



Myoepithelial Carcinoma of the Nasal Cavity: A Case Report

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Abstract

Background: Myoepithelial carcinoma is a rare epithelial tumor typically originates in the salivary gland tissues. We report a case of myoepithelial carcinoma arising in nasal cavity.

Methods: A 53-year-old man presented with a 2-month history of symptoms of nasal obstruction and epistaxis. Computed tomography revealed an enhancing mass occupying entire left nasal cavity, with obstructive sinusitis in paranasal sinuses. Medial maxillectomy was performed.

Results: Microscopic analysis revealed multi nodular tumor with solid, reticular, trabecular, and pseudoacinar growth patterns. Tumor cells were monomorphic round to oval cells, with eosinophilic cytoplasm and round hyperchromatic nuclei. Clear cells were rare. The tumor cells showed diffuse immunoreactivity for calponin, smooth muscle actin, p40 and p63, and immuno negativity for PLAG1. Electron microscopy demonstrated intracytoplasmic myofilaments in tumor cells. The tumor did not harbor EWSR1 gene rearrangement by break-apart FISH.

Conclusion: This is an additional rare case of sinonasal myoepithelial carcinoma, especially with ultrastructural and molecular study.

Keywords: Myoepithelial carcinoma; Malignant; Nasal cavity; Sinonasal

Introduction

Myoepithelial carcinoma (MC) is an uncommon neoplasm of the salivary gland, and especially rare in non-salivary gland tissues [1,2] MC of the sinonasal tract is as rare as that of the lung, and only 11 cases have been reported in the English literature. Recently, EWSR1 gene rearrangement has been identified in salivary gland MCs, especially in clear cell and rhabdoid variants. Herein, we report an additional case of sinonasal myoepithelial carcinoma with ultrastructural and molecular study.

Case Presentation

A 53-year-old man was admitted with symptoms of nasal obstruction and epistaxis, anosmia, postnasal drip, and headache of 2-month duration. He had a history of chemoradiation therapy for poorly differentiated carcinoma of both nasal cavities 6 years earlier. Paranasal sinus computed tomography revealed a 4.2 x 3.1 x 2.7-cm enhancing mass occupying the entire left nasal cavity, with destruction of the nasal septum and involvement of the right nasal cavity (Figure 1, Panel A and B). Obstructive sinusitis in the maxillary, sphenoidal, and ethmoidal sinuses were also present. Regional lymph node metastasis was not identified on CT scan. Fusion whole body F-18 fluorodeoxyglucose positron emission tomography (PET) identified a hypermetabolic mass in both nasal cavities. Medial maxillectomy was performed for suspected nonkeratinizing carcinoma. Main mass resection including medial maxillary sinus wall, nasal floor, perpendicular plate and vomer was performed and other parts of maxillary sinus wall were reserved. Multiple resection margins were identified by frozen section during surgery, and all submitted resection margins were confirmed to be free of tumor. The resected mass consisted of multiple fragmented soft tissues. The cut surface of the tumor was grayish white, soft, and granular (Figure 1, Panel C).

Microscopically, the tumor was a well-defined non-encapsulated multi nodular mass (Figure 1, Panel D). It contained solid, reticular, and sheet-like structures, with trabecular and pseudoacinar growth patterns (Figure 1, Panel E). Myxoid matrix occupied the intercellular spaces.

The tumor consisted of monomorphic round to oval cells, with eosinophilic cytoplasm and

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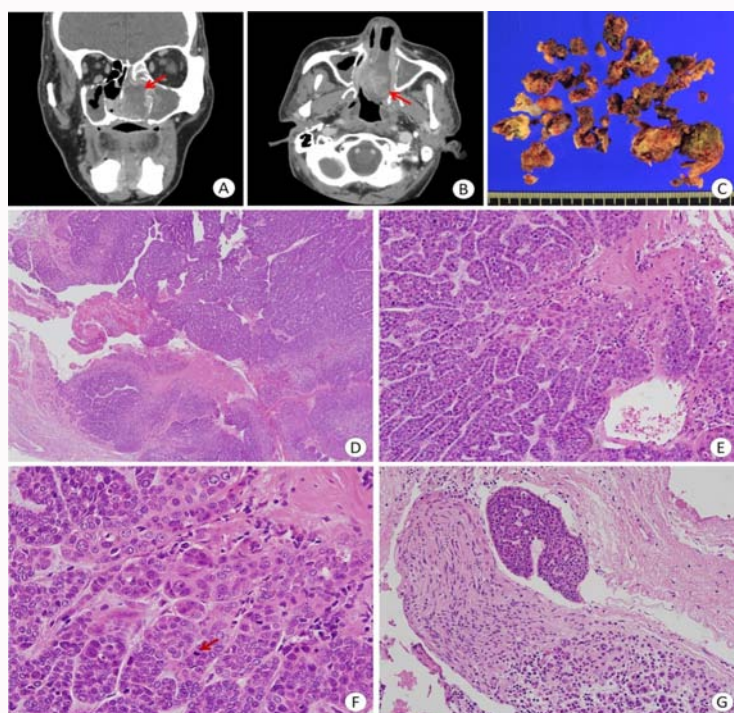


