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Clear cell neoplasm

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Abstract

We are reporting four cases of clear cell neoplasm. Local infiltration and destruction was observed in one case while in a second case, originating in the sublingual gland, metastasis to the lymph nodes occurred. The behaviour of these neoplasms has prompted the suggestion that these tumours be designated carcinomas rather that noncommittally tumours or neoplasms (Batsakis and Regezzi, 1977).

The histopathological characteristics of our four cases conform to those that have been articulated and believed to be the distinctive features of these tumours (Batsakis and Regezzi, 1977). It is hoped that ours and similar reports will be helpful towards clearing the diagnostic and taxonomic confusion regarding these tumours.

Introduction

Clear cell neoplasms of the minor and major salivary glands are uncommon. They reportedly constitute less than one per cent of all primary tumours of the salivary glands (Klijanienco *et al.*, 1989). These tumours are thought to be distinct entities characterized by the presence of two cell forms, an inner epithelial component presumed to originate from the intercalated ducts and the outer layer usually containing glycogen and presumed to originate from the myoepithelial cells (Batsakis, 1980). Their histopathological appearance varies greatly depending on the relative presence of the two cell components (Saksela *et al.*, 1972; Batsakis, 1980; Luna *et al.*, 1985; Singh *et al.*, 1988). Their behaviour spans a broad range from benign to aggressive with local and distal metastases (Corridan, 1956; Singh and Cawson, 1988; Palma and Blandamura, 1989). Because of the variable histopathological appearance and clinical behaviour, they have been reported by a variety of names. Furthermore, most if not all of these non-mucinous, glycogen and non-glycogen containing tumours should be considered 'at least low grade malignancies' (Batsakis and Regezzi, 1977).

What seems to add to the difficulty in the diagnosis of individual tumours is the fact that, histopathological clues of metastasis are lacking (Batsakis and Regezzi, 1977). There are those who believe, however, that the degree of differentiation of the cellular component, as discerned by light microscopy, correlates well with the behaviour of these tumours (Singh and Cawson, 1988).

With respect to their cell of origin, the intercalated duct cell of the salivary glands has been mentioned as its progenitor (Corridan, 1956; Chaudhry *et al.*, 1983; Klijanienco *et al.*, 1989), while others suggest the myoepithelial cells 'on the basis of morphological criteria' (Saksela *et al.*, 1972). It has been pointed out, however, that this begs the question since the semipluripotential characteristics of the intercalated duct cells enable them to give rise to ductal, acinar and even myoepithelial cells (Batsakis and Regezzi, 1977).

Case reports

Case 1

A 58-year-old white woman presented to the clinic of our dental school seeking routine dental care. The patient's past medical history was positive for hypertension and allergy to penicillin. She did not smoke and drank only one mixed drink per month.

During our preliminary examination a largely submucosal mass measuring 1.5 × 0.7 × 0.5 cm was palpated originating in the left half of the soft palate and extending toward but not involving the anterior tonsillar pillar. There were no palpable lymph nodes in the neck. The lesion was slightly mobile and asymptomatic. The patient was not aware of its presence. An incisional biopsy was initially read as adenocarcinoma of the soft palate and re-interpreted as acinous carcinoma of minor salivary gland origin. A second opinion was sought. The entire tumour was now surgically extirpated and the surgical wound was repaired with a buccal flap and split thickness skin graft. A nasopharyngeal CT scan showed an asymmetry of the soft palate with soft tissue prominence on the left side. CT scan of the upper abdomen showed normal kidneys. The histological examination of the resected tissue reads, in part as follows:

The tumour is present in the tunica propria of the palate without involvement of the overlying epithelium. The neoplasm is composed of solid sheets of cells with abundant vacuolated to clear cytoplasm and relatively small hyperchromatic nuclei with only slight pleomorphism. Mitotic activity is infrequent. In some areas there are remnants of ductal structures and myoepithelial elements. The tumour is mucicarmine negative but tumour cells do contain small amounts of PAS positive diastase sensitive material in the cytoplasm. The diagnosis was clear cell neoplasm of probable low grade malignant potential.

No further treatment was performed following surgery. The patient has been free of disease for 31 months.

