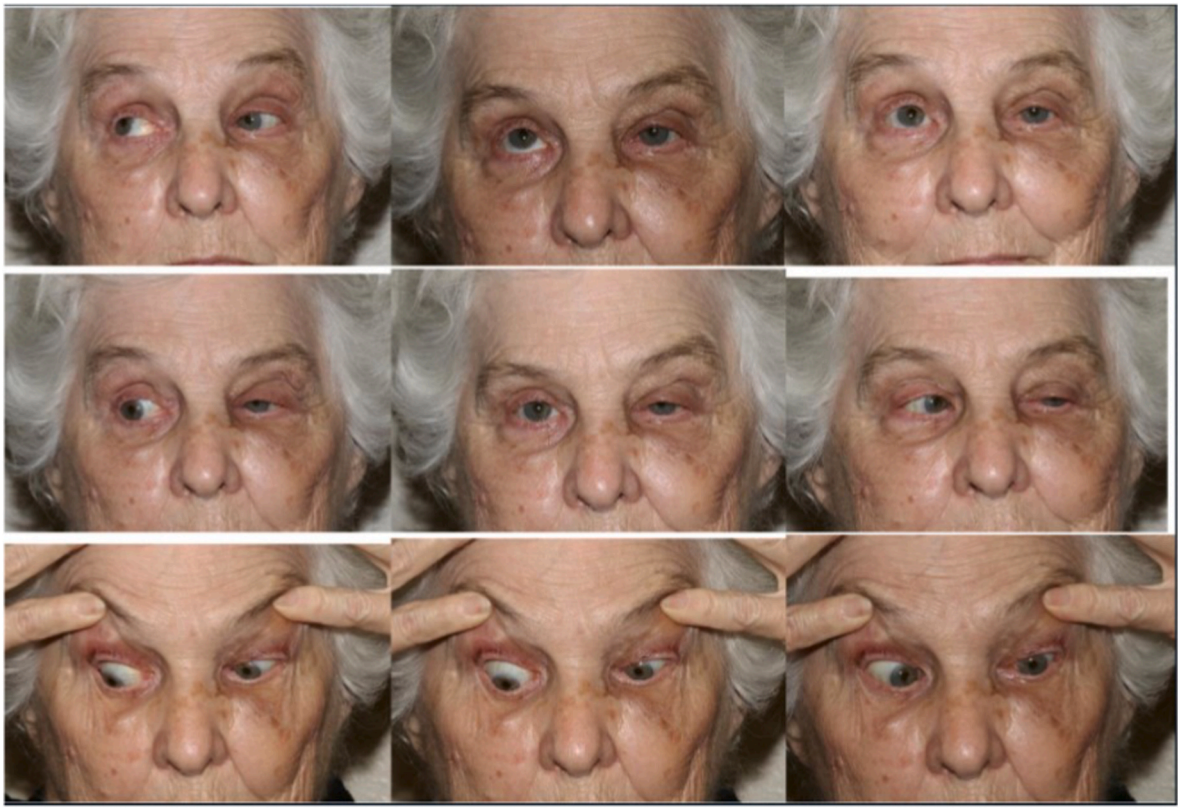

Fig. 1. The patient displays a left hypertropia in primary gaze, left esotropia, left abduction deficit, and slight limitation of motility in all cardinal fields of gaze. Also notable is a degree of left enophthalmos.

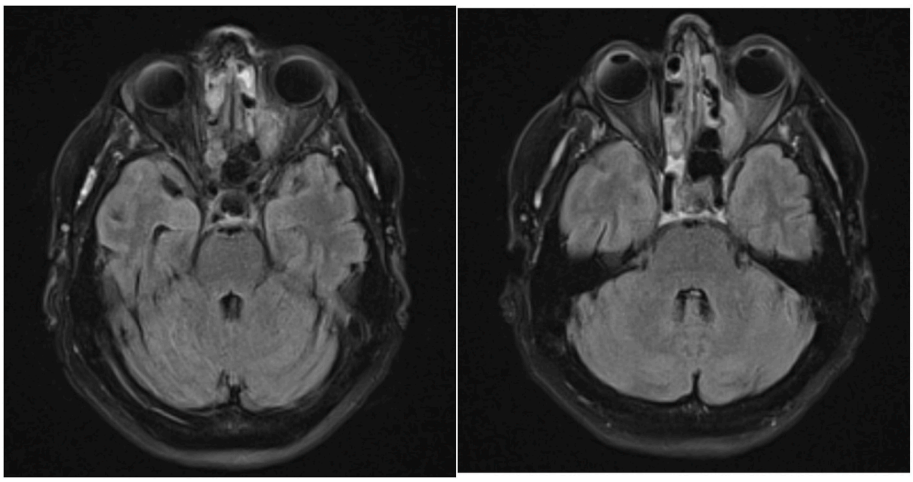

Fig. 2. A/2B: MRI Brain: Left orbital extraconal lesion measuring up to 20 mm with avid enhancement on postcontrast imaging. No definite local invasion or perineural tumor spread.

