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Pathology in Focus

Epithelial-myoepithelial carcinoma – Report of a case arising in the nasal cavity

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Abstract
We present an extremely rare case of epithelial-myoepithelial carcinoma (EMC) arising in the nasal cavity. The patient was a 56-year-old Japanese male with a polypoid tumour arising from the nasal septum. Histopathological examination revealed the tumour to consist of a solid proliferation of clear-cells and, in some areas, small or elongated duct structures with a double-layered arrangement of inner cuboidal cells and outer clear-cells. Dual differentiation toward myoepithelial and ductal cells were confirmed immunohistochemically. The occurrence of EMC in the nasal cavity is possible and this entity should be generally recognized by surgical pathologists, not only those engaged in head and neck surgery.

Key words: Nasal septum; Carcinoma; Myoepithelial tumour

Introduction

Epithelial-myoepithelial carcinoma (EMC) is a relatively new concept, previously reported as glycogen-rich adenoma (Goldman and Klein, 1972), glycogen-rich adenocarcinoma (Mohamed and Cherrick, 1975), clear-cell adenoma (Saksela *et al.*, 1972) or clear-cell carcinoma (Chen, 1983; Littman and Alguacil-Garcic, 1987). Not mentioned in previous WHO histological classification of salivary gland tumours (Thackray and Sobin, 1972), EMC has been added as a category of carcinomas in the new WHO histological classification (Seifert *et al.*, 1991) and is considered to have a low-grade malignant potential.

It occurs primarily in the parotid glands, but is described also in the histological classification of tumours of the upper respiratory tract and ear (Shanmugaratnam *et al.*, 1991), as an epithelial tumour which may occur in the nasal cavity, paranasal sinuses, larynx, hypopharynx or trachea.

We present an extremely rare case of EMC arising in the nasal cavity, one of the most unusual locations.

Case report

A 56-year-old Japanese male was referred to the Department of Otolaryngology, Kurume University School of Medicine in September 1994, with a complaint of nasal obstruction for several months and a bloody nasal drip for about two years.

On examination, in addition to a polyp of the middle nasal meatus, a yellowish white, smooth-surfaced and friable polypoid tumour based on the left posterior side of the nasal septum was observed. On computed tomographic (CT) scanning, it appeared as a soft tissue-density area extending nearly to the anterior ethmoidal foramen but mainly localized in the nasal cavity with neither enhancement nor bone destruction (Figure 1).

The tumour was excised in December 1994 under local anaesthesia using a fibreoptic technique and the postoperative course has shown no evidence of recurrence for seven months.

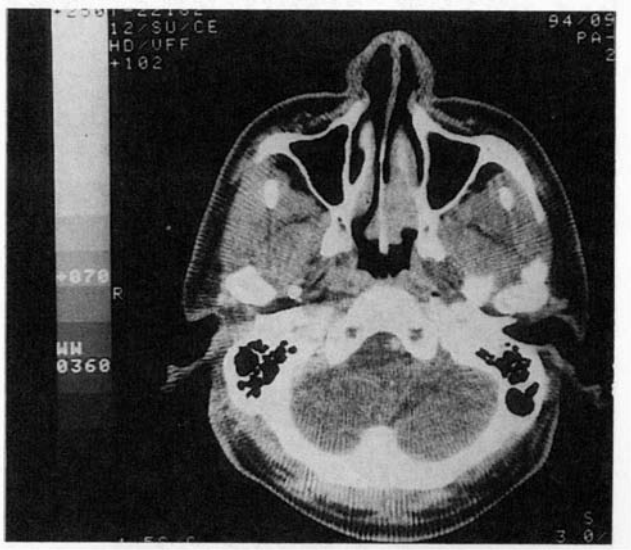

Fig. 1
Horizontal computed tomography scan. A soft tissue-density area was noted on the left side of the nasal septum.

