CAZURI CLINICE

Rare form of semi-invasive aspergillosis in immunocompetent patient: case report

Alina Croitoru[1], Boris Melloni[2], Magali Dupuy-Grasset[2], M.L. Darde[2], Manuela Delage[2], Francois Bonnaud[2]

1. National Institute of Pneumology, Bucharest, Romania;
2. University Hospital of Limoges, France

REZUMAT

Formă rară de aspergiloză semi-invazivă la un pacient imunocompetent: prezentare de caz

Aspergiloza cronic necrotizantă sau semi-invazivă este o boală ce apare mai frecvent la pacienți cu grad ușor de imunodeficiență. Prezentăm un caz de aspergiloză pulmonară cronic necrotizantă la un pacient imunocompetent, fără alte afecțiuni asociate. Boala a fost descoperită întâmplător, prin decelarea unei opacități nodulare la o radiografie toracică de rutină. Diagnosticul a fost confirmat de examenele bacteriologice și anatomopatologice. Cu tratament antifungic specific nu s-a obținut vindecarea completă, iar evoluția bolii a fost lentă, cu multe episoade de recădere.

Cuvinte-cheie: *aspergiloză, fungi, infecție pulmonară, imunocompetent*

ABSTRACT

Chronic necrotizing or semi-invasive aspergillosis represents a disease commonly occurred in patients with mild immunodeficiency. We report a case of chronic necrotizing pulmonary aspergillosis in immunocompetent patient without underlying disease. The discovery of the disease was made accidentally, by finding a nodular opacity on a routine chest X-ray. The diagnostic was confirmed by pathological and bacteriological examination. With specific antifungal treatment, no complete eradication was obtained and the patient has a slow evolution with many relapses.

Keywords: *aspergillosis, fungal, pulmonary infection, immunocompetent*

Introduction

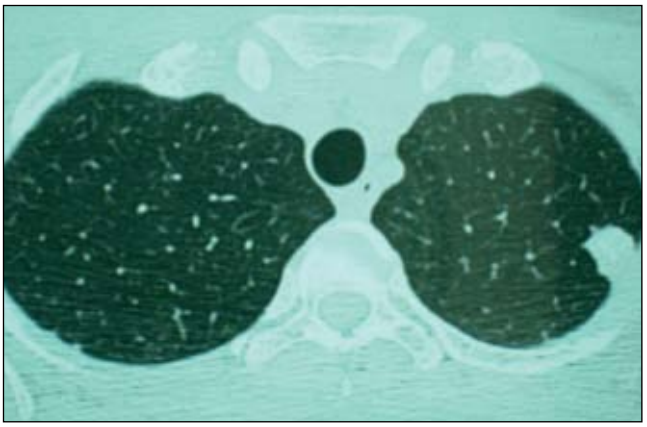
Semi-invasive pulmonary aspergillosis is a recognised complication in immunocompromised patients. Immunocompetent individuals rarely develop this infection and do so only in the presence of pulmonary or systemic abnormalities such as fibrotic lung disease, suppurative infection or corticotherapy.

Case report

A 42-year old woman was referred in 1997 to the pulmonary department for a nodular opacity of the left upper lung, incidentally discovered on routine chest X-ray. She has never smoked and had no domestic or occupational exposure, no regular medication; no history of tuberculosis contact. The clinical status was good; she was asymptomatic and physical examination was normal.

Routine blood counts showed haemoglobin: 11 gm%, total leukocyte count: 8100/mm^3, eosinophil 2,4% (absolute eosinophils count was 190). The markers of inflammation (C-reactive protein and Erythrocyte sedimentation rate) were normal; protein electrophoresis showed no abnormality. Serological markers for granulomatous and connective tissue diseases were negative. A sarcoidosis was also suspected but the serum level of angiotensin converting enzyme was normal (38 UI/l). Infectious causes were excluded: HIV infection, hystoplasma. Tumoral markers values (AFP, CA 15.3, CA 19.9, CA 125) were normal. Sputum smears for acid-fast bacilli and cultures were repeatedly negative. The RAST for Aspergillus fumigatus were negative. Pulmonary function was normal. Chest CT scan showed a well-defined solitary nodule, 15 mm diameters, in the apical segment of the culmen, near parietal pleura (Figure 1).

