

Spindle cell myoepithelioma of the parotid gland

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Myoepithelioma was recognized as a histological distinct entity by the World Health Organization (WHO) in 1991. Myoepithelial cells are believed to be of ectodermal origin. In salivary glands, the myoepithelial cells that surround the intercalated ducts are spindled, which is in contrast to the large stellate ones that envelop the acini. Myoepithelioma is a benign salivary gland tumor that consists entirely of myoepithelial cells. A 53-year-old man presented with a 1-year history of a painless mass originating from the right parotid gland. The mass grew rapidly reaching a size of approximately 6 cm. The patient had no facial paralysis. The authors performed right parotidectomy. Immunohistochemistry study of this tumor showed that it was positive for vimentin, positive for S-100, focally positive for pancytokeratin, and focally positive for p63 and that it had a Ki-67 labeling index (below 10%). Additionally, the tumor was negative for epithelial membrane antigen, negative for actin, negative for desmin, negative for CD34 and negative for anaplastic lymphoma kinase. The authors present a case of benign spindle cell myoepithelioma of the parotid gland in a 53-year-old man diagnosed after immunohistochemistry study, describing its importance, along with a brief review of the literature.

Keywords: Myoepithelioma / Parotid neoplasm

INTRODUCTION

As it is noted by Saveria and Zarbo [1], myoepithelial cells of the salivary gland were first described by Zimmerman in 1898. In 1943, Sheldon was the first to classify salivary gland tumors as myoepitheliomas in a review of 57 mixed tumors of the salivary glands, in which three salivary gland tumors were classified as myoepitheliomas. Myoepithelial cells are believed to be of an ectodermal origin. They envelop the glandular, acinar, and ductal elements of various organs, especially the breasts and salivary glands. In the salivary glands, the myoepithelial cells that surround the intercalated ducts are spindled, which is in contrast to the large satellite ones that envelop the acini [1].

Myoepithelioma was recognized as a histologically distinct entity by the World Health Organization (WHO) in 1991 [2]. It

is a benign salivary gland tumor that consists entirely of myoepithelial cells with variable cellular morphologies, including spindle, epithelioid, plasmacytoid, and clear cells. A myoepithelioma can be composed of one or a mixture of these cell types, and a variable stromal component is seen in these tumors.

Myoepitheliomas are unusual and uncommon tumors that constitute only 1% to 1.5% of all salivary gland neoplasms [3,4].

The pathologist and treating oncologist should be aware of this rare diagnosis, and it should always be a part of the differential diagnosis. However, only a morphological examination may be insufficient, even for an experienced pathologist in some cases. In such a case, the role of immunohistochemistry studies comes into play, and it should be considered to identify the diagnosis [5]. A 53-year-old male patient diagnosed with benign spindle cell myoepithelioma of the parotid gland after immunohistochemical study describes the importance of benign spindle cell myoepithelioma of the parotid gland in this literature review.

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CASE REPORT

A 53-year-old man presented with a 1-year history of a painless mass originating from the right parotid gland (Fig. 1). The mass grew rapidly, reaching a size of approximately 6 cm. The patient had no facial paralysis. Ultrasonography revealed an ovoid, homogenous, exophytic and lobulated isoechoic right parotid



Fig. 1. A 53-year-old man presented with a 1-year history of a painless rapid growing mass in the region of the right parotid gland.