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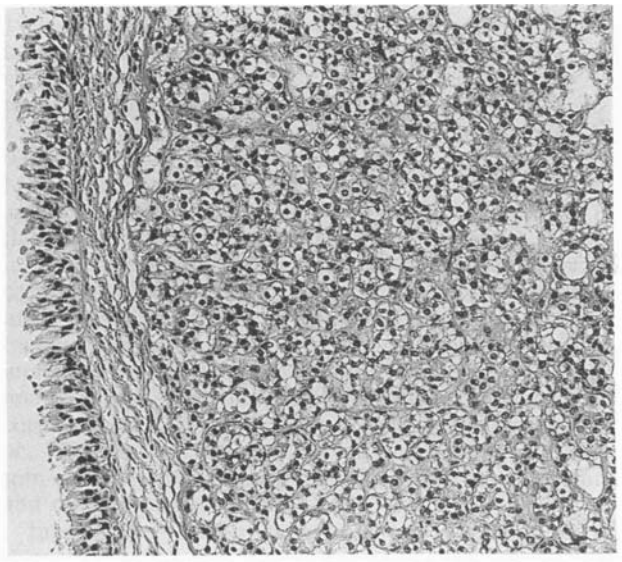

FIG. 2
Photomicrograph showing solid proliferation of clear cells. (H & E; × 100).

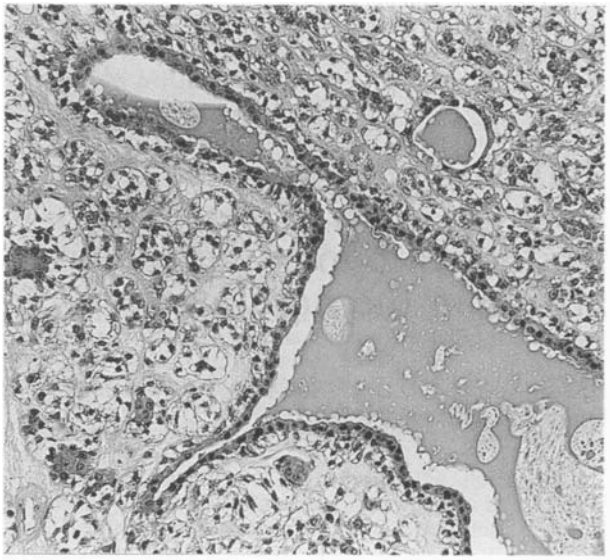

FIG. 3
Photomicrograph showing elongated duct structure involving mucoid material among clear cells. (H & E; × 100).

Pathological findings

Histopathological examination revealed a non-encapsulated tumour just beneath the nasal mucosa having a bimorphological appearance: a solid proliferation of clear-cells (Figure 2) including a pseudocribriform pattern and, in some areas, small or elongated duct structures with a double-layered arrangement of inner eosinophilic cuboidal cells and outer clear-cells (Figure 3).

The clear-cell nests were partitioned with thick or thin hyalinized fibrous stroma. Clear-cells had small round nuclei, with a limited variety of shape and size and rather haphazard polarity. They had also clear or faintly

