Case Report

Nocardiosis in a Patient with Common Variable Immunodeficiency

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Abstract

We report a case of nocardiosis in a 42 years male with common variable immunodeficiency syndrome (CVID). He presented with arthritis, subcutaneous abscess and pleural effusion. Diagnosis of CVID was made during this presentation. Serum IgG, IgA and IgM levels were markedly decreased. Nocardia asteroides was cultured from pleural fluid. He was successfully treated with intravenous immunoglobulin and co-trimoxazole.

INTRODUCTION

Common variable immunodeficiency (CVID) is the commonest symptomatic primary immune deficiency syndrome. It is characterized by primary hypogammaglobulinemia with normal B cell phenotype. The age of presentation is usually in the second decade. Clinical manifestations commonly include recurrent bacterial infections, though autoimmune and granulomatous events may also occur. Nocardiosis is chiefly an opportunistic infection in immunosuppressed individuals. However, nocardiosis in a patient with CVID has not been described earlier, though, there are some reports which suggest that nocardiosis can present in patients with CVID. We report a patient with newly diagnosed CVID who presented with pulmonary and cutaneous nocardiosis.

CASE REPORT

Mr BK, a 42 yrs old gentleman was first seen by us in April 2004. He complained of polyarticular pain and swelling since 15 days. There was fever (101°F) for 1 day at onset and redness of both eyes. Two months ago, he had loose motions lasting for 2 weeks. He was on 30 mg of prednisolone for hyperreactive airways since 2 months. His past history was significant for recurrent (5 episodes) pneumonia since 15 yrs, once requiring mechanical ventilation, 2 episodes of herpes simplex infection, 1 episode of herpes zoster and frequent viral warts in the past 2 yrs and repeated episodes of loose motions. Clinically there was mild synovitis at wrists. Investigations revealed an ESR of 60 mm at 1 hr, ACE levels were normal (32 units/ml), ANCA was negative. A clinical diagnosis of reactive arthritis (bowel related) was made. He was given symptomatic treatment with NSAIDs and steroids were tapered.

In July 2004, he was admitted with pain and swelling at left elbow, both knees and ankles and pain in the thighs of 5 days duration. He also complained of cough with mucopurulent expectoration since 1 week. Clinical evaluation revealed oral candidiasis, swollen knees and ankles, subcutaneous abscesses in the right thigh, around the right ankle, left elbow and a right sided pleural effusion.

Investigations revealed hemoglobin of 10 g/dl, total white blood count of 12,700/cumm with 83% neutrophils, 9% lymphocytes, 6% monocytes. ESR was 100 mm at the end of 1 hr. Liver function tests, blood sugar and renal parameters were normal. He had hypoproteinemia (total proteins of 3.9 g/dl), serum albumin had decreased to 1.9 g/dl (3.5 g/dl in April 2004), LDH of 180 U/L, HIV by ELISA was negative. Serum immunoglobulin levels done in view of recurrent infections in the past, showed a marked reduction of IgA - < 6.67 mg/dl (68 – 378 mg/dl), IgG - < 33.3 mg/dl (694 – 1618 mg/dl) and serum IgM – 12 mg/dl (60-263 mg/dl). Serum IgE levels were normal - 60 IU/ml (10 - 180 IU/ml). T cell function could not be done. Stool examination revealed Giardia lamblia. X-ray chest showed right basal consolidation. USG chest demonstrated a right pleural effusion. Pleural fluid analysis revealed LDH – 6158 , proteins – 2.6 gm/dl, WBC – 128000, differentials: N- 95,L-1,M-3,E-1, ADA – 94 U/L (0-36), AFB–neg. Culture of aspirate from thigh abscess and blood showed no bacterial or mycobacterial growth.
A diagnosis of common variable immunodeficiency was made. He was given intravenous immunoglobulin (IVlg) at 400 mg/kg and empiric antituberculous therapy (ATT) was started. A week later, culture of pleural fluid revealed Nocardia asteroides. This was identified by weakly acid fast Gram-positive branching filaments that were Kinyoun acid fast stain positive and also confirmed biochemically. ATT was stopped and co-trimoxazole (trimethoprim - 15 mg/kg/d and sulphamethoxazole - 75 mg/kg/d) started. On follow up at 1 month, abscesses at the ankle, thigh and elbow had decreased markedly. Serum IgG increased to 620 mg/dl. He has received 6 monthly injections of IVlg (400 mg/kg) to maintain serum IgG at >500 mg/dl along with daily co-trimoxazole. At last follow up, his pulmonary and cutaneous lesions have resolved completely, he has gained weight and has not developed any new infection.

