Unusual Cause of Chronic Cough in an Immunocompetent Host

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Abstract: *Aspergillus* infections cause a spectrum of pulmonary diseases depending on the immune status of the host. We report a rare case of a young, immunocompetent, patient who developed *Aspergillus* tracheobronchitis. Owing to primary resistance to itraconazole, the disease progressed to aspergilloma despite treatment. The condition was successfully treated with oral voriconazole.

Key Words: *Aspergillus* tracheobronchitis, voriconazole

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Aspergillus tracheobronchitis predominately affects the immunocompromised patient. The present case demonstrates that it can also develop in an immunocompetent host, and microbiological diagnosis can be delayed by the presence of concomitant infections. *Aspergillus* fungus may have a primary resistance against commonly used antifungal drugs.

CASE REPORT

A 37-year-old female homemaker presented with dry cough of 1 year, sneezing of 6 months, and decreased appetite of 3 months' duration. Chest x-ray showed cavitary lesion and fibrotic shadows involving the left upper lobe. No acid-fast bacilli were seen in 3 consecutive sputum samples. Computed tomography (CT) scan showed a thick-walled cavity involving the apicoposterior segment of the left upper lobe (Fig. 1).

Antituberculosis drugs were started on the basis of her chest x-ray and CT scan findings without much improvement.

On general physical examination, no abnormality was detected. Her lung sounds were normal and no adventitious sound was heard.

Her 3 sputum samples were reexamined and were negative for acid-fast bacilli. Her hemoglobin was 12.9 g%, total leukocytes count 17,100/mm^3, neutrophil 96%, lymphocyte 3%, and monocyte 1%, and liver and kidney function tests were normal. Her human immunodeficiency virus status was negative and serum immunoglobulin levels were as follows: IgE 665IU/mL, IgM 180 mg/dL, IgG 1280 mg/dL, and IgA 300 mg/dL. X-rays of the paranasal sinuses and lung function test were also normal.

She underwent bronchoscopy that showed multiple discrete whitish plaques involving the lower trachea, which extended up to the left upper lobe bronchus (Fig. 2). Thick purulent bronchial aspirate was collected and endobronchial biopsies were obtained. In bronchial aspirate occasional fungal elements were detected.

Endobronchial biopsy showed mild dysplastic changes in respiratory epithelial cells with dense infiltration of mixed inflammatory cells consisting of neutrophils, eosinophils, and occasionally multinucleated giant cells.

In view of the bronchoscopic finding and microbiology reports, *Aspergillus* tracheobronchitis was suspected and itraconazole 100 mg twice daily was started. Three weeks later, fungal culture showed the growth of *Candida albicans*.

With 4 months of treatment with itraconazole, she had symptomatic improvement but her chest x-rays showed worsening infiltration of the left upper lobe and appearance of a new infiltrate involving the left lower lobe. CT scan of thorax was repeated which exhibited formation of a fungal ball inside the preexisting cavity involving left apicoposterior lobe (Fig. 3). Bronchoscopy was repeated. On second bronchoscopy, the white plaques were still persisting inside the lower trachea and left main bronchus. Bronchial aspirate and endobronchial punch biopsy were also repeated. This time, biopsy showed similar histopathologic features. Bronchial aspirate was negative for acid-fast bacilli and fungal elements were seen. Itraconazole was continued.

Subsequently, fungal culture isolated *Aspergillus fumigatus* and drug sensitivity showed minimum inhibitory concentration for voriconazole (0.125 μg) and for itraconazole (> 16 μg), amphotericin B (0.06 μg), and caspofungin (> 16 μg).

She was diagnosed as having of *Aspergillus* tracheobronchitis with primary resistance to itraconazole. Voriconazole 100 mg twice daily was started (weight 38 kg).

After 3 months of the treatment with voriconazole, repeat bronchoscopy confirmed complete resolution of the mucosal lesion. Fungal cultures on bronchial aspirate were negative. Repeat CT scan of the thorax showed resolution of aspergilloma and fibrotic changes of the cavity.

