Granular cell tumor of the bronchus coexisting with a bronchogenic adenocarcinoma – case report

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SUMMARY

Pulmonary granular cell tumors (GCTs) are uncommon and usually benign and their coexistence with bronchogenic adenocarcinoma is rare. We report the case of 50-year-old woman with GCT located in the left lung hilum, which occurred simultaneously with a primary bronchogenic adenocarcinoma in the same area. Contrast CT scan of the head revealed secondary deposits in the right cerebellum, presumably of adenocarcinomas origin. Bronchoscopy revealed narrowing on the beginning of the left lingular bronchus and infiltration of the medial distal wall of the left main bronchus. Large tumor cells with eosinophilic granular cytoplasm were seen on light microscopic examination. Tumor cells fully occupied submucosa and had small, round nuclei with no signs of pleomorphism. Immunohistochemically, these cells were S-100 positive. In small area, groups of atypical oval-shaped cells of adenocarcinomas origin were noticed. This confirmed the diagnosis of GCT coexisting with adenocarcinoma. After consultation with oncologists, the patient was scheduled for further polychemotherapy and radiation treatment.

Key words: *Lung Neoplasms; Granular Cell Tumor; Adenocarcinoma; Carcinoma, Bronchogenic*

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INTRODUCTION

Granular cell tumors (GCT) are rare, usually benign mesenchymal neoplasms. They were first described by Abrikossoff in 1926 as tumors resembling embryonic myoblasts arising in the tongue, which was called myoblastenmyome (1). The term „granular cell tumor" was introduced the following year (2, 3). It is believed that these tumors are of Schwann cells origin (2, 3). GCTs can occur in almost any organ but predominantly they are found in the skin, tongue, and breast (4). Pulmonary GCTs are thought to comprise less than 10% of all GCTs (5). In the lung they can appear in trachea, predominantly in bronchial tree and very rare in peripheral lung area (6, 7). There have been few reports of pulmonary GCTs coexisting with bronchogenic adenocarcinoma. This association may be coincidental, but it has been suggested that pulmonary GCTs may be markers for an underlying malignant pulmonary tumor (8). In this article, we report the coexistence of benign pulmonary GCT with bronchial adenocarcinoma and metastatic disease in the cerebellum.

CASE REPORT

A 50-year-old female patient was admitted to the hospital for evaluation of headache, nausea, and postural instability. She had anorexia with weight loss over a past few months period and a smoking history (60 cigarettes per day). From the age of 17 she was suffering from allergic bronchitis. Because of dominant neurological symptoms, a contrast computed tomography (CT) scan of the head was performed and secondary deposits (1.5 cm) in right cerebellum with perifocal edema were described (Figure 1A). CT scan of thorax was necessary to determine the origin of the primary tumor. A thorax CT scan showed a tumor-like change in the left lung hilum, which was connected with costal pleura in stripe-associated arrangement. The tumor deformed the left lower bronchus and it was in contact with posterior wall of the left main bronchus, which had also been deformed (Figure 1B).

Physical examination was within normal limits. Hemoglobin level was 142 g/l, red blood cell count was 4.28×10^{12}, white blood cell count was 14×10^{9}, and hematocrit was 37.7%. Blood glucose level, bilirubin, urea, and creatinine blood levels were normal. Ultrasonography of abdomen was normal. Bronchoscopy revealed a narrowing at the beginning of the left lingular bronchus and infiltration of the medial distal wall of the left main bronchus. Narrowed areas did not interfere with the airflow. Samples were taken during bronchoscopic biopsy. Tissue was fixed in formalin, embedded in paraffin, and sectioned for hematoxylin and eosin (HE) staining. For immunohistochemical staining S-100 (DAKO) and Cytokeratin 7 (CK 7; DAKO) antibodies were applied.

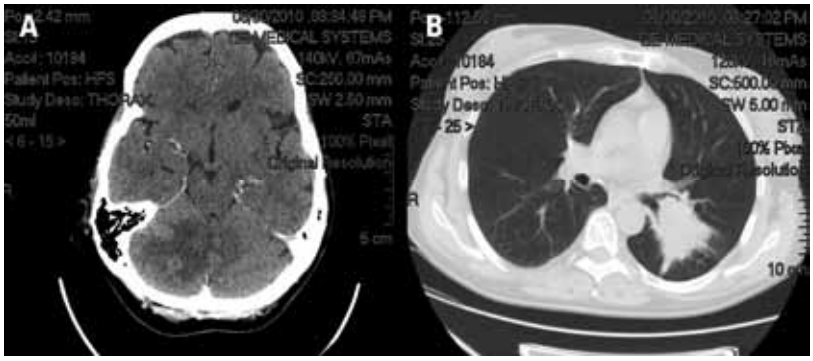

Figure 1. A) Secondary deposits (1.5 cm) in right cerebellum with perifocal edema were described; B) Thorax CT scan showed a tumor-like change in the left lung hilum, which deformed left main and lower bronchi

Pathological findings

On light microscopy, the examined bronchial tissue showed a tumor which fully occupied submucosa while mucosa showed focal squamous metaplasia. The neoplastic cells were large, uniform, rounded to polygonal with eosinophilic granular cytoplasm. Nuclei were round to oval, small, hyperchromatic and central to eccentric location. No signs of malignancy (atypia, mitotic figures, or vascular invasion) could be found (Figure 2A).

