Aspergilloma in Honeycomb Cysts and Paraseptal Emphysema: An Unusual Association

Aspergilloma en pulmón en panal y enfisema paraseptal: una asociación poco habitual

Dear Editor,

A 71-year-old male patient presented with a 1-year history of productive cough with mild hemoptysis, progressive shortness of breath, and left-side ventilatory-dependent chest pain associated with 10 kg weight loss in the past 6 months. He also reported night sweats associated with sporadic chills in the past 2 months, and use of amoxicillin for 7 days without symptom improvement. The patient denied fever and other symptoms. He had a past history of hypertension, diabetes, and a 30-pack-year smoking habit (he quit at 42 years of age). He denied a history of previous pneumonia or tuberculosis. The patient had a previous occupational history as a bricklayer, store watchman, farmworker, and roof tile cutter. He referred to past domestic bird maintenance, which he had stopped 3 years previously. On physical examination, his basal oxygen saturation was 98%; ectoscopy showed that he was emaciated and pulmonary auscultation revealed basal crepitant rales, prominent in the left hemithorax.

Laboratory test results were normal. A chest X-ray showed diffuse bilateral basal reticular infiltrates and nodular opacity in the left upper lobe. Computed tomography (CT) demonstrated peripheral cystic pattern with thick wall and basal honeycomb, and multiple intracavitary nodules of various sizes, the largest located in the left upper lobe. The larger nodule showed variation in position as the patient’s decubitus was changed (Fig. 1), suggesting the diagnosis of aspergilloma (fungus ball). Bronchoalveolar lavage (BAL) was performed and demonstrated the absence of active or residual bleeding. Gram staining of the BAL sample showed paired gram cocci. The study of malignant cells, acid-fast staining and common bacterial culture were negative. Analysis of BAL fluid showed the presence of septate and branched hyphae and positivity for galactomannan (9.26 ng/mL; normal, <0.5 ng/mL). Serology results were negative for HIV, hepatitis B, and hepatitis C and normal for rheumatoid factor, antinuclear factor, and antineutrophil cytoplasmic antibody.

This patient was diagnosed with saprophytic aspergillosis (aspergilloma) in honeycomb cysts based on imaging characteristics • mainly the characteristic shift of intracavitary nodule positions as the patient’s decubitus was changed•along with the demonstration of fungus and positivity for galactomannan, with high values on BAL fluid analysis. The diagnostic hypothesis for the underlying pulmonary disease that caused cysts and honeycomb included pulmonary idiopathic fibrosis, asbestosis, chronic hypersensitivity pneumonia and combined fibrosis and emphysema. The patient was discharged from the hospital with oral itraconazole and levothyroxine, and was managed on an outpatient basis.

Pulmonary aspergillosis can be divided into five types: saprophytic aspergillosis (aspergilloma), hypersensitivity reaction (allergic bronchopulmonary aspergillosis), semi-invasive (chronic necrotizing) aspergillosis, airway-invasive aspergillosis, and angioinvasive aspergillosis. Saprophytic aspergillosis usually develops in a preexistent cavity or ectatic bronchus from underlying disease.1 Tuberculosis is its main cause, followed by conditions such as sarcoidosis, emphysema, bullae or lung cysts, cavitated bronchogenic carcinoma, and pulmonary infarction. Any cavity or cystic space created by underlying pulmonary disease can, theoretically, harbor aspergilloma.2,3 However, studies of the association between aspergilloma and honeycomb cysts are scarce.4,5

Recognition of typical aspergilloma signs is of paramount importance. On CT, the presence of an intracavitary nodule or mass that hangs down as the patient’s decubitus is changed strongly suggests this diagnosis. Other findings include the “air crescent sign,” a sponge-like appearance, amorphous calcification within the lesion, and adjacent pleural thickening.

