



THE AGA KHAN UNIVERSITY

eCommons@AKU

---

Section of Neurosurgery

Department of Surgery

---

5-30-2016

## Cerebral aspergillosis and pulmonary tuberculosis in a child with chronic granulomatous disease

Muhammad Waqas

Sidra Zafar

Tooba Rehman

Muhammed Riyaz

Muhammad Ehsan Bari

*See next page for additional authors*

Follow this and additional works at: [https://ecommons.aku.edu/pakistan\\_fhs\\_mc\\_surg\\_neurosurg](https://ecommons.aku.edu/pakistan_fhs_mc_surg_neurosurg)



Part of the [Neurology Commons](#), [Neurosurgery Commons](#), [Pathology Commons](#), and the [Surgery Commons](#)

---

---

**Authors**

Muhammad Waqas, Sidra Zafar, Tooba Rehman, Muhammed Riyaz, Muhammad Ehsan Bari, and Romana Idress

---

## Case Report

# Cerebral aspergillosis and pulmonary tuberculosis in a child with chronic granulomatous disease

Muhammed Waqas, Sidra Zafar, Tooba Rehman, Muhammed Riyaz, Muhammed E. Bari, Romana Idrees<sup>1</sup>

Department of Surgery, Section of Neurosurgery, <sup>1</sup>Department of Pathology and Laboratory Medicine, The Aga Khan University Hospital Karachi, Pakistan

E-mail: Muhammed Waqas - shaiq\_waqas@hotmail.com; Sidra Zafar - sidrazafariqbal@gmail.com; Tooba Rehman - tooba.rehman88@gmail.com; Muhammed Riyaz - riaz\_shangla@yahoo.com; \*Muhammed E. Bari - ehsan.bari@aku.edu; Romana Idrees - romana.idrees@aku.edu

\*Corresponding author

Received: 23 March 16 Accepted: 14 April 16 Published: 30 May 16

## Abstract

**Background:** Chronic granulomatous disease (CGD) is an immune disorder that affects phagocytes. It is characterized by recurrent or persistent bacterial and fungal infections. Reports of tuberculosis (TB) in patients with CGD are rare. In developing countries, where TB is endemic, possibility of other chronic infections is often overlooked by physicians.

**Case Description:** We report the case of a 4-year-old boy who had recurrent respiratory infections and episodes of headache. He was put on antituberculosis (ATT) drugs without microbiological or pathological evidence 2 months prior to presentation. The child did not improve and was brought to our hospital where a computed tomography scan revealed multiple cerebral abscesses. These abscesses were excised. The microbiological specimen was determined to be positive for *Aspergillus fumigatus*. His tracheal aspirate was positive for *Mycobacterium tuberculosis* polymerase chain reaction assay. Further work-up confirmed the diagnosis of CGD in the child.

**Conclusion:** This report describes the course of the patient's illness in order to highlight the challenges associated with the management of these infections. We also aim to stress on the importance of pathological diagnosis before starting a therapy.

**Key Words:** Cerebral abscess, chronic granulomatous disease, tuberculosis

### Access this article online

**Website:**

[www.surgicalneurologyint.com](http://www.surgicalneurologyint.com)

**DOI:**

10.4103/2152-7806.183166

**Quick Response Code:**

## INTRODUCTION

Chronic granulomatous disease (CGD) is a rare, primary immunodeficiency disorder of phagocytes.<sup>[3]</sup> It is characterized by repeated bacterial and fungal infections with excessive inflammation and granuloma formation in the skin, liver, lung, gastrointestinal tract, lymph nodes, and bone. CGD has an incidence of 1 in 200,000–250,000 births,<sup>[8,9]</sup> and is usually diagnosed early in infancy by nitroblue-tetrazolium (NBT) negativity. Fungal infections caused by *Aspergillus* species are an important cause of morbidity and mortality in CGD. *Aspergillus fumigatus* accounts for almost 78% of all fungal infections, and is second only to *Staphylococcus*

*aureus*, which is the most frequent cause of infection in patients with CGD.<sup>[9]</sup> The most common organs affected by *Aspergillus* in CGD are the lungs; brain abscesses secondary to *Aspergillus* are very rare.

