Bronchioloalveolar Carcinoma Masked by Gravity-dependent Gradient on Computed Tomography


Abstract

A 78-year-old woman was found to have a small bronchioloalveolar carcinoma with ground-glass attenuation in the gravity-dependent gradient in the left lower lobe during a preoperative chest computed tomography (CT) evaluation, which was performed for previously-diagnosed adenocarcinoma of the right upper lobe. To remove the gravitational effect of the CT, the patient underwent a thin-slice CT in the prone position. Then, a ground-glass attenuation was revealed clearly in the left lower lobe. Postoperative pathological diagnosis was synchronous multiple bronchioloalveolar carcinomas, stage IA. This case suggests that focal areas of ground-glass attenuations on a thin-section CT in patients with BAC would be considered to be multicentric development of BAC. CT with the patient in the prone position helps to exclude the gravitational effect and narrow the differential diagnosis of ground-glass opacity, including localized forms of BAC.

Key words: ground-glass attenuation, gravity-dependent gradient, prone position

Introduction

Bronchioloalveolar carcinoma (BAC) remains one of the most enigmatic and controversial lung cancers, and it has a broad spectrum of radiographic appearances. BAC most commonly appears at initial examination as a solitary peripheral nodule, and it also often occurs as multinodular consolidation and lobar or diffuse consolidation (1-3). Other atypical features such as lobar atelectasis and cavitation, have also been described (4, 5).

Development of BAC appears to be stepwise, and the earliest lesion to be recognized is atypical adenomatous hyperplasia (AAH), the proliferative lesion of atypical epithelial cells along the alveolar septa (6). AAH and the earliest lesion of BAC show ground-glass attenuation on chest computed tomography (CT) (6, 7). Such an area of ground-glass attenuation is thought to reflect the unique lepidic growth pattern of AAH and BAC. Zwirewich et al assessed the pathologic correlation of a variety of edges and the internal characteristic of BAC seen on CT; they reported that a lepidic growth pattern along the alveolar septa with a relative lack of acinar filling accounts for the “ground-glass” attenuation at the periphery of a BAC nodule and that compact cellular growth patterns reveal higher attenuation (8).

In patients in the supine position on CT, we often see the ground-glass attenuation in the gravity-dependent area of the lungs. Because the physical density of the lung (the attenuation measured on CT) is always influenced by gravity, such a ground-glass density observed in the dependent area is called a “gravity-dependent gradient” which is determined by lung tissue, blood, and air (9-11). These components are not homogeneously distributed in the lung, and their relative proportion changes continuously during normal physiologic events. The degree of inflation can change the density of the lung rapidly and markedly. Gravity causes regional differences in density by increasing the vascular component and decreasing alveolar expansion in dependent areas. The largest changes in lung density occur in the dependent regions as a ground-glass attenuation on CT image (9).

In the present report, we describe a case of double-primary BAC with ground-glass opacity masked by gravity-dependent gradient on CT. We would like to emphasize the necessity of taking a prone position CT image, when diagnosing BAC.

Case Report

A 78-year-old woman with no history of smoking was admitted to our hospital for further evaluation because of an abnormal chest radiograph which was taken at a regular health examination (Fig. 1A). At our hospital, physical examination...
Figure 1. Chest radiograph and CT scan on admission. (A) Chest radiograph shows an undefined solitary nodular shadow in the right upper lung field. (B) A thin section CT scan depicts an 25-mm area of poorly defined nodular opacity with pleural indentation in the right upper lobe.

revealed nothing remarkable. An abdominal examination was normal. There was no peripheral edema, digital clubbing or cyanosis. In a laboratory examination, the white blood cell count was 4,000/μl with a normal differential. Hemoglobin and hematocrit were normal. CRP was not increased. Arterial blood gas analysis showed PO$_2$ of 81.0 mmHg, PCO$_2$ of 36.0 mmHg and pH 7.45. Lung function studies showed a vital capacity of 78.1% and forced expiratory volume was 1s (FEV$_1$) 100%. A tuberculin skin test (PPD) was negative. Tumor markers investigated (CEA, SLX, SCC, NSE), were within the normal limit.

A thin section CT depicted a 25-mm area of poorly defined nodular opacity with pleural indentation in the right upper lobe (Fig. 1B). Bronchoscopy showed a normal tracheobronchial tree, and transbronchial lung biopsy at the right upper lobe revealed the nonmucinous BAC. Since there was no enlarged lymph node in the hilum or the mediastinum, and no evidence of distant metastasis, we initially diagnosed her as stage IA BAC in right upper lobe. However, a thin section CT depicted the thickened gravity-dependent gradient in the left lower lobe (Fig. 2A, arrows). To remove the gravitational effect of the CT, the patient underwent a thin section CT in the prone position. Then, a ground-glass attenuation with typical radiologic features of small BAC was revealed clearly in the left lower lobe (Fig. 2B). To remove the gravitational effect of the CT, the patient underwent a thin section CT in the prone position. Then, a ground-glass attenuation with typical radiologic features of small BAC was revealed clearly in the left lower lobe (Fig. 2B). Since the cytologic distinction between BAC and reactive bronchial cells can be difficult occasionally (12), we did not perform needle aspiration biopsy to the lesion in the left lower lobe. However, intraoperative pathological diagnosis by frozen section revealed it to be localized BAC with foci of alveolar structural collapse.

