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Mucinous myoepithelioma: A report of a new variant

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Abstract

Myoepitheliomas account for approximately 1.5% of all salivary gland tumors and arise most frequently from the parotid gland. Recently, a new myoepithelioma variant, called mucinous myoepithelioma, has attracted widespread attention. These tumors are recognized as a unique subtype of myoepithelioma, characterized by the presence of abundant mucin. We herein report the findings of an 86-year-old Japanese woman who presented with a hard mass of the right parotid gland behind her right ear which was gradually increasing in size. The patient had undergone a fine-needle aspiration biopsy 4 years earlier, and a cytological evaluation of a biopsy specimen had shown features of pleomorphic adenoma. A resection was thus performed and the tissue was found to be an encapsulated, soft and solid mass, and the cut surface was observed to be a capsulated and well-defined tumor lesion with myxoid-looking foci of gray-white coloration. Microscopic examination revealed that this lesion was composed of a proliferation of bland-looking epithelial and myoepithelial cells, arranged in a solid or reticular growth fashion in an abundant myxomatous or hyalinized stroma. These neoplastic epithelial cells had centrally located small nuclei with fine chromatin and abundant clear to eosinophilic cytoplasm, often containing mucin in a uniform pattern. Immunohistochemical staining demonstrated the tumor cells to be positive for AE1/AE3, S-100 and mucicarmine. Our findings suggest this case to be one myoepithelioma variant of mucinous myoepithelioma, and more experience related to this myoepithelioma variant is necessary to better understand its biological behavior and make an accurate diagnosis for a proper treatment.

Keywords

Myoepithelioma, variant, mucin

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Introduction

Myoepitheliomas, a rare kind of tumor in the salivary gland, were initially considered to be one type of pleomorphic adenoma (PA) which was first described by Sheldon[1] in 1943. Myoepitheliomas mainly occur in adults, and there is no significant difference in their occurrence between men and women or among ages, accompanying an incidence peak in the third decade of life.[2] Myoepitheliomas account for 1.5% of all salivary gland tumors and constitute 2.2% and 5.7% of all benign major and minor salivary gland neoplasms, respectively.[3]

Although myoepitheliomas can originate in any site of the salivary gland, these tumors arise most frequently from the parotid gland.[4] The tumors typically consist of round to polygonal cells, with centrally located nuclei and varying amounts of eosinophilic cytoplasm, which is arranged in nests, cords or scattered clusters. Myoepithelioma cells often display five distinct cytomorphological features: spindle, plasmacytoid, hyaline, epithelioid and clear cells.[5,6]

Recently, a new myoepithelioma variant has attracted widespread attention: mucinous myoepithelioma.[7] These tumors are recognized as a unique subtype of myoepithelioma, characterized by the presence of abundant mucin.[8] At present, only a few cases of mucinous myoepithelioma have been reported, and the variant tumor has not been classified as a separate type in the current systems. To make an appropriate

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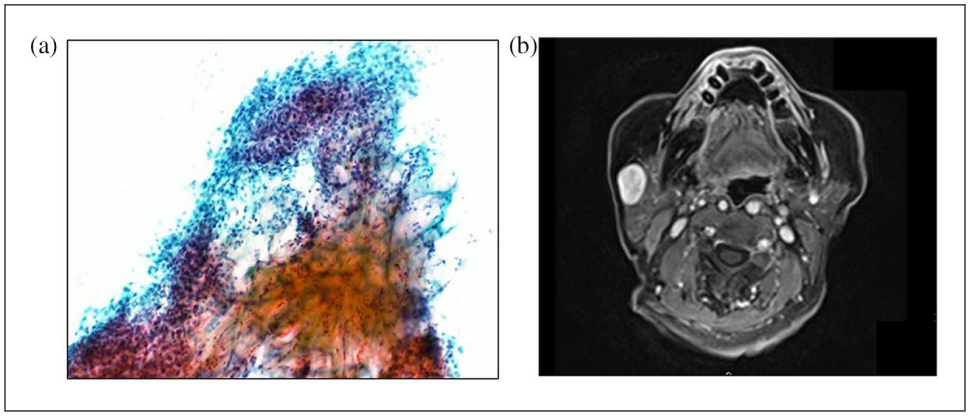

Figure 1. (a) Fine-needle aspiration smears showed cohesive aggregates of tumor cells embedded in fibrillar matrix. (b) Cerebral MRI: the parotid (arrow heads) was moderately hyperintense with internal heterogeneity.

diagnosis of this kind of tumor, the accumulation of relevant reports is necessary in order to interpret its characteristics more fully and better understand its biological behavior.

