Pergamon

Oral Oncol, Eur J Cancer, Vol. 30B, No. 4, pp. 278–280, 1994

0964–1955/94 $7.00 + 0.00

Case Report

Clear Cell Odontogenic Carcinoma. Report of a Case With Lymph Node and Pulmonary Metastases

Adriano Piattelli, Enrico Sesenna and Paolo Trisi

The authors present a case of a rare type of odontogenic tumour, recently described as "clear cell odontogenic tumour". The patient died 5 years after the initial diagnosis with lymph node and diffuse pulmonary metastases. This fact can support the view that this tumour, histologically characterised by the presence of cells with a clear cytoplasm, can behave in an aggressive way and has true metastatic potential, despite the absence of malignant cellular features.
Oral Oncol, Eur J Cancer, Vol. 30B, No. 4, pp. 278–280, 1994.

INTRODUCTION

THE ODONTOGENIC apparatus rarely gives origin to malignant tumours [1]. While malignant ameloblastomas and primary intraosseous carcinomas are well documented there is little evidence, due to the paucity of well studied and adequately followed cases, concerning the malignant variants of a newly described tumour, the "clear cell odontogenic tumour" (CCOT) [2]. Particularly lacking is reliable evidence of its biological behaviour.

CCOT is defined, in the histological typing of odontogenic tumours, as a "benign but locally invasive neoplasm originating from odontogenic epithelium" [2].

Moreover, the fact that this tumour is a distinct and separate entity and not a clear cell variant of the ameloblastoma requires, according to some investigators, further documentation and follow-up of a larger number of cases [3].

CASE REPORT

A 47-year-old male patient presented in April 1984 with a painless unilocular radiolucency in the anterior portion of the mandible extending from 44 and 33 (Fig. 1), with involvement of the lingual and vestibular soft tissues. The biopsy specimen was interpreted as "ameloblastoma" and the patient underwent a block resection extending from the right to the left premolar regions with a concurrent wide excision of the soft tissues. The postoperative period was uneventful until May 1985 when a routine panoramic radiograph showed the presence of an osteolytic lesion at the right margin of the bone excision and of a poorly demarcated radiolucency involving the right side of the mandible (Fig. 2).

The patient did not have any constitutional symptoms and underwent a full work-up consisting of complete blood counts, liver function studies, chest radiographs, upper and lower GI series, a complete bone scan, liver ecography and intravenous urography and an ENT examination. All investigations were negative with no evidence of any other primary malignant disease; no primary neoplasm was found in particular in the kidney, thyroid, major and minor salivary glands. Right submandibular and lateral cervical nodes were clinically positive. The patient underwent a right hemimandibulectomy with a right radical neck dissection.

The microscopic examination revealed islands of tumour cells separated from the stroma by a well-defined basement

Fig. 1. Orthopantomogram showing a mandibular unilocular radiolucency.

Correspondence to A. Piattelli.
A. Piattelli and P. Trisi are at the Dental School, University of Chieti, Via F. Sciucchi 63, 66100 Chieti, Italy; and E. Sesenna is at the Dental School, University of Parma, Italy.
Received 5 July 1993; provisionally accepted 8 July 1993; revised manuscript received 29 July 1993.

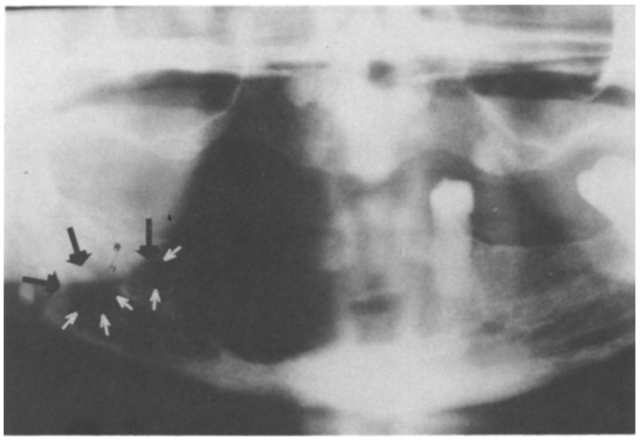

Fig. 2. Osteolytic lesion at the right margin of the previous block excision and another radiolucency encompassing the mandibular canal.

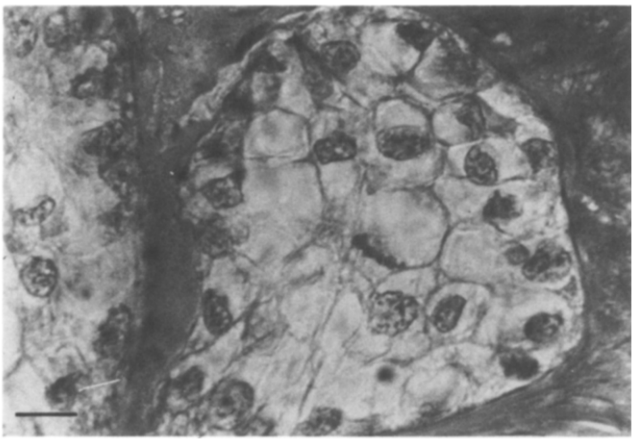

Fig. 4. High power view of the neoplastic cells showing clear cytoplasm and a rather dark nucleus (PAS). Bar = 10 μm.