Figure 1. Chest CT scan showing 1.5 cm nodule in left upper lobe with pleural contact



In these conditions, because of the lack of diagnosis, a video-assisted thoracoscopy surgery (VATS) was decided. The mass was removed and the examination revealed a nodule containing central necrosis with partial calcification and peripheral epithelial granulation tissue. Few mycosis filaments were detected, but specific stains for Aspergillus fumigatus and Mycobacterium species were negative. There was no sign of malignancy. At the moment, no treatment was decided and regular follow-up was proposed.

In February 1998, control chest X-ray and CT scan revealed several nodules in upper lobes of the right and left lung, some nodules with central excavation (Figure 2).

Contact: Dr. Alina Croitoru, Institutul de Pneumologie "M. Nasta". Șos. Viilor 90, București, 050159; haulicaalina@yahoo.com

Figure 2. Chest CT scan showing bilateral nodules of the lungs, one with central excavation

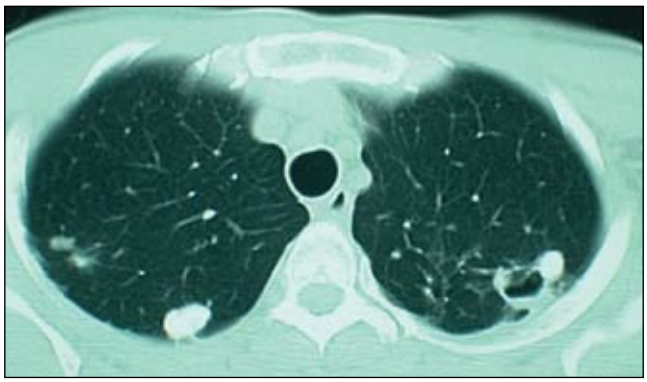
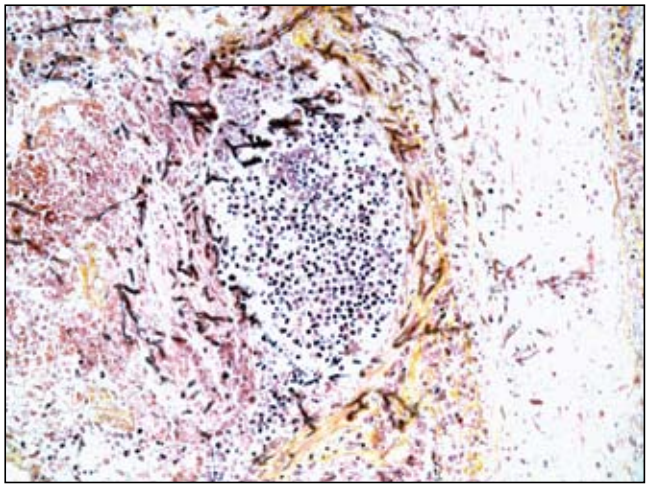


Figure 3. Pathology specimen revealing central necrosis surrounded by filaments of Aspergillus



A second VATS procedure was performed by removing one of the nodules on the right side. Pathological examinations confirmed an aspect of non-capsulated nodule containing central necrosis with multiple filaments. This time, specific staining showed septate hyphae with a right-angle branch suggestive of Aspergillus species (Figure 3 - Grocot coloration). Blood counts showed a small peripheral eosinophilia (471 elem/mm^3). The serum concentration of specific IgE against Aspergillus was increased for the first time. Complete biological analysis of phagocytosis function by polymorphonuclear leukocytes was normal.

In this condition, a treatment by itraconazole was started. Radiological improvement was observed after 3 months of treatment and total duration of therapy was 6 months.

