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Mucoepidermoid carcinoma ex pleomorphic adenoma: A rare diagnostically challenging entity

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ABSTRACT

Mucoepidermoid carcinoma (MEC) arising in pleomorphic adenoma (PA) is an extremely rare entity. Involvement of minor salivary glands by this entity has only being described twice previously. We report on a diagnostically challenging case in an 18 year old male with a large mass in the junction of the hard and soft palates that has been present for 12 months. Both cytology and incisional biopsy were inconclusive and indicated benign mixed tumour. Upon excision of the tumour with a 5 mm clear margin, histology demonstrated PA that has been replaced by small nests and cribriform islands of high-grade MEC with 13 mm of invasion beyond the original PA capsule. The tumour was composed of mostly intermediate-type cells with up to 7 mitoses per 10 high power fields. The tumour cells were positive for cytokeratin (CAM 5.2) and S100. Due to the high-grade nature and focal positive posterior margin of the resected specimen, adjuvant radiotherapy was administered. In conclusion, this case highlights the need to consider rare entities such as mucoepidermoid carcinoma ex pleomorphic adenoma in atypical cytological and histological findings. Moreover, it underlines the need to manage lesions with unconfirmed histological diagnosis with wide excision margins to avoid having involved margins post resection.

Introduction

Carcinoma ex pleomorphic adenoma (CxPA) is an epithelial or myoepithelial malignancy originating from a primary or recurrent pleomorphic adenoma (PA). It comprises approximately 3.6% of all salivary gland tumours and 12% of all salivary gland malignancies [1]. CxPA develops largely in the parotid gland and usually affects elderly patients in the 6th−7th decades of life with a history of longstanding PA. CxPA commonly behaves aggressively with features of infiltration into the adjacent glandular and extra-glandular tissues. Moreover, regional metastasizes are frequent (up to 70%) and the lesion has a high mortality rate (5-year survival rate: 25–65%) [1].

Although a number of salivary gland carcinomas have been associated with PA, mucoepidermoid carcinoma (MEC) arising from a PA is exceedingly rare [2]. We report on the diagnostic challenges encountered with a case of mucoepidermoid carcinoma ex pleomorphic adenoma (MECxPA) arising in a minor salivary gland of the palate and its clinicopathological and immunohistochemical features.

Case report

An 18 year old non-smoking male presented with a 12 month history of an enlarging mass at the junction of the hard and soft palates. Clinically a 50 mm × 40 mm asymptomatic exophytic mass was noted with no associated lymph node involvement (Fig. 1A). Contrasted computerized tomography (CT) demonstrated a heterogenous submucosal mass confined superiorly by the soft palate and uvula, laterally by the left maxillary molars and medial pterygoid muscle with no local nodal spread identified (Fig. 1 B & 1C).

An incisional biopsy was performed and microscopic sections showed stromal fragments with minor salivary glands lined by stratified squamous epithelium and free-lying fragments comprising a biphasic proliferation of epithelial and mesenchymal elements. Mitotic figures and necrosis were not seen. Furthermore, CK7 and S100 were positive in the epithelial component and p63 and GATA3 were negative. The incisional biopsy was inconclusive and merely suggestive of a benign mixed tumour not otherwise specified prompting further cytological analysis.

Fine needle aspiration (FNA) of the palatal mass showed myoepithelial groups, focal epithelial acini and myxoid stroma in a proteinaceous background. This suggested a myoepithelial rich pleomorphic adenoma or a myoepithelioma and surgical removal was advised to confirm the diagnosis. Subsequently the patient underwent surgical excision of the tumour with the overlying palatal mucosa and a 5 mm clear margin.

Histology examination of the final specimen demonstrated sections of PA that has been mostly replaced by small nests and cribriform islands of MEC surrounded by mucin (Fig. 1D & 1E). The PA component only formed the superficial submucosal portions of the tumour. The invasive MEC component appeared to have extended at least 13 mm beyond the capsule of the primary PA. This high-grade tumour was composed of mostly intermediate-type cells with up to 7 mitoses per 10 high power fields. It was positive for cytokeratin (CAM 5.2), p63 (focal), and S100 (diffusely positive). It was negative for CD117, DOG1, EMA, Synaptophysin, Mammoglobin, androgen receptor, SMA and calponin (Fig. 1F). Following confirmation of the diagnosis, the patient was referred to radiation oncology for adjuvant radiotherapy due to the tumour being high-grade and the posterior resection margin being focally involved.

Discussion

Although the majority of salivary gland carcinomas have been associated with PA, the prevalence of MEC, which is the most common salivary gland malignancy in adults, has been rarely reported [3]. A total of fourteen MECxPA have been reported (including this case), of which,