Case 2

A 69-year-old white woman presented with a freely mobile module in the left anterior maxillary vestibule measuring 0.8 × 1.0 × 1.0 cm. The lesion according to the patient, had been there for several years. No palpable facial or cervical lymph nodes were detected. The patient's medical history was positive for asthma and insulin-dependent diabetes mellitus. Following an excisional biopsy that was interpreted as a clear cell neoplasm, the patient was referred to one of the local hospitals for systemic evaluation and follow-up.

Histological examination of the resected tissue revealed sev-

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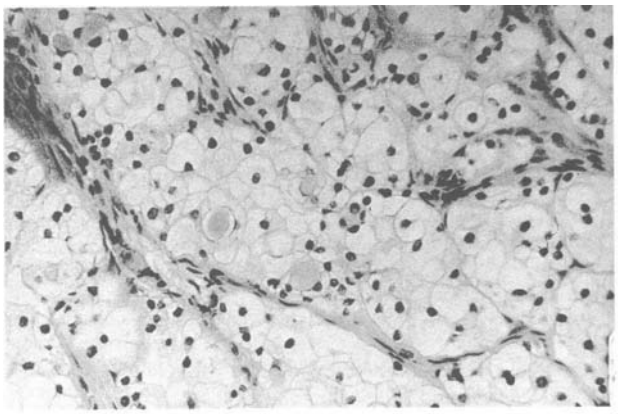

Fig. 1

eral well-demarcated sheets of epithelial tumour cells, interspersed focally with chronic inflammatory cells. The tumour cells exhibited clear cytoplasm with small, dark, isomorphic nuclei, and infrequent mitotic activities. Trabecullae of fibrous connective tissue separated the tumour masses from adjacent normal glandular tissue. PAS stains, both with and without diastase digestion were negative. CT scan of the abdomen and excretory urogram revealed a cyst on one kidney, but there was no evidence of renal carcinoma. A diagnosis of clear cell carcinoma was made. No further treatment was rendered and the patient was free of disease five months after surgery (Fig. 1).

Case 3

A 70-year-old black woman, had a mass in the right sublingual salivary gland which had been diagnosed as an adenocarcinoma in 1977. The tumour, sublingual and submandibular glands, and the cervical lymph nodes on the right side were removed. Microscopic examination revealed the lesion to be composed primarily of clear cells with no squamous component, leading to a diagnosis of clear cell carcinoma with metastasis to the lymph nodes. Eleven years later, the patient returned, complaining of a painless enlargement of the floor of the mouth in the right mandibular region, in association with severely mobile teeth and erythematous gingivae.

Histological examination of the biopsy of the soft tissue lesion from the floor of the mouth revealed syncytial masses of large, clear epithelial cells containing small, eccentric nuclei. Cellular pleomorphism and mitotic activity were not prominent. A PAS stain produced focal intense reaction in several of the clear tumour cells but prior application of diastase prevented staining of these cells with PAS. The final diagnosis was recurrent clear cell carcinoma. Although referred for definitive treatment of the neoplasm, the patient did not return and has been lost to follow-up (Fig. 2).

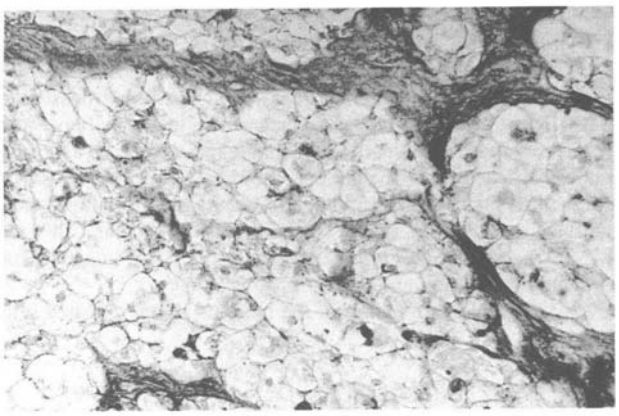

Fig. 2

Case 4

A 56-year-old white male complained of swelling on the posterior right side of the hard palate for several months. On clinical examination a 3.0 × 5.0 cm ulcerated area was identified in the right posterior palate. Radiographic evidence of some bone destruction was seen. During surgical extirpation of the lesion destruction of the greater palatine canal was found. The lesion itself had a necrotic centre.

