Hyalinizing Clear Cell Carcinoma of Palate—A Case Report

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Abstract

Clear cell carcinoma of the salivary glands is a rare tumor that represents less than one per cent of all salivary tumors. They can divided into a biphasic, epithelial-myoepithelial carcinoma or a monophasic pattern which may be myoepithelial or ductal in origin. Hyalinizing clear cell carcinoma (HCCC) of the salivary gland is a new disease that is only recognized in recent years. It is rare and the standard treatment is still under investigation. This is a report of a 64-year-old female with HCCC who presented with a painless submucosal mass over hard palate mass. Because of its rarity, it was presented and the diagnosis and treatment of this disease were discussed.

Key words: Salivary gland neoplasms, Hyalinizing clear cell carcinoma

INTRODUCTION

Clear cell carcinoma of the salivary gland has been described in the English literature in 1980 by Batsakis.¹ Salivary gland neoplasms composed predominantly of clear cells include various other lesions such as mucoepidermoid carcinoma, acinic cell carcinoma, myoepithelioma and oncocytoma, but they can be recognized by their specific histological features.² Then Chen classified clear cell carcinomas according to their morphology into two subgroups: (a) a biphasic variant composed of eosinophilic cells and clear cells with a double layered arrangement, and (b) a monophasic variant composed solely of clear cells.³ Recently, Milchgrub et al.² designated the latter subgroup as hyalinizing clear cell carcinoma.

Hyalinizing clear cell carcinoma (HCCC) is a recently described neoplasm predominantly affecting the oral cavity in adult females.² HCCC of the salivary glands is rare and accounts for less than one percent of all salivary tumors.⁴,⁵ Of the 200 cases of intraoral salivary tumors studied by Takahashi et al.⁶ in Japan, only one case of HCCC was diagnosed. The tumor cells
are characteristically clear and the stroma have areas of hyalinization. These cells are positive for cytokeratin and negative for S100 protein and smooth muscle actin. This immunohistochemical staining differentiates it from other salivary gland tumors. In that it shows predominantly clear cell component. This finding also indicates that HCCC is composed only of epithelial cells.\(^\text{2,7}\) It is considered to be a low-grade indolent neoplasm, due to rare recurrence and metastasis.\(^\text{8,9}\) Because HCCC is so rare, the presented reports are isolated examples.\(^\text{2}\) One such case over hard palate is reported for its rarity and unusual situation.

## Case report

A 64-year-old female came to our department for help due to a slow growing mass over upper hard palate for several months. Tracing her previous medical record, she had ever came to our dental department for help on 2002/9/27. At that time, chronic periodontitis of left maxillary second molar was impressed, local debridement and antibiotics were applied. At that time, the dentist had suggested her to extract that tooth, but she refused. After that appointment, this patient was loss further follow-up. Until 2004/3/12, she came back to our hospital again with the same symptom. So she was referred to our department for further treatment.

Under clinical examination, she had a symmetrical outline and normal mouth opening.\(^\text{2}\) A firm, indurated swelling mass about 1.5 x 1.5 cm over the palatal side of left maxillary second molar was noted.\(^\text{2}\) The mass was non-tender when palpated, and no specific palpable enlarged lymph node over neck was noted.

Apical film and panoramic film were taken to evaluate the dental and bony status of maxilla. Bony destruction about 1.5 x 1.5 cm and root resorption of left maxillary second molar were found.\(^\text{2}\) Compared with the previous apical film of the same region, a new locus of bony destruction over that region was found.

Incisional biopsy was performed and computed tomography was arranged at that time. Through computered tomography, a focal soft tissue tumor with destruction on left hard palate about 1.5 x 1.5 x 1.5 cm in size was discovered. Multiple subcentimeter lymph nodes were also seen in bilateral submandibular areas.\(^\text{2}\) Histopathological examination showed a tumor having hyalinizing clear cell carcinoma over left palate from minor salivary glands. She was admitted for general assessment and surgical treatment. Tracing her medical history, she had lumbosacral spondylosis, peptic ulcer and lipoma excision. No relevant family history was noted. Vital signs and the review of laboratory test were within normal limits. Chest film, abdominal echo, and TC-99M MDP whole body bone scans showed no sign of distant metastasis.

She received surgical treatment on March, 2004. The operative procedures were wide excision with maxillectomy by Weber Furgerson incision and suspected lymph nodes sampling over left submandibular region. The post-operative defect was measured about 5.5 x 4 cm over left maxilla, which was repaired with pedicle buccal fat pad flap.

## HISTOPATHOLGY

Under microscopic examination, it showed clear cells arranged in anastomosing thick trabeculae, cords, nests, or solid sheets within
a hyalinizing stroma. There were also a few eosinophilic cells. (Fig 5a,b) The tumor tissue had no connection with the overlying squamous epithelium. The tumor cells showed groups and anastomosing cords of rounded to polygonal cells with clear cytoplasm in a hyalinized stroma. It showed immunoreactivity for cytokeratin, but negative to mucin. Eosinophilic cytoplasm showed intracytoplasmic PAS-positive granules (salivary glands origin), This is not found in the clear cells (Fig 6).

The defect was repaired with buccal fat pad. The final pathological report that was a hyalinizing clear cell carcinoma of minor salivary gland, and all the section surface were free of tumor including neck lymph nodes(0/6).

The patient was discharged on the 14th post-operative day without any complications. (Fig 7a,b) She has been followed up periodically for one year post-operation and was free of locoregional recurrence. The speech function was acceptable.

