

Intracerebral *Aspergillus* abscess: case report and review of the literature

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Abstract

Intracranial aspergillosis is a rare pathologic condition, difficult to treat and often fatal, which generally affects immunodepressed patients. A case of brain abscess secondary to pulmonary localization in a patient with a non-Hodgkin lymphoma is described. The most significant clinico-pathological findings of intracranial aspergillosis are examined in the light of the relevant literature.

Keywords: Aspergillosis, brain abscess, immunosuppression, mycoses.

1 Introduction

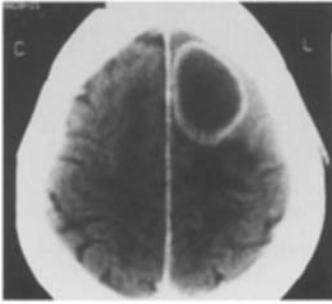
Aspergillosis is one of the most common mycotic infections of the brain, although CNS localization is rare. The clinical picture of CNS aspergillosis may express with different conditions: meningitis, meningoencephalitis, granuloma, brain abscess, vasculitis [11, 14, 17].

We report an instance of a 64-year-old man affected by a non-Hodgkin lymphoma, who developed a left fronto-parietal brain abscess secondary to a pulmonary infectious focus. The various clinical and pathological features of this rare disease are also analyzed in the light of the available literature.

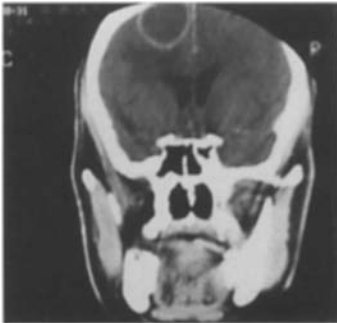
2 Case report

This patient came to our attention in July 1990 for speech and gait disturbances. Neurologic examination at admittance revealed a right hemiparesis and dysphasia. From November 1988 to December 1989

he had undergone chemotherapy (F-MACHOP protocol) following the diagnosis of non-Hodgkin lymphoma. Eight weeks after the interruption of treatment he suffered a rapid spread of a pulmonary inflammatory condition and was, therefore, admitted to the Division of Hematology of our University. Several sputum cultures disclosed the presence of *Aspergillus fumigatus*, confirmed by serologic tests for *Aspergillus* antibodies. Chest plain X-ray and CT showed two globular lesions: one, 4 cm. in diameter was located in the superior field of the left lung and the other (2 cm. in diameter) in the median field of the right lung. The patient was consequently treated with 5-fluorocytosine (6 grams daily in divided doses). During this treatment he suddenly developed the above-mentioned neurologic symptoms. A CT of the brain was obtained which showed a left fronto-parietal hypodense lesion with an enhancing ring, 4 cm. in diameter, interpreted as a "metastatic" abscess (Figure 1). Therefore, the patient was transferred to our Institute and then operated on. A left parasagittal frontal craniotomy was performed and, after dural opening, the dome of a globular lesion appeared at the cortical surface and was punctured, drawing out necrotic fluid. An anterior cleavage plane between the capsule and the surrounding cerebral tissue was hardly identified, but finally the lesion was totally removed. The hypothesis of the *Aspergillus* as the causative agent of the brain abscess was confirmed by the evidence of typical large septate hyphae of *Aspergillus fumigatus* in the culture of abscess fluid. Postoperatively, amphotericin B (600 mg./day) and 5-fluorocytosine (2 g./8 hours) therapy was established in the I.C.U. On 5th postoperative



(A)



(B)

Figure 1. Cranio-cerebral contrast-enhanced CT scan. The axial view (A) and the coronal (B) reconstruction show a left fronto-parietal abscess with ring enhancement and perilesional edema.

day an acute renal and cardiovascular failure occurred, and the patient died.

3 Discussion

Candida, *Aspergillus*, *Cryptococcus* and few species in the family of *Mucoraceae* are reported to be the organisms most frequently responsible for mycotic brain abscesses in immunocompromised patients [9, 11, 13, 16, 18, 20, 28, 29]. *Aspergillus* infection is rare and usually fatal. Only few of the 350 classified types of *aspergillus* show pathogenicity in humans: *A. fumigatus*, *A. flavus*, *A. amstelodami*, *A. sydowi*, *A. candidus* are those more often involved in CNS infection [2, 19].

Brain aspergillosis is more frequently sustained by *A. fumigatus* [15, 34]. The treatment with antibiotics, immunosuppressors, or steroids in patients with debilitating illnesses greatly enhances the chances of *Aspergillus* infection as will any process of weakening of immune system [6, 8, 19, 21, 25]. Typically

these patients are immunodefective and have leukemia, lymphoma, long standing diabetes, or renal diseases. The lung is most frequently affected, followed by the gastrointestinal tract and the brain [17].

Primitive brain aspergillosis is nevertheless very rare [7, 11, 21], and commonly the infection is secondary to lung diffusion [19, 20]. Aspergillosis typically generates large septate hyphae that are dichotomous, branching, with evidence of vascular invasion, granuloma formation, and giant cell reaction [9, 11, 13, 18, 20]. Extension of fungal invasion to surrounding neural tissue and blood vessels promotes hemorrhage, thrombosis, infarction, necrosis, meningitis, and ventriculitis [18, 20] thus causing the various clinico-pathological features of CNS aspergillosis.

Cerebral aspergillosis needs to be treated with both chemotherapy and surgery. The drugs of choice are free amphotericin B and liposomal amphotericin. 5-fluorocytosine, fluconazole, miconazole, ketoconazole, itraconazole are also used, but their effectiveness is questioned. A synergic action against *aspergillus* infection is reported for amphotericin B and 5-fluorocytosine [23]. However, the best results are achieved combining surgery and chemotherapy [15].

Although cases of survival in CNS aspergillosis have been reported [2, 14, 21, 22, 25], this pathologic condition carries an unfavourable prognosis, with a mortality ranging in different reports from 80 % to 90 % [19, 23]. Data emerging from such studies indicate that factors positively influencing the effectiveness of therapy are:

- 1) evidence of single, isolated lesion without dissemination [17];
- 2) paucity of neurologic symptoms [17];
- 3) early diagnosis [7, 10, 11, 23, 28];
- 4) preventive amphotericin B administration in patients at risk for aspergillosis [10].

Literature data, moreover, underline the difficulty of precisely determining the death causes in such patients. A possible explanation is the toxicity of the delivered drugs and particularly the proximity of therapeutic and toxic dosage of these drugs. Unexpectedly favourable outcome or sudden worsening of conditions seem not related to the patient's general condition or to the drug in use. Instead, diffusion pattern of the mycosis in the neuraxis and adequate immunologic response to infection of the patient are likely to be decisive for the final outcome. In particular, an immunodeficiency status appears responsible for the failure of various organs and systems in the preterminal stages of this mycosis.

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