We herein report a rare case of myoepithelioma which originated in the parotid gland with abundant mucin, revealing features that were the same as but also different from previous variant tumors.

Clinical summary

An 86-year-old Japanese woman with a history of leiomyoma of the uterine corpus, venous aneurysm of the lower foot, aortic valves stenosis, cardiac insufficiency and cerebral infarction presented to our center with a hard mass in the right parotid gland behind her right ear which had been gradually increasing in size. The patient had been referred to our center from another clinic to undergo a cytological analysis by fine-needle aspiration (FNA) 4 years earlier. The FNA cytological examination at that time showed features of PA. The adequate cytologic specimens consisted of mostly flat sheets of benign-like monomorphic myoepithelial-like cells, along with (fibro)myxoid stroma (Figure 1(a)). The patient reported that the mass had been slowly increasing in size over the past 4 years, and no other complaints were mentioned. No significant family history was reported.

Magnetic resonance imaging (MRI) revealed a well-defined, ovoid heterogeneous lesion with moderate hyperintensity, and the peripheral area of the lesion was uniformly thickly enhanced, thus indicating a benign minor salivary gland tumor (Figure 1(b)). The decision was made to proceed with partial excision of the right parotid gland, and the patient underwent surgery under general anesthesia.

Pathological findings

Grossly, the resected specimen consisted of an encapsulated, soft and solid mass. The cut surface revealed a capsulated and well-defined tumor lesion with myxoid-looking foci in a gray-white coloration, measuring 20×16 mm in diameter, without any fat invasion of the surrounding area. A microscopic examination revealed that this well-demarcated nodular lesion is composed of a solid proliferation of mostly bland-looking epithelial and myoepithelial cells, arranged predominantly in a solid or reticular growth fashion with pseudoglandular structures, in an abundant myxomatous or hyalinized stroma. The focal area of the tumor was adjacent to the capsule, but it had not invaded the salivary parenchyma. No glandular or ductal components, or foci of chondromyxoid stroma were observed in the tumor specimen.

On high-power view, neoplastic epithelial and myoepithelial cells were medium-sized with centrally located small nuclei and fine chromatin, with some enlarged nuclei and normal nucleoli, and large amounts of clear-to-eosinophilic cytoplasm often containing mucin in a uniform pattern confirmed by mucicarmine staining. Furthermore, a mild degree of nuclear atypia was noted, but mitotic figures were not encountered (Figure 2). Immunohistochemical staining showed that the cytoplasm of these tumor cells was positive for cytokeratins, including AE1/AE3 and CK5/6, and S-100 protein. However, it was negative for smooth muscle actin (a-SMA), p63 and calponin. Strong reactivity for α-antichymotrypsin (α-ACT) and mucicarmine was also observed in this tumor. However, no pleomorphic adenoma gene-1 (PLAG-1) or glial fibrillary acidic protein (GFAP) immunoreactivity was detected in this case (Figure 3 and Table 1).

Periodic acid–Schiff (PAS) staining was positive for spindle cells in the stroma, confirming the presence of a fibrous tissue component. The Ki67 (MIB-1) labeling index was less than 1% in the proliferating typical cells of the tumor nests (Table 1). Based on these features, without any malignant features identified, we made a final histopathological diagnosis of mucinous myoepithelioma which originated in the right parotid gland. The patient recovered from the surgery without any complications and is currently being followed up regularly. No recurrence has been detected so far.