Immunohistochemically, tumor cells were S100 positive (Figure 2B). In small area of blood, separated from the rest of the tissue sample, groups of atypical oval-shaped cells with eosinophilic cytoplasm were noticed. Nuclei of these tumor cells expressed nuclear pleomorphism and mitoses. They represented malignant cells which originated from bronchial adenocarcinoma and which were diffusely positive for CK7 antibody (Figure 3). The assays performed, confirmed the diagnosis of granular cell tumor of the bronchus coexisting with bronchogenic adenocarcinoma. Tissue samples taken from the left upper and lower bronchus revealed signs of chronic bronchitis without tumor cells.

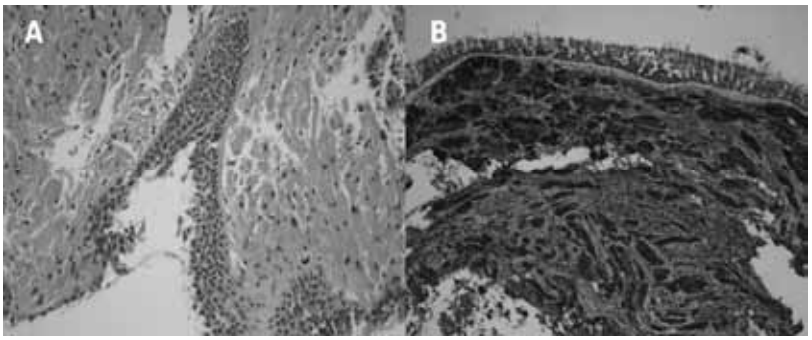

Figure 2. A) Subepithelial infiltration of large, uniform tumor cells with eosinophilic granular cytoplasm and mucosa showing focal squamous metaplasia (HE, x20); B) Immunoprofile of these tumor cells showed S-100 positivity (x40)

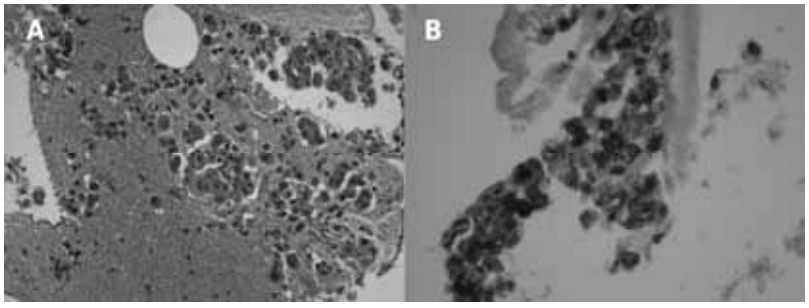

Figure 3. A) Blood with groups of atypical cells, which originated from bronchogenic adenocarcinoma (HE, x40); B) Immunoprofile of these tumor cells showed CK7 positivity (x40)

After further consultation with oncologists, polychemotherapy was required as well as radiation of the head. The patient was discharged from hospital after 11 days and scheduled for appropriate therapy protocol.

DISCUSSION

Granular cell tumors are mesenchymal neoplasms, which originate from Schwann cells and are almost always benign (9). They predominantly involve skin, breast, or tongue, and about one half of the cases are located in the head and neck region (2, 3). In lungs, they are exceedingly rare and only 6% to 10% of them involve respiratory tract (10). Since 1926, fewer than 80 cases involving lungs have been reported (11).

There is little data about inducing factors. Pulmonary GCTs are frequently associated with cigarette smoking. In our case, the patient had a long history of smoking. Because of small number of patients and the insufficient data, any speculation on, whether GCT is a smoking-related disease, would not be appropriate.

Pulmonary GCTs are usually seen in the lower trachea and central bronchi down to the segmental level. They have a tendency to occur at bifurcation sites. The GCTs in our case had a central bronchial location. Pulmonary GCTs are usually singular, but can be multiple in 7% to 25% of cases (6). When multiple tumors are present in the lung, metastases from another primary tumor must be ruled out. In our case, GCT was presented as a singular lesion.

Patients with granular cell tumors may have respiratory symptoms related to bronchial obstruction, dry or productive cough, hemoptysis, night sweats or weight loss (7). Our patient had dominant neurological symptoms due to the brain metastases with anorexia and weight loss, but there were no respiratory symptoms presented.

Although there are several case reports presenting malignant GCT with distant metastases, the clinical behavior of pulmonary GCT is believed to be benign (2, 6, 12). An extensive review of the literature revealed six cases of benign pulmonary GCTs coexisting with bronchogenic carcinoma. This review included three adenocarcinomas, two squamous cell carcinomas and one small cell carcinoma (8, 13, 14). In our case, coexistence with adenocarcinoma was reported.

Microscopically, granular cell tumors are composed of cells with abundant eosinophilic granular cytoplasm with small and uniform nucleus. While they commonly appear well circumscribed grossly, microscopically they infiltrate submucosa and area around submucosal glands and cartilage (6). Tumor cells are positive for specific neural cell markers. S-100 protein is usually expressed. Other immunohistochemical results include positive staining for neuron-specific enolase, vimentin, actin and CD68 (6). In our case, we found immunoreactivity for S-100 protein in granular tumor cells while cells of adenocarcinoma origin showed immunoreactivity for CK7.

Treatment of GCT located in respiratory tract involves curative resection. In endobronchial cases, cryotherapy or other means, such as laser or electrocautery, are used (10, 15). There are reports of patients with GCT who did not receive any treatment, but none of them died during their follow-up (15). Coexistence of GCT and bronchogenic carcinoma requests individual therapy protocol that depends on the presence of metastases, location of the tumors, and type of bronchogenic carcinoma. In our case, the patient was scheduled for further conservative therapy protocol.

Conflict of interest

We declare no conflicts of interest.

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