IJMS
Vol 27, No. 3, September 2002

Case Report

Disseminated Nocardiosis in an Immunocompromised Child with Unknown Cause

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Abstract

Disseminated nocardiosis (DN), is an infrequent and severe infection due to Nocardia species and defined as infection in two or more discontinuous organs. Most infections occur in the immunocompromised host or in persons with underlying disease. DN occurs rarely in children. In this report, we describe an 11-year-old immunecompromised child with nocardiosis involving the lung, skin, brain and bone. No predisposing factor nor any underlying disease was found to explain his immune deficiency. Diagnosis of nocardial infection is often cumbersome, resulting at times in wrong initial clinical diagnosis such as cancer and other bacterial infections (e.g. tuberculosis). Therefore, it is important to consider nocardial infection in the differential diagnosis of children with combined brain and lung lesions.

Iran J Med Sci 2002; 27(3):147-150

Keywords • Disseminated nocardiosis • immunocompromised

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Introduction

Nocardia organisms are well-recognized etiologic agents of human illness. They are free living, gram-positive, soilborne, partially acid-fast aerobic actinomycetes[1] that were first described by Edmund Nocard in 1888[2] and named after him by Blanchard in 1896.[2]

It is estimated that 500-1000 new cases of Nocardiosis occur each year in the United States[3], but most experts consider this number an underestimate[2]. The incidence rate of Nocardiosis has increased in the UK[4] and USA in recent years.[2] This organism causes serious pulmonary or disseminated infections.[2] Disseminated disease, defined as infection in two or more discontinuous organs[3], has infrequently been reported.[5-13] Most infections occur in the immunocompromised host or in individuals with underlying systemic disease, though a significant minority may occur in persons who are otherwise apparently healthy.[3,14] We describe a child with nocardiosis involving the lung, skin, brain and bone who had been immunocompromised for unknown reason.

Case Report

An 11-year-old boy living in Tehran was admitted to our hospital with a history of occasional fever reaching 40 °C which was associated

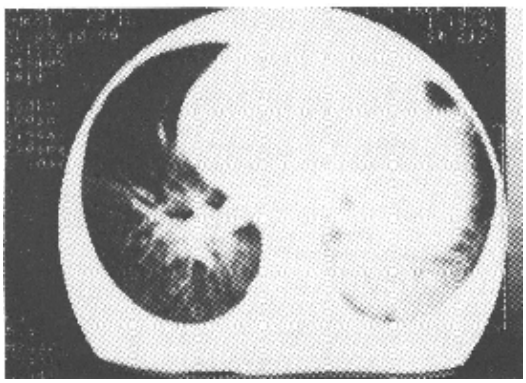

Figure 1: Chest CT scan of the patient showing a lesion in the left upper lobe of the lung

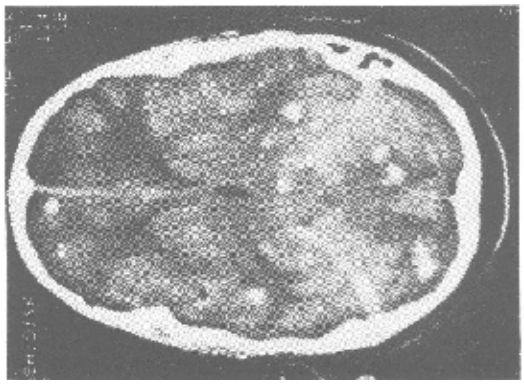

Figure 2: Brain CT scan of the patient revealing globular nodules in supra and infra tentorial area

