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A case of chronic granulomatous disease diagnosed in adulthood

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Abstract

Chronic granulomatous disease (CGD) is a heterogeneous, inherited primary immunodeficiency disease. It is characterized by granulomatous formations due to increased inflammatory response and recurrent and life-threatening infections occurring because of the defects in nicotinamide adenine dinucleotide phosphate (NADPH) oxidase system. Diagnosis is made by medical history, clinical findings, and neutrophil function tests, and is confirmed by genotyping. A 26-year-old male patient presented to our emergency polyclinic with complaints of fever, abdominal pain, diarrhea, fatigue, left ear discharge and was hospitalized in our ward for examination and treatment. Since childhood, he suffered from failure to thrive, frequent pneumonia, and skin pruritus. Since the age of 15 years, he underwent surgery for liver abscess and ear surgery due to ear discharge and chronic otitis. Ultrasonography revealed an abscess on the right psoas muscle, compressing the right kidney. Abscess culture was positive for the methicillin-sensitive strain of Staphylococcus aureus and negative for acid-resistant staining (ARB). Aspergillus spp. reproduced in the ear discharge culture. CGD, which is one of the primary immunodeficiency diseases, should be considered in patients presenting with recurrent intraabdominal abscess and respiratory system infections in adulthood.

Keywords: Primary immunodeficiency, Dihydrorhodamine 123 test, Chronic granulomatous disease

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Informed Consent
The authors stated that the written consent was obtained from the patient presented with images in the study.

Conflict of Interest
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Introduction

Chronic granulomatous disease (CGD) is an inherited primary immunodeficiency disease with a defect in the nicotinamide adenine dinucleotide phosphate (NADPH) oxidase enzyme [1]. In this disease, phagocytic cells do not produce reactive oxygen species (ROS), which are crucial to kill ingested microorganisms. It is characterized by inflammatory findings such as granuloma formation due to increased inflammatory response to some recurrent, life threatening bacterial and fungal infections [2,3]. It may be X-linked (Mutations in the CYBB gene encoding gp91phox protein) or autosomal recessive (mutations in NCF1, NCF2, CYBA or NCF4 genes coding for p47phox, p67phox, p22phox or p40phox, respectively) [1]. Most patients are diagnosed before the age of five. The use of antibiotics and prophylaxis greatly improved overall survival [4]. The most common clinical findings include infections, granulomatous diseases, inflammation, and failure to thrive [1]. Typical infections include purulent bacterial pneumonia, sinusitis, liver abscess or necrotizing fungal infections in deep tissue and the bones [5]. There are various tests based on measurement of neutrophil oxidative burst response, in which superoxide production is measured, including ferric cytochrome c reduction test, anti-HIV (by chemiluminescence assay), nitroblue tetrazolium reduction test (NBT) and dihydrorhodamine - 123 (DHR) oxidation [1].

We aimed to present a case of an adult patient who was diagnosed with chronic granulomatous disease with recurrent episodes of abdominal abscesses and respiratory infections.