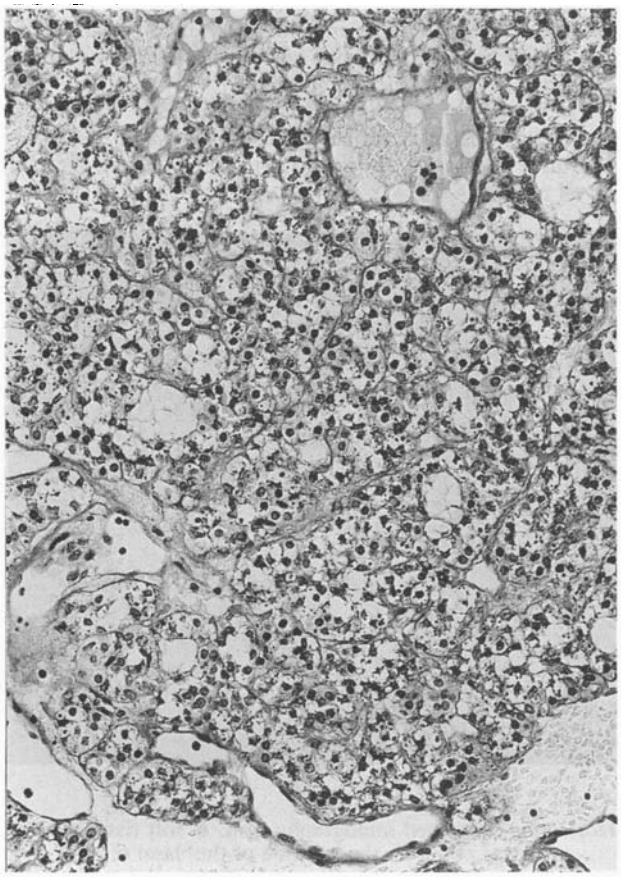

FIG. 4
Photomicrograph showing clear cells involving fine granules positive for PAS in their cytoplasms. (PAS; × 100).

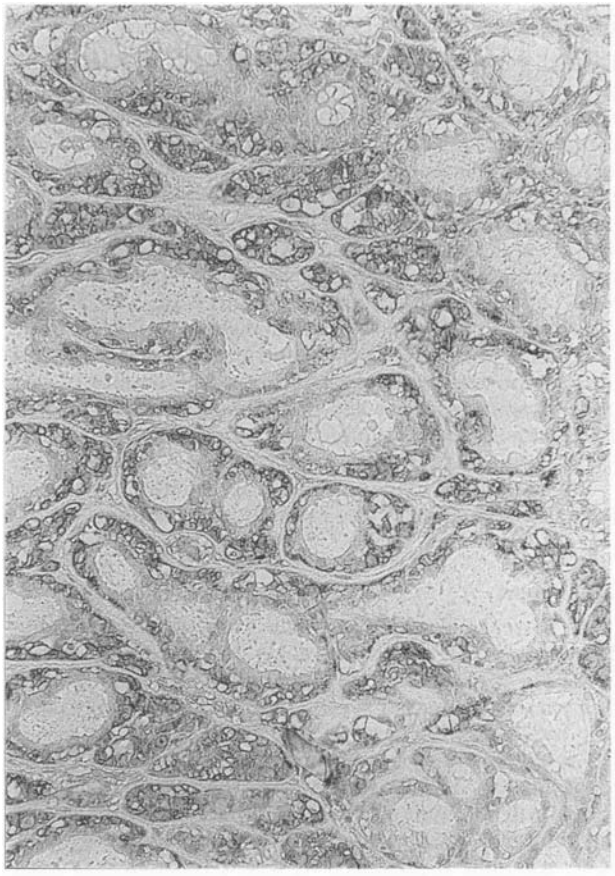

FIG. 5
Immunostaining for S-100 protein. Outer duct lining clear cells showing positive reactions. (× 100).

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TABLE I
RESULTS OF IMMUNOHISTOCHEMICAL AND HISTOCHEMICAL STUDIES

Antibody	Clear cell	Inner ductal eosinophilic cell
S-100 protein	(+)	partially (+)
α Smooth muscle actin (α SMA)	(+)	(−)
HHF 35	(−)	(−)
Amylase	partially (+)	(+)
Secretory component (SC)	(−)	(+)
PAS	partially (+)	partially (+)
PAS with prior diastase digestion	(−)	partially (+)
Alcian blue	(−)	(−)
PTAH	(−)	(−)

eosinophilic cytoplasm containing fine granular or droplet-like materials positive for periodic acid-Schiff (PAS), that were diastase digestible (Figure 4). Few mitotic figures and partial invasion into the loose connective tissue of the nasal mucosa were seen.

Inner ductal cells had eosinophilic granular cytoplasms and some contained PAS-positive granular materials that could not be digested with prior diastase treatment. No positive reactions to alcian blue (pH 2.5) were seen in any area, except in fibrous stroma, and no positive reactions to phosphotungstic acid haematoxylin stain (PTAH) were seen.

