Multiple cerebellar *Aspergillus* abscess in an X-CGD patient

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A 4-year-old male patient was the fourth child of a Turkish family. He was admitted to hospital with the complaints of headache, vomiting, drowsiness, and backache. In the past, he had developed a localized infection at the site of Bacillus Calmette-Guérin (BCG) inoculation and progressive axillary lymphadenitis, starting 3 months after BCG vaccination. He also developed pneumonia unresponsive to antibiotics, and he had been on antituberculous therapy with the presumptive diagnosis of tuberculosis (TB) for one year in the local hospital due to the endemicity of TB in that region. All the family members were healthy, no consanguinity between parents, and no family history of sibling deaths except the youngest brother (fifth child), who had also BCG adenitis and severe pulmonary infection unresponsive to antibiotics.

On admission, the physical examination revealed a confused, paraplegic child with bilateral diffuse rales on lung examination. There were 5 cm hepatomegaly and splenomegaly below the costal margins. Negative serology for HIV, rheumatoid factor, and brucella agglutination were observed in his laboratory evaluation. The percent and numbers of lymphocyte subpopulations, serum immunoglobulin, and complement levels were also normal. Cerebrospinal fluid (CSF) sample was taken to rule out CNS infection after the symptoms of recurrent seizure and vomiting. Protein level of CSF was 300 mg/dl, and sugar level was 40 mg/dl. Acid-fast bacilli were not seen in sputum stain and the culture did not yield any microorganisms. A tuberculin skin test with purified protein derivative was non-reactive (6 mm x 7 mm in diameter) and family screening for TB was also negative. Chest radiography showed bilateral disseminated lung infiltrations and calcified left axillary lymph node, and sinus x-ray was normal. Cranial non-contrast CT revealed a hypodense mass in the posterior fossa causing obstructive hydrocephalus due to the obliteration of the fourth ventricle. Cranial MRI study showed a mass composed of multiple millimetric conglomerated cystic lesions in the right cerebellar hemisphere and vermis (**Figure 1**). The signal features in MRI findings were evaluated as hemorrhage containing abscesses. The underlying cause of paraplegia was verified by spinal MRI showing a 15 x 15 mm nodular lesion at the level of T11, which may compatible with fungus ball in the subarachnoid space. Neutrophil function test with a nitroblue-tetrazolium (NBT) slide test was compatible with chronic granulomatous disease (CGD) (NBT was zero) in both the patient and his younger brother.

Chronic granulomatous disease (CGD) is a rare congenital immunodeficiency disorder in which microbicidal activity of the phagocytes is abolished.[1] Family analysis with flow cytometric dihydrorhodamine (DHR) assay, which is an ultrasensitive method for functional analysis of neutrophils also confirmed the diagnosis. The mother showed a bimodal histogram pattern of DHR assay, which is specific for the X-CGD carrier pattern.[2] He underwent surgery emergently due to the peri-lesional edema and herniation risk. Total drainage of cerebellar abscess was performed, which yielded branching septate hyphae characteristic of *Aspergillus fumigatus*. Regarding his NBT and DHR assay results, trimetoprim-sulfometaxazol (TMP-SMX; 5 mg/kg/day, iv) and liposomal Amphotericin B (LAM-B) (7.5 mg/kg/day, iv) therapies were started along with interferon-γ (IFN-γ; 50 μgr/m^2/day, subcutaneously every other day) to both the patient and his younger brother. His clinical status improved, and paraplegic symptoms, headache, and confusion also disappeared after external drainage of CSF for 3 weeks, and than ventriculo-peritoneal shunt was placed, which is still functional. The LAM-B was given for 6 months, 3 months at 7.5 mg/kg/day and then 3 months of alternate day treatment of 5mg/kg/day, along with IFN-γ (50 μgr/m^2/day, subcutaneously every other day) without serious complications. His follow up CT scan of brain demonstrated relative improvement with resolving edema, which was parallel to the clinical condition of

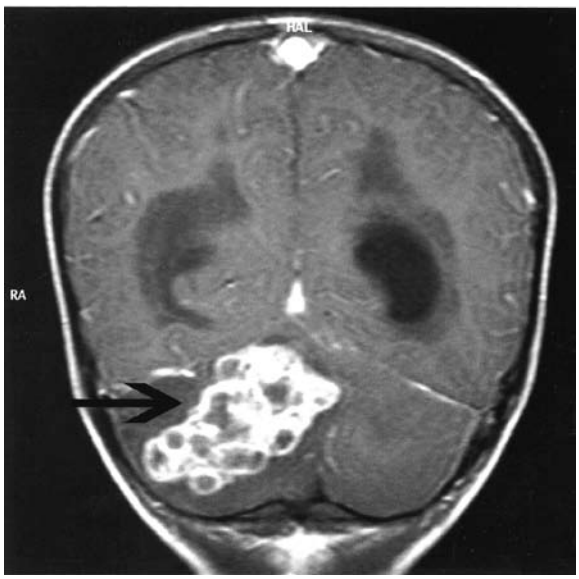

Figure 1 - Cranial MR images before medical therapy. In the right cerebellar hemisphere and vermis, there are multiple millimetric conglomerated lesions (arrow).

the patient. He was discharged with prophylactic doses of TMP-SMX (5 mg/kg/d, orally) and itraconazole (3 mg/kg/d, orally). He also receives IFN-γ prophylactically (50 μgr/m^2/day, subcutaneously 3 times a week). He is in a good general condition without any major infection and has had normal neurological findings for 5 years.

A number of patients with BCG disease (BCG-itis or BCG-osis) and tuberculosis (pulmonary or disseminated) have been reported as seen in our patient.[3,4] Our patients (both brothers) had regional BCG lymphadenitis (BCG-itis) requiring surgical drainage. Treatment of Aspergillus abscesses in CGD patients requires being aggressive both with surgical debridement and medical treatment. Liposomal formulation of Amphotericin B is accepted for the first choice of treatment with lower renal toxicity with respect to conventional Amphotericin B in CGD.[5] Combinations of L-AMB with new antifungals such as Voriconazole have also been shown to lower the treatment courses, complications, and improve the success of treatment in many reports recently in pediatric patients.[5]

In conclusion, the diagnosis and the treatment of an X-CGD case presenting with multiple nodular infiltrations on the right cerebellar hemisphere and vermis was presented. This was a case of CGD with cerebellar aspergillosis, which responded well to a combination of IFN-γ and antifungal chemotherapy with high dose LAM-B for 6 months after neurosurgical removal of the abscesses.

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