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Case presentation

A 26-year-old male patient presented to our emergency clinic with complaints of fever, abdominal pain, diarrhea, fatigue, and left ear discharge, and was hospitalized for treatment. His complaints continued for about one month. From the early ages, he had complaints of frequent pneumonia attacks and failure to thrive. He underwent liver abscess operations and ear drainage in various hospitals since the age of 15 years, and ear operation due to chronic otitis. Earlier test results were negative for methicillin-sensitive Staphylococcus aureus (MSSA), ARB, and autoimmunity markers. No pathology was detected in tuberculosis culture. In our clinic, we obtained the following test results: WBC: 21.61 K / uL, NEU: 18.09, PLT: 339000 10^{-3}/uL, EOS: 0.00283 10^{-3}/uL, CRP: 17.2 mg/dL, sedimentation: 20 mm/h, hydatid indirect hemagglutination: Negative, IgA: 658 mg/dL (60-200), IgM: 118 mg/dL (40-110), IgG: 1090 mg/dL (550-1900), Total IgE: (2500 ng/ -240), Antigliadin IgG: Negative, Antigliadin IgA: Negative, Brucella agglutination test: Negative, Grubel-Vidal agglutination test: Negative. There were no pathogenic bacteria in the stool culture, and dense leukocyte and erythrocytes were observed in stool microscopy. Metronidazole 4 x 500 mg and ciprofloxacin 2 x 400 mg were administered parenterally to the patient. Ultrasonography revealed an abscess on the right psoas muscle, compressing the right kidney. Abscess drainage was performed by the General Surgery Department. MSSA reproduced in the abscess culture, which was ARB negative. Aspergillus spp. reproduced in the ear discharge culture. Cefazolin 3 x 1 gr and Metronidazole 4 x 500 mg were administered parenterally. Considering the history of the patient and with a pre-diagnosis of primary immunodeficiency, dihydrorhodamine 123 test was requested. Trimethoprim-sulfamethoxazole (TMP-SMX) 80/160 mg tablets (2x1), itraconazole 100 mg capsules (1x2), and IV methylprednisolone (1x80 mg) were administered for the treatment of the patient whose test result were consistent with CGD. Steroid therapy was discontinued after two weeks. He was discharged with TMP-SMX and itraconazole treatment. There was no recurrence of infections during one-year follow-up. Written consent was obtained from the patient presented in the study.

Discussion

Although CGD is a heterogeneous disease, clinical findings and prognosis vary widely due to different genotype and phenotypic interactions. Patients with CGD are characterized by recurrent severe bacterial and fungal infections from infancy or childhood. In some cases, the diagnosis can be made with recurrent abnormal infections during late childhood or early adulthood [6]. The diagnosis was made at the age of 26 years, although there was recurrent hepatic abscess since the age of 15 years.

Recurrent infections, granulomatous diseases, inflammation, and weight loss are the most common clinical manifestations of CGD [1]. In our case, recurrent infections and failure to thrive were apparent.

Liver involvement is obvious and important. Liver abscess is seen in approximately 35% of patients. Until recently, almost all cases required surgical treatment [7]. Studies have shown that liver abscess can be controlled with antibiotics and corticosteroids without the need for surgical treatment [8, 9]. In our case, the patient, who was operated due to liver and psoas abscesses in various hospitals, was diagnosed with CGD. Corticosteroids and antibiotic therapy were used to control the abscess and no recurrence was observed within the one-year follow-up period.

Typically, fungal infections, more specifically, *Aspergillus spp.* are the main cause of mortality in CGD [10, 11]. The effects of fungal infections in CGD can be altered by administering a therapy of highly active antifungals using itraconazole, voriconazole and posaconazole [12]. In our case, aspergillus was found in ear drainage culture and complaints of the patient regressed with itraconazole. Infections with catalase-producing microorganisms such as *S. aureus* and Aspergillus species are seen in the preliminary plan [13]. *S. aureus*, *Burkholderia cepacia complex*, *Serratia marcescens*, *Nocardia species* and *Aspergillus species* are responsible for the majority of infections in CGD in North America [14]. In our case, MSSA was found in abscess culture and *Aspergillus spp* reproduced in ear drainage culture.

Flow cytometry is used to measure the oxidation of dihydrorhodamine 123 versus rhodamine 123 in phorbol myristate acetate (PMA) -induced neutrophils as a marker for cellular NADPH oxidase activity [15].

Antimicrobial prophylaxis (TMP-SMX, itraconazole) consists of the IFN-γ triad, an immunostimulatory treatment [1]. We started treatment with TMP-SMX, itraconazole, and corticosteroids, after which steroid treatment was gradually stopped. The patient was discharged with TMP-SMX and itraconazole therapy.

CGD, one of the causes of primary immunodeficiency, presents with recurrent infections. Therefore, the diagnosis of the disease is usually made in childhood and rarely during adulthood.

Conclusion

Our patient's complaints began at childhood and he remained undiagnosed with CGD until adulthood. In patients with recurrent staphylococcal and aspergillus infections, CGD is one of the diseases to be considered.

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