CASE REPORT

Chronic Granulomatous Disease Associated With Juvenile Rheumatoid Arthritis

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Abstract

Autoimmune disorders have been considered as a common finding in primary immunodeficiencies. Different autoimmune diseases are associated with these congenital immune defects including rheumatoid arthritis. In this report a case of Juvenile Rheumatoid Arthritis (JRA) is presented who was found subsequently to have Chronic Granulomatous Disease (CGD). This is the third case report of JRA associated with CGD in literature.

Key words: Juvenile Rheumatoid Arthritis, Chronic Granulomatous Disease, Autoimmune disorders, Primary immunodeficiency.

Introduction

The occurrence of autoimmune diseases in the setting of immunodeficiency disorders is not a new finding. The presentation of lupus erythematous in selective IgA deficiency, cytopenia in common variable immunodeficiency (CVID) and hemolytic anemia in Wiskott-Aldrich syndrome are such examples. (1) Chronic Granulomatous Disease (CGD) is one of the important disorders of immune system. CGD is an uncommon phagocytic disorder with impairment of the intracellular destruction of the microbial agents. The incidence varies between 1/200,000 - 1/250,000 in US residents. The disease is transmitted as X-linked and autosomal recessive inheritance. The most common presentations of CGD are recurrent skin and respiratory tract infections. The most common autoimmune disease observed in association with CGD is Crohn's disease (2). However, there are reports of discoid lupus erythematosis (DLE), systemic lupus erythematosis (SLE) and IgA nephropathy in patients with CGD (2). The existence of CGD and Juvenile Rheumatoid Arthritis (JRA) is rare with only two such cases been reported earlier.

JRA is chronic inflammation of the synovium with extra-articular manifestations that occurs in children less than 16 years of age. The frequency of this disease is reported as 2-20/100,000. The most common type of the JRA is oligoarticular involvement that consists 60-65% of the cases (3). We report a case of co-existence of JRA and CGD in a child, which seems to be the third reported patient in the literature.

Case Report

A six years old boy was presented with cough for ten days followed by fever and dyspnea. During the past six months he had been hospitalized three times in another hospital with the diagnosis of bacterial pneumonia and treated with different antibiotics. He was found to have JRA at the age of two years and had continuously received prednisolone, hydroxychloroquine and ibuprofen. The involved joints were both wrists. He had been operated six month ago for submandibular lymphnode abscess. He weighed 16 kg and the height was 112cm. The temperature was 38°C and other vital signs were in normal range. On examination there were decreased breath sounds in left lung with hepatomegaly and limitation of movement in both wrist joints in all directions without erythema or effusion. Other joints were normal. No significant finding was detected further in the examination. Initial laboratory investigation demonstrated Leucocytosis with shift towards left, erythrocyte sedimentation rate (ESR) of 37 and negative CRP. The diagnosis of JRA was based on a history of inflammatory joint disease and physical examination confirming the arthritis after ruling out of other causes of articular involvement such as SLE, Sarcodosis and Vasculitis Syndrome. Considering recurrent episodes of pulmonary infections, immunologic survey was performed. Intracellular oxidation dysfunction was demonstrated by standard Nitro-blue tetrazolium test (NBT=0) and was confirmed with flow cytometry. Radiography of the wrists showed widespread bony destruction and deformation. Abdominal ultrasound demonstrated hepatomegaly and chest X-ray showed diffuse opacity with bronchogram in the left upper lobe. CT-scan of the lungs demonstrated opacity in upper and lower lobes of left lung as well as posterior segment of right lung and hilar and mediastinal lymphadenopathy. Considering the abnormal phagocytosis and refractory lung lesions a CT guided biopsy was performed which was reported as acute inflammation in histopathologic examination with negative smears and cultures for bacterial, fungal and mycobacterial agents. The patient received antibiotics (Clindamycin+Ceftriaxone) with tapering of prednisolone. The fever disappeared after 24 hours and respiratory symptoms improved after one week. He was discharged after two weeks with prophylactic drugs of Itraconazole and trimethoprim/sulphamethoxazole. He is under regular observation without new infection episode. Other immunologic tests consisting of immunoglobulins level [IgG- 9.2g/l (Normal = 1.72- 10.69g/l), IgA=2.1 mg/dl (Normal =1.4-64 mg/dl), IgM=74 mg/dl (Normal = 33-126 mg/dl), IgE: 65 mg/dl (Normal = 0-170mg/dl)], serum complement components and flowcytometric analysis of peripheral blood lymphocytes [CD19= 11.9% (Normal = 6.4 - 23%), CD4=38% (Normal = 30-60%), CD8=22% (Normal =11-36%), CD3 = 69% (Normal = 59-85%)] were all normal as well as functional tests for hormonal and cellular immunity (Skin tests with recal antigens and isoagglutinins). The parents did not have any oxidative defect.