This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

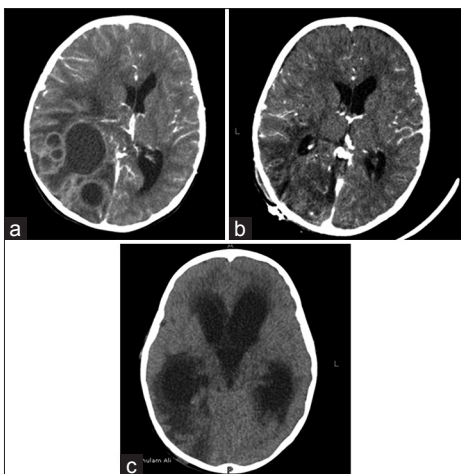
**For reprints contact:** [reprints@medknow.com](mailto:reprints@medknow.com)

**How to cite this article:** Waqas M, Zafar S, Rehman T, Riyaz M, Bari ME, Idrees R. Cerebral aspergillosis and pulmonary tuberculosis in a child with chronic granulomatous disease. *Surg Neurol Int* 2016;7:62.  
<http://surgicalneurologyint.com/Cerebral-aspergillosis-and-pulmonary-tuberculosis-in-a-child-with-chronic-granulomatous-disease/>

Although these patients have an increased susceptibility to tuberculosis (TB), reports of TB in CGD are rare.<sup>[4,7]</sup> In developing countries, where TB is endemic, there is a tendency among physicians to treat patients without a prior microbiological or pathological confirmation of the diagnosis. This can lead to a delay in the diagnosis of other potentially fatal infections. We describe this case not only because the occurrence of cerebral aspergillosis and pulmonary TB in CGD is rare but also to highlight the merit of obtaining objective evidence before embarking on a specific treatment plan.

## CASE REPORT

A 4-year-old boy was brought to the Emergency Department (ED) from a rural area with complaints of fever, headache, and weight loss. He was suffering from these symptoms for the past 4 months, which had worsened in the past week. His brother informed that the child had been unwell since infancy with several episodes of respiratory infection and has had several hospital admissions. Recently, he had started complaining of severe persistent diffuse headaches along with nausea, vomiting, and anorexia. He also suffered from low grade fever intermittently over this period of time. Physicians in his locality who had treated him with antibiotic courses for chest infections started him on antituberculosis (ATT) drugs 2 months back after an MRI, which suggested meningeal enhancement and small ring enhancing lesions. He had no history of seizures or loss of consciousness. One of his brother had passed away at the age of 8 years who was considered to suffer from disseminated tuberculosis. On examination, the child was listless, emaciated, and extremely irritable. He



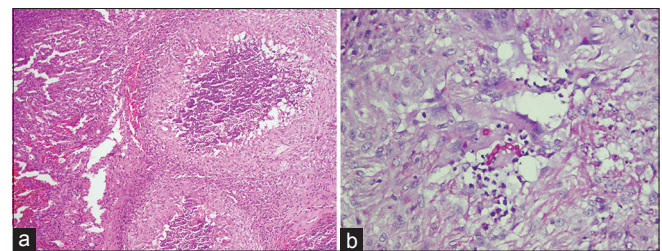
**Figure 1:** (a) An axial contrast enhanced image of preoperative CT brain showing multiple abscesses in the right parietooccipital area. (b) A corresponding postoperative image showing no evidence of residual. (c) Axial noncontrast enhanced CT scan brain at follow-up showing gross hydrocephalus

had left-sided weakness in both the upper and lower extremities.

An urgent computed tomography (CT) scan of the head showed multiple rings enhancing the left parietooccipital region, with significant surrounding edema and mass effect [Figure 1a]. His white blood cell count was 17900/uL, with neutrophils 77.4% and lymphocytes 15.7%. Hemoglobin was 10.9 and erythrocyte sedimentation rate (ESR) was 88 mm/h. We involved pediatric physicians and infectious disease specialists to perform a neuronavigation-guided craniotomy for the excision of these abscesses along with the walls, which contained thick purulent material. Microscopic examination revealed granulomas with fungal hyphae [Figure 2a and b]. Presence of *Aspergillus* was further confirmed on culture. Postoperatively, he was successfully extubated and shifted to the intensive care unit for postoperative monitoring. His weakness also improved. Considering his chronic cough and repeated chest infections, we obtained a tracheal aspirate for examination, which was positive for *Mycobacterium tuberculosis* polymerase chain reaction assay. Considering the history, we screened the child for immune deficiency disorders. Nitroblue-tetrazolium (NBT) was found to be negative, which established the diagnosis of CGD.

Intravenous (IV) voriconazole was commenced at 6 mg/kg/dose every 12 h for 2–3 days, which was later switched to 6 mg/kg/day orally. Five-drug ATT treatment was restarted for the management of pulmonary TB. He was also given broad-spectrum antibiotics. Pneumococcal and meningococcal vaccines were administered as prophylaxis, and co-trimoxazole was included in the regimen for the prevention of pneumocystis carinii pneumonia.

The child showed slow improvement, however, the treatment course was complicated by fever, seizures, and hyponatremia. Repeat CT scans did not show residual or recurrent abscesses [Figure 1b]. After stabilization of the medical condition, he was discharged. About 10 days after discharge, his family brought him to the ED with complaints of drowsiness. CT scan showed



**Figure 2:** (a) 10× magnification reveal chronic granulomatous inflammation with central neutrophilic debris and multinucleated giant cells. (b) Special periodic acid Schiff staining reveal septate fungal hyphae; 40× magnification

hydrocephalus [Figure 1c]. A temporary cerebrospinal fluid (CSF) diversion was performed, followed by a ventriculoperitoneal shunt once the CSF culture was reported negative. The child was again discharged after stabilization. He died 4 months later at home in respiratory distress. The child could not be brought to us, and hence no autopsy was performed to determine the actual cause of his death.

