Myoepithelial Carcinoma of the Parotid Gland: A Case of Adequate FNA Cytology Specimens Rendering a Conclusive Diagnosis Possible

Journal:	*SAGE Open Medical Case Reports*
Manuscript ID	SOMCR=IJSP-18-0108.R1
Manuscript Type:	Case Report
Date Submitted by the Author:	n/a
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Keywords:	Pathology
Additional Keywords:	Myoepithelial carcinoma, Salivary gland, Cytology
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Declarations

Ethics approval

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

Informed Consent

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

Case Report

R1: Myoepithelial Carcinoma of the Parotid Gland: A Case of Adequate FNA Cytology Specimens Rendering a Conclusive Diagnosis Possible

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Short running title: Cytological findings of MC.

Word count: **1,261** words (Abstract **235** words); References: 8; and 2 Figures.

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Abstract

An 80-year-old male presented with a history of a **hard right parotid mass that had gradually increased in size, with** subsequent facial paralysis**. A fine-needle aspiration biopsy was performed. The cytologic specimens** contained a substantial number of sheet-like clusters or small groups of a mixture of plasmacytoid, oval to spindled, or large epithelioid cells having hyperchromatic pleomorphic nuclei, abundant cytoplasm with occasional inclusion body-like materials, and prominent nucleoli, in a relatively clear background. We first interpreted it as a carcinoma, suggestive of myoepithelial differentiation. **Radical** parotidectomy was performed, and a gross examination of the **neoplasm** revealed a non-capsulated and ill-defined tumor lesion, **with a grayish or yellowish cut surface**, associated with fat invasion. On **a** microscopic examination, the tumor was predominantly composed of **the** solid proliferation of atypical cells including a mixture of oval to spindled, plasmacytoid, or epithelioid cells, often arranged in a trabecular and reticular growth pattern with patchy eosinophilic hyalinized stroma. Immunohistochemistry showed that **the** carcinoma cells **were** specifically positive for p63, cytokeratins and vimentin. Finally, electron

microscopy demonstrated that **their phenotype was consistent with a myoepithelial origin** containing many bundles of variably thin actin filaments. Therefore, we finally made a diagnosis of myoepithelial carcinoma (MC), defined as the malignant counterpart of benign myoepithelioma. We should be aware that owing to its characteristic cytological features, cytopathologists **may** be able to **make a** correct diagnosis **of** MC, based on multiple and adequate samplings.

Key words: Myoepithelial carcinoma (MC); parotid gland; cytopathology; myoepithelioma.

Introduction

Myoepithelial carcinoma (MC) is very rare among epithelial salivary gland neoplasms and accounts for less than 1% of cases, although it might be more common than generally believed [1,2]. MC of the salivary gland is defined as the malignant counterpart of benign myoepithelioma, displaying exclusively myoepithelial differentiation [1], and often poses a diagnostic challenge to clinicians and cytopathologists, since its entity is much more difficult to diagnose pre-operatively on small, inadequate samples. Indeed, the WHO classification in 2005 simply defined MC as an infiltrative myoepithelial neoplasm, morphologically and cytopathologically similar to myoepithelioma in part [2]. Furthermore, MC typically presents as an asymptomatic mass, like myoepithelioma, until it displays wide growth with subsequent facial paralysis. Patients with MC tend to develop metastasis due to infiltrative, progressive and locally destructive behavior [1–3]. Therefore, an early accurate diagnosis and radical surgical treatment for MC should allow for an improved quality of life and increased survival rates [3,4]. However, very few reports have described the cytological features of MC and/or myoepithelioma on fine needle aspiration (FNA) specimens.

We herein **report** an extremely rare case of MC originated from the parotid gland, potentially rendering conclusive diagnosis possible on adequate FNA cytology specimens.

