In the name of God

Shiraz E-Medical Journal
Vol. 6, No. 1 & 2, January and April 2005

http://semj.sums.ac.ir/vol6/jan2005/nocardiosis.htm

Nocardiosis, a Case Report.

Kambiz Aghasadeghi

Clinical Fellow, Section of Pulmonology, Department of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran.

Correspondence: Dr. Aghasadeghi, Department of Medicine, Nemazee Hospital, Shiraz - Iran. Telephone: +98(711) 626-1089, E mail: medicine@sums.ac.ir

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Case Report:

A 45 y/o man, a known case of chronic lymphocytic leukemia from 2 years ago, Presented with chief complaint of productive cough and fever from 2 months ago. The patient is a known case of chronic lymphocytic leukemia, followed by hematologist and received prednisolon 5mg, po, tid, and with this medication was in remission. He was relatively well up to about 2 months ago, when developed low grade fever associated with productive cough. So he referred to a general physician and received some medication without any improvement. During this period of time he developed anorexia and weight loss about 4-5 kg and his condition become worsen with generalized weakness and malaise. So he referred to a pulmonologist and a chest x-ray was recommended by him which showed infiltrations in both upper lobe with cavity formation (Fig 1). So the patient was admitted in pulmonary ward of Faghihi hospital for better evaluation. In physical examination on admission, the patient was febrile with temperature of 38-38.5ºc, he had some trash on buccal mucosa and throat but chest physical examination was completely normal. So due to findings in chest x-ray with impression of bacterial pneumonia he received some antibiotics such as ceftazidim and Amikacin.

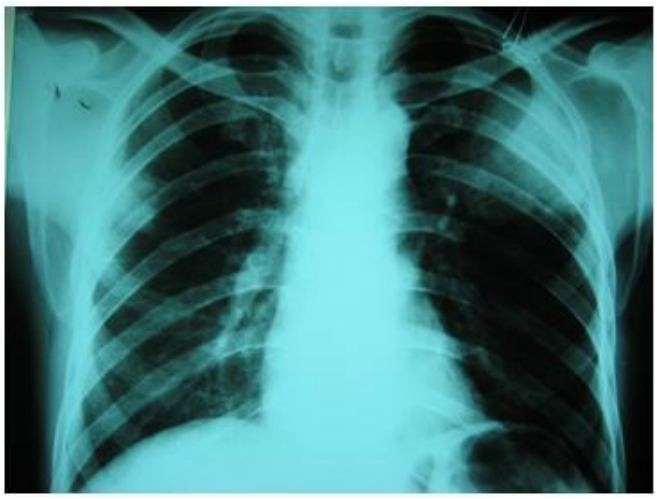

Fig 1

In hospital course, few days after starting of antibiotics, the patient become afebrile but he hadn't any improvement in respiratory symptoms. In laboratory work ups, sputum stain showed Gram-positive, beaded, branching filaments which were acid fast positive, So a fiberoptic bronchoscopy was performed for him which revealed a whitish tenacious secretions which came from right and left upper lobe bronchus. A bronchial washing was done which was negative for Acid-fast bacillus and malignancy. Finally with impression of pulmonary nocardiasis his medication was change to Co-trimoxazole, 2 adult tab, po, Q12h and previous antibiotics became discontineued. With starting of this antibiotic, he showed a significant improvement in his respiratory symptoms and general condition. So the patient was discharged from hospital and received Co-trimoxazole with the same dose as out-patient therapy. In OPD follow-up, after about 8 weeks of antibiotic therapy his complaints were completely resolved and he had about 4kg weight gain. The upper lobe infiltrations were gradually disappeared. (Fig 2).

