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Hyalinizing clear cell carcinoma of the hard palate

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Abstract
Hyalinizing clear cell carcinoma (HCCC) of the salivary gland is new disease only recognized in recent years. It is rare and the standard treatment is still under investigation. This is a report of a 42-year-old female with HCCC who presented with a painless submucosal hard palatal mass of three years duration. Wide excision of the tumour and the underlying palatal and maxillary bones was performed. Pathological examination revealed typical clear cells arranged in anastomosing trabeculae, cords, nests, or solid sheets with a hyalinizing stroma. These clear cells were positive for the periodic acid-Schiff (PAS) reaction but were negative for the mucin stain. Immunohistochemically, these neoplastic cells were positive for cytokeratin, but negative for actin. No recurrence nor distant metastasis was found during the eight-month follow-up period.

Key words: Salivary Gland Neoplasms; Carcinoma, Hyalinizing Clear Cell

Case report

A 42-year-old female presented with a painless submucosal mass of the hard palate which had been present for three years. It was enlarging gradually and, on presentation, had reached 2 cm in diameter. The lesion was located in the right hard palate near the border with the soft palate. There was no erosion, bleeding or ulceration of the overlying mucosal surface (Figure 1). A detailed examination of the head and neck revealed no other abnormal findings and no lymphadenopathy was noted. Endoscopic examination showed the nasal cavity to be intact.

Computed tomography (CT) scans showed a 2×2 cm well-defined mass in the hard palate close to the soft palate but without evidence of bony destruction. However, it was noted that the distance between the mass and the bone of the hard palate was very short (Figure 2). The CT images showed no significant enlargement of the lymph nodes in the neck. An incisional biopsy was performed and reported as HCCC, a rare salivary neoplasm. General evaluation including a chest X-ray, Technetium^{99m} whole body bone imaging and abdominal sonography showed no evidence of distant metastasis. It was, therefore, concluded that the palatal mass was a primary lesion and not a metastatic locus arising from a primary lesion elsewhere.

The tumour was treated surgically with a wide excision through a direct, intra-oral approach. The underlying palatal bone and maxilla were also excised to give an excision margin of 1 to 2 cm. The palatal defect was reconstructed with an obturator prosthesis after meticulous haemostasis.

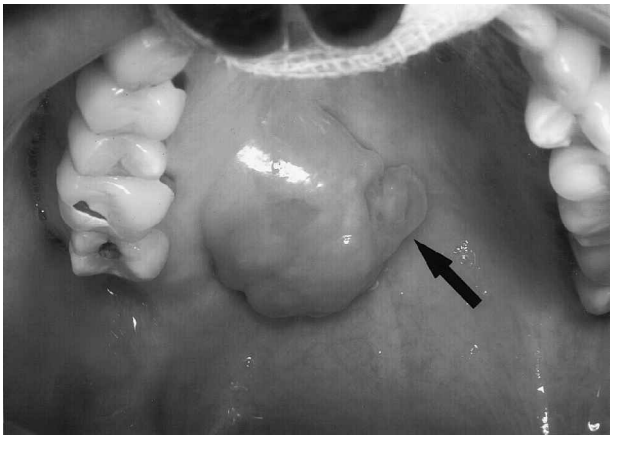

Fig. 1
Pre-operative tumour appearance. A submucosal mass of right hard palate with a biopsy defect (arrow) is shown.

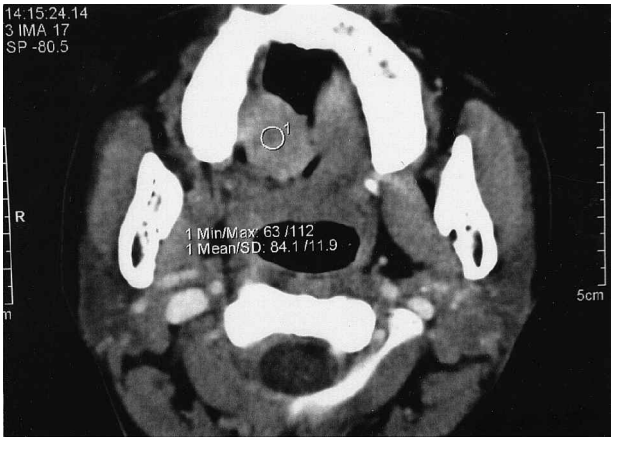

Fig. 2
An axial view of CT scan. A 2×2 cm homogenously enhanced mass locates on the right hard palate near the gingival process of the right maxilla.

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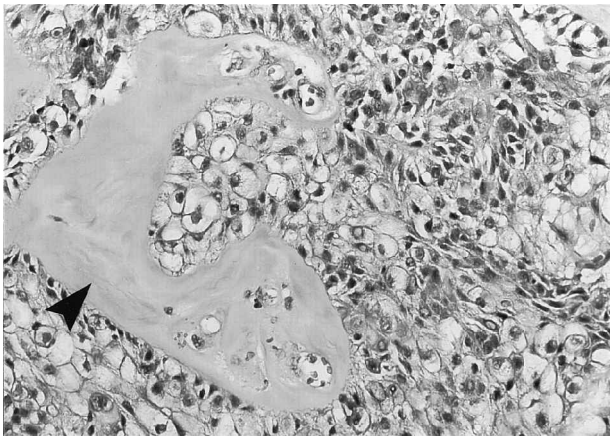

FIG. 3

Photomicrograph of clear cells and some eosinophilic cells arranged in anastomosing thick trabeculae, cords, nests, or solid sheets with a hyalinizing stroma (arrow head). (H & E; ×400)

