

# A rare presentation of chronic granulomatous disease; intracranial mass associated with aspergillosis

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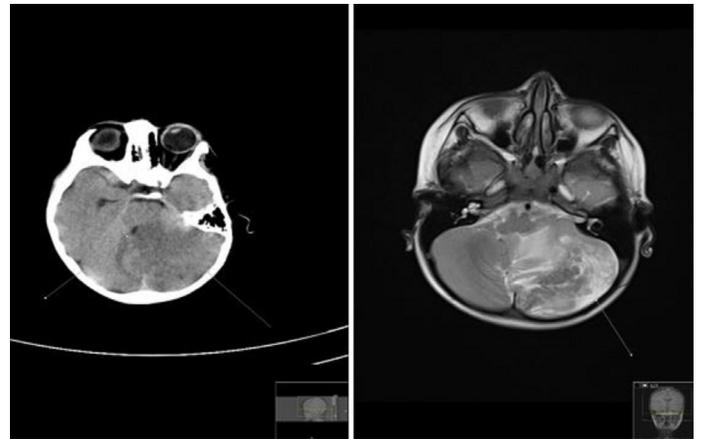
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## Dear Editor,

Chronic granulomatous disease (CGD) is a heterogeneous inherited primary immunodeficiency disorder and characterized by recurrent severe infections and granuloma formation due to defects in the nicotinamide adenine dinucleotide phosphate (NADPH) oxidase system (1,2). Although chronic granulomatous disease can be seen at any age from early childhood to adulthood, it is usually diagnosed with recurrent infections and granuloma formation under five years of age. Lung, skin, lymph nodes and liver are the most affected organs due to infection (3). *Aspergillus* species are the most common fungal infection in these patients. Cranial aspergillosis is rarely seen, and mortality is high (4). In this study, we discussed the case that was operated with the diagnosis of intracranial mass but diagnosed with CGD due to aspergillosis growth in its pathology.

A four-year, seven-month-old boy was admitted to the hospital with a complaint of headache that started two months ago and has taken antibiotics in the treatment of acute sinusitis. The patient was referred to the neurosurgery department after the patient had not received any complaints despite the antibiotic treatment and the mass was detected on the computed tomography (CT). The patient's general status is moderate, vital signs; fever was 38.3 °C, blood pressure 90/60 mm Hg, pulse 124/min, respiratory rate 28/min. The lung sounds have been coarsened. In the laboratory findings of the patient included white blood cell 10.300 / mm<sup>3</sup>, hemoglobin 9.7 g / dl, platelet 973.000 /mm<sup>3</sup>, 65% polymorphonuclear leukocytes and 35% lymphocytes observed in peripheral blood smear. As the C-reactive protein analyses displayed 4.58 "mgdl" should be corrected as "mg / dl", biochemical parameters and electrolytes were within normal limits. In

his medical history; it was learned that he was born in a cesarean section, term and weighing 3000 gr. In his family history, there was no consanguinity between his parents and his brother was healthy. Computed tomography (CT) and brain magnetic resonance imaging (MRI) of the patient were compatible with the mass (Figure 1).



**Figure 1.** Computed tomography (CT) and brain magnetic resonance imaging (MRI) of the patient were compatible with the mass

The patient was operated by the neurosurgery for a mass and aspergillus was found in the pathology. In the history, the patient was diagnosed with pulmonary tuberculosis and taken anti-tuberculosis treatment two years ago. The patient was checked to for CGD with DHR test. DHR test showed unresponsive neutrophil by PMA stimulation (Figure 2) (stimulation index) SI:1 (normal range 50-80) (R2) and DHR assay in family members also showed that mother has bimodal histogram pattern which is specific for carrier mother pattern in X-CGD. Additionally there was no residual oxidase activity of NADPH oxidase (DHR

