SPANDIDOS PUBLICATIONS

MOLECULAR AND CLINICAL ONCOLOGY 8: 209-213, 2018

Lacrimal myoepithelial carcinoma ex recurrent pleomorphic adenoma: A clinicopathological report and review of the literature

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Received August 31, 2017; Accepted October 31, 2017

DOI: 10.3892/mco.2017.1488

Abstract. Myoepithelial carcinoma is an uncommon malignant tumor of the lacrimal gland, composed of neoplastic myoepithelial cells with an infiltrative growth. The present study describes a unique case of progressive proptosis and blindness of the right eye in a 68-year-old woman following total tumor removal for lacrimal pleomorphic adenoma. Clinical study, surgical exploration, and pathology revealed lacrimal myoepithelial carcinoma ex recurrent pleomorphic adenoma, T2N0M0. In addition, 18 cases of lacrimal myoepithelial tumor that have been previously described in the literature are reviewed. The application of clinical, radiological, histopathologic, and immunohistochemical investigations may help to reach the definite diagnosis. Criteria for malignancy of lacrimal myoepithelial tumor should be the same as salivary myoepithelial tumor diagnosis, until long-term outcome data for a larger number of patients with lacrimal myoepithelial carcinoma become available.

Introduction

Histopathological typing of tumors arising in the lacrimal gland is generally similar to the classification of salivary gland, although the frequency of occurrence of individual types is different. Myoepithelial tumor (MET) is an uncommon epithelial neoplasm of the lacrimal gland and was first described in salivary gland and lacrimal gland by Sheldon *et al* and Heathcote *et al*, respectively (1,2). MET has been included in the World Health Organization (WHO) classification of salivary gland tumours since 1991. The histogenesis of myoepithelial tumor is currently regarded as tumor showing morphologic and immunophenotypic evidence towards myoepithelial cell (3). Herein, the authors report the clinical, radiological, histopathologic, and immunohistochemical features of lacrimal myoepithelial carcinoma (MEC) arising in pleomorphic adenoma of the lacrimal gland.

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Key words: myoepithelial carcinoma, myoepithelial tumor, pleomorphic adenoma, lacrimal gland

Case report

A 68-year-old Thai female patient presented with progressive painless proptosis in the right eye. For 12 years ago, she had had swelling of the right upper eyelid. She underwent total tumor removal for pleomorphic adenoma, tumor size 3 cm in greaest dimension, with intact capsule and complete surgical resected margin. For one year, 11 years later, she had noticed progressive proptosis. Three months before surgery, she developed blindness of the right eye with a large palpable mass in the superotemporal aspect of the periocular area. Physical examination showed a visual acuity of no light perception in the right eye and 20/32 in the left eye. A firm mass was palpated in the superior temporal part of the right orbit. There was proptosis and limited upward gaze of the right eye. Magnetic resonance imaging (MRI) of the orbit revealed a well-defined, lobulated, vivid inhomogeneous enhancing isosignal T1W/slightly hypersignal T2W mass measuring 38x37x33 mm. The volume was 30.626 cm^3. It located at retrobulbar portion involving extraconal-conal-intraconal spaces of the right orbit and invading of the lateral bony wall laterally, displacing the eye inferiorly, the optic nerve medially and the globe anteriorly resulting exophthalmos (Fig. 1). No regional lymphadenopathy was detected.

An incisional biopsy through the lateral orbitotomy was performed, and the diagnosis of myoepithelial neoplasm of uncertain malignant potential was made. Two months later, exenteration of the right orbit was performed. Intraoperatively, the tumor exhibited worrisome anatomic features in that is extended into adjacent periocular soft tissue. The histopathologic diagnosis was MEC arising in recurrent pleomorphic adenoma. Her postoperative course was uneventful. The patient desired no further treatment. Follow-up at 3 years revealed no evidence of tumor.