Discussion

The co-existence of the autoimmune and immunodeficiency disorders have been observed with high frequency by different studies (1). Although all the patients suffering from immunodeficiency disorders do not acquire autoimmune diseases, their risk of affliction with this group of diseases is high. Multiple factors consisting underling genetic abnormality, inflammation and environmental causes all have been proposed as etiology of developing autoimmune disorders (4). The long persistence of antigens in immunodeficient patients, can explain the high incidence of autoimmune disorders in these patients. In addition abnormalities of the immune system function (irregular immune responses) secondary to congenital immunodeficient status might be responsible in the formation of

autoimmune disorders (1,4).

The incidence of autoimmune disease is higher in patients with disorders of the humoral system (5). The rate of autoimmune disorders have been reported as 10-23% in patients suffering from CVID (6). Lee et al. studied the relation between rheumatoid disease and primary hypogammaglobulinemia and conducted that about 10-30% of these patients develop rheumatoid arthritis (7). Hematologic disorders such as thrombocytopenia and hemolytic anemia are most common autoimmune diseases observed in humoral immune deficiencies. The incidence of idiopathic thrombocytopenic purpura (ITP) in CVID patients is reported as 6.7% and 4.8% of these patients develop autoimmune hemolytic anemia (8).

The patient of the presenting report had Juvenile Rheumatoid Arthritis and after investigating the immune system for recurrent pneumonitis, the underlying immune defect of the patient was uncovered. The occurrence of autoimmune disease with CGD has been reported in several studies. More than 15% of the children with CGD suffer from typical clinical and histological finding of Crohn's disease (9). One of the common autoimmune diseases in a CGD patient is SLE. Also the incidence of SLE in the carriers of the CGD gene (Mother of the patient with X-linked CGD) is more common than normal individuals (10). The occurrence of other autoimmune diseases in CGD patients are rare findings. Narsipour et al reported the first case of IgA nephropathy with CGD background from New York in 2002 (11). Until now the occurrence of JRA in CGD cases has been reported in only two cases. Lee et al. accounted a report on a girl suffering from CGD in 1994. She had a multiarticular involvement. In the same article it was pointed to the first case of co-existence of JRA and CGD (12). In our opinion, this report is the third patient of the co-existence of the JRA and CGD. The patient, in contrast to other similar cases, presented with autoimmune disorder before diagnosis of immune deficiency.

NSAIDs are likely to be the first line of medication treatment to reduce inflammation and any pain in JRA patients. Disease modifying anti rheumatic drugs (DMARDs) are the second choice. JRA patients can use corticosteroid to reduce inflammation as well. The goal in treatment of CGD patients is to prevent infections. High doses of antibiotics over long period of time and anti fungal therapies are effective in preventing bacterial infections and infections caused by Aspergillus.

Regarding the occurrence of autoimmune disorders in patients with CGD, it is recommended to consider CGD in patients suffering from autoimmune dysfunctions, particularly when it is associated with recurrent infections.

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