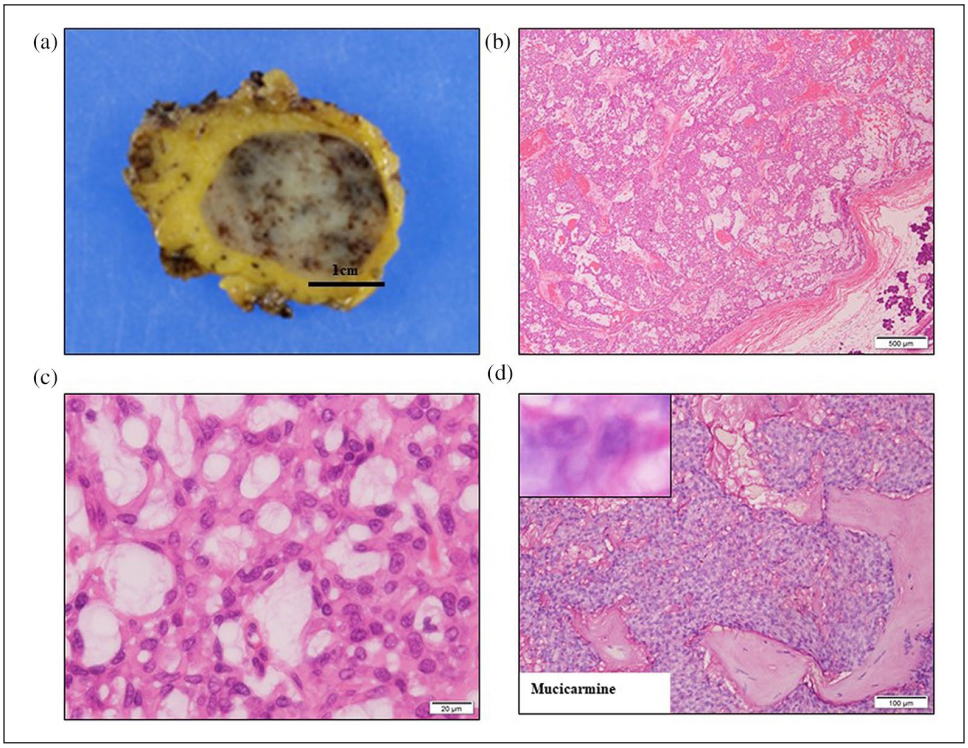

Figure 2. (a) The cut surface shows a well-encapsulated, round-shaped, yellowish-white, solid mass in the parotid gland. (b) A photograph showing the tumor covered by a fibrous capsule (40× magnification). (c) Spindle cell and epithelial cells with a myxoid matrix (100× magnification). (d) Intracellular mucin can be seen (400× magnification).