Case Presentation

A male patient in his early **80s** with double primary colonic and prostatic adenocarcinomas 4 and 2 years ago, respectively, had a chief complaint of a gradual increase in **size of a** hard mass of the right parotid gland with subsequent facial paralysis. Laboratory data, including blood cell count, **blood** chemistry and tumor markers, were within normal limits, with the exception of mildly decreased total protein (6.2 g/dL) level and white blood cell count (4,100/μL). **Neck computed tomography (CT)** showed an enhanced and relatively well-demarcated nodule with a central low-density area, measuring approximately 22 × 18 mm in diameter, arising from the right parotid gland (Figure 1A). Full-body CT **revealed** no definite evidence of metastases or neoplastic foci in the lymph nodes or other organs. In addition, an axial maximum intensity projection (Figure 1A) image **on a** coregistered ^{18}F-FDG **positron emission tomography (PET)**/CT revealed an overtly hypermetabolic area in the right

parotid gland, corresponding to the above neck CT finding. The specimen from the FNA cytology sample (Figure 1B and C) contained a substantial number of small groups, single cells (Figure 1B) or sheet-like clusters (Figure 1C) of a mixture of plasmacytoid, oval to spindled, or large epithelioid cells having hyperchromatic pleomorphic nuclei, abundant cytoplasm with occasional inclusion body-like materials, and prominent nucleoli, in a relatively clear background, on Papanicolaou stain (Figure 1B). There was no definite evidence of a necrotic or hemorrhagic background. Giemsa staining showed no metachromatic stroma. We first interpreted this picture as indicating carcinoma, suggestive of myoepithelial differentiation. Radical parotidectomy was thus performed, and a gross examination revealed a non-capsulated and ill-defined tumor lesion with a grayish to yellowish cut surface, measuring 18 × 16 mm in diameter, partly associated with surrounding fat invasion (Figure 1D). Resection was deemed likely to be complete by this histopathological examination.

Microscopically, the tumor was predominantly composed of a solid proliferation of atypical cells (Figure 2A) including a mixture of oval to spindled, plasmacytoid, or epithelioid cells, often arranged in a trabecular and reticular growth pattern with a patchy eosinophilic hyalinized stroma (Figure 2B). On a high-power view, these

neoplastic cells had medium-sized, hyperchromatic and enlarged nuclei, often conspicuous nucleoli, and abundant clear to eosinophilic cytoplasm (Figure 2B). Mitotic figures were rarely encountered. **Furthermore**, these tumor nests partly **invaded the surrounding fat**, but **there was no perineural infiltration** (Figure 2A). Immunohistochemical findings **showed** that **the** carcinoma cells were specifically and diffusely positive for p63 (Figure 2C), cytokeratins, including AE1/AE3 (Figure 2C) and CK5/6, and vimentin, whereas **they were** negative for EMA, low-weight cytokeratin (Cam5.2), S-100 protein, α-smooth muscle actin (α-SMA), bcl-2 and CEA. **The** Ki67 (MIB-1) labeling index was approximately 15% in the proliferating atypical cells of the tumor nests. **E**lectron microscopy showed that **this** phenotype **was consistent with** myoepithelial **differentiation**, **as** many bundles of variably thin actin filaments **were observed** (Figure 2D).

Based on these features, we **ultimately** made a diagnosis of MC, arising from the right parotid gland. **N**o overt benign pleomorphic adenoma components **were noted in** our thorough investigation. To date, **we have completed** approximately **one** year **of** routine follow-up **since** the surgery, and the patient remains well **without** recurrences **or** metastases.

Discussion

Since the overall **biological behavior** of MCs **of** the salivary glands **is** generally **poor**, aggressive clinical treatment in the early stage **is the** only hope for **a good** prognosis, owing to **the** higher-grade, **and** infiltrative and destructive **nature of the** tumor with frequent recurrences and distant metastases to the lung [1–5]. **I**t is **therefore** critical to establish an accurate pre-operative diagnosis by FNA cytology, **which has shown good** clinical utility **for** diagnosing salivary gland tumors**. However, the** cytological features **of** MCs have rarely **been** described in detail in the published literat**ure**, **due to the rarity of this lesions,** accounting for less than 1% **of** all epithelial salivary gland neoplasms [1–3]. To our knowledge, this is **only** the second case report of MC, **with a focus** on its cytomorphologic findings [6], **al**though there have been some cytopathological review papers of MC [7,8].