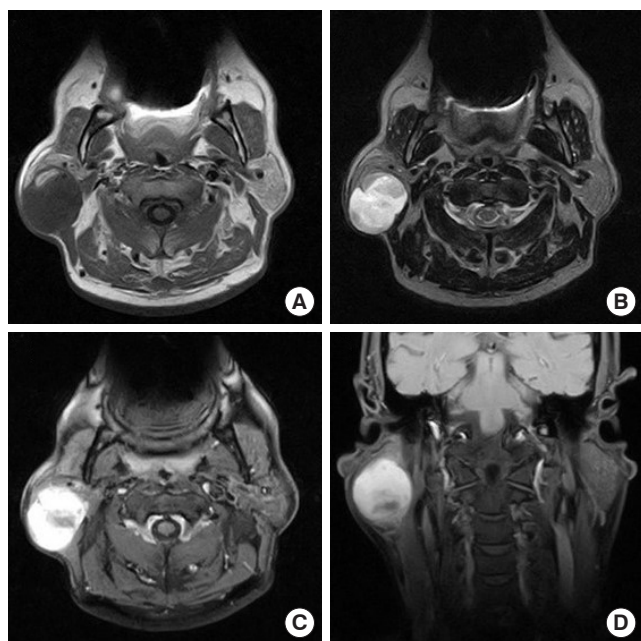


Fig. 2. Magnetic resonance images noted a large exophytic, well-margined and lobulated mass. T1WI image (A), T2WI image (B), T1WI-Gd-axial (C), and T1WI-Gd-coronal (D). T1WI, T1 weighted image; T2WI, T2 weighted image

mass measuring 4.37×3.92 cm. Magnetic resonance images noted a large exophytic, lobulated mass. T1WI (T1 weighted image; Fig. 2A) and T2WI (T2 weighted image; Fig. 2B) as compared with T1WI-Gd (gadolinium) of the axial (Fig. 2C) and coronal (Fig. 2D) views showed more enhancement in the periphery than that in the center and a relatively well-marginated mass ($5.5 \times 4.37 \times 3.92$ cm) in the right parotid gland without enlarged cervical lymph nodes. Benign mixed tumor and mucoepidermoid carcinoma were suspected. Superficial parotid gland resection including two parotid and two jugular lymph nodes was performed.

The gross specimen received in formalin was a previously bisected salivary gland tumor surrounded by yellowish brown soft tissue, measuring $7 \times 6 \times 6$ cm in total and weighing 68 g. On sectioning, there was a well-encapsulated whitish yellow myxoid tumor with areas of hemorrhagic necrosis and focal cystic change. The tumor was $5.5 \times 4.5 \times 4.0$ cm in size (Fig. 3).

The pathologist was initially suspicious of spindle cell myxoid tumor of an undetermined type with foci of an epithelial-like arrangement and hemorrhagic necrosis (Fig. 4a). Immunohistochemistry study showed that it was positive for vimentin (Fig. 4b), positive for S-100 (Fig. 4c), focally positive for pancytokeratin (Fig. 4d), and focally positive for p63 (Fig. 4e) and that it had a Ki-67 labeling index (below 10%) (Fig. 4f). Additionally, the analysis showed that the tumor was negative for EMA, negative for actin, negative for desmin, negative for CD34 and negative for ALK (Table 1). Therefore, the pathologic diagnosis was benign spindle cell type myoepithelioma with necrosis. There was no evidence of disease at the 3-year follow-up.



Fig. 3. The bisected specimen of the parotid mass consisted of an encapsulated, soft, lobulated mass with a yellow-to-white on-cut surface.

