

Primary lung adenoid cystic carcinoma: a case report and review of the literature

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Abstract: Adenoid cystic carcinoma (ACC) is a rare low-grade malignant epithelial tumor that usually originates in the salivary glands. It shows a slow progression and metastasizes rarely. A 74-year-old male patient was admitted to our clinic due to pulmonary lesions seen on a chest-X ray coincidentally. The patient, 6 years before admission, was operated on for a peptic ulcer perforation and a right hilar mass lesion, and bibasilar pulmonary nodular lesions were also found on his chest radiograph. A bronchoscopic biopsy revealed ACC and surgical treatment was offered to the patient; however, he refused it. The patient, who had a 130-pack-year smoking history, was asymptomatic on admission to our clinic. Since metastatic pulmonary lesions were present, the patient was diagnosed with stage IV lung cancer and given chemotherapy. Thorax computerized tomography, performed after treatment, revealed no change in the size or number of pulmonary lesions, and the patient has been followed since then and is still asymptomatic. This case of metastatic ACC was reported, after a review of the literature, as being a rare case, as the patient revealed no symptoms from the time of diagnosis until the end of treatment.

Key words: Adenoid cystic carcinoma, lung, asymptomatic

1. Introduction

Adenoid cystic carcinoma (ACC) shows distinct histopathological and clinical features, and it arises most commonly in the major and minor salivary glands and less commonly in other sites such as the breast, skin, uterine cervix, upper aerodigestive tract, and lungs (1). Primary ACCs of the lung, which commonly occur in the trachea and major bronchi, are very rare and account for only 0.09%–0.2% of all lung cancers (2).

The patient series of primary lung ACCs in the literature comprises a small number of cases, and the existing reports include limited data about the prevalence, clinical course, and treatment modalities of the disease and the response to treatment (3–15). The present case was reported as being an interesting one, since primary lung ACC is a very rare disease and since the patient was asymptomatic from the time of diagnosis until the end of treatment, although the disease showed an endobronchial localization with pulmonary metastases.

2. Case report

A 74-year-old male patient was admitted to our clinic due to pulmonary lesions seen coincidentally on a chest X-ray (Figure 1a). The patient, 6 years before admission, was operated on for peptic ulcer perforation and a right hilar

mass lesion, and bibasilar pulmonary nodular lesions were also found on his chest radiograph. Thorax computerized tomography (CT) performed at that time revealed similar lesions and a bronchoscopy was performed. During the bronchoscopic examination, a necrotic endobronchial lesion obstructing the right middle lobe bronchus was seen. The bronchoscopic biopsy of the lesion revealed an ACC and surgical treatment was offered to the patient; however, he refused.

The patient, who had a 130-pack-year smoking history, was asymptomatic on admission and had no coexisting diseases. The vital signs, physical examination, and laboratory findings were all normal. Thorax CT showed a right hilar mass and an accompanying atelectatic region as well as bibasilar nodular lesions (Figure 1b). The bronchoscopic biopsy specimens were reexamined and reported as an ACC (Figure 2). There was no metastasis seen upon abdominal and cranial CT examination. Bone scintigraphy showed an intense uptake of Tc-99m MDP in the thoracic vertebrae. Thoracic magnetic resonance imaging revealed prominent compression and loss of altitude of the 6th, 8th, and 10th vertebrae. Since the patient had a history of trauma, the neurosurgical consultation concluded that the patient did not have metastatic lesions but rather lesions due to trauma.

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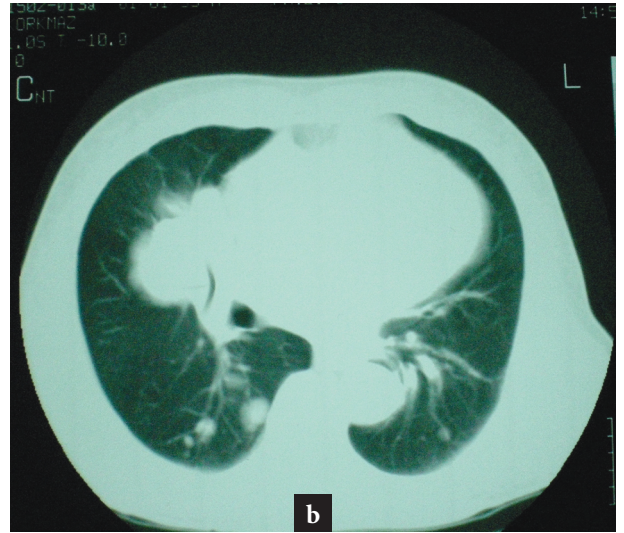
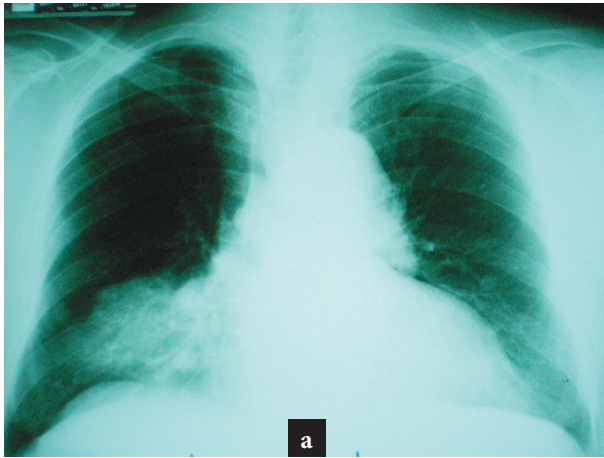