The cytological features of MCs variably reflect the histopathological ones **and** are **typically** diverse **at times** lacking malignant characteristics [1,6–8]. FNA cytologically shows small to large clusters or single cells of spindled, plasmacytoid, epithelioid, or clear cells, or a mixture of these cells, suggestive of myoepithelial

differentiation [1,2,6–8]. **These** tumor clusters/cells display the presence and/or absence of significant nuclear hyperchromatism and pleomorphism or abnormal mitotic figures, **along** with scant to abundant fragments of metachromatic stroma, often without any evidence of **necrosis or hemorrhaging** [1,6–8]. In this context, not only myoepithelioma but **also** cellular pleomorphic adenoma should be included in the differential diagnoses of MC. Furthermore, **epi-myoepithelial carcinoma** is another important differential diagnosis, but its cytology findings are considered to show bimodal population of large clear myoepithelial cells and small cuboidal ductal cells**, forming tubular, trabecular, and/or pseudopapillary structures, with the occasional absence of metachromatic stroma** [1,6]. As in the present case, since the specimens were adequate, the cytologic features were similar to those of MC**,** as described above, even though benign myoepitheliomatous foci or **stromal** fragments **have** very rarely **been reported**. **However**, a **conclusive** and accurate diagnosis of MC after distinguishing from myoepithelioma **based** on cytology **alone might be impossible to achieve**, due to cytomorphologic variety, sampling errors, **a** lack of considerable experience, and/or misinterpretation. Therefore, in any cases with a strong clinical suspicion of malignant salivary gland tumors, multiple **rounds of** CT-guided **(**if

possible) FNA cytology **should** be performed and that suspicion should be raised to alert the cytopathologists, at the very least.

Finally, **the findings of** the current immunohistochemical analyses **suggest** that immunostaining for specific myoepithelial markers, such as p63, **along** with MIB-1 labeling indices on cytological smears or cell block preparations might be useful for **the differential diagnosis with** myoepithelioma, pleomorphic adenoma or **epi-myoepithelial carcinoma**.

Conclusion

We **encountered** a case of MC arising from the parotid gland, tentatively diagnosed as a carcinoma, suggestive of myoepithelial differentiation, on the examination of **FNA samples** cytology. All cytopathologists should be aware that not only **the** clinicopathologically characteristic feature, but also multiple**,** adequate FNA specimens, might lead to a correct and conclusive diagnosis. **Further** cytomoprphological studies **with the collection and examination of a larger number of MC cases** will be further required to determine whether **or not** cytology specimens **alone** can distinguish MC from other important salivary gland tumors**.**

Declarations

Ethics approval

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

Informed Consent

Written informed consent was obtained from **the patient** for their anonymized information to be published in this article.

Availability of data and materials

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

Competing Interests

The authors declare no conflicts of interest in association with this study.

Funding

None.

Acknowledgments

We would like to thank Dr. Toshitaka Nagao, Department of Anatomic Pathology, Tokyo Medical University, Tokyo, Japan, for his constructive and helpful suggestions/comments and correct diagnosis, and **we would also like to** thank Mrs. Yuka Hiramatsu for her expert technical assistance.

References

1. Ellis GL, Auclair PL: **Myoepithelial carcinoma.** In: Tumors of the Salivary Glands. *Atlas of tumor pathology. Washington, D.C.: Armed Forces Institute of Pathology* 2008, p.341–349.

2. Bell D, Di Palma S, Katabi N, Schwartz MR, Seethala R, Skalova A: **Myoepithelial carcinoma.** In: Barnes L, Eveson JW, Reichart P, Sidransky D editors. *World Health Organization Classification of Tumours: Pathology and Genetics of Head and Neck Tumours. Lyon, France: IARC Press* 2005, p.174–175.