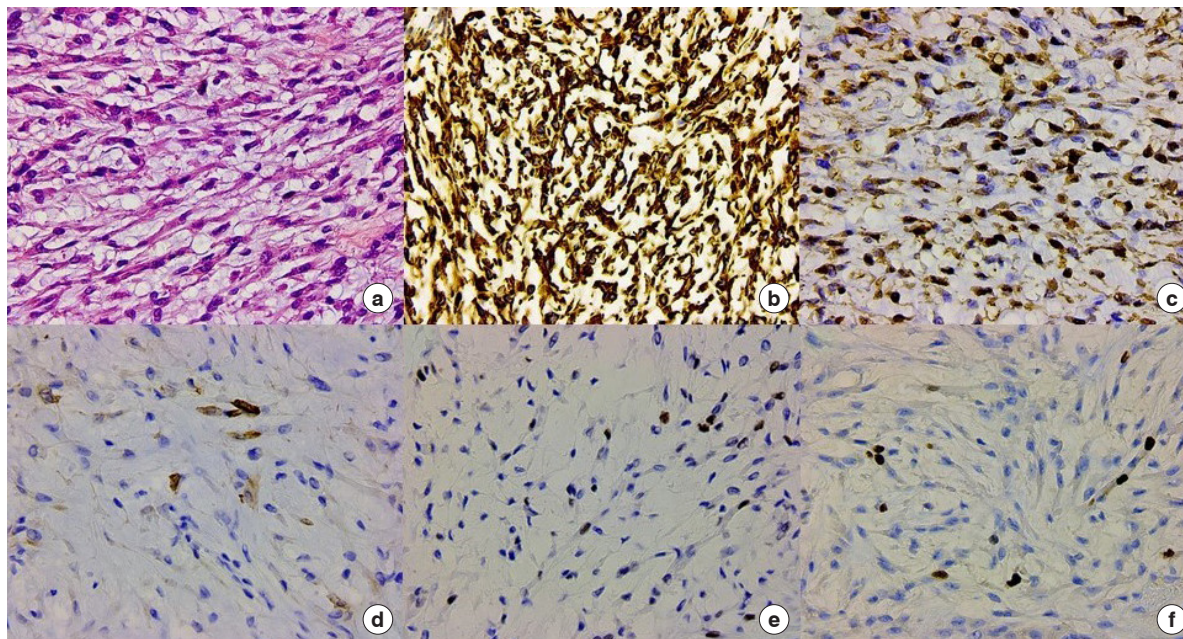


Fig. 4. Histological findings. (a) Histological study of the tumor showed spindle cell arrangement (H&E, ×400). Immunohistochemistry study showed that it was positive for vimentin (b, ×400), positive for S-100 (c, ×400), focally positive for pancytokeratin (d, ×400), and focally positive for p63 (e, ×400) and that Ki-67 was below the 10% labeling index (f, ×400).

Table 1. Management record of immunohistochemistry

No	Antigen	Company	Country	Dilution	Source	Clone	Test	Result
1	Vimentin	Dako	Denmark	1:100	Mouse	V9	Polymer (Omnis)	Positive
2	S-100	Dako	Denmark	1:2,000	Rabbit	Rabbit poly	Polymer (Omnis)	Positive
3	Pancytokeratin (CKAE1/AE3)	Dako	Denmark	1:400	Mouse	AE1/AE3	Polymer (Omnis)	Focally positive
4	P63	Dako	Denmark	1:200	Mouse	DAK-p63	Polymer (Omnis)	Focally positive
5	Ki-67	Roche	USA	Ready to use	Mouse	MIB-1	Multimer (Ventana)	Below 10% in hot spot
6	EMA	Dako	Denmark	1:200	Mouse	E29	Polymer (Omnis)	Negative
7	Actin	NOVOCASTRA	UK	1:100	Mouse	asm-1	Polymer (Omnis)	Negative
8	Desmin	Dako	Denmark	1:50	Mouse	D33	Polymer (Omnis)	Negative
9	CD34	Dako	Denmark	1:100	Mouse	QBEnd 10	Polymer (Omnis)	Negative
10	ALK-1(p80)	NOVOCASTRA	UK	1:50	Mouse	5A4	Multimer (Ventana)	Negative

EMA, epithelial membrane antigen; ALK, anaplastic lymphoma kinase.

DISCUSSION

In salivary glands and other exocrine glands, there are star-shaped cells of ectodermal origin lying between the basal lamina and the acinar and ductal cells. These cells structurally resemble epithelial cells and smooth muscles and are thus referred to as myoepithelial cells. The contraction of myoepithelial cells facilitates an expulsive secretion by rupturing “ripe” mucous cells, reducing the luminal volume and preventing the distention of acini, and other functions of myoepithelial cells are for the promotion of epithelial cell differentiation and sensory chemoreceptors, maintenance of gland patency, transportation of metabolites, formation and maintenance of the basement

membrane and tumor suppression. Myoepithelial cells are potentially differentiated into various morphologic cell types, such as the angulate/basaloid, epithelioid, clear, spindle and plasmacytoid (hyaline) cell types [6]. The different architectural arrangements found in myoepitheliomatous zones of a tumor are somewhat dependent on the type and quantity of extracellular matrix production associated with cytological differentiation, which can be classified as follows: myxoid, solid (non-myxoid), reticular, microcystic/pseudocystic and cribriform/pseudoglandular patterns [1]. Myoepitheliomas are unusual and uncommon tumors that constitute only 11.5% of all salivary gland neoplasms [3,4]. An equal sex distribution is seen in most case series [3]. The average age of tumor incidence in affected indi-

viduals is 44 years, with there being a wide age range, from 9 to 85 years [7]. The parotid gland is the primary site of occurrence of most reported myoepitheliomas (40%–50%), followed by the minor salivary glands as the second-most preferred site (of which the palate is the most common location [21%]) [3,5]. The submandibular gland accounts for 10% of tumors.

