CASE REPORT
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Disseminated Aspergillosis as the Herald Manifestation of Chronic Granulomatous Disease in an Adult Patient

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ABSTRACT

Chronic granulomatous disease is an inherited defect in intracellular killing of ingested microorganisms characterized by recurrent life threatening bacterial and fungal infections including invasive aspergillosis in early childhood.

We report a disseminated aspergillosis as the representative of adult onset chronic granulomatous disease without previous infection, with dramatic response to combination of antifungal and interferon therapy.

Keywords: Adulthood; Anidulafungin; Aspergillosis; Chronic granulomatous disease; Dihydrorhodamine; Invasive fungal infection; Voriconazole

INTRODUCTION

Chronic granulomatous disease (CGD) is an inherited disorder of nicotinamide-adenine dinucleotide phosphate (NADPH) oxidase and results in a defect in intracellular killing of ingested microorganisms characterized by recurrent life threatening bacterial and fungal infections.¹⁻³ There are one X-linked and four autosomal recessive forms of CGD.⁴⁻⁷ The incidence rate is between 1/200,000 and 1/250,000 live births.⁴ The organisms cultured from lesion of patients with CGD are generally catalase-producing including staphylococci, Escherichia coli (E. coli), Serratia; or fungi such as Aspergillus species.⁸⁻¹⁰ Recurrent or serious infections usually lead to diagnosis of CGD in early childhood, and onset of disease in adulthood is not common. Adult onset cases have been reported in adults, formerly.¹¹ Usually, they have had clinically mild phenotypes or were treated in childhood without attention to underlying diseases and causes of recurrence and extension of infections.

We report an adult case of CGD without history of infection, diagnosed with disseminated aspergillosis; and properly was treated with combined antifungal agents and gamma interferon.
CASE PRESENTATION

A 20 year-old girl was admitted due to low back pain and subcutaneous masses in left thigh and left temporal part of scalp. She complained of non-productive cough, low-grade fever, anorexia, night sweats and weight loss since eight months before admission. Ambiguous abdominal pain in left upper quadrant and bulging of the left temporal part of scalp and left thigh were other remarkable complaints in recent few months. She was healthy until 8 months ago without significant past medical history.

She was an Iranian student and had two brothers. One of her brothers died with a presumptive diagnosis of acute pneumonia twenty years ago; and the other younger brother was healthy. Her parents were consanguinous and healthy.

On admission, she was ill, pale and cachectic with two non-tender soft purple subcutaneous masses in the occipital part of the scalp (2.5 x 2 cm) and lateral side of the left thigh (1.5 x 2 cm) and focal tenderness in lumbar examination. Other examinations were normal with no significant lymphadenopathy and organomegaly.

Complete blood cell count revealed 19,000 cell/ml leukocytes (80% neutrophils, 14% lymphocytes, 5% monocytes, 1% eosinophils) and normocytic hypochromic mild anemia (9 g/dl). Erythrocyte sedimentation rate at first hour was 90 mm/hr. Electrolyte profile, renal and liver function tests as well as urinalysis all were in normal range with negative virologic assays including human immunodeficiency virus (HIV) antibody, hepatitis B surface antigen and hepatitis C antibody. Tuberculin skin test was negative as were sputum smear for mycobacteria, fungal and pathogenic bacterial agents.

Figure 1. Brain CT scan revealed a subcutaneous soft tissue mass with septation in the left side of scalp.

Figure 2. Chest and abdominopelvic CT scan with contrast revealed perihilar mass in right lung (above), hypodense lesion in spleen (left below) and heterogeneous infiltrative soft tissue density in pelvic fossa (right below).
She underwent bronchoscopy with bronchoalveolar lavage and transbronchial biopsy according to the findings of chest CT scan and normal sputum analysis. All of them were unremarkable.

DISCUSSION

CGD is an inherited defect in intracellular killing of ingested microorganisms characterized by recurrent life threatening bacterial and fungal infections including invasive aspergillosis in early childhood.\(^1\)\(^2\)\(^12\) Patients usually are diagnosed in early childhood.\(^13\)\(^14\) with infective involvements of skin and lung more commonly including supplicative adenitis, abscesses and pneumonia\(^15\) followed by osteomyelitis, sepsis, urinary infection, severe gastroenteritis, oral aphthae and Crohn-like inflammatory bowel disease.\(^16\) According to the reports from Iran, the median diagnostic age is 8 years, with a diagnostic delay of 4.5 years \(^17\)\(^18\) compared to the median age of onset at four months of age and the median diagnostic age of 5.5 years in other national reports.\(^19\)\(^20\) Recently, adult cases of CGD have been reported due to novel mutations or mosaic patterns.\(^21\)\(^22\) In the latter, the patient showed a somatic mosaic for the cytochrome b (-245) beta CYBB mutation, which probably originated during her lifetime in her bone marrow.\(^22\)

Furthermore, it seems that patients with X-linked recessive form of the disease have a more serious clinical phenotype than patients with the autosomal recessive forms, based on the fact that they are diagnosed significantly earlier (mean, 3.01 years of age versus 7.81 years of age, respectively).\(^4\) Moreover, the diagnosis may be delayed due to potent antimicrobial agents that inadvertently treated many CGD-associated infections, postponing diagnosis until more severe infections indicate CGD as the underlying cause.\(^23\)

The frequency and mortality rate of fungal infections have been reduced markedly since the advent of itraconazole prophylaxis and the use of voriconazole for treatment of filamentous fungal infections (e.g., Aspergillus). Combination therapy including antibacterial and antifungal and gamma interferon, dramatically reduce the rate of severe infections from one per patient-year to almost one every year per 10 patient.\(^10\)\(^24\)\(^30\) Successful hematopoietic cell transplantation (HCT) may be a definitive cure for CGD.\(^31\)

The interesting findings in this patient, were firstly, delay in presentation of CGD until twenty years of age without any previous infections and secondly the high burden of aspergillus infection as multiple involved organs particularly the isolation of this germ from spleen and bone marrow. Usually Aspergillus infection in phagocytic disorders particularly CGD presents as local slowly progressing infection but as observed in this patient, multiple organs were affected (skin, lung, pelvic cavity, spleen, vertebrae and bone marrow).

Finally, dramatic response to combined antifungal regimen was another intriguing finding in this patient, which may help us in treatment of other patients with disseminated aspergillosis. After 6 months, the patient was in healthy condition. She was afebrile and gained 6 kg weight while all paraclinic abnormalities resolved consisting of 20 mm/hr ESR, 11 mg/dl hemoglobin and significant reduction in size of pulmonary, splenic and pelvic masses while she was taking itraconazole 400 mg per day and she was supposed to continue for further six months of this treatment and then received antibacterial and antifungal prophylaxis.

We conclude that CGD should be considering in all patients with recurrent catalase positive microorganisms as well as fungal infections regardless of the age, although it usually manifests in children.

REFERENCES

Adult Onset Disseminated Aspergillosis in Chronic Granulomatous Disease


