Chronic *Fusarium* Infection in an Adult Patient with Undiagnosed Chronic Granulomatous Disease

Davoud Mansoori,1 Navid Ahmady Roozbahany,1 Hussein Mazinany,1 and Alireza Samimagan2

1Research Center for Tuberculosis and Pulmonary Diseases, Masih Daneshvari Hospital, Tehran, and 2Department of Internal Medicine, Bandarabbas Medical University, Bandarabbas, Iran

Disseminated *Fusarium* infection is a rare disease that is usually limited to immunocompromised patients. It more commonly occurs in patients with acute leukemia and prolonged neutropenia. We report a case of chronic *Fusarium* infection in an adult patient with undiagnosed chronic granulomatous disease (CGD), a primary immunodeficiency disorder in which phagocytic cells are defective in generating superoxide anion and its metabolites. The case is important because the patient had no manifestations of CGD until she was almost 60 years old and because this is, to our knowledge, the first reported case of *Fusarium* infection in a patient with CGD.

*Fusarium* infection in humans is rare. In healthy hosts, most infections occur following receipt of a traumatic soft-tissue inoculation. In immunocompromised patients, inhalation or inoculation due to a minor trauma can lead to disseminated *Fusarium* infection. *Fusarium* species, in particular, *Fusarium solani*, are common causes of keratitis. They are also common causes of onychomycosis, endophthalmitis, and skin and musculoskeletal infections.

The disseminated form of infection most commonly occurs in patients with acute leukemia and prolonged neutropenia. Skin lesions occur in 60%–80% of patients and usually manifest as multiple papules or deep painful nodules. They are most commonly located on the trunk and face [1]. Diagnosis is made on the basis of isolation of the fungal agent from blood samples or from skin biopsy specimens of suspicious lesions. *Fusarium* species produce catalase. The optimal treatment for this infection has not been confirmed, but high-dose amphotericin B can be the drug of choice [2]. Among patients with the disseminated form of *Fusarium* infection, the mortality rate is high (range, 50%–80%). The risk of mortality completely depends on the underlying disease(s) in and the immune function of the patient. In this article, we describe a case of chronic *Fusarium* infection with multiple soft-tissue abscesses in an adult patient with undiagnosed chronic granulomatous disease (CGD).

**Case report.** A 54-year-old married Persian woman presented to the hospital in July 2002 because of skin lesions with multiple fistulas on the left upper extremity (forearm and elbow). She had a 3-year history of such lesions, and results of microbiologic studies performed in 2 separate centers demonstrated that *F. solani* was the causative agent. She underwent surgical drainage and received medical treatment with multiple courses of amphotericin B, fluconazole, and itraconazole. Until 1 month before presentation, she had received amphotericin B therapy (25 mg every other day). At presentation, the skin lesions were partially healed.

In 1974, the patient was successfully treated for meningitis due to *Mycobacterium tuberculosis*, but no documents were available that mentioned that the diagnosis was based on microbiologic data. She had also a history of basal cell carcinoma on the face, which was cured by surgical excision. She had a 3-year history of respiratory symptoms that involved productive cough. Physical examination revealed skin lesions (as described above) and a coarse crackle at left lung apex; there were no other abnormal clinical findings.

The hemoglobin level was 14 g/dL, the WBC count was 8100 cells/µL (57% neutrophils and 35% lymphocytes), and the platelet count was 237,000 platelets/µL. The erythrocyte sedimentation rate was 72 mm/first hour. The induration of the PPD reaction was 25 mm in diameter, and the fasting blood sugar level, the blood urea nitrogen level, and results of creatinine and liver function tests were normal. A high-resolution CT scan of the lungs showed mild bronchiectasis and air trapped in the right middle lobe and lingula. Findings of CT scan of the perinasal sinuses were normal.

