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Eur J Cardiothorac Surg 1995;9:286-288

Eur J Cardio-thorac Surg (1995) 9: 286–288

European Journal of
Cardio-thoracic
Surgery

Bronchovascular mucormycosis: an urgent surgical problem

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Abstract. The case of a 70-year-old male with lymphoblastic leukemia is reviewed, who presented the rare and almost always fatal complication of pulmonary mucormycosis, but who was treated satisfactorily with amphotericin B and surgery. The risk of massive hemoptysis in the course of mucormycosis that invades the lung vessels, makes us believe that surgery is an essential part of the management of this disease. It is suggested that the patient be operated as soon as the diagnosis is obtained, as we did in our case, to avoid other risks in combined management with amphotericin B. [Eur J Cardio-thorac Surg (1995) 9: 286–288]

Key words: Mucormycosis – Hemoptysis – Immunocompromised host

Mucormycosis is a fungus disease of the Mucorales type. *Mucor* fungus, together with those of Entomophtorales, make up the Zygomycetes class with pathological species in: *Rhizopus*, *Absidia*, *Mucor* and *Cunninghamella* that cause five clinical forms of mucormycosis, a) rhinocerebral, b) cutaneous, c) gastrointestinal, d) pulmonary and e) disseminated. It particularly affects immunocompromised hosts, patients with diabetes mellitus, metabolic acidosis, malignant hematological diseases, chronic renal failure, steroid therapy, malnutrition, transplanted patients, etc. [3].

Case report

We present the case of a 70-year-old male, a night watchman and smoker of 20 packs/year, with a history of prostatic syndrome. He had been diagnosed as having type L2 acute lymphoblastic leukemia a month and a half before, but was in complete remission at the time of writing, maintained with neuromeningeal prophylaxis with methotrexate and mercaptopurine.

Received for publication: February 18, 1994
Accepted for publication: December 9, 1994

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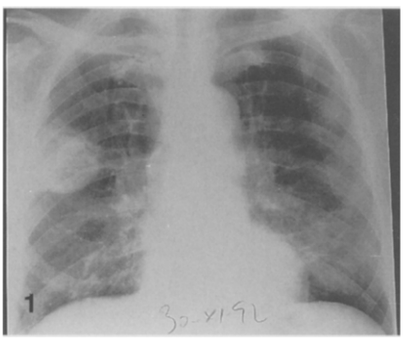
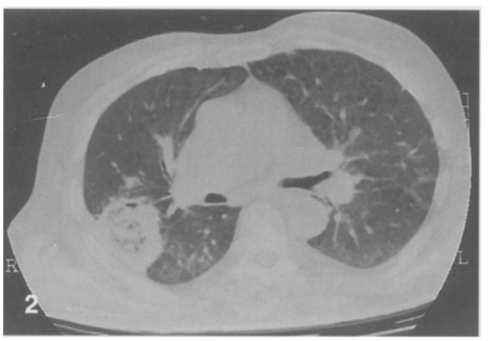
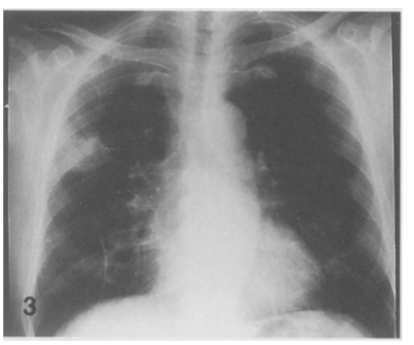
He presented at admission due to a fever (38.5 °C) of 36 h duration, that was accompanied by an insistent dry cough, and a constant right pleural pain, not irradiating, that increased with each bout of coughing. On physical examination, his blood pressure was 140/80 mmHg, heart rate 80/min and respiratory rate 24/min, and he had generalized pallor. Cardiac ausculation demonstrated a systolic murmur in the aortic area and pulmonary auscultation moist sounds in the left base, with disminuition of these in the right middle and upper fields. The rest of the examination was without any relevant findings. Blood analyses showed leucocytes 12,980, red blood cells 2,530,000, hemoglobin 8.5 g/dl, hematocrit 23.9%, neutrophiles 88%, lymphocytes 3%, monocytes 5%, eosinophiles 1% and platelets 233,000. The biochemical analyses were normal, as were the coagulation tests. In the posteroanterior and lateral chest X-rays of the thorax a well-defined round mass was observed in the posterior segment of the right upper lobe in the lateral view (Fig. 1). The blood gas analysis disclosed: ph 7.50, PaO_2 61 mmHg, $PaCO_2$ 32.6 mmHg, HCO_3 25.9 mm/l, with an oxygen saturation 93%. The initial diagnosis was established as pneumonia of the right upper lobe. We took into consideration that we were dealing with an immunocompromised host, but not with a neutropenic patient. He was treated with cefotaxime 2 g intravenously (I.V.) every 8 h and eritromycine 1 g I.V. every 6 h.