Figure 1. Chest X-ray (a) and thorax CT (b) on admission, revealing a right hilar mass and an accompanying atelectatic region, as well as bibasilar nodular lesions.

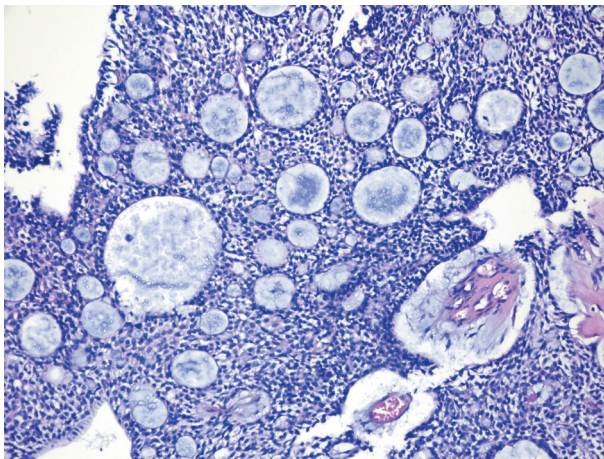


Figure 2. Tumor cells usually showing a cribriform pattern and having narrow cytoplasm with oval-round nuclei in the basophilic material (hematoxylin and eosin, 200 \times).

Although the radiological examinations of the reported patient at the time of diagnosis could not be obtained, it was considered that the patient had no metastasis in 2004 since surgery was offered to him for treatment. In the thorax CT performed in 2006, there were 2 metastatic lesions in the right lower lobe. The number and size of the metastatic lesions were found to have increased during the follow-up, although the patient was still asymptomatic. Due to the patient having metastatic pulmonary lesions, he was evaluated as having stage IV lung cancer and a chemotherapy regimen (cisplatin and gemcitabine) was prescribed. The patient, who had no change in the number and size of metastatic nodules after the therapy, was

considered to have a stable disease and was admitted to a follow-up program.

3. Discussion

ACC, which shows a slow progression and has a high long-term survival rate, is generally considered as a low-grade malignancy. Primary lung ACC affects both sexes equally and tends to occur in the 4th and 5th decades of life (16,17). The development of the disease has no association with cigarette smoking or other carcinogens (17,18).

The tumor has 3 major histopathologic growth patterns, namely cribriform, tubular, and solid. The most commonly found subtype is the cribriform pattern, which was also diagnosed in our case (17). Tumors with solid patterns have the worst differentiation and prognosis (16,17). However, there remains no definite relation between histologic subgroup and prognosis. In one of the studies investigating the relation between histologic subgroup and survival, a correlation was detected, whereas in others, no correlation was found (3,10,12).

The patients with centrally located ACC are usually asymptomatic on admission (4,7,9,10,17,18). Most patients with lung ACCs in the patient series by Moran et al. had symptoms due to obstructive pathology such as cough, wheezing, dyspnea, and hemoptysis (10). Although primary lung ACCs mostly affect the trachea and major bronchi, they may present as peripheral masses, or with Pancoast syndrome (15,19,20). Patients with peripheral ACCs in the literature were usually reported to be asymptomatic and the ACCs were seen on chest X-rays incidentally (15). The reported patient, although having a centrally located lesion, was asymptomatic both on admission and during follow-up.

