SHORT COMMUNICATION
ΒΡΑΧΕΙΑ ΔΗΜΟΣΙΕΥΣΗ

Giant cell tumor of major salivary glands in association with pleomorphic adenoma

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Γιγαντοκυτταρικός όγκος των μεγάλων σιαλογόνων αδένων σε συνδυασμό με πλειόμορφο αδένωμα

Περίληψη στο τέλος του άρθρου

Key words: Giant cell tumor, Pleomorphic adenoma, Salivary glands

Extraosseous osteoclast-like giant cell tumors have been described in the soft tissues and parenchymal organs such as pancreas, thyroid, lung, liver, breast, ovary and kidney.[1–3] Similar lesions have also been reported in the parotid and other major salivary glands.[1–6] In some cases the giant cell component was admixed with carcinomatous elements whereas in others it occurred in an apparently pure form.[1,6]

This is a report of a patient with a giant cell tumor located in the submandibular salivary gland in association with a pleomorphic adenoma.

CASE REPORT

A 55 year-old woman presented with a mass in the submandibular region which had enlarged during the previous few months and was thought to be a cystic lesion. Radiographs of the mandible and cranium were unremarkable. A total excision of the gland was performed and some mandibular bone adjacent to the mass was also resected.

On gross examination, the tumor mass measured 7.0×7.0×2.5 cm and it appeared to be well defined. The cut surface was grayish, solid and locally lobulated like the salivary gland.

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Five weeks after surgery, the patient was reviewed because of a recurrent mass measuring 4.5×4.0×2.0 cm in the same region. A second operation was performed at which a wide excision including soft tissues and the ramus of mandible was made. Gross examination of this specimen showed a well-defined nodule of firm consistency and homogenous appearance. The cut surface was solid and reddish.

Slides from the pathologic specimens from the first and second operations were prepared from formalin-fixed and paraffin embedded blocks of tissues and stained with hematoxylin and eosin. The following special stains were used on sections from the first specimen: Periodic acid-Schiff (PAS), van Gieson's and Alcian blue at pH 2.5 and 0.5. In addition, sections were stained immunohistochemically for monoclonal antibodies to low and high molecular weight cytokeratin (monoclonal mouse anti-human, DAKO), S-100 (rabbit anti-cow, DAKO), vimentin (monoclonal mouse, DAKO), lysozyme (rabbit anti-human, DAKO) and human and bovine osteonectin (kindly performed by Prof. Dr Med A. Schullz at the University of Giessen). Immunostaining was performed using alkaline phosphatase anti-alkaline phosphatase complexes (DAKO) and the monoclonal antibodies as previously described.[7,8]

Microscopic features

The histologic features of the first specimen were those of residual salivary gland parenchyma admixed with what appeared to be two different tumors abutting on each other, but with no areas of transition between the two. One tumor was a pleomorphic adenoma formed the usual admixture of epithelial structures and abundant myxochondroid stroma (fig. 1). The other tumor was composed of two major cell types, multinucleated giant cells, which were morphologically indistinguishable

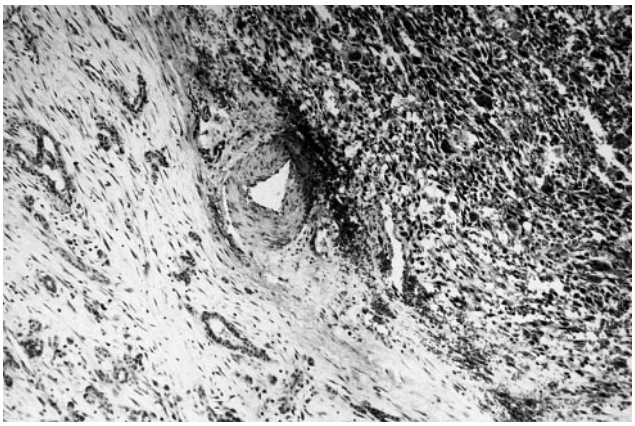

Figure 1. Giant cell tumor component is separate from the features of pleomorphic adenoma (HE×200).

from bone osteoclasts, and spindle or round-shaped mononuclear cells (fig. 2). The osteoclast-like giant cells were regularly distributed and the cell margins were generally sharp. The nuclei were round or oval with homogenous chromatin distribution and a distinct usually single nucleolus; their number per cell ranged from 2 to 20. The cytoplasm was abundant, acidophilic and in some cells had vacuoles. The mononuclear cells and their nuclei were oval or spindle-shaped, and hyperchromatic, with cytoplasm moderate in amount and acidophilic (fig. 2) and scanty mitotic activity. The background was highly vascularized and foci of hemorrhage were present. At the periphery of the tumor there were inflammatory cells and between the mononuclear cells hyalinized collagen bundles. Areas of cartilage and osteoid with osteoblastic rimming were identified (fig. 3). The small bone segment resected in the first operation showed no pathologic features.

