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Case report

Adenoid cystic carcinoma of the orbit with bilateral cavernous sinus extension: A case report

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ABSTRACT

Introduction and importance: Adenoid cystic carcinoma (ACC) is an uncommon malignant epithelial tumor of the salivary and lacrimal glands. Orbital ACC is rare, originating commonly from the lacrimal gland, with only a few cases reported without lacrimal gland involvement. Deep orbital ACC may be associated with extension into skull base structures, and further intracranial invasion.

Case presentation: We report a 47-year-old gentleman who presented with insidious onset of bilateral proptosis, left ophthalmoplegia, and loss of vision. Imaging revealed left orbital infiltrative mass with intracranial invasion and bilateral cavernous sinus extension. The lacrimal gland was not involved clinically nor radiologically. Histopathology showed ACC with classical cribriform pattern. There was no evidence of primary source of tumor or metastasis.

Discussion: ACC of the orbit commonly originates from the lacrimal gland. Only a few cases of orbital ACC without lacrimal gland involvement were found in English literature. Workup for our patient did not reveal a primary source of tumor. Tumor may have risen from ectopic orbital lacrimal gland tissue, extension from non-orbital sites, or through perineural or hematogenous spread. Only one case of bilateral cavernous sinus extension has been previously reported. Treatment for advanced orbital ACC is exenteration in most cases. However, due to the advanced nature of disease in our patient, palliative radiotherapy was the treatment of choice.

Conclusion: Orbital ACC of non-lacrimal origin is rare and is associated with high morbidity and mortality. Early recognition and treatment are key for preventing organ and life-threatening complications such as advanced intracranial spread.

1. Introduction

Adenoid cystic carcinoma (ACC) is a neoplasm of epithelial origin most commonly arising from salivary glands. In a study of the lacrimal gland (LG) lesions in a referral eye institute in our area, ACC was the commonest malignant epithelial neoplasm of the LG [1]. ACC of sino-nasal origin and of the LG is characterized by perineural and intracranial extension, local recurrence, and distant metastasis [1,2]. Deep orbital primary ACC not originating from the lacrimal gland is very rare and has been presumed to be possibly originating from ectopic lacrimal gland tissue [3]. To the authors' knowledge only one case of bilateral cavernous sinus orbital ACC spread has been reported in the literature [4]. We report a similar case of deep orbital ACC with bilateral cavernous sinus involvement and intracranial extension. The previously reported case was mimicking a meningioma both radiologically and at the initial histopathological sampling. The tumor in our case was mostly occupying the orbital cavity and the diagnosis of ACC was confirmed on initial biopsy. This case report has been prepared and reported in accordance with the SCARE criteria [5].

2. Presentation of case

A 47-year-old gentleman presented to our Oculoplastics Division complaining of progressive left eye proptosis of more than one year, associated with pain, gradual decrease in vision and numbness of the left side of the face for the last 3 months. His medical history was pertinent for glaucoma and diabetes, and he was receiving topical anti-glaucoma medications in both eyes with eventual loss of vision in his right eye due

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to advanced glaucoma two years prior to his recent presentation. His diabetes was controlled on oral medication. He had no previous surgeries. On examination, he had no light perception in the blind right eye with an afferent pupillary defect and his visual acuity measured 20/100 in the left eye. Color vision was mildly subnormal on the left. The intraocular pressure in both eyes was normal on topical anti-glaucoma medications. External examination showed restricted left eye extraocular motility (EOM) in all directions of gaze (frozen globe), while the EOM was full in the right eye. Exophthalmometry measurements at a base of 108 measured 21 mm on the right and 27 mm on the left with 6 mm left proptosis. Left sided facial paresthesia was also noted. Anterior segment examination was normal, while fundoscopic exam showed a pale disc with advanced cupping on the right, and an elevated disc with blurred margins on the left. His laboratory investigations were unremarkable.

MRI imaging showed a left infiltrative deep orbital mass, occupying most of the left orbital cavity, highly enhancing with contrast with extension into skull base and left cavernous sinus, crossing to the right cavernous sinus with extension into the contralateral right orbital apex. The lacrimal glands on both sides were radiologically unremarkable and the orbital lesion did not seem to be originating from the lacrimal gland nor to be related to the lacrimal gland fossa. There was no bone excavation, remodelling, or destruction in the superolateral aspect of the orbital roof to suggest any lacrimal gland lesion (Fig. 1A, B, & C). The radiological findings were consistent with an infiltrative process suggestive of malignancy. In view of the clinical findings above and the radiological alarming invasion, the necessity for diagnostic biopsy of this orbital lesion was discussed with the patient by the oculoplastic surgeon. Biopsy techniques and their advantages versus disadvantages were also explained. The patient agreed on the plan for incisional biopsy under local anesthesia by the same orbital surgeon.

