Pergamon

Oral Oncol, Eur J Cancer, Vol. 32B, No. 3, pp. 210–212, 1996

Printed in Great Britain
0964–1955/96 $15.00 + 0.00

0964-1955(95)00096-8

Granular Cell Ameloblastoma: a Case Report with Histochemical Findings

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A case of granular cell ameloblastoma (GCA) was studied by light microscopy and histochemistry. Microscopically, the lesion showed small groups or large clusters of granular neoplastic cells, with pyknotic and hyperchromatic nuclei, oriented away from the basement membrane, in a back-to-back arrangement. The "granular change" is thought to be due to a dysfunctional status of neoplastic cells, and the pathogenesis of this tumour seems to be age-related. The prognosis of GCA is good, generally corresponding to that of the classical ameloblastoma; as yet, only one case has been described with a more aggressive biological behaviour (high recurrence rate). Copyright © 1996 Elsevier Science Ltd

Keywords: granular cell ameloblastoma, lysosomes

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INTRODUCTION

Various oral tumours, such as granular cell ameloblastic fibromas, granular cell ameloblastomas (GCA), granular cell tumours and congenital epulides may be composed of granular cells [1]. The granular cells show the same morphology in all these lesions of the oral cavity, even if their origin is different.

In particular, the neoplastic cells exhibiting prominent cytoplasmic granularity in GCAs [2, 3], which account for only 5% of all ameloblastomas [2], arise from ameloblasts [4, 5]. Ultrastructural [2, 4, 5] and histochemical [2, 6] studies suggest that their granules are lysosomes [1, 2, 5, 6].

We report a histological and histochemical study of a case of GCA, with 3-years follow-up data.

CASE REPORT

A 44-year-old man was admitted to the Institute of Dental Discipline of the University "Federico II" of Naples, Italy, in January 1990, with a history of a painless swelling which had arisen a few months before in the left maxillary region. Clinical examination revealed a well-circumscribed swelling, which radiographically appeared as a large, multilocular radiolucency, located between the canine and the first molar of the left upper jaw (Fig. 1).

The patient was treated with conservative surgery and the healing process proceeded normally without any signs of recurrence 3 years later.

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Received 5 Jan. 1995; provisionally accepted 30 Aug. 1995; revised manuscript received 13 Dec. 1995.

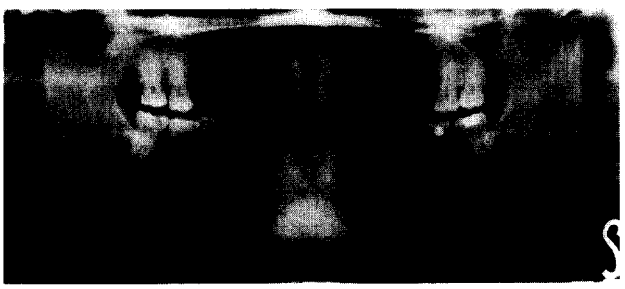

Fig. 1. Radiograph showing a large, multilocular radiolucency, located between the canine and the first molar of the left upper jaw.

Histopathological examination of the lesion revealed an ameloblastoma of the granular cell type.

HISTOLOGICAL FINDINGS

Sections from formalin-fixed paraffin-embedded representative blocks were stained with haematoxylin and eosin.

Histologically, the lesion was composed of nests or organoid clusters of neoplastic cells embedded in a fibrous stroma. Tumoral nests were constituted peripherally by elongated ameloblastic cells, and centrally by large, eosinophilic, granular cells (Fig. 2). The epithelial cells of clusters typically showed polarisation of their nuclei to the distal ends, with a palisading arrangement (Figs 3, 4). The granular cells, occurring in small groups or large islands, showed cell outlines, usually clear, but varied considerably both in size and shape. Their nuclei were pyknotic and hyperchromatic and

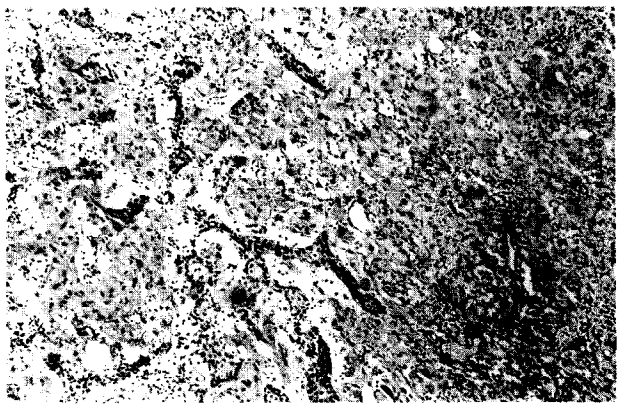

Fig. 2. Granular cell ameloblastoma. The lesion consisted of strands of elongated epithelial cells and granular neoplastic cells with clear cytoplasm (HE, × 150).