Immunohistochemical studies were performed on formalin-fixed, paraffin-embedded sections using primary antisera for S-100 protein (Dako, Kyoto, Japan), α smooth muscle actin (α SMA; Dako, Japan), human muscle-actin-specific monoclonal antibody (HHF 35 Dako, Japan), amylase (The Binding Site, Birmingham, England) and secretory component (SC; Dako, Japan).

Clear cells in the solid portion as well as outer ductal clear cells showed positive reactions for antisera of S-100 protein (Figure 5), SMA and partially for amylase but negative for HHF 35 and SC. Inner ductal eosinophilic cells, on the other hand, were positive for antisera of amylase, SC and partially for S-100 protein but negative for SMA and HHF 35. The tumour was diagnosed as an epithelial-myoepithelial carcinoma, myoepithelial clear cell predominant variant.

The results of immunohistochemical and histochemical studies are summarized in Table I.

Discussion

Donath *et al.* (1972) described eight cases of a unique form of carcinoma, which they considered to be derived from the precursor cell of the intercalated duct in 1972. Corio *et al.* (1982) presented sixteen cases of this neoplasm as EMC of intercalated duct origin characterizing both myoepithelial and ductal cells by ultrastructural studies. So far, many investigators have reported ultrastructural (Daley *et al.*, 1984) or immunohistochemical studies (Luna *et al.*, 1985; Palmer, 1985; Makek and Grant, 1988; Collina *et al.*, 1991; Fonseca and Soares, 1993; Witterick *et al.*, 1993).

In our case, clear-cells are interpreted as myoepithelial cells because of their glycogen content seen histochemically and positive reactions for S-100 protein and SMA by immunohistochemistry. The additional finding that some of both myoepithelial and ductal cells shared positive reactions for S-100 protein and amylase suggested the existence of intermediate cells or dual differentiation and supported the theory proposed by Donath *et al.* (1972).

Recently EMCs arising in unusual sites have been reported: lacrimal gland (Ostrowski *et al.*, 1994), tracheal gland (Horinouchi *et al.*, 1993), bronchus (Nistal *et al.*, 1994), subglottic region (Mikaelian *et al.*, 1986) and also the maxillary sinus (Luna *et al.*, 1985; Fonseca and Soares, 1993). However, to our knowledge, no case report describing EMC of the nasal cavity has been published.

Ostrowski *et al.* (1994) insist on the potential for its occurrence in the lacrimal gland on the grounds that myoepithelial cells occurring in normal lacrimal glands have been generally accepted. Accepting the histological similarity between salivary glands and serous or mucous glands in the nasal cavity, it is possible that EMC could occur in the nasal cavity in addition to the maxillary sinus, although this conflicts with its appearance in serous parotid glands. We believe that EMCs can occur in any gland, serous or mucous, where a double-layered arrangement of myoepithelial and ductal cells is seen.

Although the present case was expected to be, on balance, benign because of slight cellular atypia and polypoid growth with obscure infiltration, the literature demonstrates a wide variety in the malignant potential of EMCs case by case, from minimally aggressive epithelial-myoepithelial tumours (Horinouchi *et al.*, 1993; Nistal *et al.*, 1994), to the tumours with distant metastasis (Luna *et al.*, 1985; Porgel, 1985; Noel and Bronza, 1992) or intracranial invasion (Luna *et al.*, 1985; Morinaga *et al.*, 1992).

Confusingly, the prognostic factors of EMC are still controversial. Although Collina *et al.* (1991) state that no correlation was found between microscopic features and clinical behaviour, Hamper *et al.* (1989) state that differentiation and tumour size were of minor prognostic significance and Morinaga *et al.* (1992) reported that frequent mitotic figures indicated poor prognosis. In view of these comments, the only means left to be recommended is thorough histological study, case by case, in order to confirm the extent of their aggressiveness, such as perineural or intravascular invasion. In addition, the usefulness of irradiation therapy, although estimated to be of some benefit by a few authors (Makek and Grant, 1988; Witterick *et al.*, 1993), has not been used as much as chemotherapy. Further studies are needed.