Histological examination of the specimen revealed multiple lobules of neoplastic cells extending throughout the lamina propria. The lobules were composed of sheets and strands of epithelial cells with clear or faintly granular cytoplasm. The cells exhibited large, ovoid nuclei with prominent nucleoli, but mitotic activity and cytological pleomorphism were not detected. The diagnosis was clear cell neoplasm of minor salivary gland origin. The patient was lost to follow-up after surgery (Fig.3).

Discussion

Clear cell tumours of the salivary glands are rare (Spiro *et al.*, 1973). Consequently, the accumulated experience regarding these tumours, even in major diagnostic and treatment centres, is small.

To complicate matters further, their morphology is variable, and there is yet to be broad agreement on the progenitor cells. It is not surprising, therefore, that these tumours are reported under a variety of diagnostic terms.

Beyond the light-microscopy structural descriptive interpretation, ultrastructural studies, histochemical and immunochemical studies have been utilized in the study of these tumours. Several observations have thus been made. Firstly, a biphasic cellular composition consisting of cells similar structurally to the intercalated ductal epithelium, and cells structurally akin to the myoepithelial cells. The relative position of these cell types with an interposed hyalin-like ground substance is reminiscent of the normal gland. It is claimed that 'the combination of the two cell types, the matrix, and glycogen-positivity (often seen in the myoepithelial derived cells) is not duplicated by any other defined salivary gland neoplasm' (Batsakis, 1980).

With respect to biological behaviour, clear cell neoplasms of the major and minor salivary glands are thought to be low grade malignancies (Batsakis and Regezzi, 1977) because in spite of their benign appearance they are capable of local infiltrative growth and destruction as well as metastasis with poor prognosis (Batsakis and Regezzi, 1977; Klijanienco *et al.*, 1989). However, their ability to metastasize is thought to be unpredictable by some due to the lack of histopathologic markers (Batsakis and Regezzi, 1977) while others have voiced the view that aggressivity and metastatic potential correlate well with the degree of cellular differentiation, as discerned by light microscopy (Singh and Cawson, 1988).

The four cases we are contributing to the literature conform

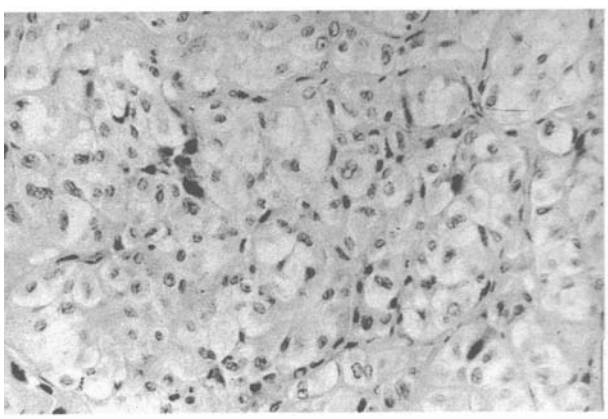

Fig. 3

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both morphologically and behaviourally with previous reports. Our findings support the view that morphological clues to the behaviour of these tumours are not readily discerned. There is ample evidence in the literature to demonstrate the broad behavioural range of these neoplasms. In a report of 16 cases of epithelial-myoepithelial carcinoma, another designation of clear cell neoplasm, over a seven year period, out of eight patients on whom follow-up information could be obtained, five reported recurrences ranging from nine months to 28 years from the time of diagnosis. In one case, metastasis to the kidneys was responsible for the patient's death (Corio *et al.*, 1982).

A case of clear cell carcinoma of the larynx, thought to be derived from minor salivary glands, metastasised to the adjacent lymph nodes. Its behaviour was aggressive resulting in the patient's death 10 months following the diagnosis (Palma and Baldamura, 1989).

The case of Klijanienco *et al.* cited above, a clear cell carcinoma of the soft palate which had arisen from a pleomorphic adenoma, metastasized to the pharynx. Following surgery and radiotherapy, however, no recurrence was noted one year after termination of therapy.

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