In the second specimen, features of pleomorphic adenoma were absent and it was composed of mesenchymal tumor only, consisting of regularly scattered osteoclast-like giant cells among round or spindle-shaped mononuclear cells. Foci of osteoid-like material were present. A focus of invasion was found in the ramus of mandible.

The standard special stains PAS, Alcian blue, van Gieson's, were noncontributory.

Immunohistochemical features

The epithelial cells of the pleomorphic adenoma showed strong positivity for both low and high weight cytokeratin and S-100, but none of the mononuclear or giant cells stained positive. The spindle cells and a few of the multinucleated cells reacted with vimentin but all failed to stain for lysozyme. Immunostaining for osteonectin revealed a faint labeling of cells lying adjacent to or within the osteoid-like material, indicating osteoblastic differentiation.

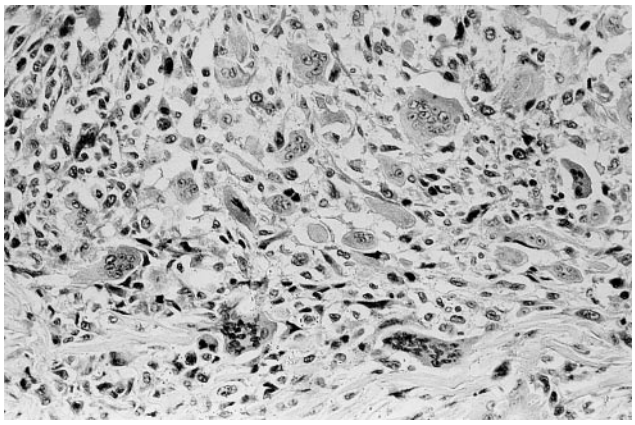

Figure 2. Giant cell tumor composed of numerous large, multinucleated osteoclast-like giant cells in a background of atypical mononuclear cells (HE×200).

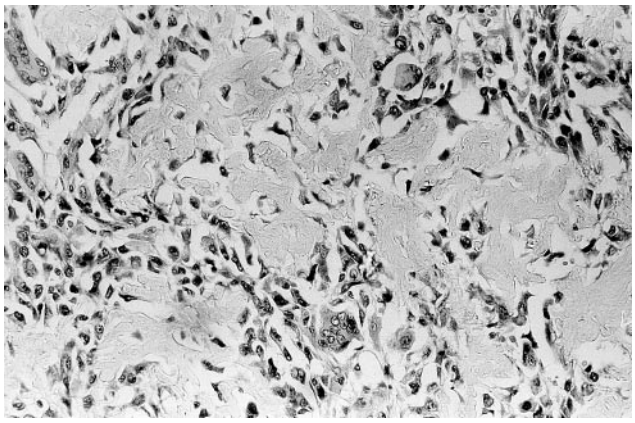

Figure 3. Foci of suggestive osteoid formation (HE×200).

COMMENT

The tumor in this case is similar to the giant cell tumor of salivary glands reported in the literature, with an additional component of pleomorphic adenoma.[1,3,4,6]

It has been reported that the giant cell salivary gland tumor has three patterns: it may be in association with pleomorphic adenoma, or adenocarcinoma or with no complications. In whatever pattern, however, the tumor has a clear border with the surrounding tissue. Therefore, this giant cell tumor seemed not to be developed as a part of a carcinoma or adenoma.[4]

The differences in behavior and histologic appearance have reflected a variable histogenesis for these giant cell tumors. Some investigators have considered them to be mesenchymal appearing but epithelially derived pleomorphic malignant neoplasms.[4,5] Other investigators have considered them to be benign or malignant mesenchymal neoplasms while still others have interpreted them as stromal reactive lesions.[2,3] Light and electron microscopic features and immunohistochemical analysis has been used to support these interpretations.[2,3] The light and electron microscopic features of the giant cells have been reported to be indistinguishable from those in giant cell tumor of bone.[1] Immunohistochemical techniques have not contributed important information.[1,3–5] In the case presented, with immunohistochemical analysis, the epithelial cells of pleomorphic adenoma showed positivity for cytokeratin but in the mesenchymal tumor no positivity was found. Moreover the giant cells were unreactive for S-100, a marker for myoepithelial cells and lysozyme, a marker for histiocyte/macrophage cells. These findings supported the mesenchymal nature of the tumor and the foci of bone formation in the tumor strengthened this interpretation, but we have not been able to identify this giant cell tumor.

Although there have been a few patients reported as summarized in table 1, it is suggested that these were low grade malignancies.[4] Many of the giant cell tumor of other

Table 1. Summary of general features of previously reported giant cell tumours of major salivary glands.