The patient was admitted and a thorax scan (CT) was performed in which a mass was observed in the right upper lobe in the posterior segment, with a thick wall, of a non-homogeneous content and with a thick halo, that suggested an aspergilloma (Fig 2). Macrophages with pigment and a little mesothelial cellularity were obtained after a fine needle aspiration guided by CT The serology for *Chlamydia*, *Coxiella* and *Legionella* were negative, while *Mycoplasma* was positive with low titers. He had a normal temperature, and a stable clinical conditions was observed from the eight day after admission, while the radiological pattern was unaltered when compared with the initial one. As a result of this we decided to perform







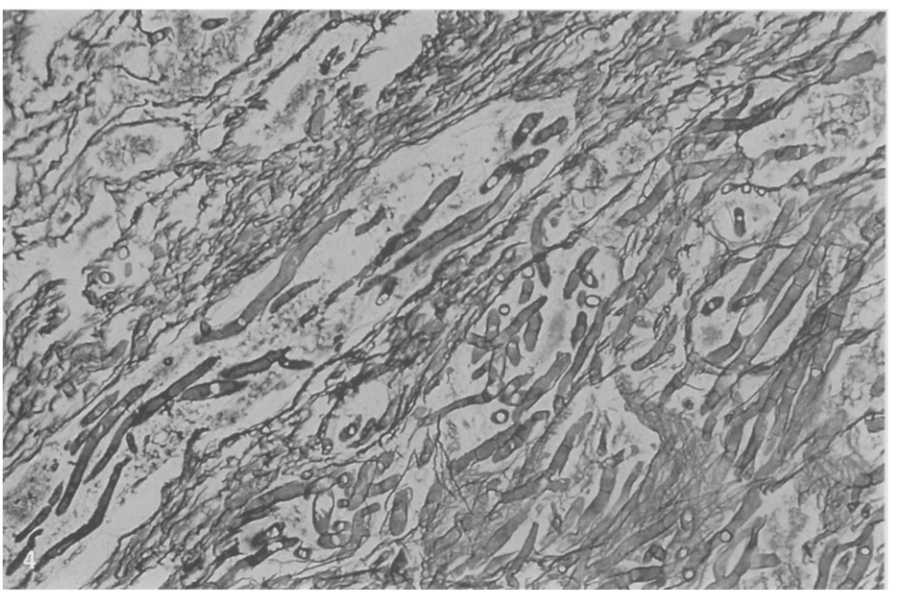


Fig. 1. Posteroanterior chest X-ray opacity with a well delimited mass in the right upper lobe

Fig. 2. Thorax CT scan mass in the posterior segment of the right upper lobe, with a thick wall and non-homogenous content

Fig. 3. Posteroanterior chest X-ray: persistence of the lesion, without resolution, in the right upper lobe

Fig. 4. Pathological findings. Pseudohyphaes from *Mucor* in lumen and wall of a vessel (Gomori × 250)

a bronchoscopy. We observed a membrane with fibrinoid material in the right upper bronchial lobe, which was also found to be partially occluding with acute inflammatory signs and diffused anthracotic images. The bronchial aspirate was negative with Gram and Ziehl stains, with scanty neutrophils, negative aero-anaerobic cultures and negative *Nocardia* culture. The bronchial biopsy showed inflammatory membranes containing abundant *Mucor*.

