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Case Report

Nasopharyngeal Myoepithelial Carcinoma Mimicking Nasopharyngeal Carcinoma

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Abstract.

Myoepithelial carcinoma (malignant myoepithelioma) (MC) is a rare tumor, defined as a malignant salivary neoplasm composed almost exclusively of tumor cells with myoepithelial differentiation. It can arise in unusual location sites, such as the nasopharynx, and may be difficult to approach. Nasopharyngeal MC can sometimes present as a nasopharyngeal mass which may be mistaken for primary nasopharyngeal carcinoma (NPC). The treatment strategy for nasopharyngeal MC is different from NPC, and maximal surgical resection of the main lesion is still considered as the mainstay of therapy. Herein we present a 32-year-old man with a nasopharyngeal mass which was initially mistaken as NPC, and which was later confirmed as MC after a comprehensive review of the pathology.

Keywords **:** myoepithelial carcinoma, nasopharynx

病例報告

鼻咽肌上皮癌模仿鼻咽癌

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中文摘要

肌上皮癌（惡性肌上皮瘤）是一種罕見的腫瘤，其定義為惡性唾液腺腫瘤合併所有癌細胞幾乎皆具有肌上皮分化。它可以出現在不尋常的位置，例如鼻咽，而這使得它們

可能很難被探究。鼻咽肌上皮癌有時可表現為鼻咽部的腫塊病灶，因而可能被誤認為原發性鼻咽癌。鼻咽肌上皮癌的治療不同於鼻咽癌，儘可能地手術切除主要病變仍被認為是主要的治療方式。這裡，我們提出一個 32 歲的男性罕見個案，有鼻咽腫塊，起初，被臆斷為鼻咽癌；然而，在病理切片的審查複閱後，鼻咽肌上皮癌的診斷才被確立。

***關鍵字*:** 肌上皮癌、鼻咽

INTRODUCTION

Myoepithelial carcinoma (malignant myoepithelioma) (MC) is defined as a malignant salivary neoplasm composed almost exclusively of tumor cells with myoepithelial differentiation [1]. It is a rarely occurring tumor with a reported incidence of 0.2% of all salivary gland tumors [2]. Most reported cases of MCs arise in the parotid gland (48-75%), followed by the minor salivary glands (reported sites include the palate, cheek, gum, nasal cavity, maxillary sinus, nasopharynx, infratemporal fossa, oral cavity, base of tongue, supraglottic larynx), and the submandibular gland [3-10]. Herein, we reported the rare case of nasopharyngeal MC with initial presentation of nasopharyngeal mass which mimicked nasopharyngeal carcinoma (NPC).

CASE REPORT

A 32-year-old master sergeant presented to our facility complaining of neck stiffness and shoulders pain for the last six months. Three months later, magnetic resonance (MR) imaging of the cervical spine revealed a subcutaneous nodule in the level VB of the neck (Figure 1A). He thereafter developed tinnitus, blood-tinged nasal discharge and headache five months later and visited our hospital again. The pathology of the neck nodule excisional biopsy showed metastatic carcinoma. During hospitalization, MR imaging of the neck revealed tumor infiltration of the nasopharyngeal mucosal space with extension to the bilateral petrous apex and clivus and necrotic metastatic nodes in the bilateral level II of neck (Figures 1B, 1C, 1D). The patient's nasopharyngeal mass pathology revealed a poorly differentiated carcinoma. Therefore, advanced NPC, cT4N2M1, stage IV was preliminarily diagnosed. He underwent concurrent chemoradiotherapy (CCRT) with weekly cisplatin after the diagnosis. However, his symptoms became worse despite the ongoing treatment.

We reviewed the pathology of the patient's biopsies in the multidisciplinary team meeting. Microscopically, the tumor cells had polymorphous patterns with enlarged, pleomorphic nuclei with distinct nucleoli as well as eosinophilic or vacuolated cytoplasm arranged in sheet-like and reticular patterns infiltrating in both neck and nasopharyngeal tissue (Figures 2A, 2B). The immunohistochemical (IHC) staining showed immunoreactive for epithelial cell markers, including cytokeratin and epithelial membrane antigen (EMA) (Figure 2C), and myoepithelial markers, including smooth muscle actin (SMA), S-100 (Figure 2D), calponin, glial fibrillary acidic protein (GFAP) and p63. The diagnosis of nasopharyngeal MC was revised one month later after initial approach, but an intensive therapeutic strategy with combined modalities using maximal surgical resection and radiotherapy (RT) [11,12] was not feasible because of his poor performance status. The patient received palliative chemotherapeutic regimens with tri-weekly doxorubicin plus cisplatin and tri-weekly docetexal after the CCRT. Poor response was noted and the patient exhibited an intolerance to chemotherapy. Supportive med-