The right upper lobe was resected, and histopathologic examination revealed nonmucinous BAC, stage T1 N0 M0 (Fig. 3A). Simultaneously, the left lower lobe was partially resected. Noguchi et al reported that localized BAC with foci of alveolar structural collapse (so called type B) showed no lymph node metastasis, rare vascular and pleural invasion, a low mitotic rate, and excellent prognosis (100%, 5-year survival) (13). Therefore, we performed partial resection of the left lower lobe for preservation of lung function. Histopathologic examination of the left lower lesion also showed nonmucinous BAC, stage T1 N0 M0 (Fig. 3B). We finally diagnosed this case with double primary BAC.

Discussion

BAC represents 1.5–6.5% of all primary pulmonary neoplasms, and its prevalence is said to be rising (2). BAC occurs at a strikingly high rate in women; 30–50% of the cases of BAC are women (2). This higher rate is especially noticeable in localized forms of BAC, as found in the present patient. It is currently believed that BAC may actually have two distinct clinical entities, its focal and diffuse forms, with identical histologic features (14). On initial examination, BAC most commonly appears as a solitary, well-circumscribed, peripheral pulmonary nodule, which rarely evolves into diffuse diseases; these patients have an excellent prognosis after resection. In its diffuse form, BAC has varied appearances, including multinodular, lobar, and diffuse consolidation. The progress is rapid
and aggressive, and patients have limited survival regardless of intervention (1–3). Most patients with the focal form of BAC are asymptomatic, and the disease is usually detected only at routine radiologic examination (2, 3).

Although BAC has a wide spectrum of radiologic appearances, the focal form often has distinctive features. In several reports, the features of solitary BAC were extensively described (7, 8, 14–19). Kuhlman et al suggested the characteristic CT features of solitary BAC after reviewing CT in 30 cases (16). These features included a peripheral or subpleural location, pseudocavitation, heterogeneous attenuation, pleural tags, and star-shaped irregular margins. In addition, focal areas of ground-glass attenuation at CT could be an early sign of localized BAC. Jang et al also speculated that areas of ground-glass attenuation may represent an early stage of BAC (7).

Recent progress in image analysis has made small parenchymal lung lesions such as AAH easily detectable. The typical CT finding of AAH is the same as the early stage of BAC.
(6, 7). AAH has come to be suspected as being a precursor lesion of BAC of the lung based on studies of surgically resected pulmonary material (20, 21), and AAH is now categorized as a precursor lesion of adenocarcinoma in the new lung tumor classification of the World Health Organization (22). Some studies provide evidence for a strong association between AAH and primary lung adenocarcinoma and lend weight to the AAH/adenoma-carcinoma hypothesis (22–27). The finding of multiple AAH lesions in patients with multiple lung cancers, together with the report of AAH in a patient with multiple synchronous lung cancers in Li-Fraumeni syndrome (28) and multiple AAH lesions associated with tumors which have deletions in the tuberous sclerosis complex (TSC-1) region on 9q (23), suggest underlying genetic abnormalities in this disease. We should remember therefore that multiple AAH, a precursor of BAC, may exist somewhere in the lungs in patients with lung cancer. We should be especially careful to read the area of gravity-dependent gradient which usually shows ground-glass attenuation on CT.

The gravity-dependent gradient is usually depicted in the dependent zone of the lungs on routine CT. The gradient in attenuation between dependent and non-dependent zones of the lung can be explained by gravitational differences in perfusion and inflation. Occasionally, some kinds of diffuse lung diseases which occur in the dependent zone are masked by the gravity-dependent gradient. Hwang et al reported that CT with the patient in the prone position help to narrow the differential diagnosis among various diseases and help diagnose or exclude subtle diseases in the posterior part of the lung, respectively (29). The present patient was in the prone position, and the pressure gradients were reversed. Then, the small BAC could be clearly observed. CT from prone patients is valuable in assessing suspected multicentric AAH or BAC in the gravity-dependent gradient.

In conclusion, a focal area of ground-glass attenuation on a thin-section CT is one of a variety of appearances of BAC and could be considered its multicentric development. CT with the patient in the prone position are helpful to narrow the differential diagnosis of ground-glass opacity, including localized forms of BAC or to exclude the gravitational effect.

References