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Case Report

Mucoepidermoid carcinoma of the lung with initial presentation of microangiopathic hemolytic anemia and thrombocytopenia

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ABSTRACT

Mucoepidermoid carcinoma is a rare entity of lung malignancy that is subclassified into high-grade or low-grade types according to its histological features. High-grade mucoepidermoid carcinoma is a more aggressive form of malignancy, with a tendency towards lymph node involvement and distant metastasis. Cancer-related microangiopathic hemolytic anemia as a less common situation of paraneoplastic syndrome may be encountered with metastatic malignancy, but has not been reported previously in mucoepidermoid carcinoma of the lung. Herein, we report a 78-year-old male patient who presented with hemoptysis for one day. Laboratory tests showed microangiopathic hemolytic anemia and thrombocytopenia. A chest X-ray demonstrated consolidation in the left lung field. Chest computed tomography revealed a mass in the left upper lobe, and a subsequent bronchoscopic biopsy was performed. The histopathological results indicated a high-grade mucoepidermoid carcinoma. Magnetic resonance imaging of the brain demonstrated leptomeningeal carcinomatosis. The patient refused systemic chemotherapy, and palliative radiation therapy only was conducted for local disease control. The patient has performed well for 12 months to date since diagnosis of the tumor.

1. Introduction

Mucoepidermoid carcinoma (MEC), a type of salivary gland tumor, is a rare neoplasm of the lung accounting for <1% of all lung tumors.[1] Histological grade is a significant prognostic indicator: low-grade pulmonary MECs grow slowly, and patients have an excellent prognosis with a 95% five-year survival rate, while high-grade pulmonary MECs tend to exhibit metastases and tumor recurrence, and lead to death.[1,2] Cancer-related microangiopathic hemolytic anemia (CR-MAHA) as a kind of paraneoplastic syndrome is usually found in metastatic malignancy; however, it has not been reported previously in mucoepidermoid carcinoma of the lung.[3] Following a literature search, we believe that our case represents the first documented report of CR-MAHA related to pulmonary MEC in the English literature.

2. Case report

A 78-year-old Taiwanese male with a medical history of type 2 diabetes mellitus under oral hypoglycemic agent control for 9 years and a history of cigarette smoking for 20 years was admitted to our hospital due to complaint of a dull anterior chest pain for 1 week and blood-tinged sputum for 1 day. His vital signs were stable. On physical examination, pale skin and jaundice were found. Laboratory tests showed typical features of microangiopathic hemolytic anemia (hemoglobin 9.5 g/dL, total bilirubin 2.65 mg/dL, direct bilirubin 0.65 mg/dL, lactate dehydrogenase 1117 U/L, and fragmented red blood cells in a peripheral blood smear) and thrombocytopenia (platelet count 17 $\times$ 10^3/μL). His coagulation profile was within normal limit (prothrombin time 12.0 seconds, control 12.1 seconds, activated partial thromboplastin time 30.2 seconds, plasma fibrinogen 363.2 mg/dL, fibrinogen degradation product 2.9 μg/ml and D-dimer 170 ng/mL). Due to a lack of other causes of primary thrombotic microangiopathies, CR-MAHA was diagnosed later after lung cancer was evidenced. The patient received plasma exchange with fresh frozen plasma for 10 days, following which

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complete remission of microangiopathic hemolytic anemia and thrombocytopenia was achieved.

A chest X-ray demonstrated consolidation in the left lung field (Fig. 1). A chest computed tomography (CT) scan revealed a 4.6-cm mass lesion in the left upper lobe of the lung with involvement of the left upper lobe bronchus and associated consolidation (Fig. 2). Further investigations were arranged in order to rule out lung cancer. A [^{18}F]2-Deoxy-2-fluoro-D-glucose (FDG) positron emission tomography (PET) scan revealed metastatic lymph nodes at the aortopulmonary, subcarinal and right supraclavicular regions. Magnetic resonance imaging of the brain revealed leptomeningeal carcinomatosis in the right temporoparietal region (Fig. 3). A bronchoscopic biopsy was performed, and pathohistologic study revealed the tumor to be composed of atypical squamoid cells, intermediate cells and mucous cells arranged in angular nests or irregularly-shaped glands in the submucosa (Fig. 4a). The surface epithelium showed no squamous metaplasia nor dysplastic change. The mitotic activity measure was 2 per 10 high-power fields. Immunohistochemical staining demonstrated consistent expressions of p63 and p40 in the cells and mucin and D-PAS in the intracytoplasmic vacuoles (Fig. 4b). The result of study for TTF-1 was negative. The final histological diagnosis was high-grade MEC based on the above morphological and immunohistochemical features.

Due to old age and the advanced stage of the disease, the patient rejected systemic chemotherapy. Palliative radiation therapy was conducted for local disease control. The patient has performed well for 12 months to date since diagnosis of the tumor.