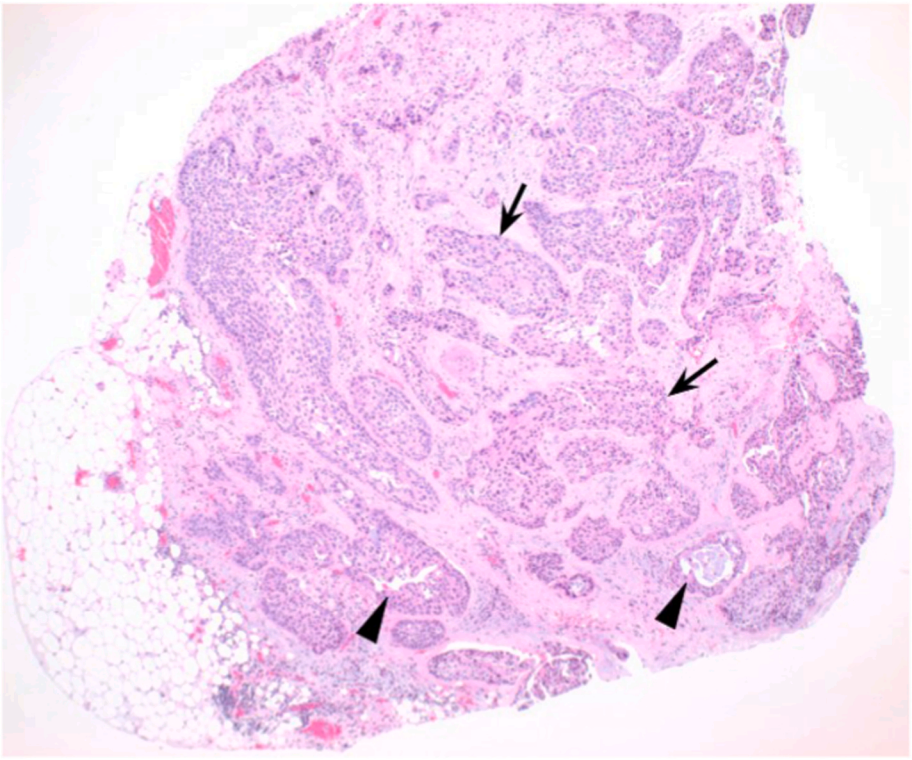

Fig. 3. Arrows: Lobules and cords of atypical squamous cells. **Arrowheads**: Lobules of atypical glandular cells.

cells exhibited increased Ki-67 expression (approximately 20–30%). The specimen underwent fluorescence in situ hybridization (FISH) for MAML2/CRTC1 translocation for which it was negative; the MAML2 gene was intact. A diagnosis of adenosquamous carcinoma was made.

The patient was further evaluated by the Otolaryngology (ENT) service who performed endoscopy and determined the patient to have SCC involving the spheno-ethmoidal recess bilaterally with orbital extension. ENT performed surgery consisting of excision of her right ethmoido-sphenoid sinus cancer, left orbital exenteration, and bilateral neck dissection and reconstruction. Additionally, she received adjuvant chemotherapy consisting of cisplatin 25 mg/m2 IV weekly with radiation therapy. Histopathology from her radical neck dissection revealed moderately to poorly differentiated squamous cell carcinoma with few foci with possible glandular features, invading skin dermis, soft tissue, and skeletal muscle, and involving deep margin. Prominent perineural invasion and lymphovascular invasion was identified. Histopathology from her sinus mass removal revealed invasive moderately to poorly differentiated adenosquamous carcinoma present in her nasal septum margins, sinuses, dural margin, with extension intracranially.

The patient is continuing to receive adjuvant concurrent radiochemotherapy for local control.