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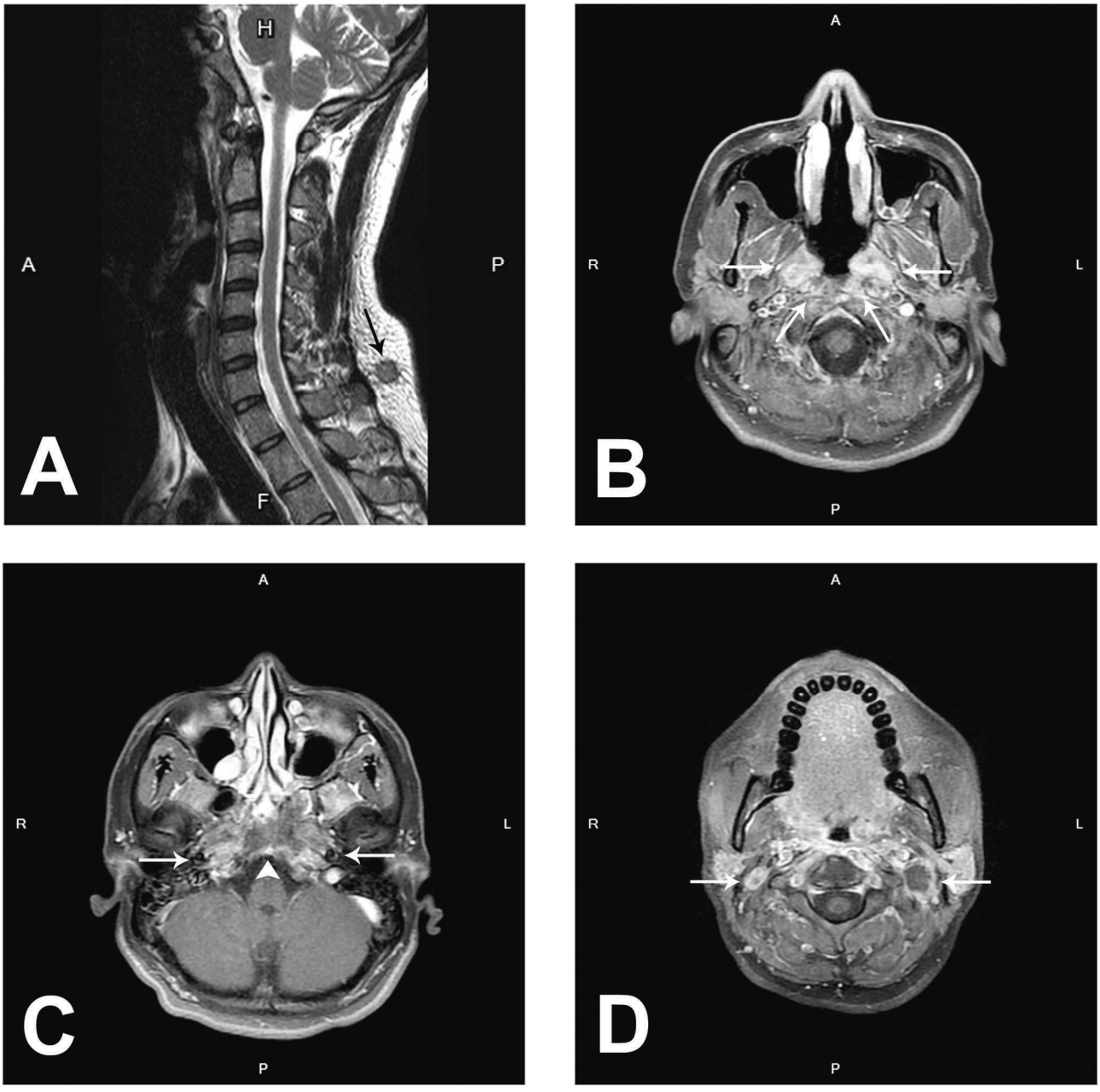

Figure 1. (A) T2-weighted MR imaging of the C-spine revealed an 1.2-cm metastatic nodule in the level VB of the neck (arrow). (B, C, D) Post-contrast T1-weighted MR imaging of the nasopharynx showed tumor infiltration in the nasopharyngeal mucosal space on both sides (arrows in B) with extension to the bilateral petrous apex (arrows in C) and clivus (arrowhead in C) and necrotic metastatic nodes in the bilateral level II of the neck (arrows in D)

ical treatment was given thereafter. He died of the disease eight months after the disease diagnosis.