Figure 1: Paranasal sinus CT shows an enhancing mass (red arrows) throughout the left nasal cavity with obstructive sinusitis in the paranasal sinuses. (A) Coronal view and (B) transverse view. (C) Gross examination revealed that the specimen consisted of multiple fragmented soft masses. (D) The tumor is non-encapsulated but well defined. It was invading adjacent tissue. (E) The tumor showed multinodular architecture with gland-like growths and thin fibrous septa. (F) Tumor cells are round to oval shape and have eosinophilic cytoplasm with nuclear polymorphism, and prominent mitotic activity (arrow). (G) The tumor has invaded the adjacent nerve tissue.

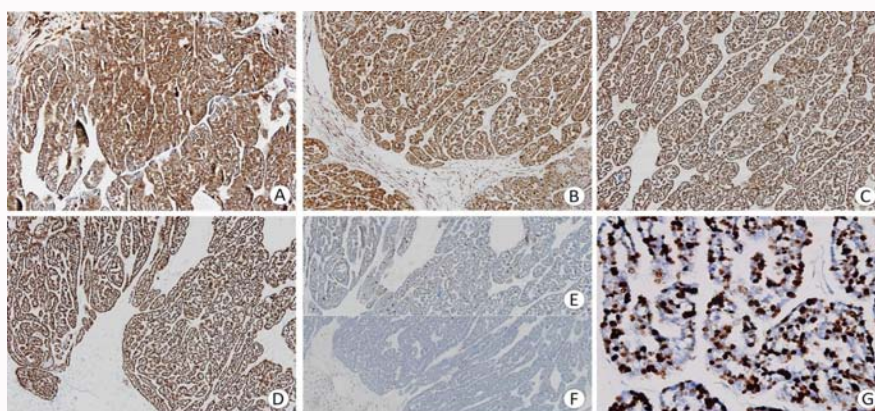


Figure 2: The tumor shows strong immunopositivity for SMA (A), calponin (B), p40 (C) and p63 (D). And the tumor shows lower immunoreactivity for LMW CK (E), and shows immunonegativity for CD117 (F) Immunohistochemistry analysis revealed that the Ki-67 labeling index was 50–60% (G).

hyperchromatic nuclei. Cytoplasmic clearing was not evident. The tumor cells showed mild nuclear pleomorphism, high mitotic activity (56/10 high-power fields) (Figure 1, Panel F), and perineural invasion (Figure 1, Panel G). The peculiar growth pattern and intercellular myxoid matrix suggested myoepithelial differentiation. Immunohistochemical examination confirmed the myoepithelial differentiation by diffuse positivity for smooth muscle actin (SMA) (1:200, Dako, Glostrup, Denmark) (Figure 2, Panel A), calponin (1:1,000, Neomarkers, California, USA) (Figure 2, Panel B), p40 (1:100, Biocare, California, USA) (Figure 2, Panel C), and p63 (1:200, Dako, Glostrup, Denmark) (Figure 2, Panel D). Immunostaining for low-molecular-weight cytokeratin (LMW CK) (1:500, Cell Marque, California, USA) and CD117 (1:400, Dako, Glostrup, Denmark) was performed for differential diagnosis. LMW CK-positive cells were

only sparsely identified (Figure 2, Panel E), and no CD 117-positive cells were present (Figure 2, Panel F), unlike in cases of epithelial-myoeplithelial carcinoma or adenoid cystic carcinoma, respectively. Result of immunohistochemical staining for PLAG-1 (1:25, Novus, Missouri, USA) was also negative. Break-apart fluorescent in situ hybridization for EWSR1 was performed with commercially available probe (Vyvis, Downer's Grove, IL, USA). The results were evaluated by fluorescence microscopy by scoring tumor cells at 1000 magnification field. We evaluated tumor nuclei in 5 fields and calculated average percent of split signals. The result of the space between two signals greater than two signal distance was considered a split signal and this interpretation was based on generally accepted guidelines of Vysis. In our case, 5 fields of total 1200 cells were counted for split signals, which comprised 6% in average (Figure 3). This result was interpreted