Incisional biopsy of the left orbital mass was obtained through a superior eyelid crease incision, which showed pinkish-grayish soft mass that was not vascular and was friable upon manipulation. There was no clear invasion of surrounding tissues. Multiple small biopsies from the left orbital tissue were taken and sent for histopathological examination. The patient tolerated the procedure well with no complications.

Histopathological examination showed malignant epithelial cells proliferation with ductal and cystic configuration of the typical Swiss cheese appearance (Fig. 2A). The cystic spaces contained mucinous secretions and the basement membrane material of the pseudolumina were highlighted using Alcian blue, periodic acid Schiff, and mucicarmine staining (Fig. 2B & C). The tumor cells expressed reactivity to Cytokeratin 7 marker as well as p63, and CD117 (Fig. 2D, E, & F). The overall histopathological appearance, the special stains, and the immunohistochemical staining were highly suggestive of ACC with a classic cribriform pattern.

It was decided to rule out another primary source for the tumor in the body since this neoplasm was deeply seated primarily in the left orbit with no actual connection to the ipsilateral lacrimal gland. PET scanning was ordered, which did not show any primary tumor elsewhere.

Staging CT of the neck, chest, abdomen, and pelvis showed enlarged cervical lymph nodes but did not reveal any metastasis. The patient was referred to the oncology team and the ENT service at a general hospital for further management. After discussing the case in the tumor board, the tumor was considered to be inoperable at this stage and the patient was started on a course of high dose palliative radiotherapy. The guarded prognosis was explained to the patient and necessary psychological support was provided by the medical team.

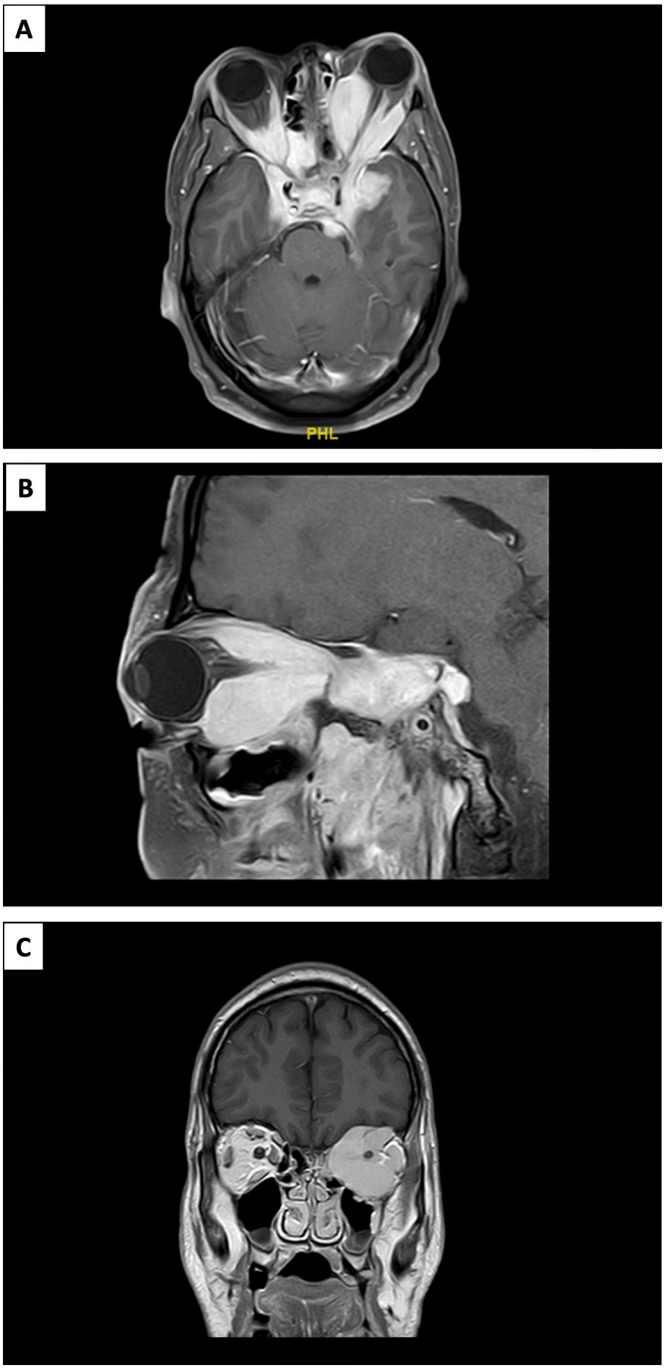

Fig. 1. T1 weighted MRI with Gadolinium enhancement obtained from (A) axial, (B) sagittal, and (C) coronal planes demonstrating bilateral enhancing intraorbital masses invading the sphenoid sinus with intracranial and perineural spread into both cavernous sinuses, suprasellar region, left middle cranial fossa and left cerebellopontine angle.