Primary lung ACCs, which were initially classified as bronchial adenomas, are slow-growing, unencapsulated malignant tumors that tend to invade the perineural and submucosal region (4). Perineural invasion is seen in 40% of cases and the tumor characteristically extends along vascular structures, bronchi, bronchioles, and lymphatics (17,18). The disease may involve regional lymph nodes, usually with direct extension. High-grade tumors are much more aggressive and tend to spread radially into the adjacent lung parenchyma rather than along the airways (16). The metastases that are usually seen in the late stages of the disease mostly involve the lung, bone, liver, brain, and mediastinal lymph nodes (17,18).

The primary treatment modality for primary lung ACC is surgery. However, the difficulty of obtaining clear surgical margins in most cases, due to perineural invasion, increases the risk of local recurrence after resection (17,18). There are some studies showing that the prognosis is better in patients with primary lung ACC who were treated surgically (7,9). In the study by Kanematsu et al., 11 patients with primary lung ACC were treated surgically and 5 patients were treated with radiotherapy because of extensive tracheal invasion of the tumor in 4 patients and poor pulmonary function for a pneumonectomy in 1 patient. The 5-year and 10-year survival rates were 91% and 76% in the resected group and 40% and 0% in the nonresected group, respectively. In the resected group, 3 patients died. On the other hand, all patients died in the nonresected group (7). In another study that investigated the effect of surgical resection on prognosis, the survival rate for surgical patients with primary lung ACC was 73% at 3 years, 57% at 5 years, and 45% at 10 years. On the other hand, the survival rate for nonsurgical patients with primary lung ACC was 74% at 3 years, 53% at 5 years, and 31% at 10 years. The difference in survival between surgical and nonsurgical patients was statistically significant ($P < 0.01$). Researchers suggest that complete surgical resection, when achievable, provides patients with the best chance of long-term survival (9). However, the patients who were treated nonsurgically or underwent incomplete surgical resection had advanced disease, and so rendering these results was difficult.

Since ACCs have a propensity to spread submucosally and perineurally, adjuvant radiotherapy is routinely recommended in all resectable tumors of this cell type (11). Although primary radiotherapy is recommended for inoperable patients, the role of radiotherapy in the primary management of this tumor is still controversial. Gelder and Hetzel reported 34 cases of tracheal ACC treated either with surgical resection or primary radiotherapy. No difference in survival was observed between the 2 treatment groups

at the 5- and 10-year follow-ups (5). On the other hand, Grillo and Mathisen described significant improvement in median survival with complete resection followed by postoperative irradiation, as opposed to radiotherapy alone. They reported a median survival time of 118 months with resection and postoperative irradiation, compared with 28 months with radiotherapy alone (6). Maziak et al. reviewed their experience with 38 patients with ACC of the upper airway. Of the 38 patients, 32 were treated by surgical resection and reconstruction. The other 6 patients, with unresectable tumors, were treated with radiotherapy alone. Of the 32 patients undergoing resection, 26 received adjuvant radiotherapy. Local recurrence of the primary tumor in the airway was documented in 8 of the 32 patients. In contrast, 5 of the 6 patients treated with primary radiotherapy had local recurrence. There was no significant difference in mean survival between these 2 categories. Of the patients who had residual tumor after resection, 16 had a mean survival of 90 months and the other 16 patients, with complete resection and negative margins, had a mean survival of 119 months; there was no significant difference in these survival data. Although the survival differences did not reach statistical significance, the authors pointed out the trend for increased survival in the group undergoing complete resection, particularly at 10 years: complete resection of 69% and incomplete resection of 30%. They therefore suggested that adjuvant radiotherapy might have an effect on survival (8).

The role of chemotherapy in the treatment of metastatic lung ACC is controversial (14). The reported case, due to presence of metastatic pulmonary lesions, was evaluated as stage IV lung cancer and a chemotherapy regimen was prescribed by the Medical Oncology Department. Since the patient had no change in the number and size of metastatic nodules after 4 cycles of therapy, he was considered to have a stable disease and was admitted to a follow-up program.

In conclusion, primary lung ACC has a better survival rate than the other lung cancers. In the early stages, surgical resection is the first choice of treatment, especially for the tracheal adenoid cystic carcinoma. Since these tumors have a propensity to spread submucosally and perineurally, adjuvant radiotherapy is routinely recommended in all resectable tumors of this cell type. Although primary radiation therapy is recommended for patients who have inoperable lesions, the benefit of radiotherapy is controversial. In advanced stages, there is no consensus about which chemotherapeutic agent to choose, and therefore the side effects of the agent should be considered before prescription. For asymptomatic patients, follow-up programs with the best supportive care possible may also be considered.

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