**DISCUSSION**

Common variable immunodeficiency is the most common symptomatic primary immunodeficiency disorder. It is characterized by primary hypogammaglobulinemia, though associated T-cell defects have also been described in up to 40% of patients. The disorder may occur at any age, but in most patients the onset is in the second or third decade. Most of the patients present with recurrent sinopulmonary infections. *H. influenzae, Moraxella catarrhalis* and *Streptococcus pneumoniae* are the commonest pathogens. Gut infection due to *Giardia lamblia* is common. Rarely, patients with CVID can get infected with mycobacteria, *Pneumocystis jerovici* and various fungi. Though viral infections are less frequent, herpes zoster and herpes simplex virus infection have been reported in a small number of patients.

In addition to infectious manifestation, there is also an increased incidence of malignancy, granulomatous and autoimmune diseases. Five to 40% of patients with agammaglobulinemia develop joint manifestation. The most commonly observed types of arthritis in these disorders are benign, aseptic, characteristic non-erosive polyarthritis and infective arthritis caused by *Mycoplasmas* or *Ureaplasmas*. In addition, patients with CVID show an increased prevalence of juvenile rheumatoid arthritis, systemic lupus erythematosus and Sjogren's syndrome.

Currently, the mainstay of treatment involves immunoglobulin replacement, early appropriate antibacterial therapy and management of complications. The optimal dose of IVlg is not established. A dose of 200-400 mg/kg given every 2-4 weeks to maintain the trough IgG levels above 5 g/L reduces the recurrence rate of infection. IVlg requirements need to be individualized as baseline IgG and rates of catabolism of IgG in patients vary widely.

Nocardiosis is an opportunistic infection seen in patients with malignancies, pulmonary diseases, solid organ transplants, connective tissue disease, long term corticosteroid therapy and acquired immunodeficiency syndrome (AIDS). *N. asteroides* is the predominant human pathogen, the other pathogenic species being *N. brasiliensis*, *N. otitidis caviarum* and *N. transvalensis*. The virulence appears to be associated with resistance to intracellular killing and ability to inhibit phagosome-lysosome fusion in macrophages. Nocardia are slow growing organisms and though colonies in pure culture can grow after 48 hours, mixed culture from clinical material may obscure nocardial colonies and delay diagnosis.

Clinical spectrum of nocardiosis includes primary pulmonary or cutaneous infection which may disseminate to involve the CNS, eyes (especially the retina), kidneys, joints, bones and the heart. Trimethoprim (TMP) (15 mg/kg/d) and sulphamethoxazole (SMZ) (75 mg/kg/d) is most frequently used to treat nocardiosis. All immunosuppressed patients should receive a minimum of 12 months therapy. However, there are reports of resistance to TMP-SMZ. Aminoglycosides and carbapenems are useful in such cases.

Our patient presented with arthritis, subcutaneous abscesses and pleural effusion. The past history of recurrent pneumonia, chronic diarrhea and herpes infection suggested immunosuppressed status. Serum immunoglobulin levels (IgG, IgM and IgA) were markedly decreased. Pleural fluid culture grew *N. asteroides* after 1 week. In addition to the humoral immune deficiency, steroid treatment in the past could have contributed to the nocardiosis.

In summary, we describe a patient with disseminated nocardiosis due to common variable immunodeficiency syndrome. Primary immunodeficiency disorders like CVID should be considered even in adult patients with recurrent infections after excluding other known causes of immunodeficiency. In patients with immunodeficiency, nocardiosis should be suspected when soft tissue swellings or abscesses develop in conjunction with acute, subacute or chronic pulmonary infection.

**REFERENCES**

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