Case Report

Oncocytes in Mucoepidermoid Carcinoma of the Palate: Diagnostic Challenges

Rammohan Kumar,1 Srikant Natarajan,2 K.S. Sneha,2 Nunna Sai Chitra,2 Karen Boaz,2 and Nidhi Manaktala2

1OralandMaxillofacialSurgeon,TCR MultispecialityHospital,Krishnagiri,Tamilnadu,India
2DepartmentofOralPathologyandMicrobiology,ManipalCollegeofDentalSciences,ManipalAcademyofHigherEducation,Mangalore,India

Correspondence should be addressed to Karen Boaz; karen.boaz@manipal.edu

Received 18 August 2017; Accepted 9 November 2017; Published 28 December 2017

1. Introduction

Oncocytes are large epithelial cells that contain bright eosinophilic, granular cytoplasm. The term “oncocyte” is derived from the Greek word “onkousthai” which means swollen or enlarged. The oncocyte was first described by Schaffer in 1897 who observed the presence of eosinophilic granular cells in ductal and acinar elements of salivary glands of the tongue, pharynx, and esophagus. He believed that oncocytes were the result of a degenerative phenomenon in salivary gland parenchymal cells. Zimmermann observed the presence of oncocytes in the sublingual gland and referred to these cells as “pyknocytes” alluding to their condensed nuclear chromatin or pyknotic nuclei [1]. Hamperl used the term “oncocyte” to describe large granular cells seen not only in the salivary gland tissue but also in tissues of the kidney, thyroid, parathyroid, pituitary, and adrenal glands. He suggested that individual cells or aggregates of cells could either undergo permanent modification into oncocytes as a metaplastic process or proliferate as a hyperplastic or neoplastic process [1]. Oncocytes have since been observed in the liver, pancreas, fallopian tubes, testes, stomach, and bronchi. Ultrastructural studies of tumours showing oncocytes have demonstrated increased numbers of mitochondria within the cytoplasm of the oncocyte. Histochemical studies performed to compare the concentrations of oxidative enzymes of the oncocyte to those of normal salivary gland acinar and ductal cells have shown similarities between an oncocyte and the intercalated duct reserve cell. However, some ultrastructural studies suggest that the salivary gland oncocyte may be an adaptive or compensatory hyperplastic cell occurring secondary to an undetermined somatic mutation rather than a purely degenerative process [1].

The World Health Organization (2005) classified oncotic lesions into three distinct categories of oncotypyosis, oncoyctoma, and oncotic carcinoma. Other lesions described to show oncocytes include both benign and malignant tumours like oncotic/oncocytoid variants of cystadenoma, myoepithelioma, acinic cell carcinoma, salivary duct carcinoma, and
metastatic renal cell carcinoma [2]. Oncocytic metaplasia is a feature of Warthin’s tumour and may also be a component of malignant salivary gland tumours like mucoepidermoid carcinoma, acinic cell carcinoma, pleomorphic adenoma, and oncocytic myoepithelioma [3].

In the current article, we describe the case of a low-grade mucoepidermoid carcinoma of the palate with numerous oncocyes.

2. Case Report

A 43-year-old female patient reported to a private clinic with a soft fluctuant swelling extending anteroposteriorly from the second premolar to the third molar in the right side of the palate. She had noticed a small swelling in the same site 3 years back, which was suspected to be a periodontal abscess, and the adjacent tooth was extracted. However, the swelling did not subside and gradually grew to attain the size of 4 × 3 cm. Adjacent teeth were intact and firm (Figure 1).

An incisional biopsy exhibited fibrous connective tissue stroma with predominance of mucicarmine-positive mucous cells with pale foamy cytoplasm intermixed with intermediate, epidermoid, clear, and oncocytic cells. Small gland-like structures were also seen along with few engorged blood vessels and areas of hemorrhage. Based on the histological features, a diagnosis of low-grade mucoepidermoid carcinoma was made. Following this, right hemimaxillectomy was performed, and the specimen was sent for histopathological examination.

2.1. Gross Appearance. The excisional specimen consisted of a resected palate including teeth 15, 16, and 17 with associated soft tissues measuring approximately "4.4 × 3.5 × 3.0" cm. An ulcer which was measuring approximately "0.8 × 0.6" cm was noticed on the hard palate in relation to the medial aspect of 16.