In 2002, asthenia and cough revealed imaging relapse with new rounded pulmonary opacities, bilaterally, without cavitation. The nodule diameters range from 1.5 to 3 cm. Second line therapy was proposed with caspofungine associated to voriconazole for one, respectively six months, which led to the disappearance of radiological images. Clinical and biological tolerance of the treatment was good.

Unfortunately, the patient presented another relapse two years later and the same therapy was proposed with the same result. Over the next years, she presented many episodes of relapse; every episode marked by radiological changes with minimal impact on clinical status. After each treatment there was a remission period of 1-2 years, followed by a new relapse. No complete eradication of the disease was obtained.

Discussion

Aspergillosis represents a pathological condition caused by Aspergillus fumigatus organism. Lung disease pattern is different between immunocompromised and immunocompetent patients. Invasive pulmonary aspergillosis is observed in immunocompromised patients and semi-invasive aspergillosis in patients with a mildly immune-suppressed state [2]. Aspergilloma is described in immunocompetent patients with pre-existing lesion, as cavern, cyst or bulla [1, 2]. Allergic bronchopulmonary aspergillosis is observed in immunocompetent patients with hypersensitive state.

Semi-invasive aspergillosis or chronic necrotizing aspergillosis represents a pulmonary form of Aspergillus infection in patients with pre-existing chronic lung disease, as COPD, pulmonary interstitial fibrosis or bronchiectasis [2, 3, 6]. This form is also observed in mildly immunosuppressed conditions, as diabetes mellitus, malnutrition, alcoholism, prolonged corticosteroid therapy, advanced age [3]. Few cases of fatal pneumonic forms caused by the massive inhalation of Aspergillus were described in the immunocompetent hosts. In these cases, the inhalation was followed by proliferation of fungi in the lung who became hemorrhagic with infarction, with impact on vital prognosis [4].

Radiologic findings are represented by a focal consolidation localized in the upper lobes, with thickening and distortion of adjacent pleura [1, 2, 3]. In a serie of 6 patients with semiinvasive pulmonary aspergillosis, Kim several reported differents CT aspects: lobar or segmental consolidation, mass, cavitary consolidation and small nodular opacity [3].

Pathologically, the superficial invasion of lung parenchyma induces an indolent focal process 1. Yousem 10 describes in a series of 10 cases three distinct histological forms of chronic necrotizing pulmonary aspergillosis:

1. necrotizing granulomatous pneumonia, with a central zone of infarct-like necrosis of parenchyma resulting from angioinvasive Aspergillus;

2. granulomatous bronchiectatic cavity, with a central fungus ball and subtle tongues of necrosis and inflammation extending into and through the fibrous wall of the cavity;

3. bronchocentric granulomatosis-like appearance, with a necrotizing granulomatous bronchitis/bronchiolitis associated with luminal necrose.

The diseases progress slowly over months or years. The diagnosis should be considered in the presence of persistent and progressive radiological opacities and confirmed by biopsy/ bronchoscopy specimens revealing the presence of Aspergillus. The differential diagnosis includes tuberculosis, malignancy, sarcoidosis, amyloidosis and mucormycosis.

The treatment for chronic pulmonary aspergillosis is not well defined. Besides the old treatment with amphotericin B, new treatments with itraconazol, voriconazol, micofungin or caspofungin were successfully used. The dose and duration of therapy is based on clinical and radiological response [7, 8, 9]. Unfortunately, the evolution of disease is often marked by relapses. Surgery resection has been indicated in patients without response to drug therapy. Endo reported a benefit of

surgery in a series of 10 patients with prolonged illness or hemoptysis: after surgical resection 9 patients from 10 were free of aspergillosis with a mean follow-up period of 4, 8 years [5].

Our observation concerned the case of a young, immunocompetent women who developed a insidious nodular form of pulmonary aspergilosis. Pathological examination of pulmonary nodule was compatible with semi-invasive aspergillosis. Specific antifungal treatment was initially efficient, but the evolution was marked by relapse and no eradication of the Aspergillus infection was obtained. No pathological condition was found to explain the development of the Aspergillus infection in this case, neither locally or generally.

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