Refer	No/Sex	Age	Localization	Association with	Recurrences	Metastases	Follow-up (yr)
1	3 M	30–52	Parotid	1 Ca in pleomorphic adenoma	–	–	NED/4–6
2	1 M	67	Parotid	Ductal Ca	1 yr	Lungs/2 yr	Dead/2
3	1 M/3 W	28–78	3 Parotid, 1 SM	1 adenoid cystic Ca	1 (3) yr	–	?
4	2 M	59–92	Parotid	1 ductal Ca	–	–	NED/1–9
5	1 M	53	Parotid	–	?	?	?
6	1 W	66	Parotid	Carcinosarcoma	Yes (?)	Lungs	Dead/1

Refer: Reference number, M: Man, W: Woman, SM: Submandibular gland, Ca: Carcinoma, yr: Year, NED: No evidence of disease

epithelial organs such as pancreas, thyroid and lung, have been aggressive malignant neoplasms. Some extraosseous giant cell tumors have been associated with recognisable carcinoma[2,6] and some have had a sarcomatoid stroma.[3,5,6] In giant cell tumors of salivary glands, the morphologic features and their locally aggressive behaviour show malignant potential, as far as the mononuclear cell component is concerned. The situation is not so clearcut for the osteoclast-like giant cell component in which mitotic features and signs of nuclear atypia are never found even when those features abound in the neighboring mononuclear cells. This suggests the possibility that the multinucleated cells themselves may be non-neoplastic stromal elements.[1]

In the case described, the pleomorphic adenoma was benign but the mesenchymal part of the tumor was accepted as malignant because it recurred five weeks after the first operation although it was clear that the primary mass had been completely removed and also invasion in the rames of mandible was evidence of its aggressive behavior. Three other previously reported tumors also recurred after surgery[2,3,6] (tabl. 1).

In conclusion, the nature of these extraosseous giant cell tumor remain uncertain. Whatever its histogenesis, the osteoclast-like giant cell tumor should be accepted as another distinctive tumor of the major salivary glands.

ΠΕΡΙΛΗΨΗ

Γιγαντοκυτταρικός όγκος των μεγάλων σιαλογόνων αδένων σε συνδυασμό με πλειόμορφο αδένωμα

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Νεοπλάσματα, ιστολογικώς όμοια με τους γιγαντοκυτταρικούς όγκους των οστών, έχουν περιγραφεί και στους μαλακούς ιστούς, ορισμένα μάλιστα από τα οποία εντοπίζονται στους μεγάλους σιαλογόνους αδένες. Περιγράφεται η περίπτωση όγκου, ο οποίος εντοπιζόταν στον υπογνάθιο σιαλογόνο αδένα γυναίκας 55 ετών. Ο όγκος είχε μικροσκοπική εικόνα πλειόμορφου αδενώματος, σε συνδυασμό με ευρήματα κακοήθους μεσεγχυματικού νεοπλάσματος, με γιγαντοκύτταρα οστεοκλαστικής υφής και περιοχές σχηματισμού οστεοειδούς. Ένας δεύτερος όγκος, με τα ίδια ιστοπαθολογικά χαρακτηριστικά, εμφανίστηκε 5 εβδομάδες μετά από την πλήρη αφαίρεση του σιαλογόνου αδένα.

Λέξεις ευρετηρίου: Γιγαντοκυτταρικός όγκος, Πλειόμορφο αδένωμα, Σιαλογόνοι αδένες

References

1. EUSEBI V, MARTIN SA, GOVONI E, ROSAI J. Giant cell tumor of major salivary glands. Report of three cases, one occurring in association with a malignant mixed tumor. *Am J Clin Pathol* 1984, 81: 666–675
2. BALOGH K, WOLBARSHT RI, FEDERMAN M, O'HARA CJ. Carcinoma of the parotid gland with osteoclast-like giant cells. *Arch Pathol Lab Med* 1985, 109:756–761
3. GNEPP DR. *Pathology of the head and neck*. 1st ed. New York, Churchill Livingstone, 1988:638–642
4. BATSAKIS JC, ORDONEZ NG, SEVIDAL PA, BAKER JR. Osteoclast type giant cell neoplasms of the parotid gland. *J Laryngol Otol* 1988, 102:901–904
5. ITOH Y, TANIGUTI Y, ARAI K. A case of giant cell tumor of the parotid gland. *Ann Plast Surg* 1992, 28:183–186
6. GRENKO RT, TYTOR M, BOERYD B. Giant cell tumour of the salivary gland with associated carcinosarcoma. *Histopathology* 1993, 23: 594–595
7. MOLL R, FRANKE WW, SCHILLER DI, GEIGER B, KREPLER R. The catalog of human cytokeratins, patterns of expression in normal and cultured cells. *Cell* 1982, 31:11–24
8. LAURIOLA L, MICHETTI F, SENTINELLI S, COCCHIA D. Detection of S-100 labelled cells in nasopharyngeal carcinoma. *J Clin Pathol* 1984, 37:1235–1238

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