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Case Report

Mucoepidermoid carcinoma of the lacrimal gland in a patient with the *CRTC1-MAML2* fusion gene [☆]

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ABSTRACT

Mucoepidermoid carcinoma (MEC) of the lacrimal gland (LG) is a rare entity. A 47-year-old woman was aware of periorbital swelling for 3 months. At presentation, the patient showed periorbital swelling in the right eye. CT scan showed an isodense mass in the anterior superolateral part of the orbit. MRI delineated the mass as enhancing, extra-conal tumor appearing isointense on T1-weighted sequences, and to be of mixed intensity on T2-weighted sequences. The tumor was totally resected. Microscopically, the tumor tissue was comprised of squamous, epithelioid cells, and cells with plump and clear cytoplasm. Necrosis, neural invasion, or mitotic figures were not observed. Immunohistochemical examination revealed intense staining for cytokeratin 7. A subset of the cells was positively stained with periodic acid–Schiff and mucicarmine stains. Genetic analysis revealed the presence of the *CRTC1-MAML2* fusion. The *CRTC1-MAML2* fusion may be a useful indicator for the prognosis and planning of adjuvant therapy.

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Introduction

Orbital neoplasms comprise a broad spectrum of benign and malignant tumors. MRI is particularly valuable for the eval-

uation of orbital neoplasms as it provides critical anatomic information about involved ocular structures and the occurrence of intracranial extension [1]. Clinically, lesions of the lacrimal gland (LG) are found as palpable masses in the superior lateral aspect of the orbit, and they can be categorized

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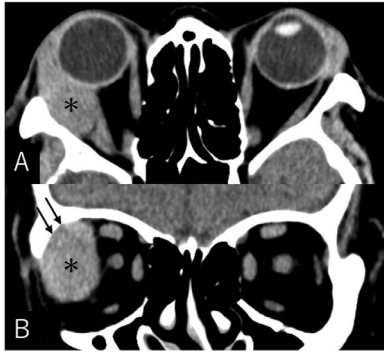


Fig. 1 – Non-contrast axial (A) and coronal (B) CT scans showing an isodense mass occupying the superolateral part of the right anterior orbit and posterolateral aspect of the eyeball (A, asterisk). Note that erosive changes are not found in the orbital wall adjacent to the mass (B, arrows).

as epithelial or non-epithelial processes. Of the LG neoplasms, pleomorphic adenoma is the most common benign epithelial tumor, while adenoid cystic carcinoma (ACC) is the most common metastatic tumor, characterized by frequent bone and perineural invasion, and extraorbital spread [2,3]. We report a case of mucoepidermoid carcinoma (MEC) of the LG, which has rarely been described in the literature [4,5].

MECs are malignant tumors that commonly affect the salivary glands, the secretory glands of the airway, and the uterine cervix. In addition to advanced histologic grade and positive nodal status, the observation of a cystic component of less than 20%, and 4 or more mitotic figures per 10 high-power fields, neural involvement, necrosis, and anaplasia are thought to be the microscopic features that herald a poor prognosis [6–8]. Recently, molecular biology techniques have been introduced to explore MECs [9–12]. Studies have revealed that MECs are frequently associated with a t(11;19) (q14-21;p12-13) translocation that results in the *CRTC1-MAML2* fusion gene, which has been suggested to indicate a favorable prognosis [9,12]. Here, we present the first LG MEC case with this genetic abnormality.

Case report

A 47-year-old woman had been aware of a painless periorbital swelling from 3 months prior to presentation. She had a medical history of cervical and kidney cancer, both of which underwent total resection, followed by an uneventful recovery without further local recurrence or metastases. At presentation, the patient showed slight proptosis and periorbital swelling in the right eye, while her visual function, and ocular motor movements were intact. A non-contrast brain CT scan showed an isodense mass occupying the superolateral part of the right anterior orbit and posterolateral aspect of the eyeball. Erosive changes were not observed in the orbital wall adjacent to the mass (Fig. 1). MRI delineated the mass as an intensely enhancing, extra-conal tumor appearing isointense on T1-weighted

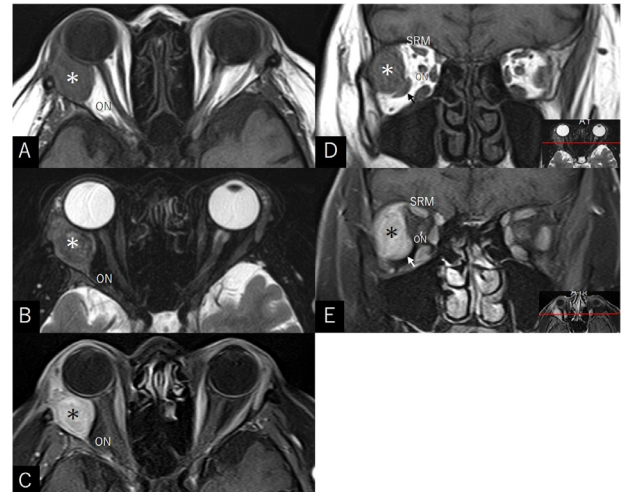


Fig. 2 – Non-contrast T1-weighted images in the axial (A) and coronal (D) planes. Non-contrast T2-weighted images in the axial plane (B). Post-contrast T1-weighted images in the axial (C) and coronal (E) planes. MRI images show an intensely enhancing, extra-conal tumor appearing isointense on T1-weighted sequences and to be of mixed intensity on T2-weighted sequences (A-E, asterisk), with the displaced lateral rectus muscle in the inferomedial direction (D and E, arrow). ON, optic nerve; SRM, superior rectus muscle.

