CLINCAL CASE

# MULTIPLE POSTERIOR FOSA ASPERGILOMAS IN A PATIENT WITH CHRONIC GRANULOMATOSIS

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## Abstract

*The invasive infection with Aspergillus fumigatus usually occurs in immunocompromised patients. CNS involvement is extremely rare in children. Usually, the diagnosis is hard, often made after the death of the patient. We describe the first report of a pediatric case of multiple CNS aspergillomas confirmed by a biopsy. We present the case of 3 years old boy who was hospitalized for evolving intracranial hypertension with a cerebellar syndrome. A brain CT showed a left cerebellar mass and early tonsillar commitment and a supra-tentorial lesion in the right occipital lobe. Therefore, a metastatic tumor was suspected and an emergency surgical intervention with cerebral biopsy and ventriculocisternostomy was performed. The cerebral biopsy revealed an Aspergillus fumigatus granuloma and further investigations showed that the patient has chronic granulomatosis due to a homozygous mutation of CYBA gene encoding p22phox. After a favorable evolution in reanimation, he continued the treatment with Voriconazole. At last follow-up, the neurological examination finds no sign of motor focus, no cerebellar syndrome or nystagmus. Walking is difficult with the enlargement of the support base. CNS invasive infection with Aspergillus fumigatus in a child is extremely rare and the presentation might mimic that of a tumor especially with a location of aspergilloma as in our case both supratentorially and infratentorially.*

**Keywords***: cerebellar aspergilloma, CYBA gene, intracranial pressure*

## Introduction

Isolated for the first time by the Italian priest Pier Antonio Micheli in 1792, Aspergillus represents a genus consisting of a few hundred mold species found in various climates worldwide. They are present in the soil, water, decaying vegetation, and organic debris. The most common fungi, among about 19 disease-causes species, is Aspergillus fumigatus who is one of the most ubiquitous of the airborne saprophytic fungi. Both humans and animals can inhale this fungus but conidia are expelled from the immunocompetent organism. The invasive infection with A. fumigatus usually occurs in immunocompromised patients with human immunodeficiency virus (HIV) infection, or chronic granulomatosis, with the mortality being very high.

Chronic granulomatosis is a genetic disease characterized by recurrent life-threatening infections with bacteria and fungi

and granuloma formation. It can be caused by defects in any of the five genes that encode the structural subunits of the NADPH oxidase, the enzyme responsible for the phagocyte respiratory burst and the generation of phagocyte superoxide. The suspicion of chronic granulomatous disease should be raised by severe or recurrent infections or abscesses involving the viscera, especially the pulmonary or hepatic parenchyma [1]. It has a variable clinical presentation and even though it can occur from infancy to late adulthood, most of the patients are diagnosed before the age of 5.

The most common site of A. fumigatus foci are the lungs and the central nervous system [2]. Cerebral aspergillosis is a rare infection of the central nervous system that represents 5-10% of all intracranial fungal pathology. It usually results from hematogenous dissemination from primary foci, which usually is located in the lungs [4].

In this case report, we present a rare case of multiple CNS aspergilloma in a 3 years old child with chronic granulomatosis who presented with a raised intracranial pressure and cerebellar syndrome.

## Case presentation

A 3 years old boy was hospitalized in March for an evolving intracranial hypertension with a cerebellar syndrome. A brain CT showed a left cerebellar mass and early tonsillar commitment and a supra-tentorial lesion in the right occipital lobe (Figure 1).

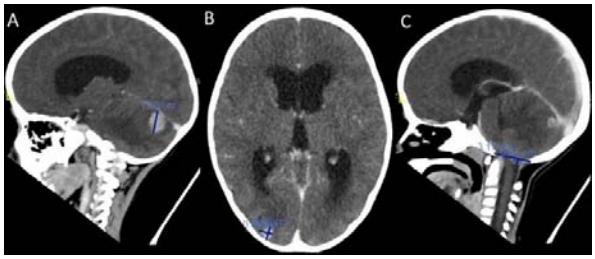


**Figure 1 – CT. A. 1.88x1.32 cm cerebellar mass situated in the left lobe, B. 1.30x2.77 cm supratentorial lesion in the right occipital lobe, C. the tonsillar commitment through Foramen Magnum**

An emergency surgical intervention with cerebral biopsy and ventriculocisternostomy was performed in the hypothesis of a brain tumor. After surgery, the child presented an acute hypoxemic respiratory failure for which he was transferred to the intensive care unit. The pneumological assessment revealed radiological white lungs, with a CT scan showing axillary and abdominal left mediastino-hilar adenomegalies associated with a left upper lingual pneumopathy focus and a left hilar mass. The parents reported of a previous small hemoptysis. A trial treatment for tuberculosis was started and a bronchoalveolar lavage was performed.

The cerebral biopsy resulted in an Aspergillus fumigatus granuloma. The further investigations revealed that the patient has a chronic granulomatosis due to a homozygous mutation of CYBA gene encoding p22phox. Aspergillus was identified in the bronchoalveolar lavage. Voriconazole was then added to Amphotericin B and anti-tuberculosis quadruple therapy Amphotericin B was relayed for Caspofungine. Cholestasis occurred since the beginning of antifungal treatment without jaundice or cytolysis, and it increased with the introduction of dual antifungal therapy and development of cytolysis without impact on hemostasis. Establishment of ursodeoxycholic acid therapy 20 mg / kg / day with continued monitoring. Abdominal ultrasound shows no hepatic lesions of infectious appearance or obstacle on the bile ducts.