Myoepitheliomas are well-circumscribed, gray-white/tan/yellow solid masses (average size, 3–5 cm) with a smooth outline [3]. Degenerative changes are usually not a feature. Tumors arising in the parotid gland are usually encapsulated, in contrast to those arising in other major glands (submandibular and sublingual) or in the minor salivary glands, which tend to lack a capsule or only have a partial capsule but are invariably well-circumscribed. Computed tomography imaging findings of benign myoepitheliomas were well-circumscribed, enhanced mass lesions with smooth or lobulated margins located chiefly in the superficial lobe and abutted on the capsule of the gland similar to that of low-grade malignant tumors [8].

Myoepithelial cells represent cell types such as epithelioid (most common), spindle, plasmacytoid, clear (least common) or mixed type cell types [4]. A mixture of these subtypes may be present in one tumor. Spindle cell myoepitheliomas have central fusiform/cigar-shaped nuclei, an eosinophilic cytoplasm, and tapered ends, and they are usually arranged in interlacing fascicles.

Myoepithelioma cells have been usually shown to be positive for cytokeratins (e.g., AE1/AE3, CK 5/6, Cam 5.2, CK-7, and CK-14) and vimentin markers in immunohistochemistry. Vimentin is reported to be positive in neoplastic myoepithelial cells and negative in normal myoepithelial cells. The neoplastic transformation of myoepithelial cells can result in a loss or modification of their smooth muscle phenotype [7]. S-100 is usually positive in neoplastic myoepithelial cells, but it is not in normal salivary gland myoepithelial cells. Calponin is the most sensitive myogenic marker [9,10]. Another variable of positivity is seen in smooth muscle actin, muscle-specific actin, smooth muscle myosin, p63 protein and glial fibrillary acidic protein markers. Many investigators have found that cells with a spindle cell morphology have the strongest immunoreactivity to smooth muscle markers, followed by epithelioid cells, with the plasmacytoid and clear cells showing a lesser, if not an absent, activity on occasion [11]. Neoplastic myoepithelium has been well established to not always retain actin expression [9,12]. Fortunately, many such confirmations can be resolved by using a combination of these markers. Usually, a combination of a keratin in conjunction with the detection of S-100, vimentin, and/or a myogenic marker is required for the confirmation of the diagnosis of myoepithelioma.

Myoepithelial carcinoma, which is known as malignant myoepithelioma, is the malignant counterpart of myoepithelioma. Malignant myoepithelioma has been added to the second edition of the WHO's histological classification of salivary gland tumors [2]. In regard to the differential diagnosis between benign and malignant myoepitheliomas, the results of Nagao et al. [10] were helpful in assessing the cell proliferative activity in those diagnosed with malignant myoepitheliomas with more than seven mitotic figures in 10 high-power fields or with a Ki-67 level index of more than 10%. According to Sciubba and Brannon [3], compared with pleomorphic adenomas, myoepitheliomas are less prone to recurrence after complete surgical resection, with only one recurrence in 16 cases observed over a period of 1 month to 7 years.

Treatment should be designed as for a benign salivary gland tumor with a margin of normal uninvolved tissue being included within the surgical excision. The recurrence rate is similar to that of pleomorphic adenomas (15%–18%) [13].

NOTES

Conflict of interest

No potential conflict of interest relevant to this article was reported.

Ethical approval

An IRB (2018-05-002) waiver for case reports was obtained from Bestian Seoul Hospital in Seoul, Republic of Korea. Written informed consent was obtained.

Patient consent

The patient provided written informed consent for the publication and the use of his images.

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