Diagnostic difficulties in lesions of the minor salivary glands

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Abstract

A wide range of lesions arise from the intra-oral salivary glands, and often present a diagnostic challenge to specialists and generalists alike. Of the salivary neoplasms, pleomorphic adenoma is the most common, but its morphological diversity may bring several other entities to mind, notably polymorphous adenocarcinoma, particularly in a small incisional biopsy. Polymorphous adenocarcinoma in turn shares features with adenoid cystic carcinoma. Immunohistochemistry and molecular cytogenetic studies can assist diagnosis in the face of overlapping morphology. The other salivary neoplasms most likely to be encountered in the oral cavity are canalicular adenoma, mucoepidermoid carcinoma, secretory carcinoma and acinic cell carcinoma. Of the non-neoplastic conditions, necrotising sialometaplasia is most likely to be misdiagnosed as neoplastic on both clinical and histological grounds. However, careful consideration of the clinicopathological features of an adequate tissue specimen will enable correct diagnosis.

Keywords cytogenetics; immunohistochemistry; mouth neoplasms; salivary gland diseases

Introduction

The histopathology of the salivary glands, and particularly of salivary gland tumours, is complex and may be problematic for even the most experienced diagnostic pathologist. Since this topic was last reviewed[1] a number of new entities have been described and terminology has been altered to more accurately reflect the behaviour and nature of some lesions. In addition, there have been advances in molecular techniques enabling more accurate diagnosis of some lesions. These changes have been incorporated into the latest World Health Organization (WHO) Classification of Head and Neck Tumours.[2] The classification contains over 40 named neoplasms, many of which show significant morphological diversity. As a result, there are overlapping features, which make differentiation between tumour types difficult. Added to this, there is also a range of non-neoplastic lesions that may resemble tumours both clinically and histologically. The purpose of this review is to provide an update on current terminology and new diagnostic techniques, and to highlight areas of diagnostic difficulty or controversy.

Tumours of the minor salivary glands

The oral cavity contains between 400 and 800 small minor salivary glands located throughout the connective tissues of the lips, cheeks, retromolar trigone, palate (including the uvula), tongue and floor of mouth. All are predominantly of mucous type, the exception being the serous glands (of von Ebner) associated with the circumvallate papillae at the interface of the anterior two-thirds and posterior third of the tongue. Theoretically, the intra-oral salivary glands can be affected by any of the salivary neoplasms recognised by the WHO, but in practice even specialist centres see only a few of these types with any frequency, thus this article will concentrate on the most commonly encountered entities and the diagnostic difficulties they pose. They are listed in Table 1.

Overall most intra-oral salivary neoplasms affect the palate, but canalicular and basal cell adenomas characteristically affect the upper lip. Indeed, whereas most swellings of the lower lip are mucocoeles, most swellings of the upper lip are neoplasms and a diagnosis of mucocoele at this site should be issued with caution. It is likely that a retromolar tumour will prove to be a mucoepidermoid carcinoma. Most diagnostic difficulties are the result of the morphological diversity of the neoplasms and the bland cytology of all but high grade lesions, which makes evidence of infiltration a critical feature in the diagnosis of malignancy. These problems are often compounded by the submission of small biopsies. For major salivary glands, FNA has been popular but should now be superseded by ultrasound guided core biopsy, which gives superior results.[3] FNA should never be used for intra-oral lesions and even core biopsies may yield insufficient tissue for accurate diagnosis. For diagnosis of minor salivary gland lesions therefore we always recommend an adequate

Salivary gland tumours most likely to be encountered in the minor salivary glands, in approximate descending order of frequency

Benign

- Pleomorphic adenoma, occasional examples of which are solid enough to merit being termed a myoepithelioma
- Canalicular adenoma

Malignant

- Mucoepidermoid carcinoma
- Adenoid cystic carcinoma
- Polymorphous adenocarcinoma
- Cribriform adenocarcinoma of minor salivary glands
- Secretory carcinoma
- Acinic cell carcinoma
- Adenocarcinoma NOS

Table 1

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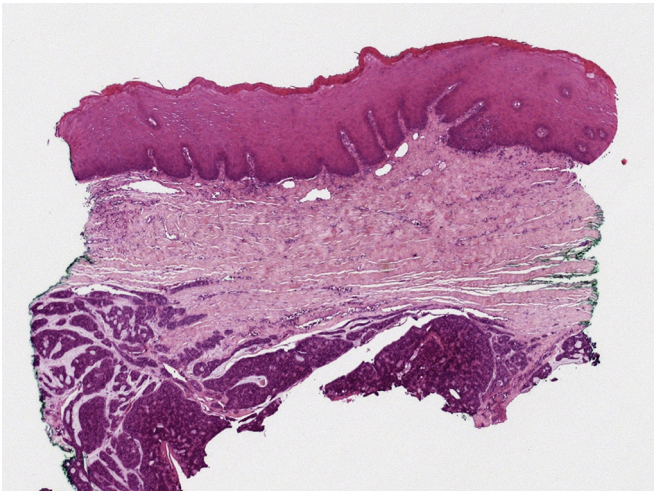

