Necrotizing Aspergillosis of Large Airways: CT Findings in Eight Patients

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Purpose: The aim of this study was to evaluate the CT findings of pathologically proven necrotizing aspergillosis of the large airways (necrotizing Aspergillus bronchitis).

Method: Medical records and imaging studies from two tertiary medical centers were reviewed for pathologically proven cases of necrotizing aspergillosis of the large airways. Fiberoptic bronchoscopic examination and CT scans of the chest were available in all cases. Two thoracic radiologists who were blinded to the clinical and pathologic data reviewed the thoracic CT scans retrospectively and reached a final decision. The CT images were evaluated for the presence, distribution, and extent of CT findings.

Results: The study included eight patients, seven men and one woman, ranging in age from 28 to 67 years (mean age 46 years). All patients had histopathologically proved necrotizing Aspergillus of the large airways and no other superimposed infections. Six patients had leukemia, one had chronic liver disease, and one had chronic obstructive lung disease. All patients had bronchial wall thickening and focal bronchial narrowing involving a lobar or segmental bronchus. The bronchial narrowing was irregular or nodular in seven patients and smooth in one. Atelectasis distal to a narrowed bronchus was present in five patients.

Conclusion: The CT findings of necrotizing bronchial aspergillosis include bronchial wall thickening, which is often nodular, and narrowing of the bronchial lumen, which is often associated with distal atelectasis.

Index Terms: Lung—Lung, diseases—Aspergillosis—Computed tomography.

INTRODUCTION

Aspergillus infection can result in a wide spectrum of pulmonary abnormalities. The histologic, clinical, and radiologic manifestations of pulmonary aspergillosis are influenced by the number and virulence of the organisms and by the patient’s immune response (1–4). The most common manifestation in immunocompromised patients is angioinvasion. Less commonly, Aspergillus may result in airway invasion, usually in the form of bronchiolitis or bronchopneumonia (3). In the large airway, aspergillosis may manifest as saprophytic colonization, tracheobronchitis, ulcerative tracheobronchitis with or without pseudomembrane formation, and necrotizing (invasive) aspergillosis. Occasionally the airway invasion may be limited to the large airways, a condition known necrotizing bronchial aspergillosis and characterized histologically by invasion of bronchial mucosa with Aspergillus. Descriptions of the findings in this condition have been limited largely to the clinical literature (4–6). The aim of the current study was to assess the CT findings in eight patients with histologically proven necrotizing aspergillosis affecting the large airways.

MATERIALS AND METHODS

During the period from January 1995 to October 2001, microbiologic and pathologic records from two large tertiary medical centers were searched for histologically proven cases of necrotizing bronchial aspergillosis. Only patients in whom necrotizing aspergillosis of the large airways were documented by either biopsy or autopsy were included in the study. Their age, gender, and immune status were reviewed. CT scans and bronchoscopic findings were reviewed for the appearance and distribu-
tion of disease. The patients were examined with either a Toshiba 900 CT unit or Asteion CT scanner (Toshiba Medical Systems, Tokyo, Japan) or a Tomoscan SR 7000 scanner (Philips Medical Systems, Best, The Netherlands). Because this was a retrospective review, several different CT scan protocols were used. Conventional CT scanning, using 10 mm slice collimation at 10 mm intervals, was performed in all patients, before and after intravenous administration of 120 ml of nonionic contrast material (Conray; Mallinckrodt Medical, St. Louis, MO, U.S.A.). Four patients also underwent thin section CT using 2 mm collimation at 10 mm intervals. CT scans were obtained at suspended end-inspiratory volume with an imaging time of 2 s. All images were retrospectively reviewed by two chest radiologists, and final decisions were reached by consensus.