3. Discussion

ACC of the orbit is rare, originating from the lacrimal gland in most cases and constitute 1 % of the orbital tumors [6]. However, there have been reported cases of primary orbital ACC without lacrimal gland involvement in the literature. Four cases involved the orbital apex with intracranial extension [3,7–9], two cases involved the medial orbit [10,11], and one case involved the inferior orbit [12]. The diagnosis of ACC in these cases with the lack of the exact origin of the tumor in relation to the LG is challenging since these cases might have atypical clinical presentation. Tse and his coauthors reported ACC that presented initially as an orbital apex mass with cavernous sinus involvement and normal appearing ipsilateral LG [13]. Tumor origin in deep orbital ACC is uncertain. Theories raised in such cases include the possibility of the tumor originating from ectopic lacrimal gland orbital tissue, or from possible occult extra-orbital tumor (such as in the sinuses) with spread

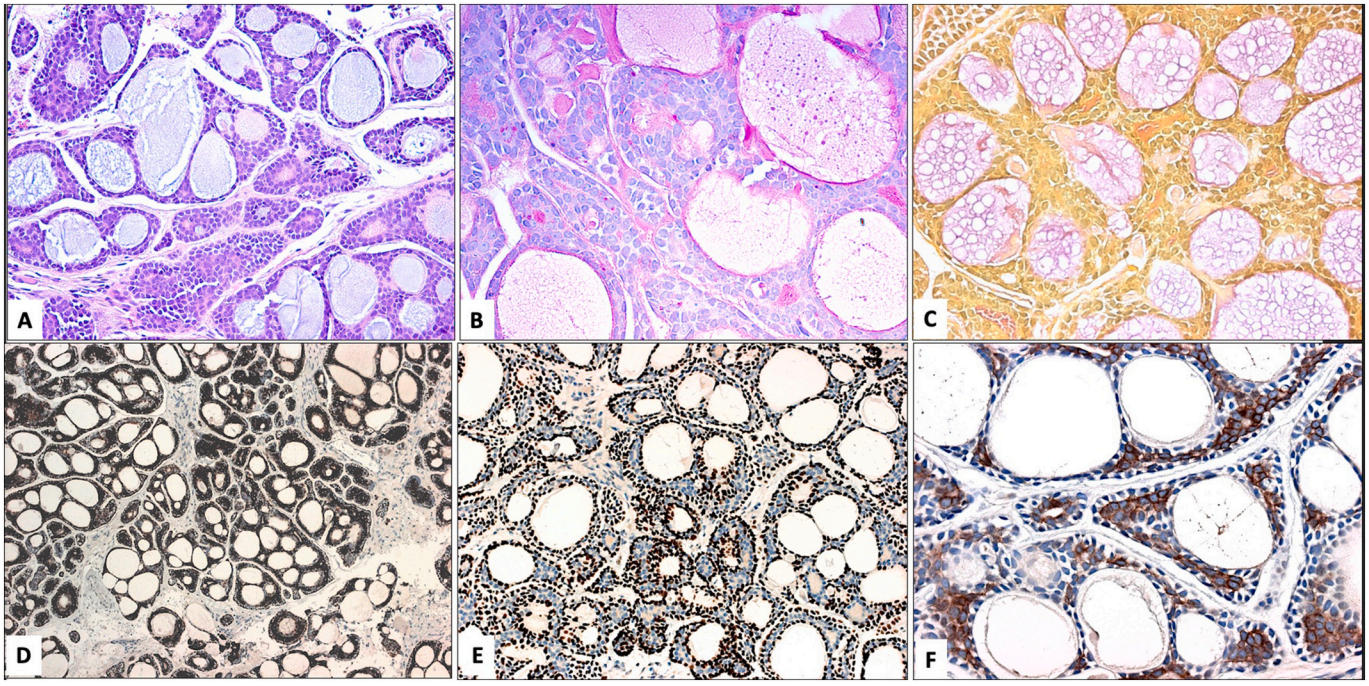

Fig. 2. A: The appearance of the left orbital tumor showing typical Swiss cheese configuration (original magnification ×200 hematoxylin and eosin).
B & C: The prominent staining of the cystic areas by periodic acid Schiff (PAS) in B and mucicarmine in C (original magnification ×400).
D, E, & F: The tumor cells demarcating the cribriform pattern of the adenoid cystic carcinoma are showing expression and reactivity to the corresponding confirmatory IHC markers (original magnification ×100 Cytokeratin 7 in D, original magnification ×200 p63 in E, and original magnification ×400 CD117 in F).

