Sarcoid Reactions Scattered in the Tumor-Bearing Lung Parenchyma and Regional Lymph Nodes Associated with Pulmonary Carcinoid

Yasunari Miyazaki, Shuji Miyake, Reiko Taki, Yasumi Ohkouchi*, Osamu Matsubara* and Yasuyuki Yoshizawa

A 77-year-old woman was admitted to our hospital because of a mass lesion in the left lung. The tumor was pulmonary carcinoid associated with sarcoid reactions in the regional lymph nodes and scattered in the resected lung parenchyma. Pulmonary carcinoid with sarcoid reactions is extremely rare. This appears to be the first case report in which tumor-related sarcoid reactions were studded within the tumor-existing lung parenchyma and confirmed not to be within the uninvolved right lung. (Internal Medicine 37: 304-306, 1998)

Key words: sarcoidosis, neoplasm, amine precursor uptake and decarboxylation system cells, bronchoalveolar lavage

Introduction

Pulmonary carcinoid tumor is a low grade malignant neoplasm believed to be derived from the amine precursor uptake and decarboxylation system (APUD) cells on the bronchial or bronchiole wall (1, 2).

In the sarcoid reaction, tumor-related sarcoid reactions have generally been reported that epithelioid cell granuloma-like sarcoidosis is observed in the regional lymph nodes, or in the parenchyma around the tumor (3, 4).

Case Report

A 77-old-woman who never smoked, was admitted to our hospital for further evaluation of a mass in the left lung on chest films. Family history revealed that her father had gastric cancer, her mother had bladder carcinoma and her son had lung cancer. On physical examination, no lymphadenopathy and no skin lesions were found. The lungs and heart were normal.

The laboratory findings on admission were within normal limits except for an electrocardiogram showing atrial premature conduction. The values of carcinoembryonic antigen (CEA), angiotensin converting enzyme (ACE) and lysozyme were also within normal limits. Radiograph of the chest on admission revealed a 1.5 cm diameter round mass in the left upper field (Fig. 1). The computed tomographic (CT) scan of the chest showed a 1.5 cm diameter round mass in the left segment (S) 1+2c and mediastinal lymph nodes of less than 1 cm in diameter (Fig. 2). An ophthalmologic consultant found no evidence of ocular abnormalities. A tuberculosis skin test was positive. Sputum cytology was negative for malignant cells.

The specimens of transbronchial biopsy (TBB) were insufficient to make a diagnosis. As the possibility of lung cancer was considered, left upper lobectomy and resection of regional lymph nodes were performed.

Histopathologic examination revealed that the tumor consisted of polygonal, low cylindrical and spindle-shaped cells and formed solid and tubular structures. Very few mitoses were observed (Fig. 3). The tumor cells were positive with Grimelius stain and immunohistochemical staining of chromogranin and N-CAM related to neuroendocrine cells were also positive. The patient was diagnosed as having typical pulmonary carcinoid. Non-caseating epithelioid cell granulomas were observed in the resected lung parenchyma and lymph nodes (Fig. 4A, B). Non-caseating epithelioid granulomas were scattered within the left upper lobe, mainly in the left S4 and S5 which are away from the tumor as well as in the left S1+2 in which the tumor was located.
Bronchoalveolar lavage (BAL) and TBB were done in the right lung, the non-operated lung. The recovery rate of BAL was 63%. The ratio of CD4 to CD8 could not be evaluated because few lymphocytes were present in BAL fluids (about 5%). The specimens obtained by TBB from five different areas of the uninvolved right lung showed no findings suggestive of sarcoidosis.

The results of the positive tuberculin skin test, normal levels...
of ACE and lysozyme, no sarcoid lesions in eyes, skin and the non-operated lung mitigated against a diagnosis of systemic sarcoidosis. Moreover, the patient has not developed systemic sarcoidosis during the follow-up period of four years.

**Discussion**

Differentiation between systemic sarcoidosis and sarcoid reactions is difficult based upon the pathological findings. Sarcoidosis is known to be a systemic disease (5) and the present case showed no evidence of sarcoidosis except in the resected lung and the regional lymph nodes. Specifically, the non-involved lung showed no granulomatous lesions even though more than five specimens were obtained by TBB. Based on the cumulative findings, we diagnosed this case as sarcoid reactions in association with pulmonary carcinoid.

The present case disclosed sarcoid reactions not only in the regional lymph nodes but also scattered in the resected left upper lobe. Tumor-related sarcoid reactions have generally been reported to be in the lymph nodes draining regions with a malignancy disease, or in the parenchyma around the tumor (6, 7).

The etiology of tumor-related sarcoid reactions is unknown. Laurberg (8) have proposed the following: 1) an immunological reaction to substances released by the tumor and transported along the lymphatic system; 2) an unrecognized sarcoidosis predisposing to lung cancer; 3) the coexistence of sarcoidosis and malignant tumor (8). The first hypothesis is likely because pulmonary carcinoid tumor is a low grade malignant neoplasm derived from APUD system cells which appear to release various substances. However, sarcoid reactions that were scattered within the left upper lobe in which the tumor was located can not be explained by these reasons. Klein et al have found the presence of HLA-B8 and DR3 antigens, as well as high levels of TNF and IL-2 in the patients with sarcoid reactions (6). HLA-B8 and DR3 antigens are known to be associated with immunologic dysfunction (primary biliary cirrhosis, primary sclerosing cholangitis, ulcerative colitis, and sarcoidosis). In addition, the secretion of cytokines could be involved as a stimulating factor that induces granuloma formation (6).

Laurberg reported that the frequency of associated sarcoid reactions is 3.2% in patients with pulmonary neoplasms, predominantly in squamous cell carcinomas (8). Histologically, squamous cell carcinoma showed a statistically significant predominance (8). However, sarcoid reactions in pulmonary carcinoid are so rare that the frequency has not been reported.

To the best of our knowledge, sarcoid reactions associated with pulmonary carcinoid was found in only one report (8). In addition, the present case showed sarcoid reactions scattered within the tumor-existing lung parenchyma as well as around the carcinoid tumor and not in the non-involved lung. The distribution of this sarcoid reaction is the first description in patients with pulmonary carcinoid tumor.

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**References**