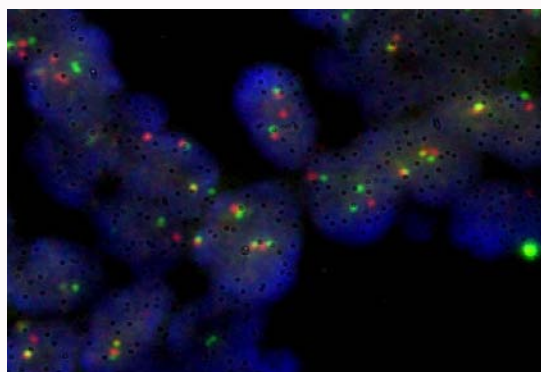


Figure 3: On fluorescent in situ hybridization for EWSR1, MC comprised 6% in average and was interpreted as negative for EWSR1 rearrangement.

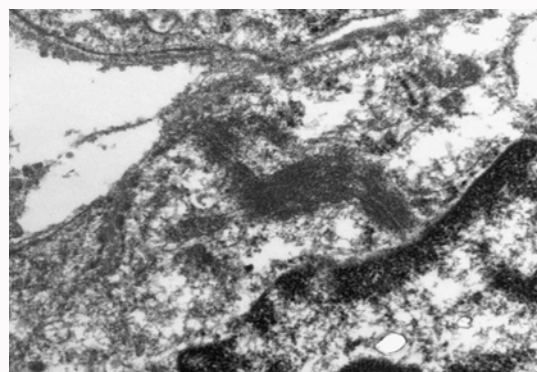


Figure 4: On electron microscopy, the tumor includes longitudinally oriented fine cytoplasmic microfilaments with focal dense bodies and pinocytotic vesicles.

as negative for EWSR1 rearrangement. Electron microscopy was performed using formalin-fixed and paraffin-embedded tissue, and revealed that the tumor included longitudinally oriented fine cytoplasmic microfilaments with focal dense bodies and pinocytotic vesicles (Figure 4). The diagnosis of myoepithelial carcinoma without EWSR1 gene rearrangement was determined. The patient received no more adjuvant treatment and has been well for 9 months after the operation.

Discussion

Myoepithelial carcinoma (MC) is a rare epithelial tumor that can originate *de novo*, from benign myoepithelioma, or as carcinoma *ex pleomorphic adenoma* [3]. MC can occur in various sites throughout the body, including the breast, lung, head, and neck [4], but most cases (75%) arise in the parotid gland [5].

Myoepithelial cells have dual features of epithelial and smooth muscle cells. When neoplastic, myoepithelial cells can appear as diverse cell types, including spindle, epithelioid, stellate, and hyaline. The characteristic architecture of myoepithelial carcinoma includes multilobulated, solid, reticular, pseudoacinar, and trabecular growth patterns [5]. Different cell types and architectural patterns can be found within the same tumor. In general, determination of the myoepithelial nature of MC can be difficult by hematoxylin and eosin staining alone due to the wide variety of cellular and histologic features [2]. Our patient had undergone chemoradiotherapy for the first diagnosis of poorly differentiated carcinoma, and medial maxillectomy was performed for nonkeratinizing carcinoma.

Immunohistochemistry is the best way to identify MC. On immunohistochemical staining, MC shows immunoreactivity for cytokeratin and at least one of the myoepithelial markers, smooth muscle actin (SMA), glial fibrillary acidic protein (GFAP), CD10 and calponin, etc [5]. Kane et al. [6] found that MC cells in most patients were

