A Case of Chronic Granulomatous Disease in which the Patient Survived a Recurrence of Suspected Aspergillus Brain Abscess

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Introduction

Chronic granulomatous disease (CGD) is one of the congenital immunodeficiencies, which affects intracellular biocidal activity through the impairment of superoxides production. Aspergillus species are a major cause of death in CGD patients and the mortality rate of cerebral aspergillosis in immunocompromised patients is reported to be nearly 100%\textsuperscript{1}. Very few reports to date have described surviving cases of cerebral aspergillosis in CGD, either with an X-linked\textsuperscript{2-3} or an autosomal recessive trait\textsuperscript{4}. Moreover, no reports could be found on the recurrence of brain abscesses in CGD. Practical information in terms of the management of a given patient and of radiological characterization concerning this devastating condition is, therefore, still limited. A case of X-linked CGD is presented here which survived a recurrence of brain abscess due presumably to \textit{Aspergillus}.

Case Report

The patient was a 22-year-old male with an X-linked CGD who had multiple episodes of infection at the ages of 13 (pneumonia of unknown etiology)\textsuperscript{5}, 15\textsuperscript{6}, 17\textsuperscript{7}, and 19. \textit{Aspergillus fumigatus} was first isolated from the lung at the age of 15. At that time, an aortography was performed for a diagnostic purpose of pseudosequestration of the lung and this mechanical injury led to a spread of the organism to the brain, and abscess formation\textsuperscript{6}. Following this episode, the patient suffered recurrence of \textit{Aspergillus} pneumonia at the ages of 17 and 19 which was successfully controlled by treatment with intravenous amphotericin B (Am B). Over the subsequent two years, he remained well with a single episode of a febrile illness which was resolved without extensive therapy.

On February 13, 1998, he came to the hospital complaining of numbness and paresis of the left lower extremity without fever or cough. An MRI of the brain (Fig. 1A) showed a small lesion surrounded by edema in the right parietal lobe which was in exactly the same position as the previous brain abscess\textsuperscript{6}. With a tentative diagnosis of the recurrence of \textit{Aspergillus} brain abscess, itraconazole (600 mg/day, 12 mg/kg body weight) was administered orally. Despite the treatment, his illness progressed during a week to

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Fig. 1  A-D. Magnetic resonance T1-weighted images of the brain. On the first visit to the hospital (A), on the day of admission (B), after 14 doses of Am B treatment (C), and after an additional 14 doses of Am B treatment (D). A high-intensity lesion with a low intensity area suggestive of brain edema (arrow heads) was observed in the right parietal lobe (A). The high-intensity lesion increased both in size and irregularity, and the surrounding edema also noticeably extended (B). Partial regression of both the high-intensity lesion and the surrounding edema was observed (C), and finally, the lesion remarkably regressed and the surrounding edema completely disappeared (D). The remaining lesion is identical with the one previously observed during the patient’s earlier convalescence[6].

Jucksonian seizures which began from clonic movements of the left lower extremity and spread to generalized convulsions. He was admitted to the hospital with a remarkable extension of the lesion (Fig. 1B).

On admission, he showed right convergence palsy with normal adduction, suggesting that the lesion involved an efferent pathway from the Perlia nucleus. A systolic vascular murmur which had been diagnosed as pseudosequestration of the lung was consistently audible on his right sternal border suggesting the persistence of the abnormal vasculature over these seven years. Gallium scintigraphy which was taken on the 4th hospital day revealed no abnormal uptake within the lesion. A brain MRI-angiography which was taken on the 18th hospital day delineated an irregular stain in the center of the lesion but no abnormal vessels around the lesion.

White blood cell count was 7,300/mm³ and CRP was 2.1 mg/100 ml. Renal function tests and serum
electrolytes were normal. Baseline urinary excretion of potassium (UexK) was 33.2mEq·K/g·creatinin (Cr) and that of magnesium (UexMg) 6.9mEq·Mg/g·Cr. Throat swab cultures and blood grew no pathogens and no serological evidence of viral or fungal infection was obtained and so, considering the patient's previous history, Aspergillus brain abscess was the only possible diagnosis and an intravenous Am B (a deoxycholate preparation) therapy was initiated.

