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Carcinoma ex pleomorphic adenoma of the minor salivary gland with pulmonary metastasis

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ABSTRACT

Carcinoma ex pleomorphic adenoma is an exceedingly rare neoplasm of the minor salivary gland. Prognostic parameters are recurrence, capsular invasion, and metastasis. We present a case of carcinoma ex pleomorphic adenoma with pulmonary metastasis to emphasize that patients treated for this condition should be investigated for distant metastasis.

Key words: • *carcinoma* • *adenoma, pleomorphic* • *mixed tumor, malignant* • *salivary glands* • *coin lesions, pulmonary*

Malignant mixed tumors are grouped into 3 categories: carcinoma ex pleomorphic adenoma (CXPA), true malignant mixed tumor (carcinosarcoma), and metastasizing mixed tumor (1-2). These tumors are characterized by high rates of recurrence, metastasis, and mortality (3, 4). There have been limited imaging findings and information for these rare neoplasms in the literature. Among these tumors, 3 cases with pulmonary metastasis were reported (5–7); however, only one was CXPA (7) and another was benign metastasizing pleomorphic adenoma (6). Herein we present a CXPA case with multiple lung metastases.

Case report

A 50-year-old male patient presented with a history of a painful ulcerative lesion at the right wall of the oropharynx. Physical examination revealed a mass at the soft palate extending into right side of the oropharynx with ulceration. Computed tomography (CT) depicted a large 3 × 4 × 3-cm ill-defined mass located at the soft palate and parapharyngeal space, which extended superiorly to the nasopharynx and anteriorly to the retromolar trigone on the right side. The tumor enhanced heterogeneously with the injection of iodinated contrast medium (Fig. 1a).

Histological diagnosis of the specimen obtained by core biopsy was pleomorphic adenoma of the minor salivary gland with no evidence of malignancy. The tumor was composed of epithelial cells dispersed in myxoid stroma. The tumor cells formed ducts, cell nests, and cell cords. The tumor capsule was not observed in the core biopsy specimens. Regarding clinical and radiological findings, it was thought that tumor might be malignant. After total excision of the tumor, histological examination revealed a tumoral structure composed of pleomorphic tumor cells. The tumor cells formed an abortive adenoid structure in myxoid stroma (Figs. 1b, c). The tumor cells had large hyperchromatic nuclei, prominent nucleoli, and scant cytoplasm. Myxoid mesenchymal stroma in the tumor area and benign pleomorphic adenoma fields in other microscopic areas were observed. The benign pleomorphic adenoma fields consisted of epithelial cells that formed ducts and cell nests in myxoid and chondroid mesenchymal stroma. The case was accepted as CXPA. Since the surgical margins were positive, radiation therapy of the primary site was performed. Four years after the initial diagnosis, the control CT showed a recurrent 3 × 2-cm tumor in the right medial pterygoid muscle and retromolar trigone (Fig. 2a). The lesion extended to the infratemporal fossa, invading the pterygoid muscles (Fig. 2b). In addition, there was a heterogeneous nodular mass at the right submandibular fossa (Fig. 2c). CT examination of the thorax revealed multiple homogeneous variable-sized metastatic pulmonary nodules (Fig. 2d). The pulmonary nodules did not have any signs of cavitation, necrosis, or calcification.