Fig. 1. Chest CT images showing peripheral cysts pattern with honeycomb at the lung bases with an intracavitary nodule positioned anteriorly in the upper left lobe (A) that shifts position when the patient’s decubitus is changed (B) (arrows). In C and D, small intracavitary nodules are visible inside cysts in the right lung (arrows).
Safeguards are needed in the rehabilitation of COPD patients:

**Dear Director**

Pulmonary rehabilitation (PR) is a comprehensive intervention based on thorough patient assessment followed by patient-tailored therapies, which include but are not limited to, exercise training, education, and behavior change, designed to improve the physical and psychological condition of patients with chronic respiratory disease and to promote long-term adherence to health-enhancing behaviors.1 Physical exercise prescription is the cornerstone of rehabilitation in COPD patients, but performance of physical exercise is not without complications.2 Studies analyzing the complications of cardiac rehabilitation (CR) have demonstrated a low incidence of fatal and nonfatal complications. However, the incidence of complications of PR in COPD patients has not been analyzed.

The objective of this retrospective analysis with longitudinal follow-up was to identify the incidence of complications in COPD patients who performed PR in two hospitals from January 2013 to September 2016.

Patients were included if they were older than 40 years, smokers or former smokers of at least 10 pack-years, with a diagnosis of severe COPD based on a post-bronchodilator spirometry showing a FEV1/FVC <0.7 and FEV1 (% predicted) <50% and were included in the PR program. The exclusion criteria were: other respiratory diseases, cardiovascular, neurological and metabolic pathologies in the acute phase or uncontrolled.

Each training session consisted of warm-up exercises of the upper and lower limbs and the spine for 20 min, followed by continuous aerobic exercise by cycling for 30 min. The initial intensity of training was 50 W, increasing progressively with tolerance to the exercise. This was followed by strengthening exercises of the upper limb muscles during 20 min, initially without resistance, and progressively increasing with the increase in tolerance, and then 10 min of stretching exercises and 10 min of relaxation exercises.

The exercise intensity was controlled by the patient using the modified Borg scale (from 0 to 10). Basal oxygen flow was increased by 1 l in oxygen carrier patients. The duration of a PR cycle was 12 weeks of 2 sessions per week.

Complications during PR were classified as major and minor. A major complication was defined as any event that determined the discontinuation of PR, and a minor complication allowed continuing the PR.

The ethics committee of the Hospital of Mataró (Barcelona, Spain) approved the study. The patients provided written informed consent to participate in PR, but since this was a retrospective study no specific consent was required for the analysis.

A total of 291 patients were evaluated, with 44 (15.1%) abandoning the PR program. Of these latter patients, 20 (45.4%) dropped out because of a lack of motivation, 9 (20.4%) due to difficulties in reaching the hospital, 8 (18.2%) for exacerbations and 6 (13.6%) due to concomitant diseases.

**Table 1** shows the characteristics of the patients included. They underwent a mean of 17.6 (range: 2.2) PR sessions with a total of 7677 h. There were 2 major complications, both in patients with previous hypertension, diabetes and dyslipidemia: 1 acute coronary syndrome in a 71 years-old patient with FEV1 (%) = 42% and peripheral artery disease and 1 debut of cardiac arrhythmia manifested as atrial fibrillation in a 60 years-old patients with FEV1 (%) = 37% and sleep apnea. Thus, the incidence of major complications was 2.7/10 000 h of PR. Three minor complications were presented: 3 musculoskeletal problems involving acute low back pain and 2 increases in the sensation of dyspnea associated with O2 desaturation during physical exercise, with the incidence of minor complications being 6.5/10 000 h of physical exercise.

To our knowledge this is the first study to evaluate the safety of physical exercise in PR programs in patients with COPD. Although the sample size of our study was small, we observed a low incidence of complications during PR.

The most severe complications were cardiovascular and may be frequent since patients with severe COPD have usually been heavy smokers, and preexisting cardiovascular comorbidity is a normal finding and may interfere with PR programs. Our sample included patients with severe COPD with a mean age of 72 years and an elevated percentage of cardiac comorbidity, hypertension and diabetes. It is therefore important to first evaluate cardiac risk in patients with COPD who are prescribed physical exercise in a PR program by performing ergospirometry to determine the origin of limitation related to exercise, in particular in those patients at highest risk.3

The major complications observed were of cardiac origin but were not life threatening. The incidence of complications such as sudden death with exercise is very low and is almost always limited

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