The differential diagnoses of EMC in our case are acinic cell carcinoma, mucoepidermoid carcinoma, oncocytoma, sebaceous carcinoma and metastatic renal cell carcinoma, all of which include variants exhibiting the predominant presence of clear-cells. Acinic cell carcinoma shows a marked positive reaction for PAS and amylase antisera and includes few myoepithelial cells. Mucoepidermoid carcinoma produces acid mucopolysaccharides, not glycogen. Oncocytoma contains numerous mitochondria, which show positive reactions for PTAH stain. Sebaceous carcinoma does not contain glycogen and renal cell carcinoma does not show ductal differentiation (Corio *et al.*, 1982; Simpson *et al.*, 1991). Clear-cell carcinoma is described in histological classification of tumours of the upper respiratory tract and ear (Shanmugaratnam *et al.*, 1991), however, differential findings are difficult to define. The most important clues to differential diagnosis are 1) a double-layered arrangement of inner eosinophilic cells and outer clear-cells and 2) immunohistochemical or electron-microscopic confirmation of myoepithelial differentiation of clear cells.

Conclusion

It is supposed that EMCs can arise not only in anatomically original salivary glands but also in various glands, such as salivary gland derivatives, sweat glands and their derivatives, wherever myoepithelial cells are involved. This tumour should be recognized by not only

those engaged in head and neck surgery, but also surgical pathologists, as further accumulation of clinical examinations and information obtained from resected specimens should be reflected in the post-operative clinical management, even if it is accepted as a low-grade malignant tumour.

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References

Chen, K. T. K. (1983) Clear cell carcinoma of the salivary gland. *Human Pathology* **14:** 91–93.

Collina, G., Gale, N., Visona, A., Betts, C. M., Cenacchi, V., Eusebi, V. (1991) Epithelial-myoepithelial carcinoma of the parotid gland: a clinico-pathologic and immunohistochemical study of seven cases. *Tumori* **77:** 257–263.

Corio, R. L., Sciubba, J. J., Brannon, R. B., Batsakis, J. G. (1982) Epithelial-myoepithelial carcinoma of intercalated duct origin. *Oral Surgery* **53:** 280–287.

Daley, T. D., Wysoki, G. P., Smout, M. S., Slinger, R. P. (1984) Epithelial-myoepithelial carcinoma of salivary glands. *Oral Surgery* **57:** 512–519.

Donath, K., Seifert, G., Schmitz, R. (1972) Zur Diagnose und Ultrastruktur des tubularen Speichelgangcarcinoms: Epithelial-myoepitheliales Schalstrukcacinom. *Virchows Archiv für pathologische Anatomie und Physiologie und für klinische Medizin* **356:** 16–31.

Fonseca, I., Soares, J. (1993) Epithelial-myoepithelial carcinoma of the salivary gland. A study of 22 cases. *Virchows Archiv für pathologische Anatomie* **422:** 389–396.

Goldman, R. L., Klein, H. Z. (1972) Glycogen-rich adenoma of the parotid gland. An uncommon benign clear-cell tumor resembling certain clear cell carcinomas of salivary origin. *Cancer* **30:** 749–754.

Hamper, K., Brugmann, M., Koppermann, R., Caselitz, J., Arps, H., Askensten, U., Auer, G., Seifert, G. (1989) Epithelial-myoepithelial carcinoma of salivary glands: a follow-up and cytophotometric study of 21 cases. *Journal of Oral Pathology and Medicine* **18:** 299–304.

Horinouchi, H., Ishihara, T., Kawamura, M., Kato, R., Kikuchi, K., Kobayashi, K., Maenaka, Y., Torikata, C. (1993) Epithelial myoepithelial tumour of the tracheal gland. *Journal of Clinical Pathology* **46:** 185–187.