Pathologic findings

The resected specimen contained a firm gray-tan mass measuring 40x40x35 mm. Cut surfaces were variably gray to

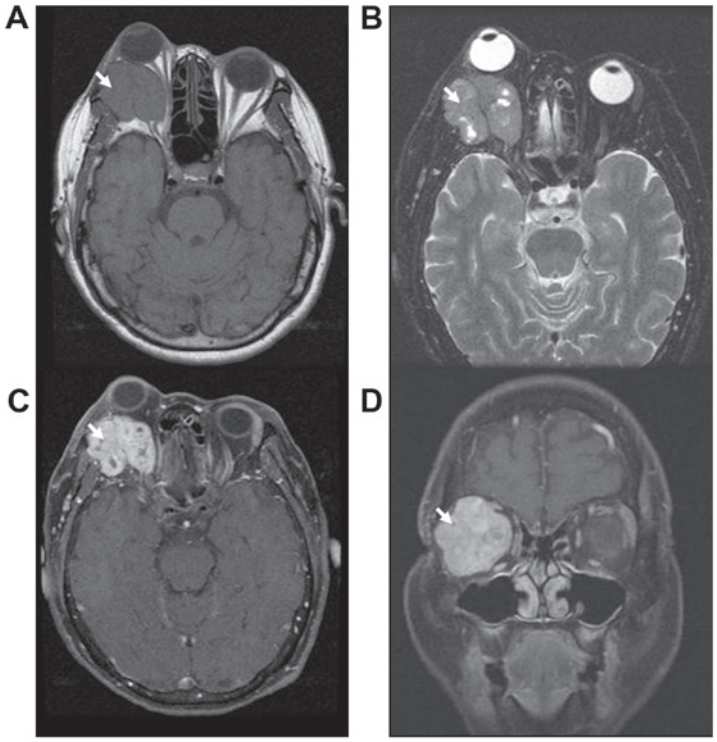

Figure 1. MRI of the orbit. (A) Axial T1W, (B) axial T2W with fat suppression, (C and D) axial and coronal T1W with fat suppression and gadolinium enhancement show a well-defined, lobulated, vividly inhomogeneous enhancing isosignal TW/hypersignal T2W mass centered at the intraconal space extending into the extraconal space and invading of the lateral bony wall laterally, displacing the optic nerve medially and the globe anteriorly resulting exophthalmos.

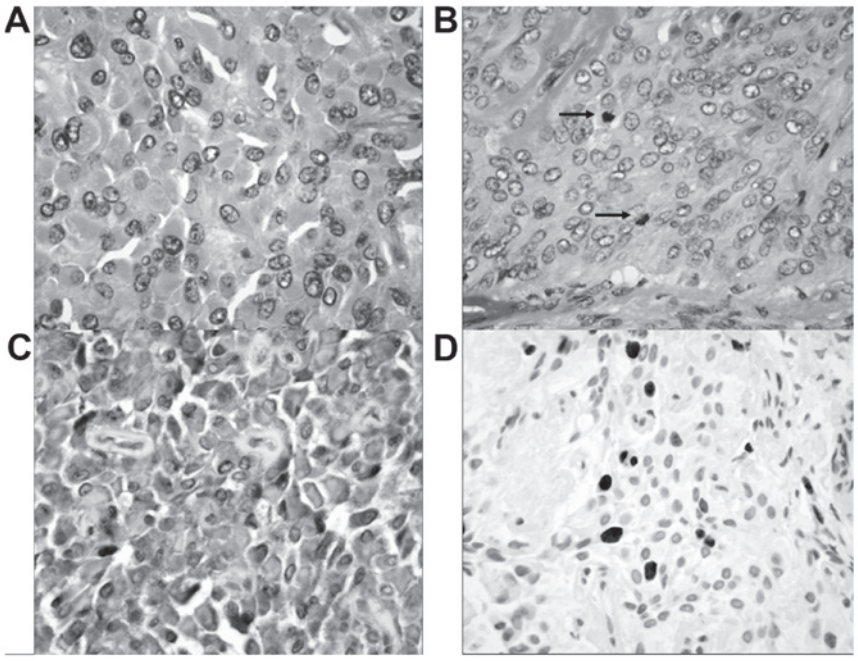

Figure 2. (A) The section of the lacrimal tumor reveals round to polygonal epithelioid and plasmacytoid cells with abundant eosinophilic cytoplasm, and nuclear pleomorphism, (H&E; magnification, x400). (B) The tumor cells are round to oval nuclei with finely distributed chromatin, small nucleoli, and increased mitotic activities (arrows) (H&E; magnification, x400). (C) The tumor cells demonstrate positivity for myogenin, and Ki67 (D), magnification, x400.

light-brown appearance. The mass had an infiltrative border not involving the margins of resection. Histopathologic examinations revealed round to polygonal epithelioid cells with abundant eosinophilic cytoplasm (Fig. 2). Occasional cells had small amounts of spindle and plasmacytoid appearance. The nuclei were round to oval with finely distributed chromatin and small nucleoli. Cellular and nuclear pleomorphisms were detected. Mitotic activity was 10/10 high-power fields (HPFs). The tumor demonstrated focal infiltration into adjacent periocular soft tissue. Angiolymphatic and neural invasions were

Table I. Summary of 19 reported cases of lacrimal myoepithelial tumors.