For the first 14 days, daily infusions of the Am B solution (30 mg/day, 0.6 mg/kg body weight) and an electrolyte solution (Na 35, K 20, Cl 115, Mg 40, each in mEq/L) were performed, each taking 12 hours. While this treatment (total Am B dose, 420 mg) resulted in a regression of the lesion (Fig. 1C), renal function was mildly impaired (serum Cr 1.7 mg/100 ml, K 3.3 mEq/L, Mg 1.1 mEq/L, UexK 64.3 mEq·K/g·Cr, UexMg 16.6 mEq·Mg/g·Cr). After a break of seven days, the therapy was resumed with alternate-day infusions of the Am B solution (30 mg) and an electrolyte solution (Na 154, K 30, Cl 109, Mg 30, each in mEq/L) each taking as long as 24 hours. The therapy was maintained for 28 days (additional Am B dose, 420 mg), preserving normal renal function (serum Cr 0.7 mg/100 ml, K 3.7 mEq/L, Mg 2.5 mEq/L, UexK 41.7 mEq·K/g·Cr, UexMg 3.6 mEq·Mg/g·Cr). Although the high-intensity lesion remained small (Fig. 1D), we considered that the active inflammation ceased because of a negative CRP value and the disappearance of surrounding edema, which was consistent with the convalescent stage of the previous episode. He was discharged from the hospital on April 16 with a mild, intermittent numbness of the left lower extremity and partial recovery of the right convergence. He has remained well to the present, 14 months after the episode.

**Discussion**

In this patient, although direct evidence could not be obtained, the fact that the exclusive use of Am B was extremely efficacious against the lesion taken together with his previous history strongly indicated that the abscess was due to Aspergillus infection. In general, the mortality rate of cerebral aspergillosis is high. In addition, to my knowledge, there has been no information in the literature concerning the recurrence of brain abscesses in CGD. In this patient, the recurrence was no more severe than the first episode, with an identical radiographical appearance. The negative finding by gallium scintigraphy was rather unexpected due to the fact that the lesion expanded in a relatively short time with a remarkable worsening of the clinical symptoms. In addition, the MRI-angiography showed no vascular invasion. These observations along with no remarkable mass effect in the MRI suggest that the inflammation was well compartmentalized without any blood brain barrier destruction, which must have been a beneficial factor for this patient.

Recently, a low dose infusion strategy of Am B has been advocated to avoid significant side effects, particularly when a deoxycholate preparation is used. Although this strategy may be available to use in candidiasis, larger doses of Am B are necessary in many cases of aspergillosis. In such situations, a longer infusion time, i.e., as long as 24 hours, might be helpful in minimizing the nephrotoxicity of Am B. The cautious use of Am B over a long infusion time on the basis of the previous experience must significantly have contributed to the favorable outcome in this patient. In addition, concerning the nephrotoxicity, an increase in the urinary excretions of electrolytes always preceded a decrease in the serum electrolytes in this patient. Monitoring UexK and UexMg can be performed with a single urine sample. These parameters are highly useful as a simple and early indicator of the nephrotoxicity of Am B.
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References


アスペルギルスによると推測された脳膿瘍を再発症した
ものの救命し得た慢性肉芽腫症の1例

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要旨
慢性肉芽腫症における真菌感染症はしばしば致命的であり、とりわけ脳膿瘍の治癒例は極めて少ない。本例は5年前のアスペルギルス脳膿瘍の旧病巣と同一部位に脳膿瘍を再発症したもので、救命し得た1例である。
症例は22歳男性。左下肢の脱力、疎れ感を主訴に来診。頭部MRIにて右頭頂一側頭葉に周辺の浮腫を伴う活動性の病変を認め、既往歴からアスペルギルス脳膿瘍の再発症と診断した。アムホテリシンB 0.6mg/kg、12時間点滴静注14日間投与にて病変は縮小傾向を示したが、軽度ながら腎機能障害が進行した。7日間投与を中断し、投与法を24時間点滴静注・隔日投与に変更、その後28日間の治療にて腎機能を維持しつつ、炎症を鎮静化し得た。