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Unusual Presentation of Primary Orbital Microcystic Adnexal Carcinoma

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Abstract

Microcystic adnexal carcinoma (MAC) is a rare and locally aggressive malignancy that occurs on the face, can invade deep tissue, and can rarely invade the orbit via perineural spread. It has been reported most often in the form of a cutaneous lesion. Although there have been 3 prior case reports of an orbital presentation of MAC, all have been from undiagnosed cutaneous or subcutaneous lesions. We report a rare case of a primary orbital MAC in a 39-year-old healthy woman who presented with progressive diplopia and enophthalmos without evidence of any cutaneous or subcutaneous lesions.

A 39-year-old healthy woman presented initially with a history of an “odd feeling” over the left orbit and forehead, followed by painless diplopia and a dilated poorly reactive pupil. MRI showed changes consistent with an infiltrative process in the left orbit involving the extraocular muscles and fat. Additional workup included serologic studies for inflammatory processes, gallium scan, CT of the chest, and mammogram, none of which revealed any abnormalities. A biopsy of orbital fat via a transnasal endoscopic approach revealed only mild chronic inflammation.

At the initial visit to our institution, the patient had a visual acuity of 20/20 in the right eye, with normal color vision, and a superior arcuate field defect. The left eye had a visual acuity of 20/30, with normal color vision, and mild superior and inferior arcuate defects. There were bilateral optic disc drusen. The left pupil was dilated and poorly reactive to both light and near stimulations. On the left eye, there was a significant limitation of movement in all directions, a deep superior lid sulcus, and 1 mm of enophthalmos. Corneal and facial sensation were equal and normal bilaterally. A more extensive orbital biopsy was recommended, but the patient declined further evaluation.

Over the next 6 years, the patient developed worsening diplopia and increasing enophthalmos. Examination at that time demonstrated normal afferent visual function in both eyes except for bilateral arcuate visual field defects consistent with optic disc drusen. The left pupil remained dilated and nonreactive to both direct and consensual light

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stimulations, and eye movements on the left were limited in all directions of gaze. She had reduced left levator function, and exophthalmometry revealed 3 mm of left enophthalmos with moderate resistance to retropulsion (Fig. 1A, B). There was decreased left corneal sensation but normal corneal sensation on the right and normal sensation on both sides of the face. Slit-lamp biomicroscopy revealed diffuse punctate epithelial erosions of the left cornea. Both optic discs contained drusen associated with moderate peripapillary atrophy.

Orbital ultrasonography and a repeat MRI showed changes consistent with an infiltrative process in the left orbit involving extraocular muscles and orbital fat (Fig. 1C, D). A positron emission tomography and a repeat mammogram revealed no abnormalities. The patient consented to orbital biopsy, at which time the orbital fat appeared somewhat gray and thickened. Microscopic examination revealed a low-grade infiltrating carcinoma composed of nests and strands of relatively bland epithelial cells that were immunopositive for cytokeratins AE1 and AE3, p53, and carcinoembryonic antigen (Fig. 2). Immunostains for CK7, CK20, CAM 5.2, CD34, and Bcl-2 were negative, with the latter suggesting that this was not a sclerosing basal cell carcinoma (sBCC). Estrogen receptor, progesterone receptor, and thyroid transcription factor 1 immunohistochemical stains were also negative, making an origin from breast, lung, or thyroid unlikely. The Ki67 proliferation index was low, and some of the tumor strands contained small “microcystic” ductules. The overall morphological and immunohistochemical profile was consistent with a microcystic adnexal carcinoma (MAC).

A consulting oncologist indicated that there was no role for radiation or chemotherapy and recommended orbital exenteration. The patient declined further surgery and is being followed with serial examinations and orbital imaging.

MAC is a rare, slow-growing, locally invasive skin tumor of eccrine and pilar origin first described in 1982 by Goldstein et al (1). It is also known as sclerosing sweat duct carcinoma (1), malignant syringoma (2), or sweat gland carcinoma with syringomatous features (3). Affected areas that have been reported include the face, scalp, neck, trunk, vulva (4), and eyelid (5–7). Orbital extension is usually through perineural spread from cutaneous lesions (7,8). Regional and isolated distant metastasis are rare (9–14). Associated risk factors include immunosuppression and previous radiotherapy; however, cases in immunocompetent patients have also been reported (15–19). Age, gender, and history of actinic damage have been implicated as risk factors for MAC, but these associations remain inconclusive (20).