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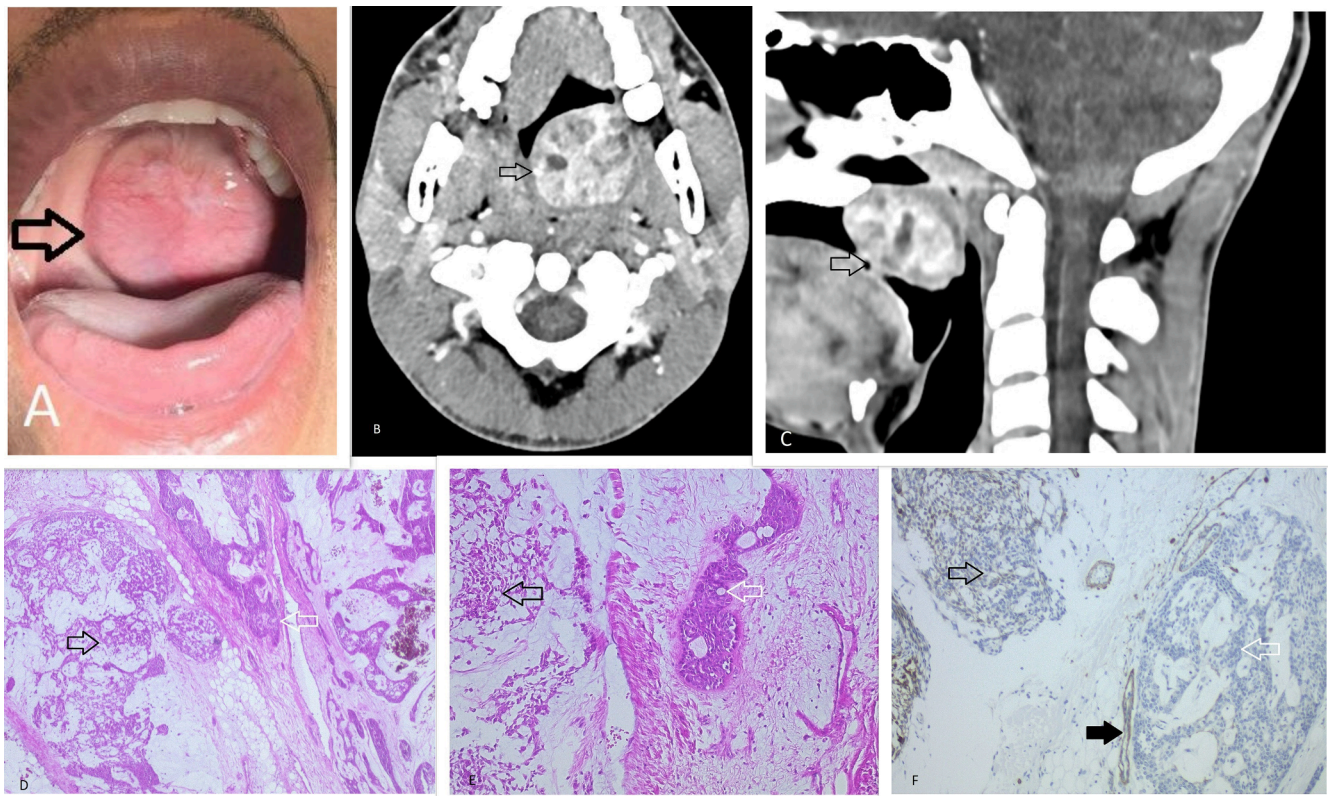

Fig. 1. **A**: Intra photograph of lesion in palate. **B**: Axial contrast CT showing extension of tumour. **C**: Sagittal contrast CT confirming no bony involvement of hard palate. **D**: H&E stained histology section (40x magnification) showing a mucoepidermoid carcinoma (white arrow) arising from a pleomorphic adenoma (black arrow). **E**: H&E stained histology section (100x magnification) showing mucoepidermoid carcinoma comprising a mixture of squamous cells, intermediate cells and goblet cells (white arrow) arising from a pleomorphic adenoma, which is composed of a mixture of ductal cells and myoepithelial cells in a myxoid stromal background (black arrow). **F**: Immunohistochemical staining with calponin (100x magnification) showing the mucoepidermoid carcinoma to be negative (white arrow) arising from a pleomorphic adenoma, which is composed of a mixture of calponin negative ductal cells and calponin positive myoepithelial cells (black arrow). The calponin stain also stains the smooth muscle of vessels (solid black arrow).

ten were high-grade MECxPA, three were low-grade and one was intermediate grade. Most lesions were located within the parotid gland while two were in the palate and one in the mandibular retromolar region [4,5]. Two were metastatic lesions within the parapharyngeal space [2,6]. Cytologic diagnosis was inaccurate in 72.7% of reported cases (only 11 cases underwent cytological exam). An enlarging mass within the affected salivary gland was present in all cases. Recurrent PA was noted in only one patient [2].

The rare occurrence of MECxPA in minor salivary glands as reported in this case proved to be a diagnostic challenge. This is due to a misleading incisional biopsy and FNA findings which both suggested a benign mixed salivary tumour. Furthermore, given the patient's young age and location of the lesion, this entity was not considered at all. Histological and immunohistochemical examination of the resected specimen confirmed a MECxPA via the presence of intermediate-type cells with focal mucus cells and positivity for cytokeratin (CAM 5.2) with loss of calponin staining for myoepithelial cells.

The transformation of PA into MEC is not considered unprecedented as there are similar phenotypic and ultrastructural features amongst intermediate cells of MEC and myoepithelial cells of PA. Mutual karyotypic alterations are also noted in both tumours, further highlighting an association between these two entities [3].

MECxPA is managed in a similar fashion to MEC. Complete surgical excision is the primary modality for management of all grades of MEC [1]. The indications for neck dissection and/or adjuvant radiotherapy are modified based on clinical assessment and risk of recurrence. Low-grade MEC display less aggressive behaviour and is routinely managed with surgical excision alone. High-grade tumours are typically managed with wide surgical excision along with neck dissection and adjuvant radiotherapy. Management of intermediate-grade tumours varies widely from local to wide excision with neck dissection and/or postoperative radiotherapy [2]. In our case, a 5 mm excision margin was performed as the lesion was thought to be benign in nature based on the FNA and incisional biopsy findings. This resulted in the posterior margin being focally involved with the tumour and hence post-operative radiotherapy was administered. No clinical or radiological signs of lymph node involvement were present and hence neck dissection was not performed.

In conclusion, this report emphasises the need to consider rare entities such as MECxPA in atypical cytological and histological findings in salivary gland tumours. Moreover, it underlines the need to rather manage lesions with unconfirmed histological diagnosis with wide excision margins to avoid having involved margins post resection.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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