2.2. Microscopic Appearance. Microscopic examination in low power showed the presence of neoplastic glandular epithelial cells that were separated from the overlying mucosal parakeratinized stratified squamous epithelium. Oncocytic cells were also seen to be intermixed with the cellular elements of mucous, epidermoid, and intermediate cells (Figure 2(a)). On higher magnification, the lesional tissue (tumour mass) was seen to exhibit large cystic spaces that were lined by mucous, epidermoid, intermediate, spindle-shaped, and few clear cells (Figures 2(b) and 2(c)). Oncocytic metaplasia was evidenced as extensive areas of polyhedral cells with granular eosinophilic cytoplasm arranged in an organoid/alveolar pattern and supported by thin fibrous connective tissue septa (Figures 2(d) and 2(e)). The connective tissue stroma surrounding the tumour mass exhibited a moderate amount of chronic inflammatory cell infiltrates, salivary gland acini, focal areas of hyalinization, engorged blood vessels, and adipocytes.

The presence of large cystic spaces lined by the classic population of three types of cells (i.e., mucous, epidermoid, and intermediate cells) accompanied by a predominance of
oncocytic cells led us to the diagnosis of a low-grade mu- 
coeidermoid carcinoma with oncocytic metaplasia.

3. Discussion

Mucoepidermoid carcinoma (MEC) is the most common 
malignant salivary gland neoplasm of the major and minor 
salivary glands. An intraosseous variant of the MEC has also 
been described. MECs are characterized by the presence of 
three types of cells: mucous, intermediate, and epidermoid 
cells in varying proportions. Minor proportion of the his-
tology may also be constituted by clear, columnar, or 
oncocytic cells.

Less frequently encountered variants of the MEC include 
oncocytic MEC, sebaceous MEC, psammomatous MEC, 
spindle cell MEC, goblet cell aggressive MEC, and sclerosing 
MEC. Although the variants do not appear to affect the 
prognosis of the tumour, the predominance of a less-
frequent histological cell type does pose a challenge to 
diagnose MEC, as it may obscure the classical histopatho-
logical features. One such variant is the oncocytic mucoe-
pidermoid carcinoma (OMEC) showing high proportion of 
oncocyes. Oncocytic change is not only a neoplastic event 
but also a component of the normal aging process. Thus, an 
MEC containing oncocyes may put the pathologist in a 
dilemma to categorize it as an OMEC or MEC with on-
cocytic metaplasia. The percentage of oncocyes in the lesion 
to discriminate these two has not been defined in the lit-
ature owing to the rarity of this variant and the relatively 

fewer number of studies documented. However, Brannon 
and Willard defined a tumour with classical histopathological 
pattern of the MEC with mucous, epidermoid, and in-
termediate cells with ≥50% showing oncocytic changes as 
OMEC [4]. Weinreb et al. studied all the MEC tumours 
containing oncocyes and included only those cases with 
>50% oncocytic elements as OMEC [3]. Jahan-Parwar et al. 
described 3 cases of the MEC (2 low-grade and 1 high-grade) 
containing >75% and >60% oncocyes, respectively [5].

MEC is the most common malignant salivary gland tum-
our which histologically shows the presence of mucous, 
intermediate, and epidermoid cells. Low-grade lesions are 
characterized by the presence of cystic spaces with abundance 
of mucous cells. High-grade lesions, on the other hand, show 
solid areas of intermediate and epidermoid cells with presence 
of necrosis and neural involvement. Low-grade MECs with 
presence of oncocyes are not difficult to distinguish from 
other oncocytoid tumours as areas of typical MEC are in-
vitably present within the tumour. When oncocytic cells 
predominate with few epidermoid and intermediate cells, the 
diagnosis becomes difficult and other oncocytic lesions should 
be considered in the differential diagnosis. The lesions 
showing the presence of oncocyes can be broadly grouped as

(1) oncocytic lesions which include oncocytosis, onco-
cytoma, and oncocytic carcinoma;