RESULTS

Eight patients were identified (seven men and one woman; age range 28–67 years, mean age 46 years). Four of the eight patients had acute myelogenous leukemia, two had acute lymphoblastic leukemia, one had chronic liver disease, and one had received prolonged low dose corticosteroid treatment of chronic obstructive pulmonary disease. One patient was a lifelong non-smoker, and seven patients were ex-smokers. Review of the clinical records of these eight patients determined that there were no concurrent comorbid diseases of the airways at the time of diagnosis of necrotizing bronchial aspergillosis. One patient had a remote history of treated uncomplicated tuberculosis. Presenting clinical symptoms in all patients were cough, sputum production, dyspnea, hemoptysis, and fever. The diagnosis was histologically proven by bronchial and transbronchial biopsy (n = 7) or at surgery (n = 1); the diagnosis was confirmed at autopsy in two patients.

CT scans were performed within a week prior to bronchoscopy (range 1–7 days, median 3 days). All patients had bronchial wall thickening and narrowing of large bronchi evident on CT. They involved the right main bronchus in three patients, the anterior segment of the right upper lobe in two, and the left main bronchus in three. Luminal narrowing was irregular or nodular in seven patients (Figs. 1 and 2) and smooth in one patient.

FIG. 1. A 46-year-old man with acute myelogenous leukemia and necrotizing Aspergillus bronchitis who presented with cough and sputum production. A: CT image obtained at the level of the carina (10 mm section) shows circumferential thickening and narrowing of the major right bronchus. Note irregular nodular areas involving the bronchial mucosal surface (arrow); bilateral areas of consolidation are also present. B: CT image obtained 1 cm below the carina (10 mm section) demonstrates an irregular left bronchial stenosis associated with an endobronchial nodule (short arrow) and ill-defined parenchymal consolidation in the left lung. Thickening of the posterior wall of the intermediate bronchus is also visible (large arrow). C: Gross pathologic specimen from autopsy shows the bronchial lumen covered by multiple whitish endobronchial nodules (arrows). D: Photomicrograph of the biopsy specimen obtained from the right upper lobe reveals an endobronchial hyphal nodule invading the bronchial epithelium. Hematoxylin-eosin; ×400.
Atelectasis distal to the narrowed or obstructed bronchus was noted in five patients, lobar in two, and complete in one (Fig. 3). Bronchial narrowing without distal atelectasis was noted in the remaining three patients. Other associated CT scan findings included bronchiolectasis and centrilobular branching linear and nodular opacities ("tree-in-bud" appearance) in two patients, bilateral ill-defined consolidation in one patient, and unilateral pleural effusion in one. There was no apparent difference between the imaging presentation of patients with underlying hematologic diseases and patients with nonneoplastic debilitating diseases.

Flexible fiberoptic bronchoscopy was used in all of our cases. Bronchoscopic findings included nodular thickening of major bronchi (n = 5), elevated pale mucosal lesions (Fig. 3B) obstructing the lumen of the left main bronchus (n = 1), smooth narrowing of the lumen of the anterior segment of the right upper lobe bronchus (n = 1), and formation of pseudomembranes in the right upper lobe bronchus (n = 1). Bronchoscopic biopsy was performed in all cases.

The pathologic specimens obtained from bronchoscopic or surgical biopsy, or autopsy, of the bronchial lesions in all cases showed characteristic features of necrotizing bronchial aspergillosis with destruction of the airway epithelium and associated acute inflammation of the mucosa. Fungal hyphae were demonstrated invading the respiratory epithelium (Fig. 1D).

FIG. 2. A 57-year-old man with acute lymphoblastic leukemia and necrotizing Aspergillus bronchitis who presented with cough and sputum production. A: CT scan at the level of the carina (10 mm section) shows irregular narrowing and obstruction of the major right bronchus (white arrow), resulting in a consolidation with some associated volume loss of the right upper lobe. B: Gross pathologic specimen from autopsy reveals intraluminal overgrowth of Aspergillus sp.