## DISCUSSION

CGD is a congenital disorder of the immune system, which is characterized by impaired NADPH oxidase activity of the phagocytes. This results in defective intracellular killing of catalase-positive microorganisms, and clinically presents as recurrent, severe infections usually in early infancy.<sup>[5,8]</sup> Although mycobacterium is catalase positive, the case reports of *Mycobacterium tuberculosis* are very few.

The child in our case presented with brain abscess caused by *Aspergillus fumigatus* with pulmonary TB. *Aspergillus* is a common pathogen in CGD patients, and most commonly manifests as pulmonary complications or as infections of the chest wall and bones. Neurological complications, especially abscesses of the brain, are uncommon and are rarely documented.<sup>[8]</sup> In fact, there has been just one report of culture-proven *Aspergillus* brain abscess in a child with CGD.

Kolb *et al.* reported the case of a child suffering from CGD along with pulmonary TB where *Aspergillus* brain abscess was highly suspected, but was not proven on microscopy or fungal culture. Another case was discussed by Frank *et al.* where *Aspergillus* growth was proven in culture and the child was successfully treated with itraconazole and interferon.<sup>[5,7]</sup> In the present case, we used voriconazole to treat the patient. The drug has been shown to be efficacious against *Aspergillus*.<sup>[2]</sup>

Alsultan *et al.* reviewed literature on intracranial abscesses in CGD and found four cases of intracranial aspergillosis.<sup>[1]</sup> A case reported by Pollack *et al.* differed from the current report in having epidural abscess and skull osteomyelitis.<sup>[6]</sup> Three of the four cases reported belonged to the pediatric age group whereas only two had supratentorial *Aspergillus* abscesses. All the cases were managed surgically, but with different antifungal agents.<sup>[1]</sup>

This case highlights several issues of medical and surgical importance. In endemic areas, where incidence of TB is very high, it is a common practice among physicians

to start patients on ATT drugs on the basis of history, examination, and nonspecific blood tests such as ESR. This child had several key features in history to suggest the possibility of an underlying immune disorder. Important hints were not recognized and the diagnosis had a significant delay. Another important point to note from this case is the need for a close clinical and radiological follow-up because of the high risk of acute hydrocephalus that warrants urgent surgical intervention.

## CONCLUSION

Coexisting cerebral aspergillosis and pulmonary TB in CGD is rare. Surgical excision of abscesses is essential to reduce the mass effect as well as to establish a diagnosis. However, these patients need prolonged antifungal drugs and a close follow-up because they are at a high risk for the development of hydrocephalus and recurrence of abscesses. This case also stresses on the fact that no treatment should be offered to such patients without a definite pathological diagnosis in the form of biopsy or culture.

## Financial support and sponsorship

Nil.

## Conflicts of interest

There are no conflicts of interest.

## REFERENCES

1. Alsultan A, Williams MS, Lubner S, Goldman FD. Chronic granulomatous disease presenting with disseminated intracranial aspergillosis. *Pediatr Blood Cancer* 2006;47:107-10.
2. Herbrecht R, Denning DW, Patterson TF, Bennett JE, Greene RE, Oestmann JW, et al. Voriconazole versus amphotericin B for primary therapy of invasive aspergillosis. *N Engl J Med* 2002;347:408-15.
3. Johnston RB Jr. Clinical aspects of chronic granulomatous disease. *Curr Opin Hematol* 2001;8:17-22.
4. Kloss S, Schuster A, Schrotten H, Lamprecht J, Wahn V. Control of proven pulmonary and suspected CNS aspergillus infection with itraconazole in a patient with chronic granulomatous disease. *Eur J Pediatr* 1991;150:483-5.
5. Lee E, Oh SH, Kwon JW, Kim BJ, Yu J, Park CJ, et al. A case report of chronic granulomatous disease presenting with aspergillus pneumonia in a 2-month old girl. *Korean J Pediatr* 2010;53:722-6.
6. Pollack IF, Pang D, Schuit KE. Chronic granulomatous disease with cranial fungal osteomyelitis and epidural abscess: Case report. *J Neurosurg* 1987;67:132-6.
7. Saulsbury FT. Successful treatment of *Aspergillus* brain abscess with itraconazole and interferon- $\gamma$  in a patient with chronic granulomatous disease. *Clin Infect Dis* 2001;32:E137-9.
8. Seger R. Chronic granulomatous disease: Recent advances in pathophysiology and treatment. *Neth J Med* 2010;68:334-40.
9. Stasia MJ, Li XJ. Genetics and immunopathology of chronic granulomatous disease. *Semin Immunopathol* 2008;30:209-35.