membrane (Fig. 3); in some areas the basement membrane was poorly defined and the tumour cells infiltrated the surrounding connective tissue. In some areas the tumour infiltrated the bone. There was also involvement of the inferior mandibular nerve. The tumour was mainly composed of large cells with dark and central or peripheral nuclei and cytoplasm that was abundant and clear: the nuclei were not in a parabasal position (Fig. 4). The stroma was composed of a fibrous connective tissue with few cells. There was no palisading of the neoplastic cells at the periphery of the tumour islands. Histochemically many cells contained periodic acid-Schiff (PAS)-positive granules. Mitoses were rare. There was no evidence of calcium salts deposits or signs of glandular differentiation. Several of the lymph nodes were heavily infiltrated by a tumour tissue composed mainly of clear cells identical to those of the mandibular neoplasm (Fig. 5).

The histopathological diagnosis was of "clear cell odontogenic carcinoma with lymph node metastases". The postoperative course was uneventful. Three years after the last operative procedure the patient developed diffuse pulmonary metastases and was treated with a cycle of chemotherapy, the patient died 5 years after the first admission. No autopsy was performed.

DISCUSSION

Clear cells can be found in periodontal and gingival cysts in adults or as rests of the dental lamina in the connective tissue of these cysts [4, 5]. Odontogenic tumours of the jaws with a large or predominant component of clear cells are exceedingly rare [6]. Only the calcifying epithelial odontogenic tumour (CEOT) has been reported to exhibit clear cells [6, 7]: in these tumours there is however a frequent deposition of calcium salts usually in the form of Liesegang rings. Moreover, even in CEOT the clear cells are not a constant finding [6]; only 7 cases of CEOT with a clear cell component have been described [4]. Waldron *et al.* [7] in 1985 reported 2 cases of a neoplasm in which it was possible to see areas of follicular ameloblastoma together with abundant areas composed mainly of clear cells. Similar cases were described by Slootweg and Muller [8], Guilbert *et al.* [9] and Odukoya and Arole [10].

Hansen and coworkers [6] in 1985 presented 3 cases of a previously unreported neoplasm of putative odontogenic origin. All their cases were located centrally in the jaw bones, were composed for the most part of sheets and islands of uniform, vacuolated clear cells without evidence of deposition of calcium salts and amyloid and with no glandular differentiation. One of these cases was studied ultrastructurally and histochemically by Eversole *et al.* [11] who concluded that this

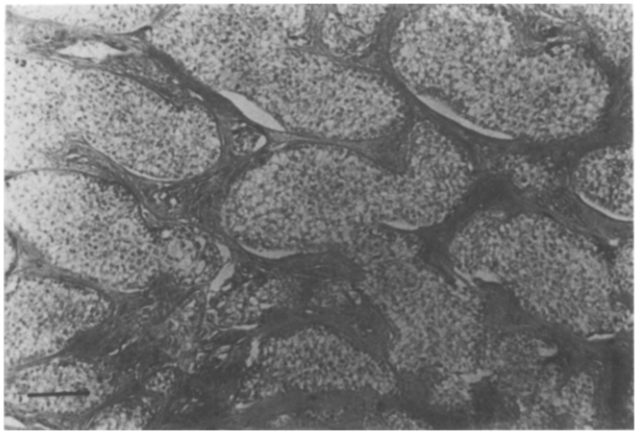

Fig. 3. The neoplastic islands are composed by large clear cells. There is no evidence of calcium salts deposit (PAS). Bar = 100 μm.

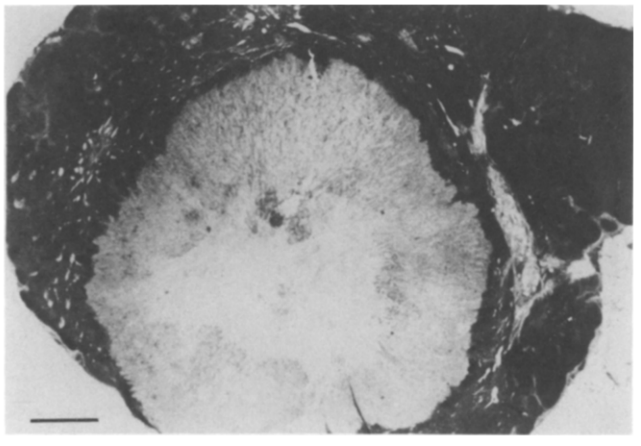

Fig. 5. Regional lymph node heavily infiltrated with metastatic neoplastic cells. (haematoxylin and eosin). Bar = 2.5 mm.

tumour was probably of odontogenic origin with features similar to the presecretory ameloblasts in the developing enamel organ, and moreover the neoplasm failed to recapitulate the features of the enamel organ (stellate reticulum, ameloblastic differentiation, a resemblance to the dental lamina). Only one of the lesions recurred and there was no evidence of metastatic disease. For these reasons they thought that this was a tumour with only a locally aggressive capability and termed the neoplasm "clear cell odontogenic tumour". In 1989 Bang and coworkers [12] described 3 more cases of the same neoplasm: one of these patients presented lymph node metastases and one bilateral pulmonary metastases. For these reasons the authors termed the tumour "carcinoma" and recommended aggressive therapy.

