Chronic granulomatous disease

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ABSTRACT

A 2½-year-old child presented with multiple discrete granulomatous lesions on the face and flexural regions since the age of 2 months along with lymphadenopathy. The patient also had recurrent bouts of pyodermas and respiratory tract infections. Biopsy of the lesion showed necrosis of tissue with suppuration and histiocytes but no evidence of tuberculosis, fungal infections or atypical mycobacteria. Lymph node biopsy also showed necrosis with suppuration but no infective organism. Nitroblue tetrazolium test was negative indicating that the neutrophils failed to oxidize the dye. We are reporting here a rare case of chronic granulomatous disease.

Keywords: Chronic granulomatous disease, Congenital immunodeficiency disorder, Nitroblue tetrazolium test

INTRODUCTION

Chronic granulomatous disease (CGD) is a congenital immunodeficiency disorder of phagocyte bactericidal function with X-linked recessive inheritance, characterized clinically by granulomatous lesions in the skin, lymph node, lung, liver, GIT and bones. The basic pathology in this disease is a defect in the subunits of nicotinamide adenine dinucleotide phosphate (NADPH) oxidase, whose normal functioning is essential for killing of phagocytosed bacteria by neutrophils using the myeloperoxide-halide system.[1] The main defective subunit is gp91 phagocyte oxidase.[2] An autosomal recessive form with a defect in the p22 phagocyte oxidase has also been described. Consequently, these patients develop recurrent bacterial infections by Staphylococcus aureus, Chromobacterium violaceum, Nocardia species, Serratia marcescens, legionella and atypical mycobacteria. Fungal infection by aspergillus is also common. The respiratory and the gastrointestinal tracts are the commonest affected systems in CGD. The laboratory diagnosis of CGD is by the nitroblue tetrazolium test (NBT). We report a 2 and 1/2 year old boy with this disorder.

CASE REPORT

A 2½-year-old boy born of a non-consanguineous marriage presented with multiple discrete raised skin lesions on the face, neck and flexural regions since the age of 2 months. The lesions first developed as skin-colored tender nodules over the axilla and gradually enlarged and ruptured to form large granulomatous masses. Similar lesions developed over the groin, periauricular region and submental region over a period of one year. In between, the child also developed recurrent fever, respiratory tract infections and pyodermas. Various physicians gave him multiple...
courses of antibiotics and antituberculous drugs but the lesions failed to heal.

Examination revealed a small for age, sick and febrile child with a protuberant abdomen. Dermatological examination showed multiple, discrete, well-defined, erythematous, moist, fleshy, granulomatous plaques of various sizes and shapes distributed symmetrically over the submental, preauricular, retroauricular, axillary and groin regions overlying the lymph nodes [Figure 1]. The cervical, axillary and inguinal lymph nodes were enlarged bilaterally and were discrete, non-tender and mobile.

Blood hemogram showed microcytic hypochromic anemia with reactive lymphocytosis in the peripheral smear. Liver and renal function tests, VDRL, TPHA and ELISA for HIV were negative. Pus culture and sensitivity did not show any organism. X-rays of the chest, skull and long bones were normal. Mantoux test was negative. Cultures for fungus, Mycobacterium tuberculosis and atypical mycobacteria were negative. Ultrasound abdomen showed hepatosplenomegaly with para-aortic lymphadenopathy. A skin biopsy showed necrosis with supplicative inflammation and plenty of histiocytes. FNAC from cervical lymph nodes yielded sheets of neutrophils with multiple histiocytes. Lymph node biopsy also showed necrosis with suppuration and histiocytes, but there were no fungi, tuberculous or atypical mycobacterium [Figure 2]. The NBT test
revealed the inability of the patients’ neutrophils to oxidize NBT into blue formazan [Figure 3] compared to the control [Figure 4]. A final diagnosis of CGD was made.

DISCUSSION

The presentation with multiple granulomatous lesions, recurrent pyodermas and respiratory infections; absence of fungi, tuberculous bacilli or atypical mycobacteria by investigations; and negative ELISA for HIV pointed to a diagnosis of the congenital immunodeficiency disorder, chronic granulomatous disease. The NBT test clinched the diagnosis of CGD. The NBT depends on the capability of normal neutrophils to reduce the colorless NBT dye to blue formazan during phagocytosis, while in CGD this is not possible and hence a negative test is diagnostic.[3]

Chemiluminescence and bacteriocidal assays are the other tests to diagnose CGD. Even though patients with CGD are prone to recurrent bacterial infections, organisms like streptococci and pneumococci cannot cause infections as these bacteria produce their own hydrogen peroxide to allow the myeloperoxidase-halide system to function during phagocytosis.

Respiratory involvement in the form of recurrent pneumonia, lung abscess and empyema is very common.[4] Gastrointestinal tract involvement is in the form of malabsorption, oral ulcers, perianal abscesses and fistulae.[5] However, in our patient, there was no clinical or laboratory evidence of respiratory or gastrointestinal tract involvement.

There is no definite treatment for CGD. Proper skin care and hygiene are very important. Frequent antibiotic therapy may be required. Long-term therapy with trimethoprim-sulfamethoxazole is now used.[6] Aspergillus infections of the lung and bones may require itraconazole even though the response may be poor. Subcutaneous gamma-interferon is now advocated as a new modality of therapy.[7] Bone marrow transplantation may be done if other modalities of therapy fail. Gene therapy may have a role in the future.

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REFERENCES