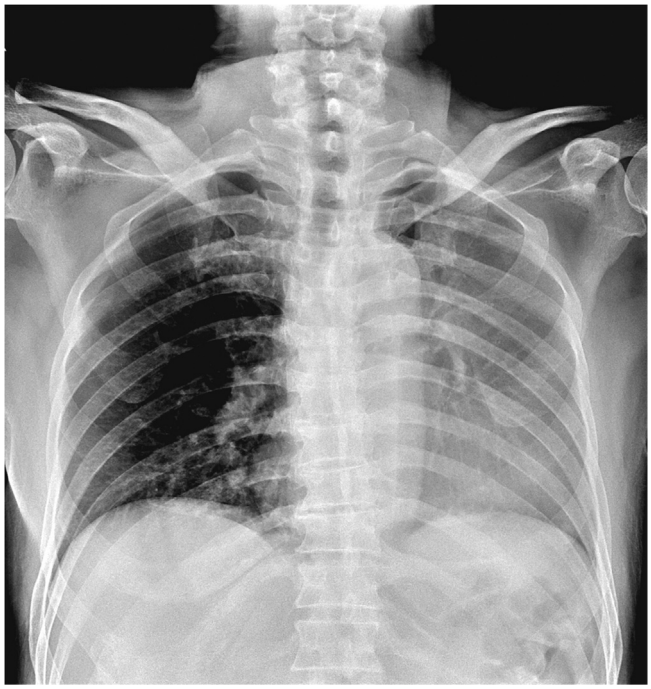

Fig. 1. Chest X-ray showed consolidation in the left lung field.

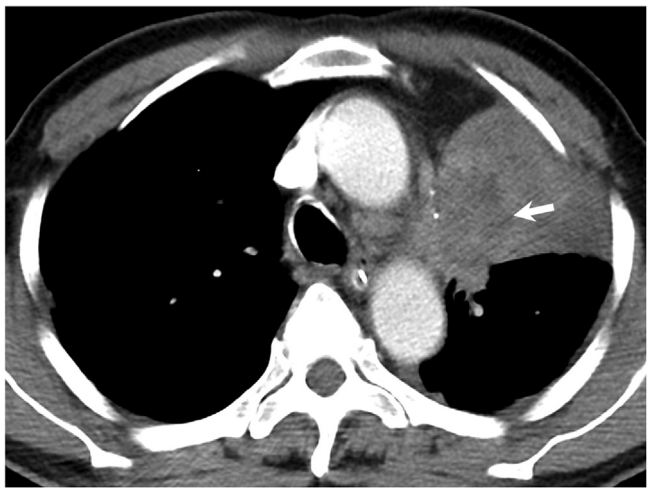

Fig. 2. Computerized tomography imaging with contrast enhancement of the chest demonstrated a heterogeneously enhanced (4.6 × 3.8 cm) tumor in the left pulmonary hilar region (arrow), causing obstruction of the left upper bronchus and partial collapse of the left upper lobe of lung.

3. Discussion

MEC is a rare entity of lung malignancy, representing 0.1–0.2% of all pulmonary tumors.[1] Wang et al. reported the average age of the patients to be 44.35 ± 17.10 years.[2] It is most often seen in young adults, although all age groups (3–78 years) can be affected. No similar risk factors for bronchial carcinoma such as cigarette smoking or asbestos exposure appear to be associated with MEC.[4]

MECs most often arise from the major salivary glands, such as the parotid or submandibular glands. The World Health Organization classifies pulmonary MECs as “salivary gland type” tumors, and pulmonary adenoid cystic carcinomas and epimyoepithelial lung carcinomas belong to the same classification.[5] Pulmonary MECs mostly arise in the proximal bronchi. An unusual case of MEC arising from bronchogenic cysts has been reported.[6] Grossly, the average tumor size at diagnosis is 2.2 cm (ranging from 0.5 to 6 cm) according to the literature.[4] In our patient, the tumor arose from the left upper lobe bronchus and measured 4.6 cm in diameter. Histologically, MECs feature composite mucus-secreting, squamous, and intermediate cell types, and are subclassified into low- and high-grade types. Low-grade MECs consist primarily of a glandular element and mucus-secreting cells. On the contrary, high-grade MECs are mainly composed of sheets or nests of squamoid and intermediate cells, and mucus-secreting cells account for smaller populations. Moreover, high-grade MECs present cellular necrosis and cytological atypia such as nuclear pleomorphism or significant mitotic activity. Histological grade is a significant prognostic indicator, and high-grade MECs tend towards metastases and tumor recurrence, and lead to death.[7]

Image study, such as chest CT, plays a supplementary role in the diagnosis of pulmonary MECs with help in identifying pulmonary tumors and their extent. Although pulmonary manifestations of pulmonary MECs in CT image studies are variable and nonspecific, they tend to present as a well-defined ovoid or round tumors with moderate to marked heterogeneous contrast enhancement.[8] Wang and colleagues reported some differing features in CT studies between low- and high-grade MECs: a central bronchial nodule with markedly homogeneous contrast enhancement may suggest low-grade MECs, while high-grade MECs may appear with peripheral, ill-defined margins and lobular-shaped nodules with lower heterogeneous contrast enhancement.[2] To predict the tumor grade, FDG-PET scan is generally accepted nowadays as an efficient preoperative imaging modality to assess nodal stage and post-surgical prognosis. A tumor lesion with an increased FDG uptake, with a maximum voxel-based standardized uptake value greater than 6.5, tends to be a high-grade MEC, a lymph node involvement or a recurrent MEC.[9]

The typical symptoms of pulmonary MEC patients are related to bronchial obstruction and lung atelectasis, such as a cough,

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