3. Nagao T, Sugano I, Ishida Y, Tajima Y, Matsuzaki O, Konno A, Kondo Y, Nagao K. **Salivary gland malignant myoepithelioma: A clinicopathologic and immunohistochemical study of ten cases.** *Cancer* 1998, **83**: 1292–1299.

4. Savera AT, Sloman A, Huvos AG, Klimstra DS. **Myoepithelial carcinoma of the salivary glands: A clinicopathologic study of 25 patients.** *Am J Surg Pathol* 2000, **24**: 761–774.

5. Kane SV, Bagwan IN. **Myoepithelial carcinoma of the salivary glands: A clinicopathologic study of 51 cases in a tertiary cancer center.** *Arch Otolaryngol*

Head Neck Surg 2010, **136**: 702–712.

6. Sehgal S, Goyal P, Singh S, Kumar A. **Fine-needle aspiration cytology of myoepithelial carcinoma of salivary gland: diagnostic challenge to cytopathologist.** *J Cytol*, 2013, **30**: 207–210.

7. DiPalma S, Alasio L, Pilotti S. **Fine needle aspiration (FNA) appearances of malignant myoepithelioma of the parotid gland.** *Cytopathology*, 1996, **7**: 357–365.

8. Chhieng DC, Paulino AF. **Cytology of myoepithelial carcinoma of the salivary gland.** *Cancer*, 2002, **96**: 32–36.

Figure Legends

Figure 1. The findings of neck CT and ^{18}F-FDG PET/CT at surgery, FNA cytomorphologic, and gross examinations of the MC specimens. (A) Neck CT (lt.) shows an enhanced and relatively well-demarcated nodule with a central low-density area, measuring approximately 22 × 18 mm in diameter, arising from the right parotid gland (arrowhead). An axial maximum intensity projection image on coregistered ^{18}F-FDG PET/CT (rt.) shows an overtly hypermetabolic area in the right parotid gland, corresponding to the neck CT finding. **(B)** The FNA cytology specimen (Papanicolaou staining) contains a substantial number of small groups or single cells of a mixture of plasmacytoid (inset), oval to spindled, or large epithelioid cells having hyperchromatic pleomorphic nuclei, abundant cytoplasm with occasional inclusion body-like materials, and prominent nucleoli, in a relatively clear background. Original magnification: 400×. **(C)** Furthermore, the FNA cytology (Papanicolaou staining) shows a substantial number of sheet-like clusters of atypical myoepithelial-like cells. Original magnification: 400×. **(D)** A gross examination from the surgical specimen shows a non-capsulated and ill-defined tumor lesion with a grayish to yellowish cut surface, measuring 18 × 16 mm in diameter, partly associated with surrounding fat invasion

(arrows). Bar = 1 cm.

Figure 2. Microscopic and ultrastructural examinations of the parotid gland MC.

(A) Microscopically, this tumor is predominantly composed of **the** solid proliferation of atypical cells, involving the surrounding fat. Original magnification: 40×. **(B)** Those proliferating tumor nests contain a mixture of oval to spindled, plasmacytoid, or epithelioid cells, often arranged in a trabecular and reticular growth pattern with a patchy eosinophilic hyalinized stroma. On **a** high-power view, the neoplastic cells have medium-sized, hyperchromatic and enlarged nuclei, often conspicuous nucleoli, and abundant clear to eosinophilic cytoplasm (inset). Original magnification: 200× (inset, 400×). **(C)** Immunohistochemical findings **show** that those carcinoma cells are specifically and diffusely positive for p63 (lt.) and cytokeratins, including AE1/AE3 (rt.). Original magnification: 100×. **(D)** **E**lectron microscopy **shows that** the **phenotype** of the carcinoma cells **exhibits** myoepithelial differentiation, containing many bundles of variably thin actin filaments. Bar = 1 μm. N = Nucleus.