DISCUSSION

MCs are tumors of epithelial origin that may occur with preexisting benign lesions like pleomorphic adenomas or benign myoepitheliomas, but they can also

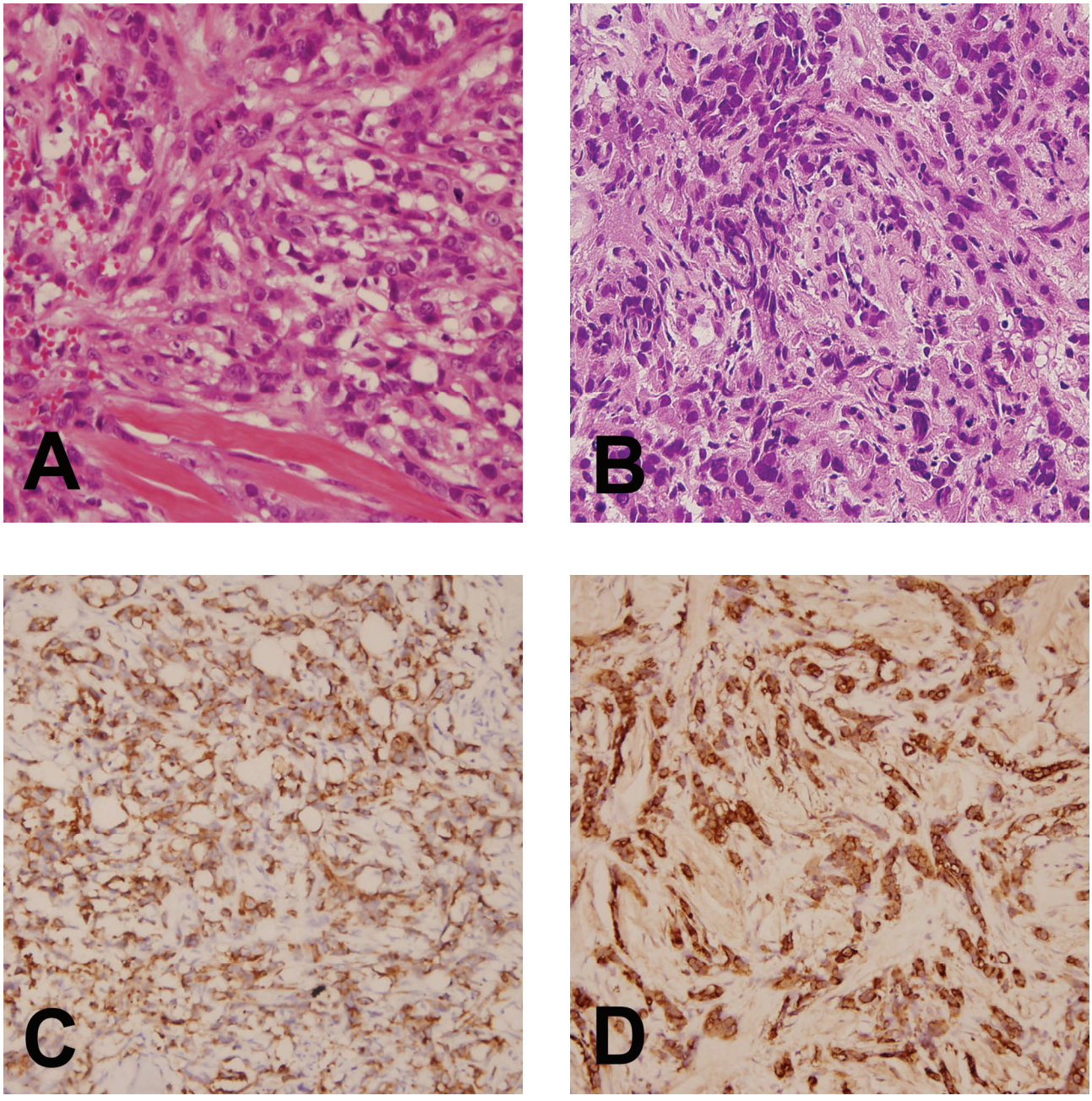

Figure 2. The pathological exams of the metastatic nodule (2A) and the primary lesion (2B) revealed similar findings. Tumor cells have polymorphous patterns with enlarged, pleomorphic nuclei with distinct nucleoli as well as eosinophilic or vacuolated cytoplasm arranged in sheet-like and reticular patterns infiltrating in both neck and nasopharyngeal tissue (H&E, 400X). The immunohistochemistry (IHC) staining showed positive for (C) epithelial membrane antigen (EMA, 200X) and (D) S100 (200X). (IHC was done using diaminobenzidine substrate and the brown color indicated expression of staining.)

