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Hyalinizing clear cell carcinoma of the base of the tongue

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Abstract
Clear cell carcinoma of the salivary glands is a rare tumour that represents less than one per cent of all salivary tumours. They are divided into a biphasic, epithelial-myoepithelial carcinoma and a monophasic pattern which may be myoepithelial or ductal in origin. The latter is accompanied by prominent fibrohyaline stroma and has been described recently as hyalinizing clear cell carcinoma (HCCC).

Most of the HCCC occur in the oral cavity, and are associated with minor salivary glands, unlike the biphasic pattern which is more common in the major salivary glands. In the oral cavity, the commonest site is the palate followed by the lips and the buccal mucosa. Its occurrence in the oropharynx and the larynx is extremely rare.

Key words: Tongue; Carcinoma

Introduction

Clear cell carcinoma of the salivary glands is rare and accounts for less than one per cent of all salivary tumours.[1,2] Uncertainty in the past as to its histogenesis and biological behaviour has resulted in a proliferation of terms for these neoplasms including clear cell adenoma, clear cell carcinoma, glycogen rich clear cell adenoma, glycogen rich clear cell carcinoma, tubular carcinoma, epithelial-myoepithelial carcinoma etc.

They can be divided into two distinctive patterns, a biphasic epithelial-myoepithelial carcinoma and a monophasic pattern that has been shown to be either myoepithelial or ductal in origin.[3] Milchgrub *et al*. have recently described the latter as hyalinizing clear cell carcinoma.[4] They found HCCC to occur more commonly in the minor salivary glands than in the major salivary glands. Of the 11 patients found to have the distinctive pattern, nine occurred in the minor salivary glands of the oral cavity (82 per cent). They are low grade malignant neoplasms with few reported cases of cervical lymph node metastasis.

Of the 200 cases of intraoral salivary tumours studied by Takahashi *et al*.,[5] seen in Japan, only one was diagnosed to have clear cell carcinoma. Intraoral salivary tumours were found to be more common in the palate followed by the lips and the buccal mucosa, accounting for 83 per cent of the cases. Such lesions were usually benign. The rest of the tumours occurred on the gingiva, floor of the mouth and the tongue and were predominantly malignant.

As clear cell carcinoma is so uncommon, the majority of the reports are isolated examples.[1] Its occurrence on the base of the tongue and the larynx is extremely rare. One such case occurring on the base of the tongue is reported for its rarity and unusual situation.

Case report

A 35-year-old male presented with a painless swelling in the throat along with a foreign body sensation of one year duration and change in voice of two months duration. Clinical examination revealed a three by two cm oval, smooth, raised yellowish-white lesion with prominent vessels running on its surface on the base of the tongue extending from the midline towards the right tonsillo-lingual sulcus, obscuring the view of the laryngeal inlet, (Figure 1). The mass was firm and non-tender on palpation. He had palpable jugulodigastric and submandibular lymph nodes on the right side, each about two by one cm, firm and non-tender.

Excision biopsy of the mass was performed using bipolar cautery aided by a broad microlaryngoscope and operating microscope. Histopathological examination showed groups and anastomosing cords of rounded to polygonal cells with clear cytoplasm in a hyalinized stroma. Periodic acid Schiff (PAS) phosphotungstic acid haemotoxylin (PTAH), and mucicarmine tests were carried out and cells were found to be positive for PAS. Immunochemistry was not performed as the majority was non-specific. For example, S100 can be strongly positive to absent. Although these tumours are cytokeratin and epithelial membrane antigen (EMA) positive, this does not differentiate them from other lesions that mimic HCCC.

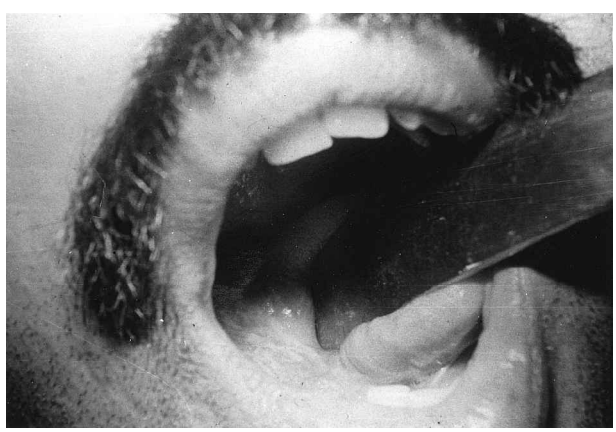

Fig. 1
Mass at the base of the tongue.

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After two weeks, a transcervical transmandibular approach for wide excision of the lesion was performed. The defect was reconstructed with a tongue flap. Resection was preceded by a supraomohyoid neck dissection and frozen section biopsy of the isolated nodes, that were uninvolved. The tumour was found extending to the right vallecula and into the musculature of the base of the tongue for approximately 2 cm. Histopathological examination reconfirmed the diagnosis with tumour free margins.

The patient was discharged on the 10th post-operative day without any complications. He has been followed up for one year post-operatively and has been found to be free of locoregional disease with good, acceptable speech.