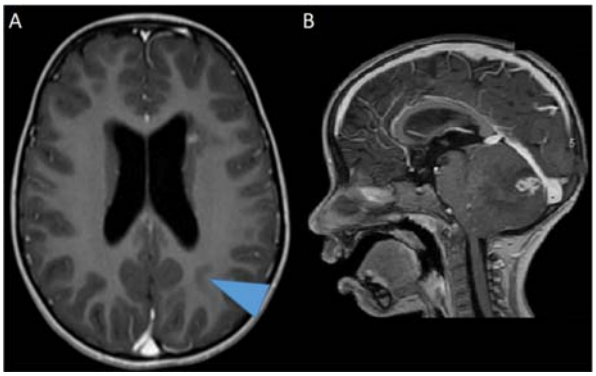


**Figure 2 – MRI. A. The new punctiform lesion in posterior left parietal white matter (triangle), B. The reduction of perilesional edema around the cerebellar lesion**

After a favorable evolution in reanimation, the treatment with Voriconazole was continued and an oral candidosis with erosive lesions occurs but without any other infectious complication. On the cerebral MRI performed

one month later, a new punctiform lesion in posterior left parietal white matter was found. The cerebellar lesion decreased in size from 41 x 27 mm previously to 35 x 26 mm. The right occipital lesion almost disappeared with instead a discreet meningeal residual enhancement. A reduction of perilesional edema, especially around the left cerebellar lesion with decrease mass effect on the fourth ventricle was observed. The cerebellar tonsils were still in a low position but without any clear sign of commitment (Figure 2).

A control thoracic CT was also performed and it founds a decrease in size of lymphadenopathy and pneumonia (Figure 3).

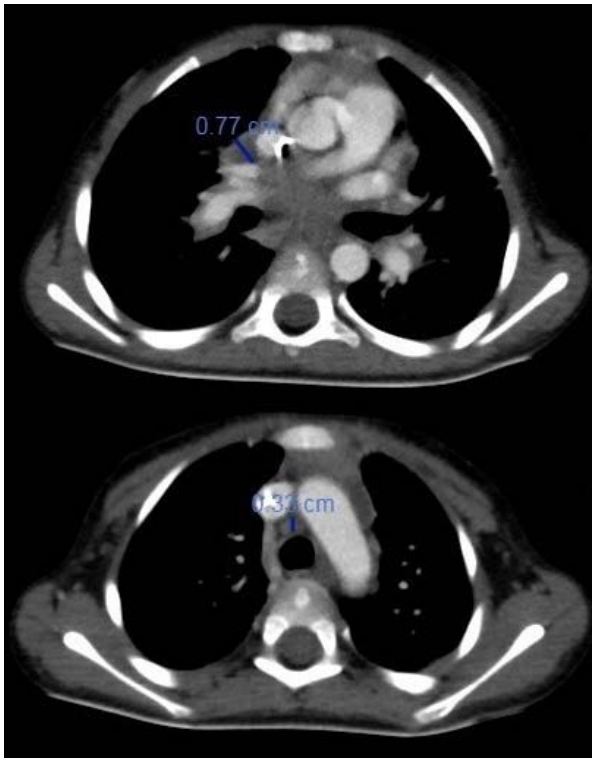


**Figure 3 – The decreased in size lymphadenopathy from the thoracic level**

One month later the child presented a recurrence of the intracranial hypertension reappears and the CT showed an active hydrocephalus for which a ventriculoperitoneal shunt was placed in emergency. The evolution was good, without any neurological complication.

At last follow-up, the neurological examination found no sign of motor focus. The cerebellar examination was difficult but there is no cerebellar syndrome or nystagmus. Walking was difficult with enlargement of the support base. There was no meningeal syndrome and the abdomen is without particularity and VP shunt scars are clean. Due to the gravity of the infectious presentation of this septic family granulomatosis and the absence of the donor, a bone marrow allograft was indicated. The transplant will be performed once the obtained control of the infection will be considered as satisfactory.

## Discussions

The mortality rate in immunocompromised patients with cerebellar aspergillosis ranges from 75% to 100%, despite the intensive treatment with Amphotericin B. Usually the diagnosis is hard, often made after the death of the patient [5], [6]. Aspergillus spores have a predilection for the anterior and middle cranial fossa [7], [8]. The location of aspergilloma in our case is quite rare, being located in the posterior fossa and occipital lobes, both supratentorially and infratentorially. Aspergillus abscesses in the cerebellum are extremely rare, and only a few cases of purely cerebellar aspergillosis have been reported [9], [10-12]. This is the first report of a pediatric case of multiple CNS aspergillomas confirmed by biopsy. Only Sheng Chen et al. described so far another case of multiple aspergillomas confirmed by biopsy, though their patient was significantly older, at 43 years old patient [13].

Even though the central nervous system fungal abscesses are well described, the management of the patients tends to be controversial due to the high mortality of this pathology. There are authors that suggest that the most effective treatment would be resection combined with administration of antifungal drugs [14-15].

In our case, only a partial resection was performed due to the multiple locations of the lesions. However, combined with antifungal therapy it allows to treat the infection.

## Conclusion

In conclusion, we report a case of 3 years old boy, with an immunodeficiency caused by familial chronic granulomatosis with multiple aspergillus granulomas in the lungs which

hematogenous and the central nervous system, being located in the posterior fossa, both in the cerebellum and in the occipital part of the brain revealed by raised intracranial pressure.

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