immunopositive for vimentin, calponin, and S100 protein (positive in 82–100% of cases). In other studies, SMA and p63 expression rates were less common (35% and 28%, respectively), and Ki-67 labeling indices were low (4–10%). In our case, the tumor cells showed diffuse and strong immunoreactivity for calponin and p40. Moreover, tumor cells in our case showed very strong immunopositivity for SMA, p63, and high Ki-67 labeling index (50–60%) unlike cases reported in the literature. The PLAG1 (pleomorphic adenoma gene 1) is a proto-oncogene, and its chromosomal aberrations result in gene fusion with CTNNB1, CHCHD7, LIFR, and TCEA [7]. Transcriptional upregulation and the protein overexpression of PLAG1 had reported in case of pleomorphic adenomas and myoepitheliomas. Diagnostic value of PLAG1 immunostaining as diagnostic marker in salivary gland tumors is limited, [7] and immunohistochemical study about PLAG1 of myoepithelial carcinoma in salivary gland has not been reported, yet. In our study, the tumor cells showed immunonegativity for PLAG1. Electron microscopy has shown that myoepithelial cells include longitudinally oriented fine cytoplasmic microfilaments with focal dense bodies and pinocytotic vesicles, desmosome and intermediate filaments [5]. In our case, myofilaments typical of MC were identified by electron microscopy.

MC should be differentiated from adenoid cystic carcinoma, polymorphous low-grade adenocarcinoma (PLGA), and basaloid squamous cell carcinoma [6,8]. Adenoid cystic carcinoma is usually strongly positive for c-KIT (CD117) [9] and our case was immunonegative for c-KIT. Cells of PLGA have bland edges, rare mitotic figures and are negative for myoepithelial markers [10]. In basaloid squamous cell carcinoma, tumor cells have minimal cytoplasm, and single cell necrosis and comedonecrosis are common, and the cells are immunonegative for S100 protein, SMA and GFAP [11]. Recently, EWSR1 gene rearrangement has been identified in clear cell and rhabdoid variant MC of the salivary gland [12]. EWSR1

Table 1: Pathologic and clinical characteristics and outcomes of reported cases of myoepithelial carcinoma of the sinonasal tract in the literature.

Author/ year	Case	Sex/ (Mean) age	Site	(Mean) Size (cm)	Surgery	Adjuvant therapy	Metastasis	Outcome
Xu et al. [3]	4	NA	Nasal cavity	NA	Sleeve resection	NA	NA	NA
Shubhada et al. [6]	5	M,F/ 45.4	Nasal cavity	4.3	Wide excision, maxillectomy	Absent	Absent	Recurrence (2/5 cases)
Roggen et al. [2]	1	M/67	Sinonasal tract	7.0	Radical hemi-maxillectomy	Absent	Absent	NA
Fredrik et al	1	F/45	Sinonasal tract	5.4	Craniofacial resection	RTx	Absent	NA
Present case	1	M/53	Nasal cavity	4.2	Medial maxillectomy	Absent	Absent	NED

NA: Not Available; RTx: Radiotherapy; NED: No Evidence of Disease.

gene is a frequently rearranged gene that is fused with various partners in many sarcomas [12]. Among the salivary gland tumors, hyalinizing clear cell sarcoma was first found to harbor EWSR1-ATF fusion. Skalova et al. [13] analyzed 94 salivary gland carcinomas with prominent clear cell component and found rearranged EWSR1 in 26 cases of 83 myoepithelial-derived carcinomas with clear cell change, and found poorer prognosis of EWSR1 rearrangement cases. EWSR1 gene rearrangement in non-salivary MC is not well known, except for soft tissue cases [14]. We were prompted to confirm EWSR1 gene status in our sinonasal MC, and the present non-clear cell type MC did not show EWSR1 rearrangement.

In the English literature, 11 cases of myoepithelial carcinoma of the sinonasal tract were reported (Table 1). Almost all patients were in middle age, with no gender predilection. The tumors usually had firm, solid, and non-encapsulated features, and the mean size was about 4–7 cm. The growth patterns were solid sheet like, trabecular, cord-like, and multinodular. Tumor cells were usually round to oval, with eosinophilic cytoplasm and mild nuclear pleomorphism. The treatment of choice was surgical excision and some patients underwent adjuvant chemo-radiation therapy. Two of 11 cases had tumor recurrences.

MC is a locally aggressive neoplasm that exhibit diverse clinical outcomes [3]. The treatment of choice is complete surgical excision, and selective neck dissection may be indicated if nodal metastases are suspected [15]. Efficacy of radiation therapy and chemotherapy has not been established. In our case, the patient has presented with local recurrence 6 years after first manifestation. This relatively slow progress might be related with absence of EWSR1 gene rearrangement. Since there was no evidence of metastasis, medial maxillectomy was performed but the lesion could not be completely excised. Although the patient has been well for 9 months after the operation, the probability of disease progression is supposed.

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