with chills and malaise. He had pleuritic chest pain localized in his left upper chest. He had a nonproductive cough without dyspnea or cyanosis. Laboratory findings included: a leukocyte count of 21000/µl, a hemoglobin level of 11g/dl, a platelet count of 645000/µl, an ESR of 42 in the first hour and a normal urinanalysis. CT scan showed a lesion in the upper lobe of the left lung and anterior mediastinum (Fig 1). Needle biopsy revealed nonspecific inflammatory lesions and in the open biopsy, inflammatory changes with nonspecific interstitial fibrosis were noted. Cytologic evaluation of the specimen did not show any evidence of malignancy and direct test was negative for acid-fast bacilli. Sputum smear and culture were also negative. The patient was discharged on a regimen of amoxicillin. Six days later, he was again admitted with a fever of 39°C. Where upon treatment with cefazolin and gentamycin was initiated. On bronchoscopy, there was no evidence for tuberculosis. Although antibiotics were discontinued for suspicion of drug fever, however, an intermittent fever persisted for another month. Hematologic malignancies were ruled out on the basis of the normal tests and peripheral blood smear. By the time the patient started experiencing severe headaches. Brain CT scan revealed globular nodules with distinct margins both in supra and infra tentorial spaces, which was thought to be suggestive of tuberculoma (Fig 2). Phenytoin 100mg (IV BID) and dexamethasone 8mg (IV TDS) was administered for five days and then replaced by oral corticoesteroids. Bronchoscopy and biopsy were again negative for malignancy and tuberculosis. One positive and two negative PCRs were reported for tuberculosis. Triple treatment with isoniazide, pyrazinamide and rifampin was initiated but no improvement was seen after a month. Immunologic assessment showed an intact humoral and complement systems but a deficient cellular immunity (CD_4=24.6% with a normal range of 27-57%, CD_8=25.9% with a normal range of 14-34%). No predisposing disease that could cause a decrease in CD_4 (T helper suppression) was found. ANA, ANCA, HBsAg, Anti-HIV (two times) and a anti-HCV were all negative. Entering the sixth month, the patient's headaches worsened and two skin erythematous skin lesions 1cm in diameter appeared on the left arm and the right thigh. These lesions and also the site of the needle biopsy of the lung became fistulized, secreting a small amount of highly viscous, colorless and odorless fluid. *Nocardia* was detected in the direct test of specimen from skin and the culture of specimen was positive for the organism. A biopsy from the left frontal lobe of the brain revealed multiple foci of granulation tissue with acid-fast staining organisms. Culture was again positive for nocardia. Therefore antituberculosis therapy was discontinued and treatment with trimethoprim-sulfamethoxazole (10 mg/kg/day IV) was initiated. Within two weeks, patient's skin lesions resolved and fever subsided; pulmonary condition improved and headache was alleviated. The patient remained symptom free until the present time (six months after the treatment) without evidence of recurrent nocardiosis.

Discussion

Nocardial infections are usually opportunistic, occuring in patients with predisposing conditions such as lymphoreticular neoplasms, chronic pulmonary disorders, diabetes, immunosuppressive therapy, suppressed T-cell immunity, renal and cardiac transplantation, dysgammaglobulinemia, chronic granulomatous involvement, trauma, mycobacterial infections and alcoholism.[2, 5, 14-19]

Pulmonary disease can be acute, subacute or

Table 1: Cases of nocardial infection in children under 14 years of age reported since 1980

Case	Age(y)/Sex	Source of diagnostic Material	Treatment (duration)
1	6/M	Liver/node biopsy	Trisulfapirimidines (8 mo): relapse, then TMP-SMX
2	3/F	Abscess (face)	TMP-SMX(3 mo)
3	5/M	Cervicofacial	TMP-SMX
4	7/M	Lympocutaneous	Sulfisoxazole
5	5/M	Cervicofacial	Methicillin=penicillin G, then dicloxacillin
6	2/M	Scalp abscess, osteomyelitis of skull	Sulfisoxazole [craniotomy, (I&D)]
7	5/M	Abscess of axilla	Sulfadiazine
8	3/M	Lymphocutaneous	Trisulfapyrimidines
9	1/F	Abscess of arm	Sulfisoxazole
10	2/M	Submandibular abscess	(I&D), methicillin, then dicloxacillin

Outcome: *All cases recovered*

chronic.[20] A wide variety of radiographic features may be seen. [5,20] The skin lesions manifest as subcutaneous abscesses, cellulitis, mycetoma or infected ulcerations.[20] CNS involvement occurs, usually with abscess formation in 23%.[21] Meningitis is rare and is often secondary to the rupture of an abscess.[4] Disseminated nocardiosis has a mortality rate as high as 85-100%. Increased awareness of it as an opportunistic infection in susceptible patients may lead to earlier diagnosis and lower mortality.[4] The diagnosis of nocardiosis requires isolation of the organism from the patient.[22] There is no serological test which could routinely be used to identify patients with nocardial infections[22] and the radiological findings and blood smear are so nonspecific that many of the cases[23], such as ours could end in a wrong diagnosis.

The mean age of patients affected with nocardiosis is usually over 40 years.[5, 15] Although rare in children under 11 years of age[15], however, few cases in neonates have been reported.[23] The clinical presentation and outcome of ten immunocompromized children under 14 years of age with disseminated nocardiosis and no known underlying disease reported since 1980, are presented in Table 1.

Ever since 1944[25] , sulfonamides have been the mainstay of therapy for nocardiosis. Trimethoprim-sulfamethoxazole (TMP-SMX) is now generally regarded as therapy of choice.[2, 7, 15, 16, 26] The required duration of therapy is unknown, but reports recommend 6 weeks in localized forms of nocardiosis and 6 months to 1 year in disseminated nocardiosis.[4, 15, 16]

Nocardiosis may be difficult to diagnose resulting often in wrong initial diagnosis; cancer and infection with mycobacteria (as in this case), or *pnuemocystis carinii* are the most frequent alternative diagnoses.[15, 20, 23, 27]

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