Authors, year	Age (years)	Sex	Side	Size (mm)	Variant	Nature	(Refs.)
Heathcote *et al*, 1990	Middle	F	NA	31x25x17	Spindle	Benign	(2)
Herrera, 1990	68	M	Left	35x30x25	Epithelioid	Malignant	(4)
Font *et al*, 1992	23	F	Left	30x25x17	Spindle	Benign	(5)
Ni *et al*, 1992	NA	NA	NA	NA	Spindle	Benign	(6)
	NA	NA	NA	NA	Spindle	Benign	
Grossniklaus *et al*, 1997	76	F	Right	9x9x9	Mixed	Benign	(7)
Okudela *et al*, 2000	34	M	Right	25x15x18	Mixed	Malignant	(8)
Iida *et al*, 2001	77	M	Left	NA	Spindle	Malignant	(9)
Bolzoni *et al*, 2005	46	M	Right	18x16x16	Plasmacytoid	Benign	(10)
Pasquale *et al*, 2005	57	F	Left	35x25x15	Epithelioid	Benign	(11)
Wiwatwongwana *et al*, 2009	84	M	Left	32x26x22	Epithelioid	Malignant	(12)
Weis *et al*, 2009	NA	NA	NA	NA	Mixed	Benign	(13)
	NA	NA	NA	NA	Epithelioid	Malignant	
Argyris *et al*, 2013	39	F	Left	16x11x13	Epithelioid	Malignant	(14)
von Holstein *et al*, 2013	NA	NA	NA	NA	NA	Malignant	(15)
Eldesouky *et al*, 2014	NA	NA	NA	NA	NA	Benign	(16)
Moret *et al*, 2014	88	M	Right	35x17x25	Spindle	Malignant	(17)
Rabade *et al*, 2014	27	M	Right	30x20	Clear cell	Malignant	(18)
Present case	68	F	Right	40x40x35	Epithelioid	Malignant	

M, male; F, female; NA, not available.

Table II. Clinicopathological characteristic of 19 reported cases of lacrimal myoepithelial tumors.

Characteristics	Benign	Malignant	P-value
Mean age (years)	50.50±22.13 (range, 23-76)	60.62±23.84 (range, 27-88)	0.495
M:F ratio	1:4	3:1	0.049
Right:left ratio	1:1	1:1	0.135
Size (mm)	24.60±10.78	30.43±7.89	0.303
Histopathologic variant			0.046
Epithelioid	1	5	
Spindle	4	2	
Plasmacytoid	1	0	
Clear	0	1	
Mixed	2	1	
NA	1	1	

M, male; F, female; NA, not available.

not identified. There was no intracytoplasmic mucin. There were small foci of myxoid stroma, representing the residual pleomorphic adenoma. Immunohistochemiscal stains of the epithelioid, spindle, and plasmacytoid cells were diffuse positive reactivity for cytokeratin AE1/AE3, S100 protein, vimentin, myogenin, muscle-specific actin, and α-smooth muscle actin. The tumor cells did not express sarcomeric actin, desmin, h-caldesmon, epithelial membrane antigen (EMA), glial fibrillary acidic protein (GFAP), HMB45, estrogen receptor, and progesterone receptor. The proliferation (Ki67) of the tumor cells was 10.26%. The tumor was completely excised. The pathologic diagnosis was lacrimal MEC arising in recurrent pleomorphic adenoma.