(2) benign lesions like pleomorphic adenoma, Warthin’s 
tumour, and oncocytic myoepithelioma which shows 
oncocytic metaplasia;

| S. no. | Lesion | Microscopic appearance | Differentiating feature from OMEC |
|-------|--------|------------------------|---------------------------------|
| (1)   | Oncocytic mucoepidermoid carcinoma | Predominance of oncocyes showing granular eosinophilic cytoplasm along with large cystic structures lined by mucous cells, epidermoid cells, and intermediate cells | |
|       | —      | Unencapsulated foci of oncocytic cells appearing in multiple separate nodules. The lesion contains residual (nononcocytic) salivary gland parenchyma | Absence of epidermoid, mucous, and intermediate cells either focally or predominantly |
| (2)   | Oncocytosis | Encapsulated tumour exhibiting an organoid/alveolar growth pattern separated by thin fibrous connective tissue septa | Encapsulation. Absence of mucous, epidermoid, and intermediate cells |
| (3)   | Oncocytoma | Oncocytic cells exhibit pleomorphism. Infiltration into the salivary gland parenchyma in the form of trabeculae, sheets, and nests | Absence of mucous, epidermoid, and intermediate cells and presence of atypical features |
| (4)   | Oncocytic carcinoma | Encapsulated, presence of chondromyxoid areas, characteristic melting pattern seen | Encapsulation. Chondromyxoid areas, presence of ducts |
| (5)   | Pleomorphic adenoma | Papillary cystic lesion with bilayered oncocytic epithelium overlying lymphoid stroma | Absence of mucous cells, not infiltrative |
| (6)   | Warthin’s tumour | Forms a solitary mass or multiple nodules and invades in broad fronts. Predominantly cellular with less fibrous stroma. Tumour cells arranged in organoid sheets which are traversed by ramifying blood vessels. Prominent growth pattern: microcyst pattern | Absence of/minimal fibrous stroma. Absence of mucous cells, epidermoid, and intermediate cells |

Table 1: Difference between OMEC and other oncocytic lesions.
(3) Malignant lesions exhibiting oncocytes which include mucoepidermoid carcinoma and acinic cell carcinoma;

(4) Metastatic lesions with oncocytes which include hepatocellular carcinoma, thyroid carcinoma, and renal cell carcinoma [3].

As with all pathologies, adequate sampling of the excised specimen is needed to eliminate errors in diagnosis that may occur due to restricted/selective sampling.

The distinguishing features of these oncocytic lesions are summarized in Table 1.

Oncocytic MEC has been reported to occur most often in the parotid gland [6], followed by the submandibular gland [7], and only in 3 cases in the minor salivary glands. Of these cases, individuals from the 2nd to the 8th decade were affected with a slight male predominance. All cases of OMEC were of low grade showing large cystic spaces histologically with a good prognosis [4]. The pathogenesis of the oncocytic change in salivary glands has been attributed to degenerative cell changes, metaplastic transformation, or an adaptive/compensatory mechanism secondary to an undetermined somatic mutation [1].

A lesion showing predominance of oncocytes obscuring the classical histological features of the MEC may be difficult to diagnose based on routine histopathology. The primary aim would be to identify the lesion as malignant. Studies have shown that p63 is a reliable marker to help in the distinction of OMEC from other tumours. The rationale for using p63 in the diagnosis of OMEC is its expression in the epidermoid component of the conventional MEC as opposed to the peripheral staining pattern in oncocytoma and oncocytic carcinomas [3]. Recently, studies have shown that MECs result from a recurrent t(11;19)(q21;P23) translocation resulting in an MECT1-MAML2 fusion [8]. This fusion gene can be used to identify and arrive at a diagnosis of MEC in cases where the tumour is composed predominantly of oncocytes [9].

4. Conclusion

A pathologist must remain cognizant of the rare diagnosis of oncocytic mucoepidermoid carcinoma of the palate which has a good clinical prognosis. Although oncocytic changes are predominantly age-related or seen in benign lesions, similar change may be occasionally encountered in oncocytic carcinoma or oncocytic mucoepidermoid carcinoma. It may be worthwhile to additionally assess the expression of p63 in diagnosing these malignant oncocytic lesions especially in the absence of a reliable criterion to histopathologically differentiate metaplastic and neoplastic oncocytic lesions.

Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.