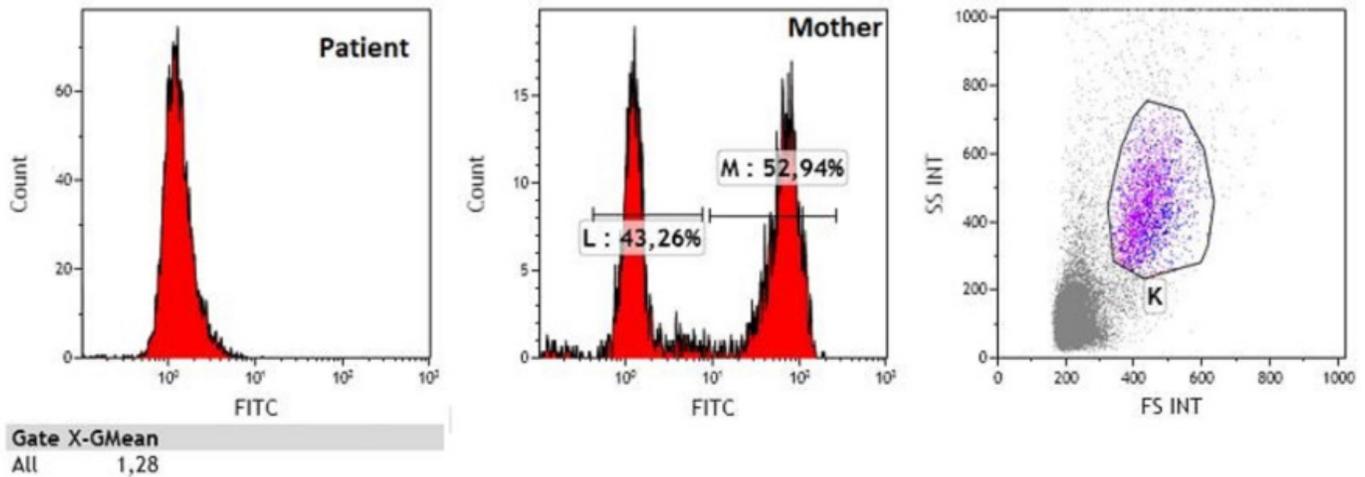
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SI:1). The serum immunoglobulin level and lymphocyte subgroups were investigated and found between the normal ranges. While following up, the patient became unconscious and cranial CT was compatible with hydrocephalus. Then ventriculoperitoneal shunt was

implanted. In the chest X-ray, infiltration (aspergilloma?) developed in the right upper zone (Figure 3). The treatment of voriconazole and interferon gamma was started at 50 mcg /m<sup>2</sup> twice a week. In follow-up, the patient was dead due to neurologic complication.



**Figure 2.** DHR Assay with flow cytometry of patient and mother neutrophil (bimodal neutrophil pattern of mother diagnostic for X-CGD in patient)



**Figure 3.** Chest X-ray, infiltration (aspergilloma?)

The common feature in patients with CGD is that they are characterized by severe bacterial and fungal infections recurring from infancy or childhood. Some cases may also be diagnosed with recurrent unusual infections in late childhood or early adulthood (3,4). Although fungal infections are seen less frequently than bacterial infections, they are the most important cause of mortality. Aspergillus species appear as the most common fungal infections, the infection begins with the inhalation of the fungal pathogen, leads to pneumonia, spreads to the ribs and spines and can metastasize to the brain. Neurological problems occur as; brain abscess, granulomatous disease

in central nervous system, leptomeningeal and focal brain lipid macrophage loaded infiltrations (6). In our case, invasive aspergillus infection, which was initially thought to be an intracranial mass but spread to the brain, was detected in the resected mass.

Diagnosis is based on medical history, clinical findings and neutrophil function tests in which respiratory burst cannot be achieved and confirmed by genotyping. Patients with a history of clinically recurrent, serious or unusual organisms should be examined for CGD and neutrophil function tests should be performed. Individuals with a family history of CGD should be screened in neonatal or postnatal early stages. In our case, diagnosed with X-CGD by DHR assay and genetic analysis for mutation point in CYBB gene was undergoing.

Today, the main treatment methods are antibiotic and antifungal prophylaxis, interferon-gamma prophylaxis, treatment of acute infections and inflammatory complications, hematopoietic stem cell transplantation and gene therapy. In our case, voriconazole and interferon gamma treatment were started at 50 mcg /m<sup>2</sup> twice a week.

In conclusion, intracellular pathogens such as aspergillus cause rarely intracranial severe infections and mostly fetal in patient diagnosed with CGD.

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