Osteoclast-like giant-cell tumor of the parotid with salivary duct carcinoma: Case report and cytologic, histologic, and immunohistochemical findings

Maryam Kadivar, MD, APCP; Yalda Nilipour, MD; Alireza Sadeghipour, MD, APCP

Abstract
Primary giant-cell tumor of the salivary gland is a rare lesion with an incompletely characterized histogenesis. To the best of our knowledge, only 16 cases have been previously documented in the English-language literature. We report a new case, which occurred in a 75-year-old man who presented with a parotid mass and cervical lymphadenopathy. The patient underwent a left total parotidectomy and cervical lymph node dissection. As far as we know, ours is the only reported case of a primary giant-cell tumor of the salivary gland in which the patient presented with lymph node metastasis. Because so little is known about giant-cell tumor of the salivary gland, we use the occasion of this case report to describe the cytologic, histologic, and immunohistochemical characteristics that we observed.

Introduction
Primary giant-cell tumor of the salivary gland is a rare, relatively recently known tumor that is usually associated with the presence of another primary tumor of the salivary gland. It was first described by Eusebi et al in 1984. Since then, 15 other cases have been reported in the English-language literature, most of them in elderly men; the most common presenting symptom in these cases was a painless, growing mass.

Of the 16 previously reported cases, 14 (87.5%) occurred in the parotid gland. In 8 cases (50.0%), the pure form of this tumor was reported; in the remaining half, the giant-cell tumor component was admixed with a clearly identifiable carcinomatous element—usually salivary duct carcinoma and less frequently carcinoma ex pleomorphic adenoma. The presence of the carcinomatous component is a risk factor for early metastasis.

In this article, we describe what we believe is only the 17th reported case of primary giant-cell tumor of the salivary gland, and the first case in which the patient presented with lymph node metastasis. We place special emphasis on the cytologic, histologic, and immunohistochemical aspects of this case.

Case report
A 75-year-old man, a heavy smoker, presented with a painless, fixed, and slowly growing left parotid mass of 2 years’ duration. Left cervical lymphadenopathy, which had been present for approximately 3 months, was also noted. Physical examination revealed that the facial nerve was intact. Findings on skeletal radiography were unremarkable.

Fine-needle aspiration was performed with a 22-gauge needle. Two smears were prepared. One was air-dried and stained by the Wright-Giemsa method, and the other was fixed in 95% alcohol and stained by the Papanicolaou method.

Cytologic findings. The Papanicolaou smear was nondiagnostic, but the Wright-Giemsa stain was richly cellular and populated by three components: (1) numerous osteoclast-like multinuclear giant cells, (2) multiple malignant-appearing mononuclear and multinuclear cells, and (3) broad, tightly cohesive, flat sheets of large polygonal epithelial cells (figure 1):

• The osteoclast-like giant cells contained multiple relatively monomorphic and bland-looking nuclei (ranging from 3 to 25 per cell) with abundant cytoplasm. Some also demonstrated engulfment of tumoral epithelial cells.
OSTEOCLAST-LIKE GIANT-CELL TUMOR OF THE PAROTID WITH SALIVARY DUCT CARCINOMA: CASE REPORT AND CYTOLOGIC, HISTOLOGIC, AND IMMUNOHISTOCHEMICAL FINDINGS

• The malignant-appearing, highly atypical mono- and multinuclear cells were characterized by a high nucleus-to-cytoplasm ratio, enlarged and irregular nuclei, coarse chromatin, and prominent nucleoli. Some also exhibited prominent intranuclear inclusions.

• The polygonal epithelial cells were arranged in flat and branching sheets with few tubuloacinar features. These cells contained eosinophilic cytoplasm and enlarged round to oval, relatively monomorphic nuclei with finely granular chromatin. Some had prominent nucleoli.

The cytomorphologic features of this case yielded a spectrum of findings. Although a number of disorders can be considered in the differential diagnosis of the pure form of giant-cell tumor, the benign appearance of giant cells, the coexistence of sheets of polygonal epithelial cells, and the presence of mono- and multinuclear cells with malignant features certainly limit the possibilities. Based on a combination of cytologic findings, we considered the diagnosis to be a “giant-cell–rich carcinoma.”

**Gross examination.** A left total parotidectomy and cervical lymph node dissection were performed. The tumor was found to be 6.5 cm in its maximum dimension and arising from the parotid gland. Cross-sections of the tumor revealed that it was solid and brownish-yellow with multiple areas of hemorrhage and necrosis.

