PARA VERTEBRAL ABSCESS AND RIB OSTEOMYELITIS DUE TO ASPERGILLOUS FUMIGATOUS IN A PATIENT WITH CHRONIC GRANULOMATOUS DISEASE.


From the Department of Immunology and Allergy, Department of Pediatric Infectious disease, Children Medical Centre, Tehran University of Medical Sciences, Tehran. I.R.Iran

ABSTRACT

Chronic granulomatous disease is an infrequent primary immunodeficiency characterized by defective intracellular killing of ingested microorganisms thereby making patients highly susceptible to recurrent life threatening bacterial and fungal infections. In this study, we review the medical course of an 8 yr old girl with AR-CGD. She suffered from recurrent dermal and deep abscesses, retractable salmonellosis, disseminated BCGosis, recurrent aspergillus infection presenting as mandibular osteomyelitis and pulmonary involvement with invasion to rib and vertebral bodies. Despite of longterm IV amphotericin B, itraconazole and IFN-γ administration, and surgical interventions (drainage and resection), she died in spite of long term antibiotic anti fungal prophylaxis and interferon-gamma administrations, invasive aspergillosis resistant to current conventional therapies is the cause of 1/2 to 1/3 of CGD deaths.

Keywords: Chronic granulomatous disease. Invasive aspergillosis. Complications.

INTRODUCTION

Chronic granulomatous disease (CGD), a spectrum of genetic underlying defects which lead to complete absence or malfunction of NADPH-dependent oxidase in phagocytic cells.

It is inherited in 95% of cases by X-linked pattern (mutations in Xq 21.1) in others by mendelian autosomal recessive pattern Cmutation in chromosomes 7q 11.23,1q25,16q24,(1,3,9,16)

Major clinical manifestations are recurrent
Para vertebral abscess

respiratory infections, dermal and deep organ abscess formation, osteomyelitis, lymphadenopathies and hepatosplenomegaly. Granulomatous reaction, due to the incomplete resolution, is another prominent sign. Wide spread granuloma formation leads to the gastric antral or urethral stenosis, granulomatous colitis, liver fibrosis, cirrhosis and chronic lung disease. (3,10,11,19)

Offending organisms are catalase positive germs such as s.aureus, g. enteric bacilli, p. aeroginosa , s.mercesence, legionella and different fungi like aspergillus , candida and mycobacteria.

Invasive aspergillosis spread over various contagious organs. The underlying defective host defense mechanisms and infection with resistant germs make its management extremely difficult. (3,11,17,18)

PATIENT

An 8yr old girl with AR-CGD initially had been presented with frequent dermal staphlococcal abscesses since 3 months of age, besides retraceable salmonellosis and deep abscesses during infancy. At the age of 3, she had received anti tuberculous drugs for disseminated BCGosis with lung involvement. Suffering from several episodes of staph. and Aspergillus dermal abscesses, she was admitted in hospital due to nuchal lymphadenitis and mandibular fungal osteomyelitis, with concomitant evidences of lung and rib involvement. Surgical drainage, treatment with amphotricin and itraconazole controlled the catastrophe.

The following year, she was admitted for elbow arthritis and lung and rib involvement. Six months later, searching for causes of chronic RUQ pain and fever the investigative stage of the liver abscess formation and lung and rib involvement, was revealed. She thus received long term broad spectrum antibiotics, metronidazole, amphotericin, IFN-gamma and itraconazole prophylaxis.

The disease presented as a localized dermal abscess on her right hemithorax, with underlying lung involvement and rib osteomyelitis due to aspergillus (culture). Despite 1.5 months therapy with IFN-gamma and high dose IV amphotericin, there had been no response, thus the rib was removed surgically. A few days later, she became paraplegic with spasticity and developed positive plantar reflexes. MRI showed an invasive extended paravertebral abscess. The neurosurgeon drained all the suctionable pus, which had pushed the cord posteriorly. Smear and dural biopsies showed fungal hyphae. Therefore, Itraconazole was added to the previous regimen.

As an out patient, she was given itraconazole, cotrimoxazole and cephalaxine.

Finally, two months later she was admitted to PICU for severe respiratory distress, fever, oliguria, cachexia, infected surgical wounds, wide bed sore on her right buttock and hepatomegaly. Chest roentgenograms showed bilhar pneumonia, a wide consolidation on right upper lobe and destruction of several nuchal vertebrae. Abdominal sonogram detected hepatomegally and right kidney hydrenephrosis.

She developed hypocalcemia and severe hypokalemia which should have been corrected before amphotericin administration. Despite correction of electrolyte disturbances and an umbrella of broad spectrum antibiotics, itraconazole and IFN-gamma, she died 4 days later.

Lab data:

Flowcytometry (including, T & B lymphocytes CD markers, CD11, CD18)=NL
NBT=0
NBT of parents and other siblings = NL (>90%)
Chemiluminescence: complete defect.
Chemotaxis assay: NL-elevated complement assays:NL

DISCUSSION

CGD is an infrequent primary immunodeficiency due to complete absence or malfunction of NADPH-Oxidase in phagocytic cells, resulting from survival of cutaneous positive organisms within cells. Consequently patients are susceptible to bacterial and fungal infections. (1,4) Despite marked improvement in their life expectancy which has been brought about by IFN-gamma prophylaxis, the quality of their lives has not changed much.

Chronic inflammation due to incomplete resolution of infections ending up in granuloma formation renders functional impairment of vital organs causing gastric antral or urethral stenosis,
granulomatous colitis, liver fibrosis, cirrhosis, lung fibrosis and cor pulmonale.\(^{(3,10,11,19)}\)

Patients are still susceptible to life-threatening infections especially from pathogens like aspergillus. Invasive aspergillosis disseminates into various contagious organs. Following pulmonary aspergillosis, there are reports of invasion to bony thoracic cage such as ribs and vertebral bodies with subsequent spinal paralysis, heart and liver involvement.\(^{(3,10,11,17)}\)

Despite specific antifungal therapies the mortality of invasive aspergillosis in CGD is high and causes \(\frac{1}{3}\) to \(\frac{1}{2}\) of deaths. In the absence of minimal oxidative metabolism in CGD neutrophils, managing invasive aspergillosis is extremely difficult. Another possible etiology is infection with microorganisms resistant to conventional therapies containing amphotericin B. A. Terrus and A. nidulans appear to have been increasingly isolated from patients with invasive disease. These are innately resistant to amphotericin B.\(^{3,5}\)

Ozhasin et al reported a very courageous interesting medical challenge. They controlled an invasive disseminated aspergillosis in a CGD patient by concomitant bone marrow transplantation, granulocyte colony stimulating factor mobilized granulocyte transusions and liposomal amphotericin B.\(^{11}\)

Van't HEK et al managed a similar case with voriconazole, a novel broad spectrum antifungal triazole.\(^{17}\)

REFERENCES