2. Discussion

Adenosquamous carcinoma involving the orbit is rarely reported on in literature. There have been documented case reports of ASC arising in the bulbar conjunctiva as well as ASC of the lacrimal gland, however, no reported cases of sinonasal ASC with orbital extension.[6,7] This is a rare

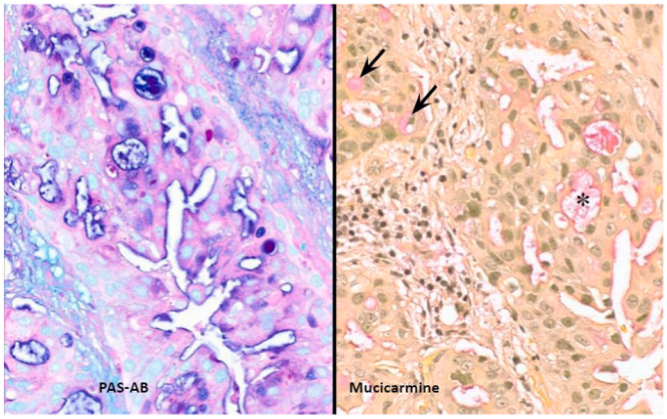

Fig. 4. Left panel: Magenta PAS staining and Alcian blue staining indicating the presence of acid mucopolysaccharide. Right panel: Intra- (arrows) and extracellular (asterisk) mucin highlighted by the mucicarmine stain.

case of head and neck sinonasal, specifically spheno-ethmoidal, adenosquamous carcinoma with secondary orbital extension resulting in compressive optic neuropathy.

Sinonasal malignancies (SNM) account for less than 1 percent of all neoplasms and only 3 percent of all head and neck cancers. SNMs most commonly involve the maxillary sinus, followed by the nasal cavity, the ethmoid sinuses, and the frontal and sphenoid sinuses rarely.[8] In the latest literature review of 93 cases, Masand et al. reported that 47.4 percent of cases had regional metastases and 24.7 percent had distant metastases.[4] Yoshimura et al. reported in a retrospective study that the rate of correct ASC diagnosis from initial biopsy specimens is approximately 31.6 percent, with an incorrect diagnosis of SCC occurring in 7 of the 19 patients.[4] It is proposed that it is difficult to obtain a histological diagnosis of ASC before treatment due to smaller biopsy sizes lacking both components of the tumor, the squamous cell component and the adenocarcinomatous component.[4] Immunostaining may be positive for the individual squamous (cytokeratin 5/6, p63, CD44) and adenocariconmatous (CEA, CK7, CAM5.2) components.[3] Special staining of the intraluminal content with PAS and mucicarmine often reveals positive evidence for mucin production but is not fundamental criteria for diagnosis. Some tumors, despite the true neoplastic glanduloductal formation, may not contain mucin. Glandular components are typically associated with an intracellular and intraluminal material that is mucicarmine, PAS, and Alican Blue positive.[3] Various authors in the literature have used a wide range of immunohistochemical (IHC) markers. Some of the commonly used markers include pancytokeratin for epithelial cells, carcinoembryonic antigen for tumor progression, Ki 67 for proliferation rate, p53 for tumor suppression, and p63 for squamous differentiation.[3]

Mucoepidermoid carcinoma should always be on the differential for ASC as MEC can be a masquerader of ASC due to its similar morphologic features.[3] It is imperative to distinguish these two entities as the biologic behavior and prognosis of ASC are much worse than that of poorly differentiated MEC and SCC. FISH testing for CRTC1-MAML2 translocation can be helpful if positive as ASC is never MAML2 translocation positive. However, if results are translocation negative, this is less indicative as although ASC is negative, 20–30% of MEC can also be negative.[9]

There is nearly unanimous agreement about the first-choice treatment of adenosquamous carcinoma, which is thorough resection with an adequate surgical margin. However, there is no clear consensus on additional postoperative therapies, including radiation and chemotherapy.[4] Despite treatment, ASC carries a poor prognosis with a 5-year survival of approximately 22% and 50% of patients dying from their disease after a mean period of 23 months.[10] Fig. 6 shows the patients MRI imaging approximately seven months post-surgical intervention, radiation therapy, and chemotherapy treatment.

Our case demonstrates the first occurrence of sinonasal ASC with orbital extension presenting with ophthalmologic symptoms including: compressive optic neuropathy causing painless vision loss and ocular muscle restriction leading to an abduction deficit and esotropia. Upon original orbital mass biopsy, a diagnosis of adenosquamous carcinoma