Results of testing for hepatitis B surface antigen (HBs), antibody to HBs, antibody to HIV, and antibody to hepatitis C virus were negative. IgG, IgM, IgE, IgA, total hemolytic activity, and complement C3 and C4 levels were within normal limits. Results of neutrophil chemotaxis testing and flow cytometric analysis of PBMCs, including CD3 (total) T cells, CD4 (helper) T cells, CD8 (suppressor) T cells, CD19 (B) cells, CD56 (natural...
killer) cells, and adhesion molecules (CD18, CD11a, CD11b, and CD11c on lymphocytes, neutrophils, and monocytes), were normal. The results of cutaneous Candida testing were positive. Anti-diphtheria and anti-tetanus antibodies and serum zinc level were within normal limits.

CGD was confirmed by the nitroblue tetrazolium test. This test was performed 1 time each in 2 different centers, and the reported results showed that 5% and 0% of total activity was present. In addition, the result of chemiluminescence testing was 60 million electron volts (mev) per 15 min, compared with the normal control value of 1500 mev per 15 min. These tests were performed in accordance with standard methods of immunology laboratories. Prophylactic antibiotic therapy with itraconazole and trimethoprim-sulfamethoxazole was administered. Additional follow-up revealed no symptoms, and the patient’s general condition was favorable.

Discussion. CGD is an inherited disease in which the nicotinamide adenine dinucleotide phosphate oxidase complex is unable to produce superoxide anion and its metabolites, which are required by phagocytes for intracellular killing activity [3]. This defect leads to recurrent bacterial and fungal infections, particularly with pathogens that are catalase positive. Aspergillus species, Staphylococcus aureus, Serratia species, Nocardia species, and Burkholderia cepacia are the most common pathogens found in patients with CGD [4, 5].

CGD is a primary immunodeficiency disorder, and most cases are diagnosed at childhood. The X-linked form is more common, but autosomal recessive forms have also been described [4].

Primary immunodeficiency disorders are rare in adults and have 3 possible manifestations. First, some primary immunodeficiency disorders can manifest for the first time during adulthood. For example, common variable immunodeficiency, IgA deficiency, IgG subgroup deficiencies, and some complement deficiencies may have no manifestations during childhood [6–8]. Second, primary immunodeficiency disorders sometimes have a mild phenotype that leads to latent manifestation at older ages. Mild forms of CGD, Bruton disease, adenine deaminase deficiency, and Wiskott-Aldrich syndrome are some examples [9]. Some primary immunodeficiency disorders are controlled during childhood by appropriate antibiotic therapy and by other therapies that are administered without a definite diagnosis, and the patients may survive to adulthood. Third, the immunodeficiency disorder may be initially diagnosed during adulthood but with complications different from those that appear in children. Patients with known primary immunodeficiency disorders can be treated by conservative therapies, such as bone marrow transplantation, intravenous IgG therapy, or enzyme (e.g., adenine deaminase) replacement. These patients can live for a long period of time without presenting for evaluation to physicians who care for adults [10].

The patient described in this article had no symptoms for a long period of time, and CGD could be diagnosed only after the development of chronic Fusarium infection, which occurred when the patient was 54 years old. Most patients with CGD receive this diagnosis during the first years of life. Some older patients with CGD have also been described. In such patients, mild phenotypes are considered to be the reason for the unusually late manifestations. Autosomal recessive CGD has a milder phenotype than X-linked CGD [9]. On the basis of our accumulated data and the absence of reports of Fusarium infection in patients with CGD in the literature, we propose that this is the first reported case of Fusarium infection in a patient with CGD.

The presented case is important because this is the first reported case of Fusarium infection in a patient with CGD, and because the patient had no manifestations of CGD until she was almost 60 years old, with no evidence of infection during childhood. Our patient had meningitis due to M. tuberculosis at the age of 28 years, and Lau et al. [11] have described 6 Chinese patients with CGD and pulmonary tuberculosis. However, tuberculosis associated with CGD is rarely reported in the United States, and we had not observed any cases of tuberculosis associated with CGD in any of our other Persian patients. Therefore, we think that meningitis due to M. tuberculosis in our case cannot be explained by the patient’s underlying immunodeficiency.

References