sequence and mixed intensity on T2-weighted sequence. The right lateral rectus muscle was displaced in the inferomedial direction by the tumor (Fig. 2). The patient underwent tumor resection via lateral orbitotomy. The tumor lying under the periorbita was whitish in color, elastic, hard, and less vascular. Adhesions were not noted between the tumor and the periorbita or lateral rectus muscle. However, a part of the tumor had adhesions to the lacrimal gland, which was easily dissected and detached. Consequently, gross total resection was achieved (Fig. 3). Microscopically, the tumor tissue was comprised of squamous, epithelioid cells and cells with plump and clear cytoplasm. The latter cells proliferated in alveolar patterns or formed gland-like structures. Necrosis, neural invasion, or mitotic figures were not observed. Immunohistochemical examination showed intense staining for cytokeratin 7 and negative staining for cytokeratin 20. In addition, staining of a subset of the tumor cells with clear cytoplasm using periodic acid-Schiff and mucicarmine stains revealed an MIB-1 labeling index of 8% (Fig. 4). Furthermore, genetic analysis demonstrated the presence of the *CRTC1-MAML2* fusion gene (Fig. 5). Postoperative whole-body FDG-PET and/or CT did not identify any abnormal accumulations. Based on these findings, we diagnosed the patient with low-grade MEC originating from the LG. Immediate adjuvant chemoradiation therapy was not administered, but the patient was placed under close observation.

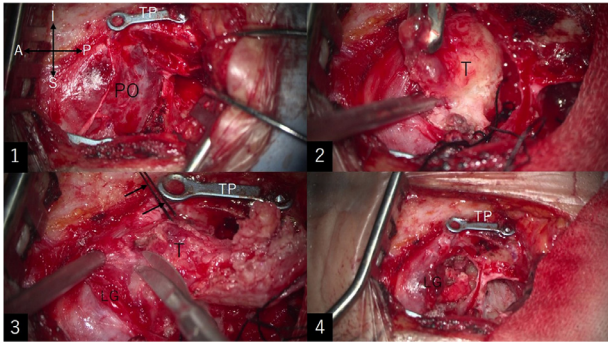


Fig. 3 – Intraoperative photos showing the following: 1. completion of lateral orbitotomy, 2. early stage of tumor resection, 3. tumor being dissected from the lacrimal gland, and 4. completion of tumor resection. A, anterior; I, inferior; LG, lacrimal gland; P, posterior; PO, periorbita; S, superior; T, tumor; TP, titanium plate; Arrows in 3: threads hung to the lateral rectus muscle near the attachment site of the eyeball that allow intraoperative identification of the muscle when pulled.

Discussion

Due to only a few documented cases, LG MECs are not well understood. Therefore, currently, there are no defined treatment strategies [4,5]. Orbital neoplasms comprise a broad spectrum of benign and malignant pathologies, with ACC being the most common malignant tumor of the LG [2,3]. In our case, presurgical CT did not show any bone erosion that results from large tumors, which excluded the diagnosis of ACC and aided with the positioning of the surgical window that allowed to expose the tumor located in the superolateral part of the anterior or-

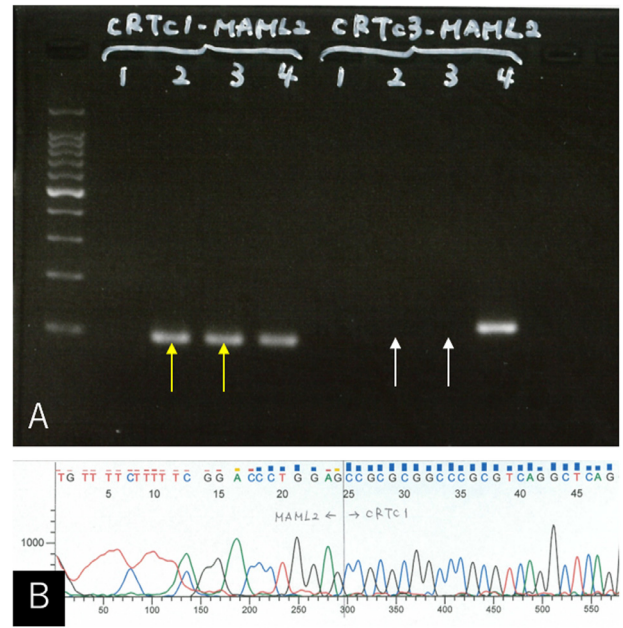


Fig. 5 – Results of immunoelectrophoresis (A) and direct sequencing (B) showing the presence of the CRTc1-MAML2 fusion (A, yellow arrows and B) and the absence of the CRTc3-MAML2 fusion (A, white arrows) (Color version of the figure is available online.)