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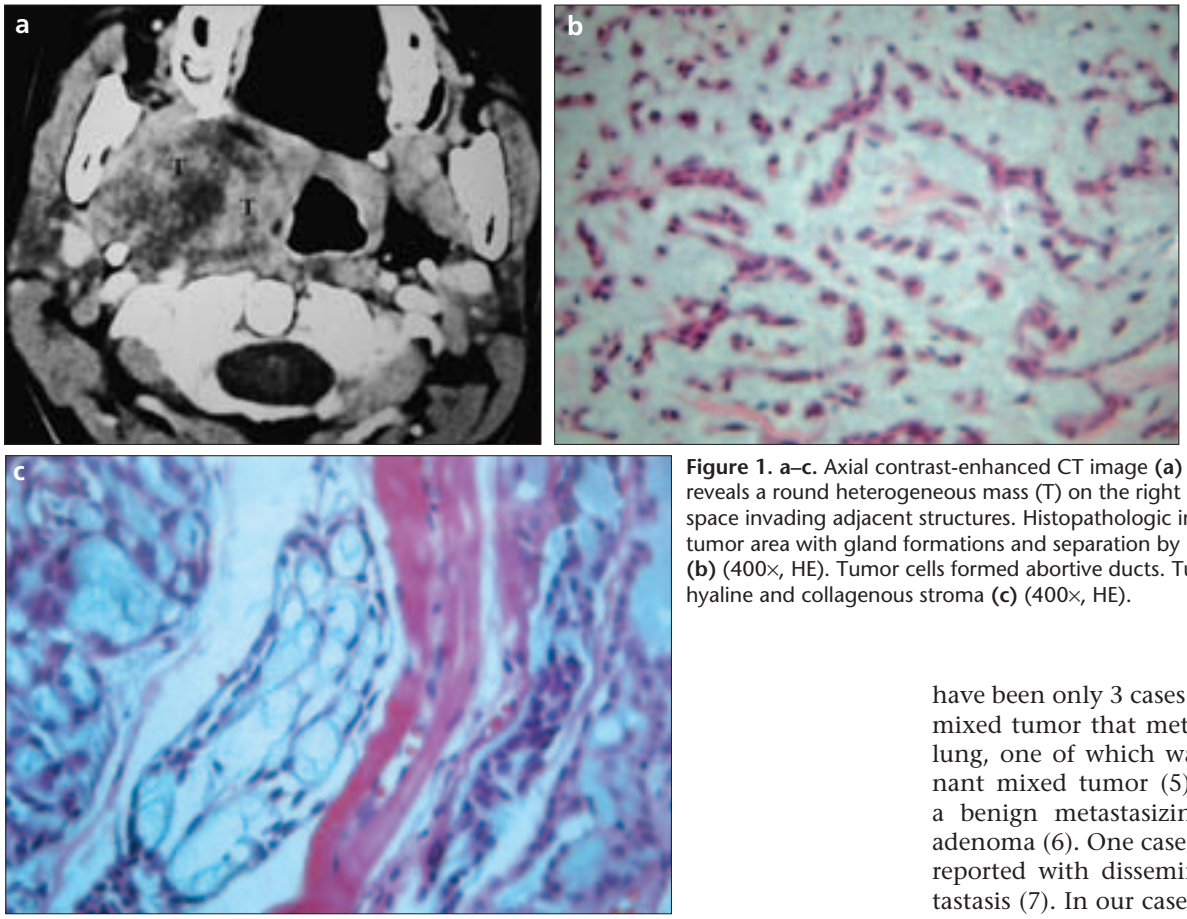

Figure 1. a–c. Axial contrast-enhanced CT image **(a)** of the oropharynx reveals a round heterogeneous mass (T) on the right parapharyngeal space invading adjacent structures. Histopathologic images **(b, c)** show tumor area with gland formations and separation by myxoid stroma **(b)** (400×, HE). Tumor cells formed abortive ducts. Tumor cells in the hyaline and collagenous stroma **(c)** (400×, HE).

The case was accepted as stage IV malignant mixed tumor and chemotherapy was started. At follow-up, scanning tests revealed no metastasis, except in the lungs; however, the follow-up lung CT showed no regression in number or size of the metastatic nodules.

The patient who was followed-up and treated accordingly by the medical oncology department died of the disease 5 years after the diagnosis.

Discussion

Malignant mixed tumors represent approximately 11.6% of all malignant neoplasms of the salivary gland and mostly originate from major salivary glands (1). CXPA comprises the vast majority of malignant mixed tumors. Location in the minor salivary gland is uncommon and occurs in less than 7% of all cases (8–10). The majority of CXPAs develop from epithelial components of pleomorphic adenomas that display aggressive behavior (1–3). Prognostic parameters are recurrence, capsular invasion > 9 mm, and metastasis (2). In our case, malignant mixed tumor of the minor salivary gland developed from epithelial components of the pleomorphic adenoma. It recurred with invasion to some of the adjacent structures and with distant metastasis.

CXPA may have various CT appearances: (a) it may be similar to a pleomorphic adenoma with no evidence of malignancy, (b) it may occur with focal necrosis, wall irregularity, or infiltrating margins, or (c) it may have an entirely aggressive CT appearance (11). Since most CXPAs have high-grade cellularity, they have fairly low signal intensity on both T1- and T2-weighted images (11). Therefore, low T2-weighted signal intensity should alert radiologists that the tumor might be CXPA.

It is reported that CXPA involves regional nodes with a frequency nearly equal to the distant metastatic rate (3). Olsen and Lewis reported that metastasis (either initial or delayed) occurred regionally in 37 (56%) and distantly in 29 (44%) of 66 patients (4). Malignant mixed tumors metastasize regionally and in distant areas, such as the lungs, hilar and cervical lymph nodes, bone, and central nervous system (1, 3–5, 12, 13). To the best of our knowledge, there have been only 3 cases with malignant mixed tumor that metastasized to the lung, one of which was a true malignant mixed tumor (5) and the other a benign metastasizing pleomorphic adenoma (6). One case with CXPA was reported with disseminated lung metastasis (7). In our case, regional recurrence, regional metastasis to the submandibular lymph node, and distant metastasis to the lungs occurred. There were multiple metastatic nodules in both lungs, the largest of which was 5 × 3 cm. CT examination revealed that the metastatic pulmonary nodules had neither calcification nor cavitation. Radiological findings, including multiple round variably-sized nodules, were consistent with typical hematogenous metastasis (14); however, those were not only peripherally, but also centrally located. According to American Joint Committee on Cancer (15), the case was initially stage II and later progressed to the stage IV. CXPAs generally display aggressive behavior. They have high recurrence and metastatic rates, which vary from 25% to 75% (1) Recurrence and regional and distant metastases are predictive of extremely poor prognosis (7, 8). In one series, disease-specific survival was 45% at 3 years and 37% at 5 years (4); however, median survival was 27% at 1 year after detection of any type of progression and 5% at 3 years after detection of distant metastasis (4). Our case died 5 years after diagnosis, 1 year after recurrence and distant metastasis.