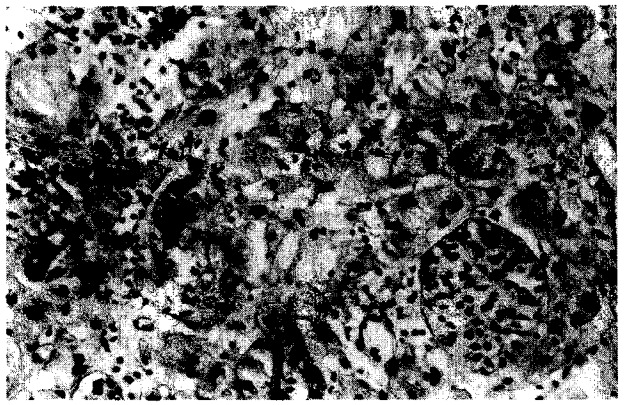

Fig. 3. Granular cell ameloblastoma. The epithelial cells of the tumour showed palisading and polarisation of the nuclei toward the distal ends. Large, eosinophilic, granular cells occurred in small groups or large clusters; their nuclei were pyknotic and hyperchromatic and orientated away from the basement membrane in a back-to-back arrangement (HE, × 250).

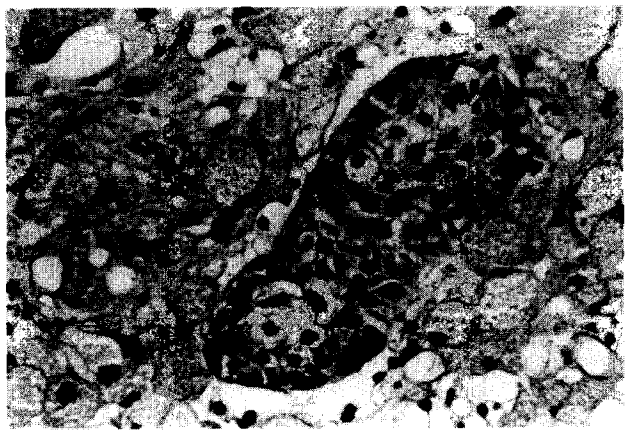

Fig. 4. Granular cell ameloblastoma. High-power view of the lesion (HE, × 400).

characteristically orientated away from the basement membrane in a back-to-back arrangement.

HISTOCHEMISTRY

For the histochemical study, sections were fixed in cold formal calcium, kept in cold gum sucrose overnight and sectioned with a cryostat. Then, PAS (Periodic Acid Schiff) stain with and without diastase digestion, Hale's dialysed iron staining and the Alcian blue stain at pH 2.5, 4 and 5.8 were performed before and after hyaluronidase digestion (Table 1).

The cytoplasmic granules were found to be PAS-positive before and after diastase digestion, oil red O-weakly positive, and negative after staining with phosphotungstic acid haematoxylin, Alcian blue and NASD-chloroacetate esterase. Focally we found residual areas of stellate reticulum-like cells.

Granular cells were stained intensely for acid phosphatase, moderately for α-naphthyl acetate and β-glucuronidase; conversely, they were found negative for alkaline phosphatase activity.

DISCUSSION

As pointed out previously, GCA represents a rare variant of ameloblastoma. Moreover, cases of classical ameloblastoma with only focal presence of granular cells have to be differentiated from the pure variant of GCA, in which the neoplastic granular cells are diffusely present and predominate. In this case, the granular cells occur in all the tumour follicles, replacing completely or in part the stellate reticulum-like cells.

Concerning histogenesis, the granular cells of ameloblastomas are of epithelial nature, and arise from ameloblasts. Conversely, the granular cells found in other lesions of the oral cavity are of mesenchymal derivation.

Histochemical and ultrastructural studies of GCA have suggested that the cytoplasmic granularity was due to the high content of lysosomes [1, 2], but the function of the ameloblastic cells is still completely unknown [2, 4, 5]. However, it has been shown that the numerous lysosomes represent the epiphenomenon of an increased cellular activity of the tumour ameloblasts in digesting unwanted components [2].

During normal amelogenesis, ameloblasts show an increase in autophagic lysosomes between the secretory and absorptive stages and from reduced ameloblasts to squamous epithelium [7]. Thus, the odontogenic epithelium seems to undergo granular changes under certain conditions [2]. The high activity of acid phosphatase in our case could confirm that the cytoplasmic granularity is due to high lysosome content, as shown in the histochemical studies of Nasu *et al.* [3].

It is currently thought that the granular change probably occurs as a consequence of an altered function of tumour cells, a hypothesis supported further by the finding that this tumour is age-related [2].

Moreover, in some instances granular cells show intracytoplasmic crystalloids [3], which probably constitute variant types of lysosomes, possible due to cellular degeneration [3].

The prognosis of granular cell ameloblastoma is similar to that of the classical ameloblastomas. Only one case has been described with an aggressive biological behaviour, with high recurrence rate [8].

Table 1. Histochemical stains used in diagnosis of GCA

Stains	Specificity	Reactivity of granular cell granules
PAS	Glycogen	+ +
PAS with diastase	No glycogen	+ +
Hale's dialysed iron	Acid mucopolysaccharide	?
Alcian blue pH 2.5	Mucin (highly acidic)	−
Alcian blue pH 4	Mucin (slightly acidic)	−
Alcian blue pH 5.8	Mucin (neutral/slightly acidic)	−
Oil-red O	Lipid	+
Phosphotungstic acid haematoxylin (PTAH)	Intracellular filaments	−
NASD-chloroacetate esterase	Mast cells—myeloid series	−
Duray's technique	Lysosomal acid phosphatase	+ + +
α-Naphthylacetate	Substrate of esterhydrolases of carboxylic acids	+
β-Glucuronidase	Hydrolysis of glycosyl compounds	+
Alkaline phosphatase	Hydrolysis of glycosyl compounds	−

In our case, a 3-year follow-up without clinical recurrences confirmed the reported good prognosis of the completely excised classical granular cell type of ameloblastoma.

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