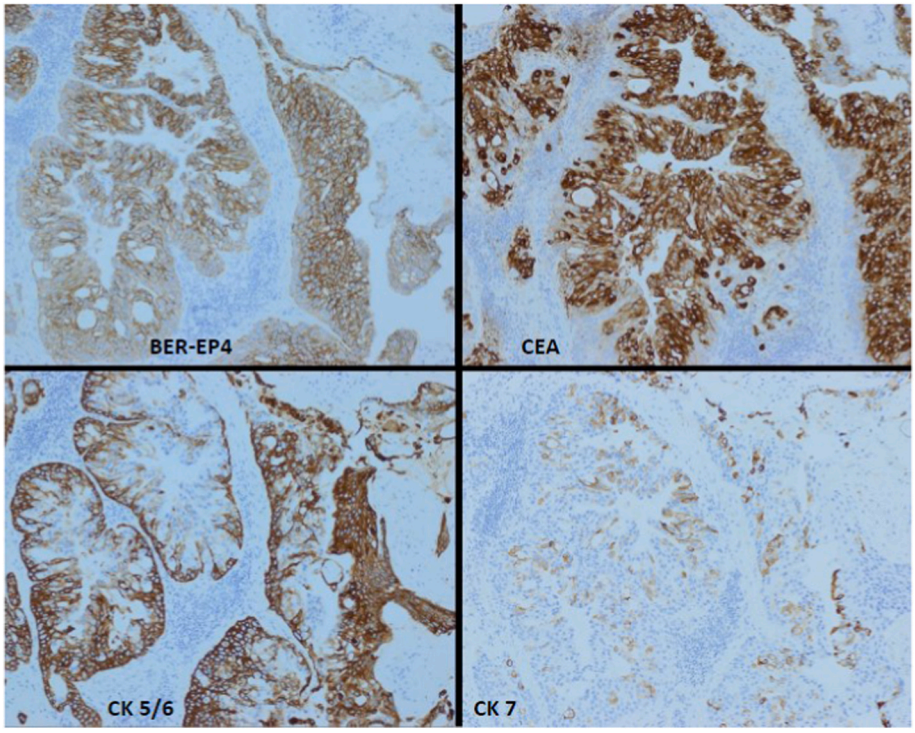

Fig. 5. Immunohistochemical studies revealed positive staining of tumor cells for BER-EP4, CEA (carcinoembryonic antigen), cytokeratins 5/6, and cytokerating 7. Note the focal CK7 staining in the glandular tumor cell component and the lack of CK7 staining in the squamous component (lower right panel).

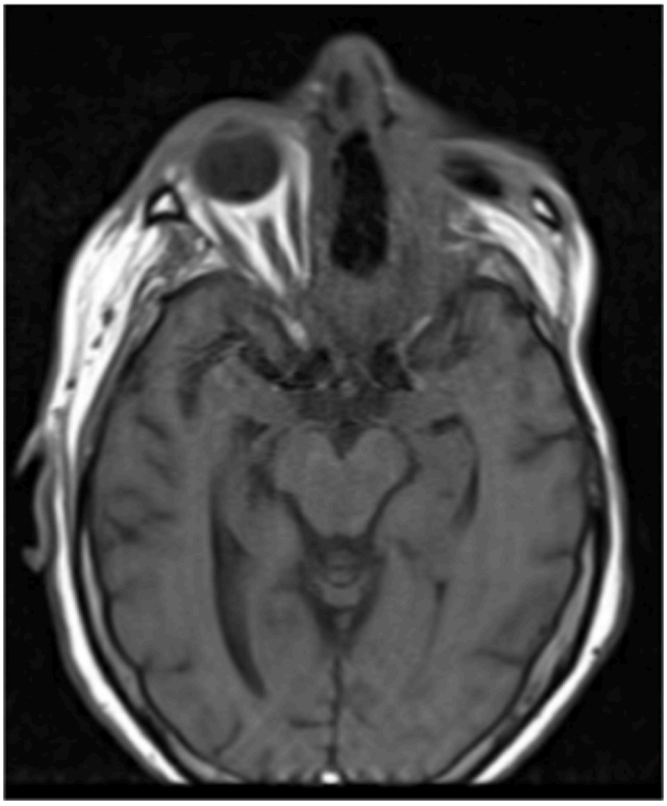

Fig. 6. MRI Face with and without Contrast: Imaging approximately 7 months post left orbital exenteration, tumor resection, bilateral neck dissection with reconstruction, and radiation therapy. Extensive postsurgical changes are noted with plaque-like enhancement involving the floor of the anterior cranial fossa that extends into the interhemispheric fissure that may reflect scarring or residual malignancy.

vs. mucoepidermoid carcinoma was considered. The biopsy showed stromal and intracytoplasmic staining with PAS and mucicarmine. Additionally, the biopsy demonstrated immunohistochemical staining congruent with reports of ASC in literature including disclosure for: CEA, p63, CK 5/6 and Ki-67. This case contributes to the limited literature of sinonasal adenosquamous carcinoma, explores orbitotomy techniques for adequate extraconal mass biopsies of the entity, reviews histology of ASC of the head and neck, and presents the first case of sinonasal ASC with orbital extension causing ophthalmologic symptoms.

Statement of informed consent/patient consent

Informed consent to publish an identifiable photograph was obtained from the study participant. Written consent to publish this case has not been obtained.

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Declaration of competing interest

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