**DISCUSSION**

The clear cells in the clear cell tumors contain glycogen, mucin or lipids. Clear cell tumors in the oral cavity constitutes a heterogenous group of lesions which may be odontogenic, metastatic or salivary gland in origin. Odontogenic originated neoplasms, which may be characterized by a clear cell component, include odontogenic carcinoma, ameloblastoma and calcifying epithelial odontogenic tumor (Pindborg tumor). Most metastatic in such character were derived from renal cell and thyroid.
Fig. 2. Compared with the previous film of the apical region of left maxillary second molar, apparent bony destruction truly exist as time goes by.
Fig. 3. Bony destruction about 1.5 x 1.5 cm in size over left posterior maxilla and root resorption of left maxillary second molar (2004/03).

Fig. 4. A focal soft tissue tumor with bony destruction of left hard palate about 1.5 x 1.5 x 1.5 cm in size (white arrow).
Fig. 5a. A pseudocapsule solid tumor with intact hard palate mucosa (H&E, 40X).

Fig. 5b. Clear cells (wide arrow) and eosinophilic cells (narrow arrow) are separated by variable amounts of hyalinized stroma (H&E, 200X).
Fig. 6. Eosinophilic cells (narrow arrow) show intracytoplasmic PAS-positive granules (salivary glands origin), but not found in the clear cells (wide arrow) (PAS, 200X).

Fig. 7a. 6 months later after tumor excision.
cell carcinomas and rarely from the prostate, bowel or the liver. Clear cell tumors of salivary gland origin are usually malignant including acinic cell carcinoma, mucoepidermoid carcinoma and the clear cell variant of the myoepithelial carcinoma.

HCCC is a new and rare salivary gland neoplasm which occurs in the intraoral minor salivary glands.\textsuperscript{(10)} From 1994 to 2004, only 13 cases of salivary glands were published in the English literatures.\textsuperscript{(2,13,14)} It happens more commonly in the sixth and the seventh decades and women are affected twice as often as men. 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.\textsuperscript{(11)} 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. Cells with eosinophilic and granular cytoplasm are also noted. They show minimal nuclear pleomorphism and a very low mitotic index with infiltrative borders. Immunohistochemically, the tumor cells express cytokeratins and epithelial membrane antigen. The special and immunohistochemical stains were essential for the definitive diagnosis. The clear cells were glycogen–rich and showed a positive PAS reaction and negative Congo–red amyloid staining. Myoepithelial antigens (smooth muscle actin, musclespecific actin, and S–100 protein) are not expressed in HCCC. Mucin stain, positive in mucoepidermoid carcinoma is negative in HCCC. These findings are useful to rule out any other possible neoplasms that present with clear cell morphology.

Fig. 7b. 6 months later after tumor excision.
Ultrastructurally, the tumor cells contain abundant glycogen, desmosomes, peripheral tonofilaments and apparent interdigitating microvilli with actin myofilaments and dense bodies, providing evidence of epithelial differentiation without myoepithelial differentiation. As clear cells are known to be present in many salivary gland tumors, demonstration of CK positivity and S100 and SMA negativity would be necessary for a diagnosis of HCCC\(^{(12,13)}\). The tumor cells are also positive for carcino- embryonic antigen (CEA) and epithelial membrane antigen (EMA).

The differential diagnosis of tumor mass over palate should include pleomorphic adenoma of the minor salivary gland\(^{(5,11)}\) 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 absence of heterogenous architecture, increased vascularity, and intracytoplasmic lipid as found in HCCC.

Nowadays, limited experience of this pathology leads the authors to consider HCCC as a low-grade malignancy. Distant metastasis has been reported only in one case in the literature, in which a primary lesion in the hypopharynx had metastasized to the lung.\(^{(15)}\) As clear cell carcinoma is rare, few treatment protocols have ever been described. Being a tumor of low malignant potential, wide surgical resection is the treatment of choice with, or without, pre/post-operative radiotherapy. A regular follow-up is needed as recurrences are known to occur even after several years following the primary treatment.

Our case of HCCC was happened seen in an old female and she was successfully treated by wide excision and the defect was reconstructed by buccal fat pad. Due to its low malignant potential, and uninvolved resected margins without lymph nodes metastasis, post-operative radiotherapy was not considered. The patient was followed up for one year post-operatively and was found to have no locoregional recurrence up to date.

**CONCLUSION**

In conclusion, HCCC is a rare salivary gland neoplasm. The clinical course is slowly progressive. Because it is considered as a low-grade malignancy, wide excision is the treatment of choice nowadays. Adjuvant radiotherapy may be unnecessary if the lesion is excised with an adequate safety margin.

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硬顱唾液腺透明細胞癌之一病例報告

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摘要
唾液腺透明細胞癌是一個十分罕見之唾液腺腫瘤，估所有唾液腺腫瘤不到百分之一的比例。在組織學之特徵上合併有上皮與肌上皮癌兩種組織。此外這種腫瘤也可以只含有肌上皮或唾液腺管單一組織來組成。唾液腺透明細胞癌是近幾年才被確立之唾液腺惡性腫瘤，且由於病例十分罕見，故目前並無一個明確之標準治療方式。本篇報告提出一位64歲女性罹患硬顱唾液腺透明細胞癌經手術治療及門診追蹤之後，目前狀況穩定，並將此患者的病程作爲日後討論及研究的參數。

關鍵詞：硬顱唾液腺。