through perineural extension, or even through hematogenous spread as a form of distant metastasis [3]. To our knowledge, Arsene et al. reported the only case of bilateral cavernous sinus extension of ACC found in the literature [4]. Their case is very similar to ours in many aspects, but in their case, meningioma was initially suspected rather than ACC based on radiological findings and initial histopathological examination. Initially, a lymphoproliferative process was suspected in our patient due to the clinical and the radiological presentation, however the biopsy of the lesion was positive for a low-grade ACC with typical cribriform pattern.

Our patient presented to us one year after the onset of his proptosis, which might have contributed to a more advanced disease. Another poor prognostic factor in our patient was the significant intracranial spread, extending into the skull base and bilaterally into the cavernous sinus. Due to the aggressive nature of the tumor, and the degree of intracranial spread, our patient received palliative radiotherapy outside our facility.

Similar to the case described by Macri et al. [7], lacrimal gland involvement was not suspected radiologically or clinically in our case, and the patient refused further biopsy of the lacrimal gland, as his tumor was advanced and surgical treatment was not offered. Although microscopic extension into the ipsilateral left gland could be present, we believe that considering the advanced nature of the tumor and the extensive invasion present, macroscopic lacrimal gland involvement would have been locally evident in the anterior orbit way before the tumor have attained this huge size and before these deep intracranial and cavernous sinus invasions. Multiple investigations including CT, MRI and PET did not identify any alternative primary tumor sites, in this case, which suggested that the orbit was the primary source of the ACC.

Optimal treatment of orbital ACC is unclear. In cases of ACC of the lacrimal gland, exenteration with adjuvant radiotherapy or chemotherapy is often performed [14]. Yang and his coauthors commented on the difficulty in managing ACC that extends to the cavernous sinus such as in our case. They described resection of the tumor via endonasal approach using endoscopy [15]. Others have suggested high dose proton beam radiotherapy for ACC of the skull base [16]. Intracranial extension into the skull base is a devastating complication which may present as diplopia, trigeminal neuralgia, and extraocular motility deficits, mainly 6th nerve palsy. Slow and insidious growth of tumor is characteristic of ACC, and late presentation is a common theme in these cases [9]. Even though molecular studies for *MYB* rearrangement have been a useful diagnostic tool in ACC of the LG, its status was not found to have a relationship to the clinical outcome of the tumor [17]. While such molecular studies might not be available in many centers, tissue diagnosis in orbital diseases aided by the presence of experienced histopathology/cytology staff remains the gold standard for tumors as well as in selected inflammatory conditions [18,19]. On the other hand, ACC diagnosis is also challenging histopathologically. The morphological appearance can be aided using immunohistochemical markers [20].

4. Conclusion

We present an advanced rare case of orbital ACC involving multiple skull base structures and the cavernous sinus bilaterally. A high index of suspicion is needed when dealing with orbital masses, and urgent tissue diagnosis and management are better guided depending on the case and the available diagnostic tools in each facility.

Provenance and peer review

Not commissioned, externally peer reviewed.

Consent

General informed written consent was obtained from the patient including permission for anonymous use of imaging and for reporting. A copy of the written consent is available for review by the Editor-in-Chief of this journal upon request.

Ethical approval

IRB is not required for case reports. However, information was obtained and reported in a manner that was compliant with the standards set forth by the Health Insurance Portability and Accountability Act, and the Declaration of Helsinki as amended in 2013.

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Guarantor

Hind M. Alkatan.

Research registration number

Not applicable.

CRediT authorship contribution statement

FMA: Review of chart for data collection, literature review and first draft of the case report. HA: The primary treating ophthalmic surgeon providing tissue biopsies. Review of the first draft of the manuscript. HA: Histopathological examination and final tissue diagnosis. HMA: Histopathological examination, images, review of the manuscript, and submission of revised manuscript as a corresponding author.

Declaration of competing interest

None.

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