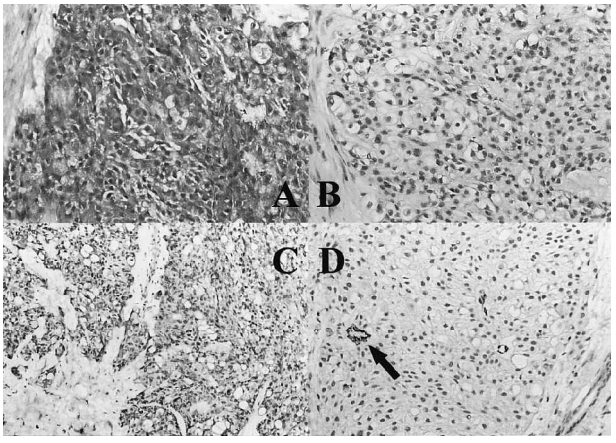

FIG. 4

Special stains of the clear cells reveal strong reaction for PAS (A) but negative for mucin stain (B). Immunohistochemically, these neoplastic cells are positive for cytokeratin (C), but negative for actin (D) (Avidin-biotin complex method, DAB as chromogen). The internal control (arrow), the vessel, is positive for actin (×100)

Grossly the tumour was firm, measuring 2.5 × 2 × 1 cm beneath the oral mucosa. The cut surface was yellowish white and elastic. The tumour was relatively well circumscribed but, on careful inspection, was locally infiltrative. Microscopically, it showed clear cells arranged in anastomosing thick trabeculae, cords, nests, or solid sheets within a hyalinizing stroma (Figure 3). There were also a few eosinophilic cells. The mass had no connection with the overlying squamous epithelium and was infiltrative at the margins. The surgical excision margins, palatal and maxillary bones were free of tumour. The neoplastic cells were positive for the periodic acid-Schiff (PAS) reaction but negative for the mucin stain (Figures 4(a) and 4(b)). Immunohistochemically the neoplastic cells were positive for cytokeratin (Novocastra, Newcastle, UK; mouse monoclonal, clone AE1/AE3) but negative for actin (Zymed, San Francisco, CA, USA; mouse isotype: IgG1, clone ZAC34) (Figures 4(c) and 4(d)). Mitotic figures with one to two mitoses per 10 high power fields were noted in only one area of the sections examined. The whole specimen demonstrated the homogeneous appearance described above and there was no evidence of any other concurrent pathology.

The patient has been followed up for eight months after operation with no evidence of recurrence or distant metastasis.

- **Hyalinizing clear cell carcinoma (HCCC) of a salivary gland is a new disease entity**
- **The palatal tumour was widely excised together with the underlying palatal and maxillary bones**
- **The histology and immunohistochemistry are described**
- **No local or distant recurrence has been found at eight-months follow up**

Discussion

HCCC is a rare salivary gland neoplasm occurring predominantly in adult females.[1] Most cases originate from the minor salivary glands. The oral cavity, including the base of tongue and palate, is the most common site.[1–3] This case was also an adult female who presented with a painless tumour of the hard palate. After the initial report which included 11 cases, very few additional cases have been reported. Rare cases had been reported in the larynx, nasopharynx, hypopharynx, mandible and maxilla.[1,4–6]

Clinically, as with this case, HCCC usually presents as a slowly growing and painless submucosal mass. Local regional lymph node metastasis has been found in only a few cases. In their first report of HCCC, Milchgrub *et al.* reported cervical lymph node metastasis in only two out of a total of 11 patients.[1] Interestingly, these two patients with histological evidence of mitotic figures were the only cases with cervical lymph node metastasis. Our case presented without cervical lymph node metastasis. However, mitotic figures were noted in one area. Furthermore, no palpable cervical lymph node metastasis was detected during the eight-month follow-up period. This is contrary to the previous literature.

To date, limited experience of these lesions leads the authors to consider HCCC as a low-grade malignancy. Distant metastasis has been reported only in one case where a primary lesion in the hypopharynx metastasized to the lung.[6] The indolent clinical course suggests that local wide excision with, or without, radiotherapy may be the treatment of choice. On histopathological examination, a 1 to 2 cm safety margin was adequate for complete excision of the neoplasm in this case. This may prove to be a useful guide for head and neck surgeons. Post-operative radiotherapy has been performed in some reported cases. Nevertheless, it may be unnecessary when the tumour is removed with a wide margin of surgical clearance.

Pathologically, this case demonstrated a special feature of HCCC, infiltrative clear cells arranged in anastomosing thick trabeculae, cords, nests, or solid sheets within a hyalinizing stroma. Eosinophilic cells were found less frequently. The differential diagnosis of HCCC includes epithelial-myoepithelial carcinoma, acinic cell carcinoma with extensive clear cell change, mucoepidermoid carcinoma, clear cell oncocytoma, sebaceous carcinoma, metastatic renal cell carcinoma, pleomorphic adenoma, and Pindborg tumour. The use of 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, muscle-specific actin, and S-100 protein) are not expressed in HCCC. Mucin stain, positive in mucoepidermoid carci-

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noma is negative in HCCC. These findings rule out other possible neoplasms that present with clear cell morphology. In addition, although rare, clear cell carcinoma can arise in pleomorphic adenoma of a minor salivary gland.[7] Therefore, great care should be taken to exclude other concurrent pathologies occurring in the specimen. Our report demonstrated a HCCC arising *de novo*.

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

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