MAC usually is misdiagnosed clinically and histologically because of its inconspicuous features. It can present as a slow-growing plaque or nodule on the eyelid or the central face area, commonly the upper lip and nasolabial folds, that can mimic a basal cell tumor or a chalazion (6,14). Pathologically, it can mimic a sBCC, trichoadenoma, syringoma, eccrine carcinoma, desmoplastic trichoepithelioma, or metastatic breast cancer (21–23). Late recognition is common and can be associated with local tissue destruction at the time of diagnosis.

The main histological features of MACs include eccrine and pilar components. The cell of origin is believed to be an adnexal keratinocyte capable of dual differentiation (23). Biopsy findings include cords and nests of uniform keratinocytes, keratin-containing cysts, and foci of ductal differentiation in a sclerotic desmoplastic stroma (7). The tumor cells express a distinctive pattern of staining for epithelial membrane antigen (24), carcinoembryonic antigen (24,25), cytokeratin AE1/AE3 (23,24), and focal expression of Bcl-2 that differentiate them from sBCCs and dTEs (22,26).

Treatment options for MACs include wide local excision, Mohs micrographic surgery (MMS), and exenteration when there is orbital involvement. Standardized surgical margins have not yet been defined. Radiation can be considered as an adjunctive therapy; however, this tumor has been shown to be fairly radioresistant (4,14). Reported recurrence rates range from 40% to 60% depending on the treatment modality, with lower rates after MMS (24,27,28); however, these statistics may be an overestimate as there is often misdiagnosis at the time of excision, and positive margins can sometimes be misread.

Secondary enophthalmos may be caused by a number of conditions, including bone growth arrest; trauma; orbital varix with secondary bone erosion; orbital fat atrophy from inflammation (e.g., lupus erythematosus profundus), infection, or radiation; wasting disorders (e.g., Parry-Romberg hemifacial atrophy, linear scleroderma); scirrhous carcinoma, most commonly from breast metastasis; and silent sinus syndrome. To our knowledge, there are no reported cases of orbital MAC causing acquired enophthalmos.

We are aware of 3 reports of orbital involvement by MAC in the literature (7,8,25). Hoppenreijds et al (7) described 3 patients with lesions of the eyelid and medial canthal region, 2 of whom developed orbital invasion after local excision. Cooper and Mills (8) described a patient who developed a lesion on the left lip and left side of the nose that was resected but recurred about 2 years later at which time it involved the left orbit and the turbinates. A patient reported by Marshall et al (25) presented initially with a subcutaneous mass below the left medial canthal tendon that was excised; the patient later developed epiphora with diplopia and was found to have an orbital mass consistent with MAC.

Our case is unique compared with prior cases in its atypical clinical presentation—a pure orbital presentation with progressive diplopia and enophthalmos and a tonic pupil. The lack of any cutaneous or subcutaneous lesions on her external examination makes this patient very unusual and raises the question of the true origin of the tumor. One possibility is that the lesion arose from a small orbital dermoid cyst or other developmental malformation containing adnexal structures. Alternatively, the eccrine lacrimal gland or its ducts may have the capacity to give rise to a MAC, although if this is true, one might expect similar lesions in salivary glands. Finally, it may be that a small undiagnosed primary tumor arose from deep skin adnexae and extended into the orbit.

MAC is a diagnosis that should be considered in patients presenting with cutaneous or subcutaneous masses that extend into the orbit, particularly when the tumor has atypical histological features. In such cases, early diagnosis and treatment are critical in the prevention of extensive tissue loss due to the aggressive and destructive nature of this

disease. In addition, our case indicates that rare cases of MAC can present as an isolated infiltrative orbital process producing progressive enophthalmos, ophthalmoparesis, and other orbital signs.

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FIG. 1. External appearance of patient (**A** and **B**) and MRI (**C** and **D**). **A.** Note left ptosis, enophthalmos, deep superior lid sulcus, and inferior scleral show. **B.** Profile highlights left-sided enophthalmos. T1 axial (**C**) and coronal (**D**) MRIs show enhancement and infiltration (arrows) of the extraocular muscles and fat.

FIG. 2.

Left orbital biopsy specimen. **A.** Diffusely infiltrating epithelial process with deep invasion and associated dense desmoplasia (hematoxylin and eosin, $\times 20$). **B.** Immunohistochemistry reveals expression of cytokeratins (dark areas) in tumor cells (cytokeratin AE1/AE3, $\times 100$). **C.** The basaloid epithelial cells form nests and cords (arrows) surrounded by sclerotic stroma and are focally carcinoembryonic antigen immunoreactive (inset, brown areas) (hematoxylin and eosin, $\times 100$; inset: monoclonal carcinoembryonic antigen). **D.** Ductule-

like structures characteristic of MAC are also present (arrow) (hematoxylin and eosin, $\times 200$).

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