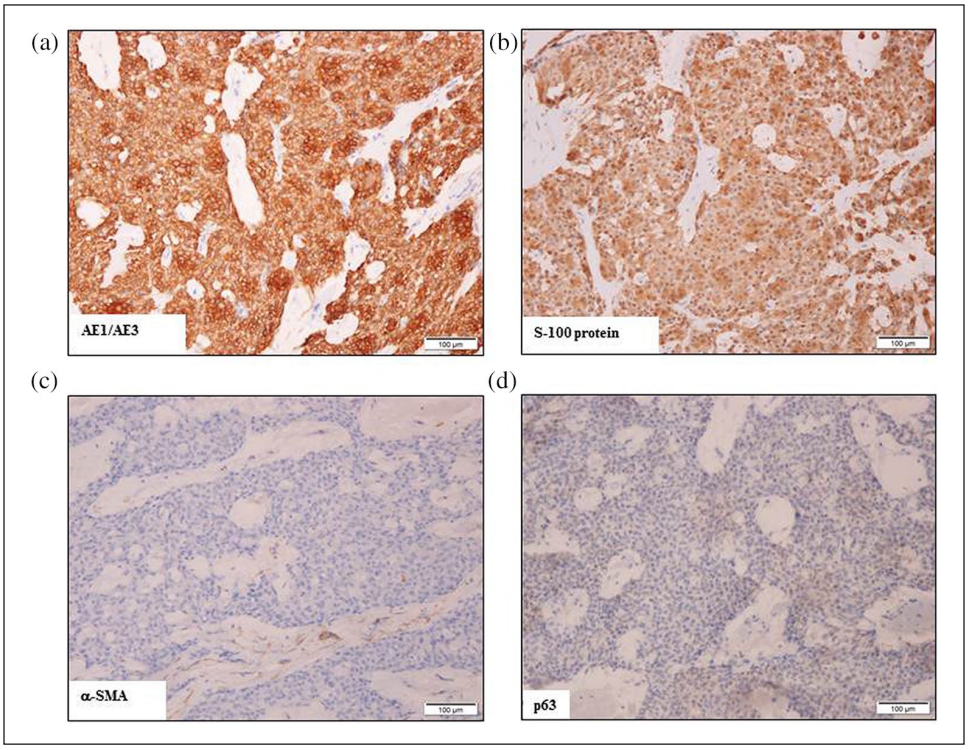

Figure 3. Immunohistochemical staining for **(**a) AE1/AE3, (b) S-100, (c) α-SMA and (d) p63.

Table 1. The summary of results from immunohistochemical and special staining.

Positive	Negative
AE1/AE3	α-SMA
CK56	P63
S-100	calponin
αACT	GFAP
Mucicarmine	PLAG1
PAS	MIB-1(< 1%)

SMA: smooth muscle actin; ACT: antichymotrypsin; GFAP: glial fibrillary acidic protein; PLAG: pleomorphic adenoma gene; PAS: periodic acid–Schiff.

Discussion

The annual incidence of salivary gland tumors varies from about 0.4 to 6.5 cases/100,000 people worldwide and accounts for 2% to 6.5% of all tumors of the head and neck.[9] Imaging of the head and neck is a noninvasive method of evaluating space-occupying lesions, including salivary gland tumors. It may preoperatively establish the intraglandular or extraglandular origin, the relationship of the lesion and facial nerve, and in some cases, whether the lesion is benign or malignant.[10] The site and size of salivary gland tumors can be easily judged by computed tomography (CT) or MRI; however, the histology of these tumors, which is more important for treatment, requires a further examination.

Patients are often asked to undergo an FNA biopsy, which is a cost-effective diagnostic modality and is useful for selecting the optimal treatment modality for salivary gland tumors in the early stages. It can help to preoperatively distinguish between inflammatory and neoplastic disease, primary and metastatic disease, lymphoproliferative and epithelial disease, and benign and malignant lesions.[11] The tissue sample underwent cytological analysis and a substantial number of small groups of cells, single cells and sheet-like clusters were found to demonstrate plasmacytoid, oval to spindle and epithelioid cells with no cytological atypia, mitosis or necrosis. Initially, the case was misdiagnosed as PA because of these cellular features. This misdiagnosis based solely on FNA has also been reported in other cases.[12] Unfortunately, FNA cannot always differentiate between these two entities since they demonstrate a similar morphology, and a specific diagnosis is established in 60%–75% of cases by cytology alone.[13] Thus, the limitations of FNA in the diagnosis of benign salivary gland tumors should be underscored, and at the very least, several FNA biopsies should be performed, targeting different areas of the tumor each time.

Myoepitheliomas are uncommon, accounting for $<1.5\%$ of all salivary gland tumors. The most common site of myoepithelioma is the parotid gland, occurring in approximately 40% of cases, in the head and neck region.[14] Myoepithelioma has been reported to be frequently misdiagnosed as PA based on evaluations of paraffin tissue sections. The gross inspection of typical myoepitheliomas shows a well-circumscribed, glistening cut surface of solid, tan or yellow-tan colors, which were closely similar to the findings of this case. Histologically, myoepitheliomas are composed principally of spindle-shaped cells and often exhibit a variety of cell morphological variants, such as plasmacytoid, hyaline, epithelioid and clear cells. Such tumors are observed as a pure cell type or a mixed cell type, while rarely show ductal differentiation. The stroma may be myxoid or hyalinized, but usually chondroid or myxochondroid components are seen in myoepitheliomas.[15]