The forced spirometry disclosed FVC 4.18 l, FEV_1 2.83 l, FEV_1/FVC 67.70% and echocardiogram showed an aortic double lesion and a probable slight left ventricle hypertrophy. Finally, we added amphotericin B (5 mg/day) to the antibiotic treatment. Due to the lack of radiological improvement (Fig. 3) we decided on a surgical intervention, 51 days after admission, and carried out a right posterolateral thoracotomy, through the fifth space. A fixed abscess between the posterior segment of the right upper lobe and the point of the middle lobe adhering to the parietal pleura was observed. A wedge resection of the posterior segment of the right upper lobe and one edge of the middle lobe was performed, followed by local parietal pleurectomy.

The pathological findings revealed bronchopneumonia with cavitation, a fixed abscess and invasive mucormycosis. The presence of gram-positive bacteria and chronic inflammatory signs were seen. The cavity seemed to be lined partially by bronchial mucous and in its interior there was a fibrinopurulent abscess with fixed material and an addition of fungi corresponding to *Mucor*, that occasionally infiltrated blood lumens. Fragments of parietal pleura with hemorrhagic signs were also seen (Fig. 4). The clinical, as well as the radiological, follow-up with amphotericin B was satisfactory at the time of discharge, and the patient is at present in good health 18 months after surgery.

Discussion

Pulmonary mucormycosis associated with cutaneous manifestations belongs to a disseminated disease, while manifestations of a necrotic pleural or trachea-bronchitis have also been described. The most common symptom is fever associated with dyspnea with a radiological pattern of lung infiltration of segmentary or lobar distribution or, more curiously, coin lesion with a tendency to cavitation without accompanying pleural effusion [8]. A typical CT pattern has not been described. Pulmonary infection is the most common cause of morbidity and mortality in the immunocompromised patient, with mucormycosis being the third most common opportunistic pulmonary mycosis [4].

Infection can be through the inhalation of angiospores, although occasionally it can proliferate in cutaneous wounds or pass through intact mucous membranes arriving at the alveolus, where the macrophage function is inhibited, and starts to germinate to the hypha tissue invasive phase. The fungus penetrates the bronchial wall and the internal elastic layer of the blood vessels, predisposing to a rupture. The infiltrating growth of mucormycosis toward pulmonary vessels results in hemorrhage, ischemia, infarction or tissue necrosis. Hyphae may also dissect between the internal elastic membrane and media of

the large pulmonary arteries, leading to fatal hemoptysis. *Mucor* is always pathogenic except in some rare cases of simple colonization in the course of other diseases (tuberculosis, cancer, etc.). The opposite is also true, mucormycosis is usually not pathogenic in immunocompetent subjects, but may become pathogenic in locally or systemically immunocompetent patients. Tuberculosis, bronchial carcinoma and acute lymphoblastic leukemia – as in our case – are examples of the pathogenic potential of mucormycosis in an appropiate clinical environment [1].

The diagnosis is based on a fine needle aspiration guided by CT or open lung biopsy. In our case, a bronchial biopsy was performed, demonstrating the presence of *Mucor* [5]. When a diagnosis cannot be made, surgical treatment is justified with the suspicion of cavity neoplasia, unresolved pneumonia with an abscess or a fungus ball, or the presentation of massive hemoptysis. A bronchopleural fistula may appear as a postoperative complication. In cases of error, late diagnosis or surgical rejection, massive hemoptysis and pleural empyema are recognized as lethal complications of pulmonary mucormycosis [2]. Given the high mortality rate (70–80%) due to the difficult diagnosis, if there is not a high suspicion index it is necessary to use invasive diagnostic technique. Early diagnosis and a combination of surgery and antifungal therapy are basic to achieve control of a potentially curable infection. In very ill patients the pulmonary lesion can be drained or an aspiration may also be performed. Since mucormycosis may become more frequent in the future, particularly in association with HIV infection, a surgical approach may be indicated in patients with acceptable life-expectancy, taking into account the considerable intraoperative risk for the patient and staff [6].

Tedder et al. [7] recently reported a review of 30 patients treated at this institution and 225 cases in the literatur with a hospital mortality rate of 65% for patients with isolated pulmonary mucormycosis, 96% for those with disseminated disease and 80% overall. The mortality in patients operated on was 11%, while it was 68% in those not operated on. The most common causes of death were fungal sepsis (42%), respiratory insufficiency (27%) and hemoptysis (13%). Our case supports the combination of antifungal agents and surgical resection for localized pulmonary mucormycosis versus surgery or antifungal therapy alone.

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