Littman, C. D., Alguacil-Garcic, A. (1987) Clear cell carcinoma arising in pleomorphic adenoma of the salivary gland. *American Journal of Clinical Pathology* **88:** 239–243.

Luna, M. A., Ordonez, N. G., Mackay, B., Mackay, B., Batsakis, J. G., Guillamondegui, O. (1985) Salivary epithelial-myoepithelial carcinomas of intercalated ducts: A clinical, electron microscopic, and immunohistochemical study. *Oral Surgery* **59:** 482–490.

Makek, M., Grant, J. W. (1988) Epithelial-myoepithelial carcinoma of the parotid gland associated with a primary carcinoma of the lung. *International Journal of Oral Maxillofacial Surgery* **17:** 134–137.

Mikaelian, D. O., Contrucci, R. B., Batsakis, J. G. (1986) Epithelial-myoepithelial carcinoma of the subglottic region: A case presentation and review of the literature. *Otolaryngology – Head and Neck Surgery* **95:** 104–106.

Mohamed, A. H., Cherrick, H. M. (1975) Glycogen-rich adenocarcinoma of minor salivary glands. A light and electron microscopic study. *Cancer* **36:** 1057–1066.

Morinaga, S., Hashimoto, S., Tezuka, F. (1992) Epithelial-myoepithelial carcinoma of the parotid gland in a child. *Acta Pathologica Japan* **42:** 358–363.

Nistal, M., Garcia-Viera, M., Martinez-Garcia, C., Paniagua, R. (1994) Epithelial-myoepithelial tumor of the bronchus. *American Journal of Surgical Pathology* **18:** 421–425.

Noel, S., Bronza, J. P. (1992) Epithelial-myoepithelial carcinoma of salivary gland with metastasis to lung: report of a case and review of the literature. *Head and Neck* **14:** 401–406.

Ostrowski, M. L., Font, R. L., Halpern, J., Nicolitz, E., Barnes, R. (1994) Clear cell epithelial-myoepithelial carcinoma arising in pleomorphic adenoma of the lacrimal gland. *Ophthalmology* **101:** 925–930.

Palmer, R. M. (1985) Epithelial-myoepithelial carcinoma: an immunohistochemical study. *Oral Surgery* **59:** 511–515.

Porgel, M. A. (1985) Follow-up report on epithelial-myoepithelial carcinoma of intercalated duct origin. *Oral Surgery* **59:** 172–173.

Saksela, E., Tarkkanen, J., Wartvaara, J. (1972) Parotid clear-cell adenoma of possible myoepithelial origin. *Cancer* **30:** 742–748.

Seifert, G., Sobin, L. H., Batsakis, J. G., Brocheriou, C., Cardesa, A., Dardick, I., Ellis, G. L., Eveson, J. W., Gusterson, B. A., Shanmugaratnam, K. (1991) *Histological Typing of Salivary Gland Tumours.* 2nd Edition, Springer-Verlag, Berlin, pp 23–24.

Shanmugaratnam, K., Sobin, L. H., Barnes, L., Cardesa, A., Ferlito, A., Friedmann, I., Heffner, D. K., Hellquist, H. B., Hyams, V. J., Krueger, G. R. F., Micheau, C., Nascimento, A. (1991) *Histological Typing of Tumours of the Upper Respiratory Tract and Ear.* 2nd Edition, Springer-Verlag, Berlin, pp 37–38.

Simpson, R. H. W., Clarke, T. J., Sarsfield, P. T. L., Gluckman, P. G. C. (1991) Epithelial-myoepithelial carcinoma of salivary glands. *Journal of Clinical Pathology* **44:** 419–423.

Thackray, A. C., Sobin, L. H. (1972) *Histological Typing of Salivary Gland Tumours.* World Health Organization, Geneva, p 16.

Witterick, I. J., Noyek, A. M., Chapnik, J. S., Heatoce, J. G., Bedard, Y. C. (1993) Observation on the natural history of a parotid epithelial-myoepithelial carcinoma of intercalated duct. *Journal of Otolaryngology* **22:** 176–179.

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