DISCUSSION

Aspergillus tracheobronchitis is a rare form of *Aspergillus* infection where the infection is limited entirely or predominately to the tracheobronchial tree. It is defined as the isolation of *Aspergillus* spp. from endobronchial

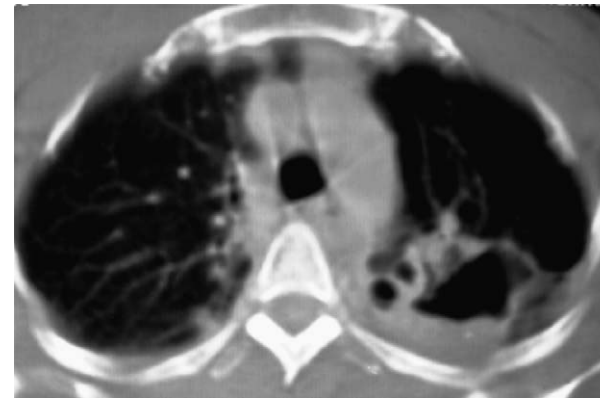

FIGURE 1. Computed tomography scan of thorax showed thick-walled cavity involving apicoposterior segment of left upper lobe.

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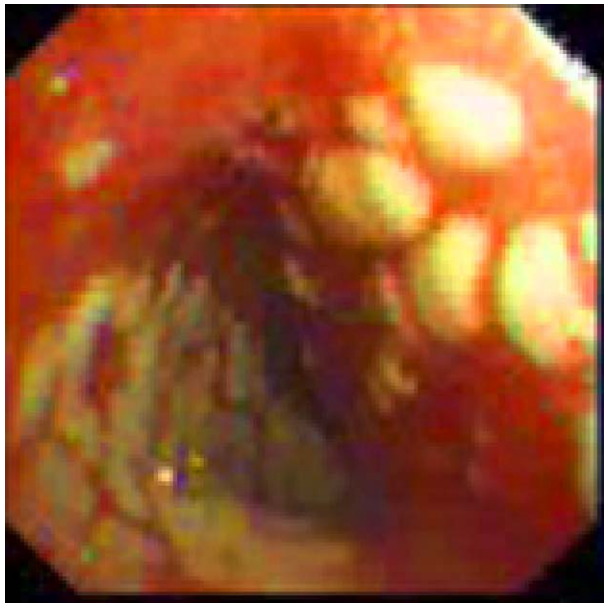

FIGURE 2. Bronchoscopy showed multiple discrete whitish plaques involving left main bronchus.

specimens, the presence of 1 or more endobronchial lesions without an alternative diagnosis, and no clinical, radiographic, or histologic evidence of invasive parenchymal disease.

Clarke et al[1] proposed 2 morphologic patterns of tracheobronchitis: (1) occlusion of the airway by pseudomembrane of necrotic tissue and hyphae, and (2) invasion of the adjacent lung parenchyma or pulmonary artery.

Aspergillus tracheobronchitis is a well-recognized infection in immunocompromised patients. Its incidence has increased over the last 20 years because of increasing use of immunosuppressive and corticosteroid therapies.

The bronchoscopic appearance of the lesion is variable and includes mild bronchitis, endobronchial ulcerations with or without pseudomembranes, and airway stenosis.

Aspergillus tracheobronchitis in an immunocompetent host carry a very high mortality rate.

Randhawa et al[2] had shown in vitro inhibition of *Aspergillus* by 5 species of *Candida* by fungistatic action,

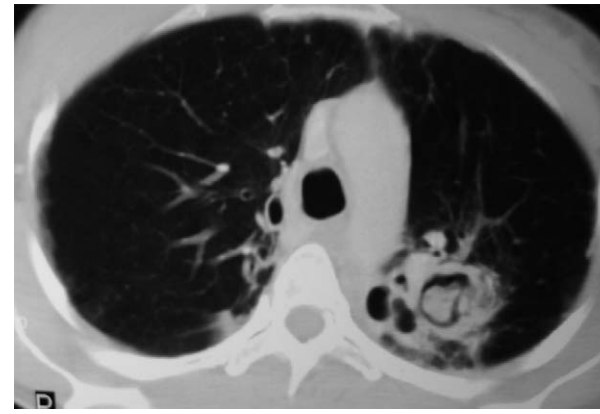

FIGURE 3. Computed tomography scan of thorax showed fungal ball involving left apicoposterior lobe.

and the authors suggested the possibility of delayed diagnosis of *Aspergillus* in mixed infections.

We report the case of an immunocompetent individual who had *Aspergillus* tracheobronchitis. Owing to fungistatic action of concomitant candidal infection, the *Aspergillus* was not isolated during the first bronchoscopy, which led to delayed diagnosis. The initial empirical treatment with itraconazole probably destroyed the concomitant *Candida* and helped the isolation of *Aspergillus* on second culture. The present case also demonstrated that inadequate treatment can favor the formation of aspergilloma and that *Aspergillus* may have primary resistance against itraconazole.

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