Some of these recognized features of myoepitheliomas were very similar to the histological findings of the present case. However, some unusual histological features, including intracellular and stromal mucin and mild nuclear pleomorphism, were also observed in this case. These unusual histological features were additionally reported in other cases. Seven years ago, Gnepp[7] described three unusual myoepithelial tumors, including two benign tumors arising in the parotid glands. The cells of those benign parotid tumors had abundant eosinophilic to foamy grayish-blue cytoplasm, often containing intracellular mucin, mild nuclear pleomorphism, fine peppery chromatin and inconspicuous nucleoli, which is very similar to our case. In addition, a careful literature review revealed several benign or malignant myoepitheliomas with similar characteristics that were published as signet-ring cell tumors or "secretory" myoepithelial carcinomas. These tumors showed unique, previously unrecognized myoepithelioma features but did not fit into the current salivary gland classification system, so Gnepp[7] described a subset of benign and malignant myoepithelial tumors containing intracellular mucin, termed the "mucinous" variant of myoepithelioma. Due to them containing intracellular mucin, these tumors often included areas of signet-ring cells. Immunohistochemically, these tumor cells often showed positivity for typical myoepithelial markers, such as CK7, p63, CK4, SMA, calponin, HHF35 and GFAP.[16,17] However, interestingly, few signet-ring cells were found in the present case, and on immunohistochemical analyses, this tumor did not stain with many myoepithelial markers but was diffusely and strongly positive for AE1/AE3, CK5/6 and S-100 protein. As some special subtypes of myoepithelioma have been reported to not stain for myoepithelial markers and tumors have been reported with a similar appearance with no documented myoepithelial characteristics, we considered this case to also be a mucinous variant of myoepithelioma.[18,19]

Thus far, only 17 mucinous myoepitheliomas have been reported worldwide, including 4 benign and 13 malignant tumors, most of which arose in minor salivary glands, with only 3 cases in the parotid (Table 2). The male-to-female ratio in these patients is approximately equal. Follow-up information was only available for five patients, and all five were reported to have a successful outcome. Thus, this myoepithelioma variant is considered to have low-grade malignancy. The main differential diagnosis for mucinous

Table 2. The summary of reported mucinous myoepitheliomas.

Case No.	Location	Benign/ malignant	References
1	Minor salivary glands	Benign	Zamecnik et al.[20]
2–8	Minor salivary glands	Malignant	Ghannoun et al.[21]
9	Parotid glands	Malignant	Singh et al.[16]
10–13	Minor salivary glands	Malignant	Bastaki et al.[22]
14	Minor salivary glands	Benign	Foschini et al.[18]
15–16	Parotid glands	Benign	Esteva et al.[8]
17	Minor salivary glands	Malignant	

myoepithelioma includes signet-ring adenocarcinoma, mucoepidermoid carcinoma, colloid carcinoma and salivary duct carcinoma of the signet-ring subtype. In addition to their own special histological characteristics, all of these tumors are negative for myoepithelial markers.

Conclusion

In this article, we reported a rare myoepithelioma variant, mucinous myoepithelioma, which has not been classified as a separate type in the current systems. Therefore, the accumulation of more experience related to this myoepithelioma variant is necessary to better understand its biological behavior and make an accurate diagnosis for proper treatment.

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Author contributions

X.G. and S.Y. participated in the conception of the study and writing and designing of the manuscript with figures and tables. X.G., S.Y., J.W., H.N. and K.F. performed the clinical imaging and/or pathological/immunohistochemical interpretation of this lesion. All of the authors have read and approved the final manuscript.

Availability of data and materials

The data set supporting the findings and conclusions of this case report is included within the article.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical approval

Our institution does not require ethical approval for reporting individual cases or case series.

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Informed consent

Written informed consent was obtained from the patient on admission for his anonymized information to be published in this article.

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