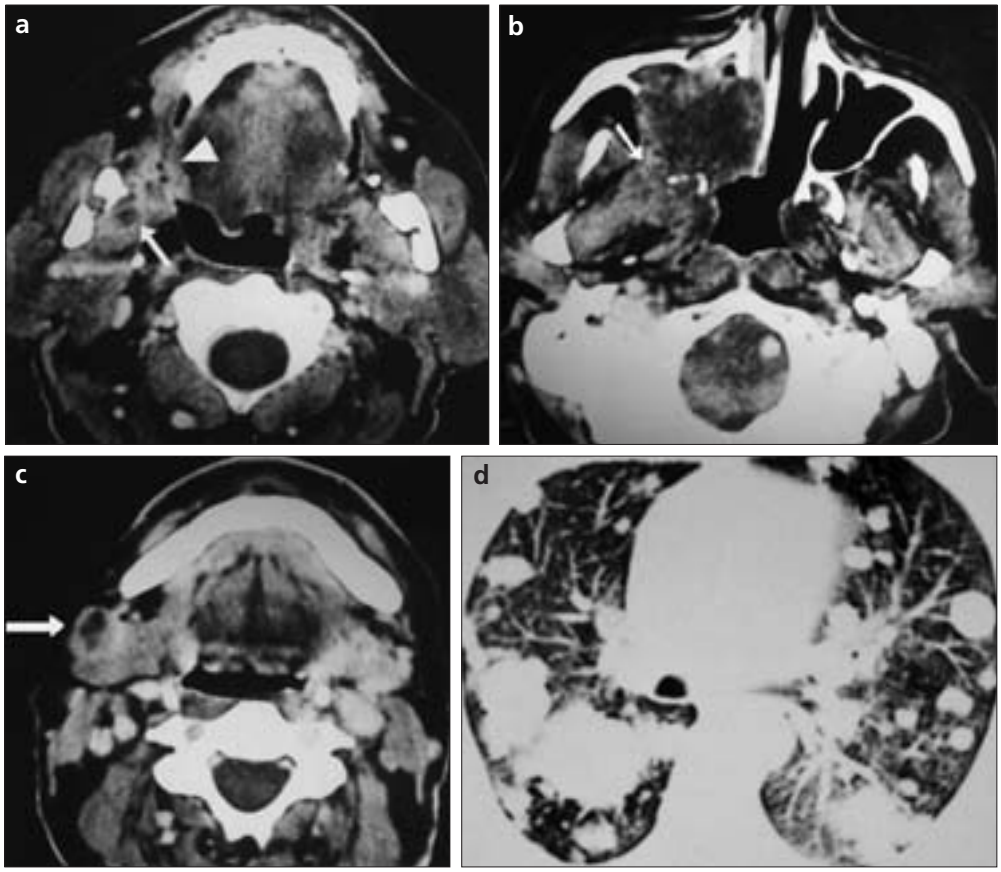

Figure 2. a–d. Axial contrast-enhanced CT images **(a-c)** show a heterogeneously enhanced mass on the right medial pterygoid muscle (**a,** *arrow*) extending to the retromolar trigone (**a**, *arrowhead*). Note tumor invasion to the anterior part of the lateral pterygoid muscle (**b**, *arrow*). A nodular mass with central necrosis (**c**, *arrow*) located anterolateral of the right submandibular gland. Axial CT image of the lungs **(d)** displays several lesions in both sides.

Because CXPA is histologically composed of both benign and malignant components, false negative diagnosis of the malignant component of the tumor, even by open biopsy, is frequent due to sampling error or misinterpretation. False negative diagnoses of malignant mixed tumors on biopsy have been reported in the literature, as in our case (16).

In conclusion, CXPA of the minor salivary gland is extremely rare and frequently misdiagnosed. When recurrence and distant metastasis occur, survival is remarkably low; therefore, early and adequate removal of malignant mixed tumors of the salivary glands is extremely critical. Although metastasis to the lungs is rare, patients treated for CXPA should be investigated for distant metastasis, such as to the lungs and bone.

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