The question of malignancy in odontogenic tumours has been controversial for many years; their ability to metastasise to the lungs appears to be well established [12], even if this has been thought by some investigators to be the result of aspiration into the tracheobronchial tree rather than of true haematogenous spread; metastases have been described also in the pleura, regional and distant lymph nodes, liver, brain, soft tissue, kidney, spleen, vertebrae, diaphragm, ilium and ribs [3, 13]. In our case, however, the diffuse bilateral lung and lymph node metastases and the lymph node involvement document beyond doubt the ability of these tumours to metastasisc [12]. We have documented moreover, invasive bone destruction, microscopic involvement of the inferior alveolar nerve and extensive soft tissue invasion; Yoshida *et al.* [14] believe these features are indicative of a malignant nature of the tumour.

The differential diagnosis should include other types of primary or metastatic head and neck tumours that can present a clear cell component, particularly salivary gland tumours (mucoepidermoid carcinoma, acinic cell carcinoma, clear cell carcinoma, epithelial–myoepithelial carcinoma of intercalated ducts, sebaceous neoplasms, pleomorphic adenoma, clear cell oncocytoma) and metastatic renal cell carcinoma or thyroid carcinoma [1, 3, 7, 9, 11, 15, 16]. In our case no primary neoplasm was found in any of these sites, suggesting that the most likely source of the tumour was odontogenic.

In conclusion, our case shows clearly that the so-called clear cell odontogenic tumour has an aggressive and metastasising potential and an early radical surgery is clearly appropriate; the tumour should then, perhaps, be labelled "carcinoma".

1. Hoffman S, Jacoway JR, Krolls SO. Intraosseous and parosteal tumors of the jaws. AFIP, Bethesda 1987, 101–106/151–154.
2. Kramer IRH, Pindborg JJ, Shear M. Histological typing of odontogenic tumours. *WHO International Histological Classification of Tumours*, 2nd ed. Berlin, Springer, 1992.
3. Regezi JA, Sciubba JJ. *Oral Pathology. Clinical-pathologic Correlations*. Philadelphia, W.B. Saunders, 1989, 274–275, 351.
4. Schmidt-Westhausen A, Philipsen HP, Reichart PA. Clear cell calcifying epithelial odontogenic tumor. A case report. *Int J Oral Maxillofac Surg* 1992, **21**, 47–49.
5. Shear M. *Cysts of the Oral Regions*, 3rd ed. Oxford, Wright, 1992, 64.
6. Hansen LS, Eversole LR, Green TL, Powell NB. Clear cell odontogenic tumor—a new histologic variant with aggressive potential. *Head Neck Surg* 1985, **8**, 115–123.
7. Waldron CA, Small IA, Silverman H. Clear cell ameloblastoma—an odontogenic carcinoma. *J Oral Maxillofac Surg* 1985, **43**, 707–717.
8. Slootweg PJ, Muller H. Malignant ameloblastoma or ameloblastic carcinoma. *Oral Surg Oral Med Oral Pathol* 1984, **57**, 168–176.
9. Guilbert F, Auriol M, Chomette G. Une forme rare d'épithélioma primitif de la mandibule: le carcinome odontogénique à cellules claires. *Rev Stomatol Chir Maxillofac* 1991, **92**, 277–280.
10. Odukoya O, Arole O. Clear-cell ameloblastoma of the mandible (a case report). *Int J Oral Maxillofac Surg* 1992, **21**, 358–359.
11. Eversole LR, Belton CM, Hansen LS. Clear cell odontogenic tumor: histochemical and ultrastructural features. *J Oral Pathol* 1985, **14**, 603–614.
12. Bang G, Koppang HS, Hansen LS, *et al.* Clear cell odontogenic carcinoma: report of three cases with pulmonary and lymph node metastases. *J Oral Pathol Med* 1989, **18**, 113–118.
13. Appel BN, Verbin RS. Odontogenic tumors. In Barnes L, ed. *Surgical Pathology of the Head and Neck*. New York, Marcel Dekker Inc, 1985, 1340–1349.
14. Yoshida T, Shingaki S, Nakajima T, Suzuki M, Fukushima M. Odontogenic carcinoma with sarcomatous proliferation. A case report. *J Cranio-Max Fac Surg* 1989, **17**, 139–142.
15. Seifert G. *Histological Typing of Salivary Glands Tumours*, 2nd ed. Berlin, Springer, 1991.
16. Ogawa I, Nikai H, Takata T, Yasui R. Clear cell variant of mucoepidermoid carcinoma: report of a case with immunohistochemical and ultrastructural observations. *J Oral Maxillofac Surg* 1992, **50**, 906–910.

Acknowledgements—This work was partially supported by the Italian Ministry of University, Research, Science and Technology (60%), and by the Italian National Research Council.