Discussion

MET is an uncommon neoplasm composed of histologically and immunohistochemically distinctive myoepithelial cells (3). Most METs arise in the salivary glands (3). Lacrimal METs are uncommon. Including the authors' patient, 19 cases of lacrimal MET have been reported (Table I). Of these cases, nine cases (50%) were considered to be malignant MET or MEC. The ages of patients range from 23 to 88 years with the mean and median ages of 57.25 and 62.5 years, respectively (2,4-18). The average age of diagnosis of benign MET was younger than MEC (50.50±22.13 vs. 60.62±23.84 years, P=0.495). The tumor sizes range from 9 to 40 mm with the mean and median sizes of 28 and 30.5 mm, respectively (2,4-18). The average size of benign MET was smaller than MEC (24.60±10.78 cm vs. 30.43±7.89 cm, P=0.303). Male patients are more likely to have MEC with a male to female ratio of 3:1 (P=0.049, Table II). Lacrimal METs

usually remain asymptomatic until they produce a mass effect. The most frequently presenting symptoms are painless proptosis, progressive periorbital swelling, diplopia, and blindness (2,4-18).

The imaging procedures such as computed tomography, and MRI may allow recognition of lacrimal METs. Imaging findings of MET show vivid enhancing isosignal T1 W and hyper-, intermediate or even hypointense T2 W (8,10). In the authors' case, the mass shows typical MRI feature and invades the lateral wall of orbit. This behavior suggests progression of slow growing malignant tumor.

The diagnosis of MET is based on histopathology and immunohistochemical studies. The lacrimal MET can easily be mistaken for variety tumors including atypical meningioma, leiomyosarcoma, and metastatic amelanotic melanoma. Atypical meningioma is excluded, as it does not immunohistochemically express myogenin, muscle-specific actin, and alpha-smooth muscle actin. Leiomyosarcoma with epithelioid feature does not demonstrate immunoreactivity for S100 protein, and cytokeratin AE1/AE3. Metastatic amelanotic melanoma may have a similar histopathology, but the tumor cells typically show atypia, and usually locate in the lymphovascular channels as well as there is no evidence of primary lesion. Negative results of HMB45 immunohistochemical stain may be helpful in excluding melanoma. Finally the definite diagnosis is lacrimal MEC.

Histopathologically, MET is classified into four subtypes composing of solid, trabecular, reticular, and mixed pattern (3). Five cellular variants are identified in MET: namely spindle, plasmacytoid, epithelioid, clear, and mixed cell type (3,12,18). Benign MET usually shows spindle cellular variant, whereas, MEC usually shows epithelioid cellular variant (P=0.046). However, different cell types and architectural patterns may be found within the same tumor. In fact, most MECs are less monomorphic than benign MET.

Most METs have benign course, however few reported patients had malignant nature. Clear criteria for lacrimal MEC have not been elaborated. On the basis of prior reports, it appears that lacrimal MET displaying infiltrative, destructive growth, marked hypercellularity, marked cellular pleomorphism, perineural invasion, lymphovascular invasion, high mitotic activity or necrosis should be regarded as indicating neoplasms with malignant potential (5,8,9). METs showing p53 expression and mitotic figure more than 7/10HPFs as well as Ki67 labeling index more than 10% are indicatory for malignancy (19). The authors suggest lacrimal MET having a few above parameters should be considered a tumor of malignant potential. Criteria for malignancy of lacrimal MET should be used as same as salivary MET until long-term clinicopathologic outcome data for a larger number of lacrimal MECs become available. Additional investigations and long-term follow-up are warranted to clarify the malignant potential of lacrimal MET.

Malignant tumor can arise either de novo or develop in a pleomorphic adenoma. Di Palma *et al* postulated that MEC has a low-grade malignancy when it arises from a pleomorphic adenoma, but may play more aggressive growth when it arises de novo (20). To our knowledge, this is the first reported case of MEC arising in recurrent pleomorphic adenoma of the lacrimal gland.

Surgical excision remains the cornerstone of management of the lacrimal neoplasms (21). Orbital exenteration is indicated where the lacrimal neoplasm is extensive and the mass has infiltrated beyond neoplastic capsule (21). Benign lacrimal tumors generally behave in an indolent manner and generally do not recur after complete wide surgical excision. However, malignant lacrimal neoplasms appear to be more aggressive may recur and metastasize. Close follow-up after wide surgical excision is recommended. The surgery will be followed by radiotherapy, chemotherapy and molecularly targeted agents, which classically belong to the armamentarium of malignant neoplasm (21).

In conclusion, lacrimal MEC should be considered in the differential diagnosis of lacrimal neoplasm. The application of immunohistochemical investigation correlating with the clinical presentation, intraoperative and radiological findings might help in making the definite diagnosis.

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