FIG. 3. CT scans in a 54-year-old man with acute myelogenous leukemia and necrotizing Aspergillus bronchitis who presented with cough and sputum production. A: CT scan at the level of the carina shows left lung atelectasis with smooth narrowing and obstruction of the left main bronchus (arrow). B: Bronchoscopic image shows multiple mucosal plaques (P) at the level of the carina. Note that the left main bronchus is totally obstructed.
DISCUSSION

Necrotizing bronchial aspergillosis is a distinct clinicopathologic form of invasive aspergillosis characterized by histologic evidence of invasion of the tracheobronchial mucosa with *Aspergillus* without lung extension (7–9). Associated underlying diseases and predisposing factors include AIDS, leukemias, lung transplantation, solid tumors, chronic obstructive pulmonary disease, and prolonged antibiotic or corticosteroid administration (3–6).

*Aspergillus* in the large airway may manifest as saprophytic colonization, tracheobronchitis, ulcerative tracheobronchitis with or without pseudomembrane formation, and necrotizing (invasive) aspergillosis. Factors that predispose to localized infection of the main bronchi instead of pulmonary parenchyma are unknown. As with more invasive forms of fungal infection, the degree of immunosuppression is probably the most important factor leading to bronchial wall invasion. Nevertheless, it has been recommended that any airway isolate of *Aspergillus* species in the immunocompromised patient be considered evidence of invasive disease until proved otherwise (10,11).

Although the CT findings of invasive pulmonary aspergillosis have been extensively evaluated, there is little documentation of the CT features of the invasive aspergillosis of the airways in the radiologic literature (3,5,6). In a report of nine patients with biopsy-proven invasive aspergillosis of the airways, Logan et al. (3) reported only two cases affecting the trachea or main stem bronchi in addition to disease of the more peripheral airways. However, no abnormality of the trachea or main stem bronchi was identified at CT in either case. To our knowledge, only one case report (8) has been published that discusses CT findings in necrotizing aspergillosis of the central bronchi with histologic correlation.

In our series, the most characteristic findings on CT and high resolution CT were peribronchial thickening, multiple endobronchial nodules, and smooth or irregular bronchial narrowing. These features correlated well with bronchoscopic and pathologic abnormalities, with the changes reflecting a progressive spectrum of the disease involving exclusively the large airways.

Mildly impaired host immunity has also been regarded as a predisposing factor in the development of necrotizing *Aspergillus* bronchitis. This form of aspergillosis is increasing in frequency and may be severe or fatal if untreated (12). Two of our patients had mild immunosuppression due to severe obstructive airway disease and chronic alcoholism. In this group of patients, the slow progression of clinical and radiographic findings (several months to years) may contribute to a delay in diagnosis (3–6). It has recently been demonstrated in lung transplant recipients that the infected bronchial anastomosis by *Aspergillus* is associated with the development of clinically significant endobronchial abnormalities (10). In these patients, rapid diagnosis and appropriate antifungal treatment are mandatory to maintain airway control and improve survival. When untreated, necrotizing bronchial aspergillosis is associated with a high mortality rate. Surgery is recommended for the treatment of mechanical complications of this infection if the patient can tolerate such a procedure safely. It should be stressed that the CT scan findings of necrotizing *Aspergillus* bronchitis are nonspecific and need to be distinguished from bronchogenic carcinoma affecting the central airways. Peribronchial thickening and narrowing of a central bronchus have been described in patients with mucormycosis, tuberculosis, as well as amyloidosis and sarcoidosis.

Our study has several limitations. It is retrospective and includes a small number of patients. The diagnosis of necrotizing bronchial aspergillosis is often delayed because patients have insidious clinical manifestations including cough, dyspnea, sputum production, fever, and constitutional symptoms (weight loss and weakness).

CONCLUSION

In conclusion, necrotizing bronchial aspergillosis is a distinct form of bronchial invasive aspergillosis that can affect patients with immune dysfunction arising from multiple causes. Although CT findings are nonspecific and may mimic lung cancer or other fungal infections, necrotizing bronchial aspergillosis should be considered when bronchial wall thickening, which is often nodular, and narrowing of the bronchial lumen, which is often associated with distal atelectasis, are seen in immunocompromised patients.

REFERENCES