occur de novo [13]. These tumors usually present as painless masses with insidious onset. When MCs occur in the nasopharynx, the symptoms are the same as those of other tumors that affect this region, such as

nasal obstruction, ear fullness, serous otitis media, and conductive hearing loss. There is also a lack of diagnostic criteria. On account of the aforementioned reasons, early detection is difficult and the diagnosis may be delayed by months or even years.

Computed tomography (CT) and MR imaging allow the site and the nature of the extension of MCs to be established. However, some MCs may appear non-invasive and could be mistaken as benign on imaging alone. In the past, very few reports have described imaging findings of MCs. Martinoli et al. reported nonspecific CT features of the MCs arising in salivary tissue on the masseter muscle [14]. In general, MCs appear isodense to muscle and moderate homogenous contrast enhancement on CT images. On MR images, MCs typically show low to intermediate signal intensities on T1-weighted images and heterogeneously increased signal intensities on T2-weighted images with a tendency to invade adjacent structures [8, 15]. In our case, the preoperative imaging findings were nonspecific and the impression was advanced NPC with metastatic nodes in the neck.

Due to the nonspecific clinical manifestation and imaging characteristics, preoperative diagnosis may be difficult or impossible for MCs. Histological examination with IHC staining studies is the most reliable and conclusive method of diagnosis. Histologically, MCs are characterized by multilobulated architectures without ductal formation and have myoepithelial differentiation. Morphologically, the tumor cells are often spindle-shaped, stellate, epithelioid, plasmacytoid (hyaline), and occasionally vacuolated with a signet ring-like appearance. Solid sheet-like formations and trabecular or reticular patterns (biphasic pattern) may form by tumor cells [16]. The presence of significant atypia, atypical mitotic figure, hemorrhage, and necrosis have been considered features of malignancy [17]. IHC analysis shows elevated expression of epithelial markers such as CK, EMA, S-100, and markers of smooth muscle origin such as SMA and calponin on the tumor cells of MCs. Current IHC criteria for the confirmation of myoepithelial differentiation are double positive for both CK and one or more myoepithelial IHC markers (i.e., S-100, vimentin, calponin, p63, GFAP, and actins) [18-21]. There are still some tumors that also show similar spindle cell composition, such as parachordoma, chordoma, extraskeletal myxoid chondrosarcoma, unusual carcinoma and even chondrosarcoma if a chondroid matrix is present and the sampling is small. Therefore, IHC studies are useful and the expression patterns may help us to distinguish MCs from other tumors.

Brandal et al. found that t(19;22)(q13;q12) translocation leads to a novel fusion gene, EWSR1-ZNF444. The significance of this new fusion gene to tumorigenesis is not clearly understood, but it may be a defining pathogenetic feature of some of these tumors [22]. In dedifferentiated MCs, nuclear accumulation of p53 and cyclin D1 has been described [23,24], and a recent article also showed an expression of platelet-derived growth factor A (PDGFA) genes in the tumor [25]. However, due to the limited number of patients that have been studied, the clinical applicability of this earlier investigation requires further inquiry.

Interestingly, MCs usually exhibit a propensity for distant metastasis more than for regional lymph node metastasis [7]. Distant metastasis has been seen to the lungs (most commonly), bone, liver, peritoneum, pleura, kidneys, brain, and skin in previous reports [4,11,26]. Unlike certain nasopharyngeal tumors for which CCRT are the preferred treatments in some cases, the application of these treatments to nasopharyngeal MCs has been disappointing. However, there are no specific guidelines for the treatment of MCs, especially in the uncommon sites. In general, complete resection with tumor-free margin remains the first choice of treatment for nasopharyngeal MCs. In addition, local radiotherapy or chemotherapy may be the most effective adjuvant strategy for the patients.

CONCLUSIONS

Nasopharyngeal MC is a rare entity, but often ob-

served as having a very aggressive characteristic. It can sometimes present as a nasopharyngeal mass which may be mistaken for primary NPC. If accurately diagnosed, an intensive therapeutic strategy with combined modalities may provide the best chance of long-term control.

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