bit and posterolateral aspect of the eyeball. Lateral orbitotomy was first described by Krönlein in 1888 and has been subject to many modifications and variations. However, the utility of this approach is limited if lesions are located deep in the orbital apex or extends into the intracranial cavity. With surgeons becoming increasingly familiar with this procedure, along with

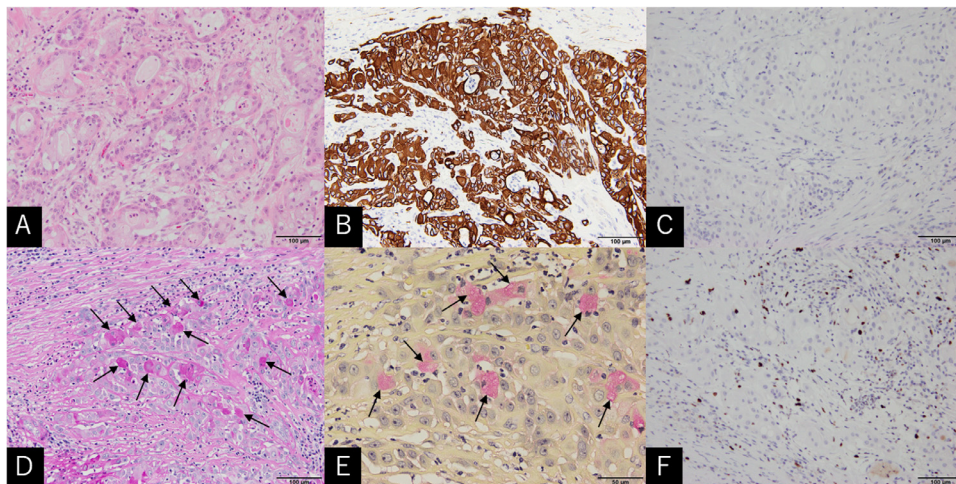


Fig. 4 – Photomicrographs of the tumor tissue are mainly comprised of squamous, epithelioid cells and cells that have plump and clear cytoplasm. The latter cells proliferate in alveolar patterns or form gland-like structures. Necrosis and mitotic figures are not found (A: hematoxylin and eosin stain). Immunohistochemical examination showing intense staining for cytokeratin 7 (B) and negative staining for cytokeratin 20 (C). Some tumor cells with clear cytoplasm are stained with periodic acid–Schiff (D, arrows) and mucicarmine (E, arrows) stains. The MIB-1 labelling index is accounted to be 8% (F).

modern microsurgical techniques, and the adoption of endoscopy, the utility of this approach has expanded to allow the treatment of intracranial pathologies [13]. The present patient underwent gross total resection of the tumor, and the histologic appearance was consistent with low-grade MEC. Postoperative whole-body FDG-PET and/or CT did not reveal any abnormal accumulations. Furthermore, the *CRTC-MAML2* fusion gene suggesting a favorable prognosis was identified. Therefore, immediate adjuvant therapy was not administered to the patient. Although the *CRTC-MAML2* gene fusion is not always detected in MECs, its presence can be definitive for the diagnosis of LG MECs, and help in planning postsurgical adjuvant therapy. The *CRTC1-MAML2* fusion gene was also useful to exclude the involvement of the previous cervical and kidney cancers from the differential diagnosis of the LG tumor. Accumulation of further cases is needed to validate the diagnostic and therapeutic implications of the *CRTC1-MAML2* fusion gene in LG MECs. Recent studies have reported that the activation of the endothelial growth factor receptor (EGFR) pathway and EGFR amplification are also implicated in LG MECs [10]. Continuous investigation using molecular biology techniques would further improve the strategies used to approach LG MECs.

In addition to aforementioned findings, variability of the arterial and venous tributaries distributed over the LG and that of the zygomaticotemporal nerve, a branch of the trigeminal nerve that gives rise to the lacrimal nerve, may influence the biological behavior of LG MECs [14,15]. Therefore, long-term follow-up of the present patient is needed.

In conclusion, *CRTC1-MAML2* fusion may be a useful indicator not only for an accurate diagnosis of LG MEC but also for predicting the prognosis, and planning of adjuvant therapy.

Author contributions

All the authors contributed equally to the study.

Disclosure of funding

None.

Ethical standards and patient consent

We declare that the present study has been approved by the institution's guidelines for human research and performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. We declare

that the patient described in this study gave informed consent prior to inclusion in this study.

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