**Histologic findings.** The histologic features were those of residual atrophic salivary gland tissue that had been invaded by what appeared to be two different tumors abutting each other; areas of transition were noted between the two masses. One tumor appeared to be an invasive malignant neoplasm that exhibited the typical features of a salivary duct carcinoma; the other appeared to be an osteoclast-like giant-cell tumor. The former was characterized by atypical epithelial cells showing a high nucleus-to-cytoplasm ratio, pleomorphic enlarged vesicular nuclei with prominent nucleoli, and a moderate amount of eosinophilic cytoplasm arranged in glandular, cribriform, comedo-like, and solid patterns. In some areas, the salivary duct carcinoma and the giant-cell tumor were separated by fibrous tissue, but in other areas, they appeared to have merged, as there was no clearly distinguishable border between them (figure 2).

The giant-cell tumor, which accounted for 60 to 70% of the tumor mass, contained two components—one multinuclear and osteoclast-like and the other mononuclear:

• A number of multinuclear, osteoclast-like giant cells were rather regularly distributed throughout the tumor. These cells featured round to oval nuclei that ranged in number from only a few to approximately 50 per cell (average: ~15). They contained homogeneous, delicate chromatin and a single small nucleolus.

• The mononuclear component demonstrated round to oval nuclei similar to giant cells, but adjacent to the area of the transition to the salivary duct carcinoma, highly malignant mono- and multinuclear tumor cells were admixed with the giant-cell tumor. Some of these were engulfed by osteoclast-like giant cells. The background was highly vascular and hemorrhagic, with multiple areas of necrosis. No areas of osteoid formation were identified. Metastatic salivary duct carcinoma was present in four intraparotid and cervical lymph nodes.

**Immunohistochemical findings.** Immunohistochemical studies were performed on a formalin-fixed, paraffin-embedded specimen. Antibodies to epithelial membrane antigen (EMA), smooth-muscle actin (SMA), cytokeratin 8 (CK8), pancytokeratin (CK), vimentin, estrogen receptor (ER), prostate-specific antigen (PSA), C-erb2, CD68, carcinoembryonic antigen (CEA), and alpha 1-antitrypsin (AAT) were used with the avidin-biotin-peroxidase complex technique.
The cells of the salivary duct carcinoma strongly and diffusely expressed epithelial markers (EMA, CK, and CK8) and C-erb2. The osteoclastic giant cells strongly and diffusely expressed CD68 and vimentin. Epithelial markers were also expressed by scattered, highly malignant cells admixed or engulfed by giant cells (figure 3). CEA and AAT expressed nonspecific reactions, and PSA, ER, and SMA were negative in both components, a finding that assisted in ruling out metastatic carcinoma originating in either the prostate gland or the breast.

Discussion
It was once thought that primary giant-cell tumor of the salivary gland was homologous to giant-cell tumor of bone, but a recent study has suggested that it is more akin to a carcinoma.2 Although the two tumors might be morphologically indistinguishable, there are some features that do enable the pathologist to differentiate the salivary gland tumor from the bone tumor and from other extraskeletal giant-cell tumors:

• The salivary tumor is biologically more aggressive.
• The salivary tumor has a carcinomatous component.
• The salivary tumor demonstrates scattered, overt, malignant epithelial cells admixed with a mononuclear component in areas adjacent to transition.
• The salivary tumor is associated with a lack of reactive bone formation at the periphery of the tumor.
• Giant-cell tumor of the jaw (mandible or maxilla) that has secondarily invaded the parotid gland can be ruled out easily by unremarkable radiographic studies and surgical findings.

Although the cellular origin of primary giant-cell tumor of the salivary gland remains uncertain, ultrastructural findings and immunohistochemical staining for CD68, lysozyme, and other histiocytic markers suggest that the giant cells are of osteoclastic or histiocytic lineage.1,3

Genotyping analysis performed by Tse et al demonstrated that the giant-cell component is a neoplastic rather than reactive lesion; they preferred the term osteoclast-type giant-cell carcinoma.2 Nevertheless, it is not clear whether this tumor is an unusual metaplastic carcinoma or if it originates in mesenchymal or stem cells.

In summary, the identification of a giant-cell-tumor-like neoplasm in a salivary gland should warrant a diligent search for a carcinomatous component because this component can be very small and focal. Preoperative diagnosis of this neoplasm may warrant a more extensive workup and therapy, including radical surgery or neck dissection followed by radiation therapy. Finally, although giant-cell tumor in association with salivary duct carcinoma is difficult to interpret accurately in cytologic smears, it should be considered in the differential diagnosis of malignant-appearing, giant-cell–rich lesions of the salivary glands.

Acknowledgment
The authors thank John Steytler, MD, for his valuable editorial comments on the draft of this article.

References