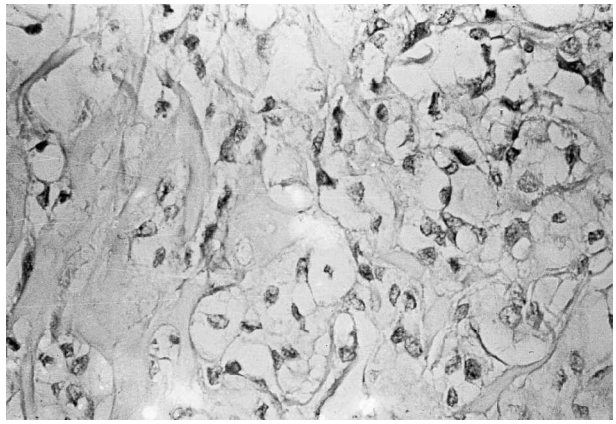

FIG. 2

Photomicrograph showing sheets of clear cells in a hyalinized stroma (H&E; ×400)

Discussion

Clear cell tumours of the oral cavity and the salivary glands constitute a heterogenous group of lesions which may be odontogenic, metastatic or salivary gland in origin. Odontogenic neoplasms, which may be characterized by a clear cell component, include odontogenic carcinoma, ameloblastoma and calcifying epithelial odontogenic tumour (Pindborg tumour). Most metastatic lesions occur from renal cell and thyroid cell carcinomas and rarely from the prostate, bowel or the liver. Clear cell tumours of salivary origin are usually malignant except for oncocytoma and myoepithelioma. Malignant salivary tumours with clear cells include acinic cell carcinoma, mucoepidermoid carcinoma and the clear cell variant of myoepithelial carcinoma. There are some unclassifiable malignant clear cell salivary tumours, for which the descriptive term clear cell carcinoma is used.[3,6]

The clear cells in the clear cell tumours contain glycogen, mucin or lipids, or they may be fixation artefacts. Special stains, immunohistochemistry and electron microscopy help in distinguishing the different clear cell tumours of the salivary glands and the oral cavity.[6–9] HCCC is a new but distinct and rare salivary neoplasm which frequently occurs in the minor salivary glands, intraorally.[9] Common intraoral sites include the palate, followed by the lips and the buccal mucosa. Its occurrence in the oropharynx and the larynx are very unusual.[10]

This monophasic type of clear cell carcinoma (HCCC) has prominent fibrohyaline stroma and is distinct from its biphasic variant, the epithelial-myoepithelial carcinoma.[6] The latter, unlike the former, is more common in the major salivary glands. It is more common in the sixth and the seventh decades and women are affected twice as often as men. They show a 35 per cent incidence of local recurrence and few patients have had regional and distant metastases.[7] The intraoral clear cell carcinoma which is usually HCCC in type, has low malignant potential, low recurrence and long survival rates.[11] It is also more common in women and few cases of cervical lymph node metastasis have been reported.

Microscopically, HCCC is characterized by the formation of trabeculae, cords, islands, and nests of monomorphic clear cells that are glycogen rich and mucin negative and are surrounded by hyalinized bands with foci of myxohyaline stroma (Figure 2). Cells with eosinophilic and granular cytoplasm are also noted. Both cell types show minimal nuclear pleomorphism and a very low mitotic index with infiltrative borders. Immunohistochemically, the tumour cells express cytokeratins and epithelial membrane antigen. Ultrastructurally, the tumour cells contain abundant glycogen, desmosomes, peripheral tonofilaments and prominent interdigitating microvilli with actin myofilaments and dense bodies, providing evidence of epithelial differentiation without myoepithelial differentiation.

The differential diagnosis in the case of the tongue should include follicular carcinoma with clear cell change arising in a lingual thyroid,[12] clear cell carcinoma arising from a pleomorphic adenoma of the minor salivary gland[2] as well as metastatic renal cell carcinoma. In metastatic renal cell carcinoma, the tumour cells are clear and have intracytoplasmic glycogen which is PAS positive, but differentiating factors from HCCC include the presence of heterogenous architecture, increased vascularity, and presence of intracytoplasmic lipid.

Of the 55 cases of salivary tumours of the tongue studied by Goldblatt *et al*., only eight per cent were found to have clear cell carcinoma.[13] Goldblatt describes four cases of clear cell carcinoma among 50 malignant salivary gland tumours of the tongue. He does not give any breakdown for these carcinomas, (HCCC), in terms of site, age or sex. Follow-up information was available for three of the four cases. Two were alive five and 10 years respectively after treatment. The first was treated by resection of the posterior one-third of the tongue and the second by hemiglossectomy and radium implant. The third patient died three weeks after tongue biopsy due to an unrelated cerebral haemorrhage. The fourth was lost to follow-up.

As clear cell carcinoma is rare, very few treatment protocols have been described. Being a tumour of low malignant potential, wide surgical resection is the treatment of choice with, or without, pre/post- operative radiotherapy.[1,4] The latter is reserved for those with recurrent lesions, or for those with lymph node metastasis.

Our case of HCCC was seen in a young male and was successfully treated by wide excision by the transcervical – transmandibular approach and the defect was reconstructed by a tongue flap. The resection was preceeded by a supraomohyoid neck dissection and frozen section biopsy of the lymph nodes. Considering its low malignant potential, and uninvolved resected margins and lymph nodes, post-operative radiotherapy was not considered. The patient was followed up for one year post-operatively and was found to have no locoregional disease. A regular follow-up is needed as recurrences are known even several years after the primary treatment.

Conclusion

A case of HCCC in the base of the tongue is reported for its rarity and unusual presentation. These are low grade malignant neoplasms with good prognosis. The treatment

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of choice is wide excision with, or without, radiotherapy. As lymph node metastasis is known, a selective neck dissection with frozen section biopsy is desirable.

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