Figure 1 An incisional biopsy of a palatal tumour, only the most superficial aspect of which is present. The tumour has a pleomorphic pattern, with evidence of local infiltration. This tumour was originally diagnosed as a pleomorphic adenoma; the correct diagnosis of polymorphous adenocarcinoma was only made after complete excision.

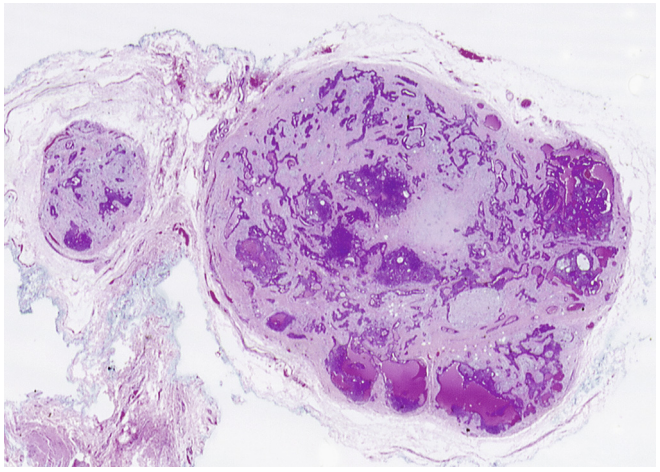

Figure 2 A pleomorphic adenoma of the upper lip, showing an apparently detached satellite of tumour in the tissue surrounding the main nodule. However, serial sectioning proved the tumour to comprise a single large nodule.

scalpel biopsy. Palatal lesions are most common and here, the biopsy should be taken down to bone. Shallow biopsies may only yield the superficial aspect of the lesion and may not be representative (Figure 1).

Pleomorphic adenoma

This is the most common salivary gland tumour, comprising about 70% of parotid lesions and 50% of minor gland tumours. Intra-orally, the most common site is the junction of the hard and soft palate. Because pleomorphic adenoma is the most frequently encountered tumour the features are well described, but its relative frequency may lead to over-diagnosis. Morphological diversity is characteristic of pleomorphic adenoma, but this is also a particular problem with small biopsies where only one histological pattern may be seen. Some of the typical features are listed in the left column of Table 2. When seen in isolation in small biopsies, these features may lead to confusion with the lesion in the right column; the consequences of a misdiagnosis are clearly apparent. The pathologist must take into account the clinical history and the site of the lesion, but even so it may be necessary to issue a differential diagnosis, with or without a favoured option. The true nature of the tumour may not become apparent until the lesion has been completely excised and examined in its entirety.

Pleomorphic adenomas are usually well demarcated, but minor gland tumours are not necessarily encapsulated. There may be no evidence of infiltration of the adjacent structures, but the lobular shape of the lesion may lead to the phenomenon of "pseudocapsular invasion", where tumour apparently extends into, and beyond, the capsule (Figure 2). This is not uncommon and should not be misinterpreted as a sign of malignancy. Carcinoma arising in pleomorphic adenoma, a well recognised entity, is more likely to complicate a major rather than a minor salivary gland lesion.

The key histopathological features of pleomorphic adenoma are a variable pattern of epithelium in a loosely fibrous matrix, which may be myxoid, mucoid or chondroid. Although present in the tumour shown in Figure 2, chondroid areas are less common in minor than major gland tumours. The epithelium is

Characteristic features of pleomorphic adenoma and lesions with which it may be confused

Feature	Resemblance
Morphological diversity	Polymorphous adenocarcinoma
Bilayered ducts and cribriform pattern	Adenoid cystic carcinoma; Cribriform adenocarcinoma
Bilayered ducts with clear outer cells	Epithelial-myoepithelial carcinoma; adenoid cystic carcinoma
Sheets of basaloid cells	Basal cell adenoma or adenocarcinoma
Lymphoid infiltration at periphery of tumour	Acinic cell carcinoma; mucoepidermoid carcinoma
Myxoid stroma	Myxoma, neural tumours
Chondroid stroma	Chondrosarcoma
Plasmacytoid cells	Plasmacytoma
Spindled myoepithelial cells	Schwannoma, other benign soft tissue tumour, or sarcoma
Squamous metaplasia	Squamous cell carcinoma
Oncocytic metaplasia	Oncocytoma

Table 2