Figure 1

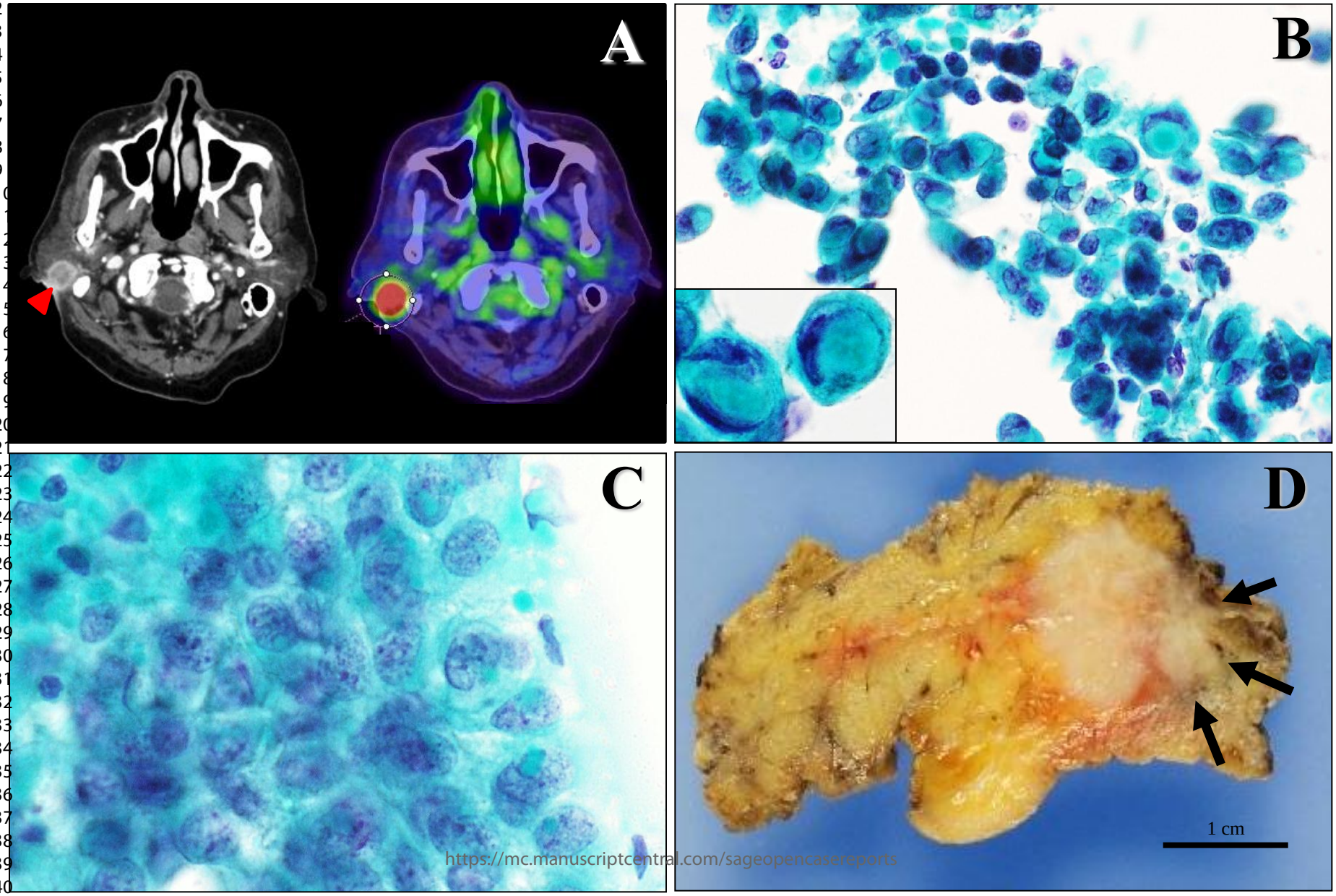

Figure 2