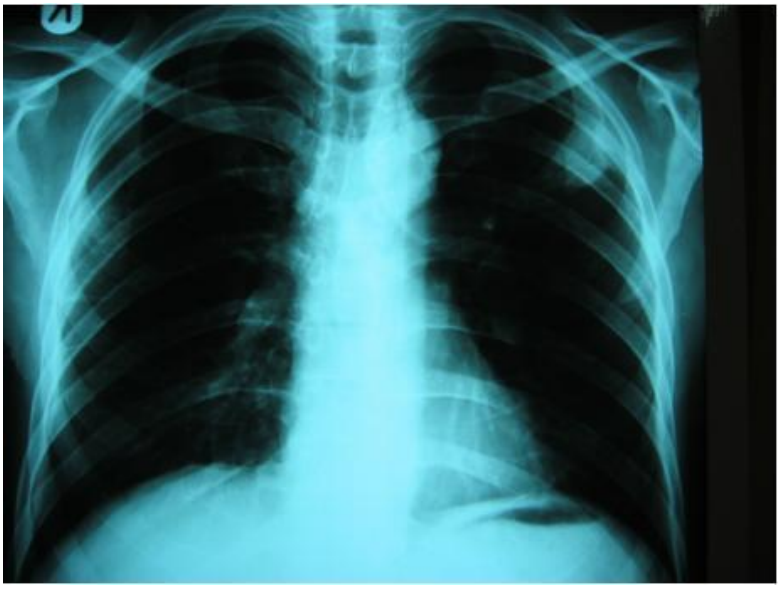

Fig 2

Therefore according to the findings in history, physical examination and paraclinics, associated with hospital and OPD course, our final diagnosis for him is pulmonary nocardiosis.
Systemic lupus erythematosus is a chronic, debilitating autoimmune disorder with unknown etiology that is characterized by the involvement of multiple organ systems[1]. Some systems that are more commonly involved include the central and peripheral nervous systems, lungs, heart, skin, serous membranes, hematological system, and the kidneys[1]. Other systems were reported to be involved too, but the prevalence of their involvement was too much lower. The disorder occurs more commonly in women especially in the childbearing ages[2].

Nocardiosis:

Pulmonary nocardiosis is a subacute or chronic pneumonia caused by aerobic actinomycetes of the genus nocardia. In humans, nocardia asteroids complex is the predominant pathogen, but there are several other species, including: No brasiliensis and N. Otitidiscaviarum. Pulmonary infection is usually produced by N. asteroids, whereas N. brasiliensis causes cutaneous and subcutaneous abscesses(1). Members of the N.asteroids complex are responsible for about 80% of noncutaneous invasive disease and for most systemic and CNS disease(2). Nocardiosis can be

distinguished from actinomycosis by a lesser proclivity for sinus tract formation and a greater tendency for hematogenous dissemination specially to the brain[3].

Nocardia species are common natural inhabitants of the soil through out the world. Pulmonary nocondiosis is usually acquired by direct inhalation of nocardia species form contaminated soil, and person-to person transmission is rare[4].

N. asteroids may be a saprophyte in the skin and in the upper respiratory tract. Respiratory colonization can occur, and in a compromised host it can progress to tissue invasion and dissemination[5]. Nocardiosis typically develops in immunocompromised persons, such those suffering from a lymphoreticular malignancy, cushing's disease, those with acquired immuno deficiency syndrom, those with transplanted organs, and those receiving high-dose corticosteroids[6]. Suppression of cellular immunity appears to play a key role in the establishment of nocardia infection[7].

Bronchopulmonary or disseminated nocardiosis can occure in various rheumatologic disease, including SLE, temporal arteritis, polyarthritis nodosa, intermittent hydarthrosis, vasculitis or uveitis[8]. Persons with pulmonary alveolar proteinosis are also at increased risk[3]. The disease usually occurs in adults, and males are affected twice as often as females[9]. The typical lesions of nocardiosis are abscesses extensively infiltrated with neutrophils. There is usually extensive necrosis, granulation tissue often surrounds the lesions, but extensive fibrosis or encapsulation is rare.

Clinical Manifestations:

The clinical presentation of pulmonary nocardiosis is variable and nonspecific with a chronic course[7]. Patients often complain of low-grade fever, fatigue, malaise, anorexia, weight loss, productive cough, and pleuritic chest pain for weeks before seeking medical attention[3]. Cough is prominent and is often productive of small amounts of thick, purulent sputum, which is not malodorous[9]. Physical examination is nonspecific, unless sites of dissemination are obvious. Disseminated disease occurs in one-half of cases of pulmonary concardiosis. The central nervous system is the most common location of disseminated disease and occurs in one-fourth of cases of pulmonary nocardiosis, typically as supratentorial brain abscesses. Other common locations are the skin and subcutaneous tissue, kidneys, bone, and muscle[10]. On chest radiographs, early nocardiosis is evident as localized bronchopneumonia. As the lesion progresses, complete lobar consolidation and eventual cavitation evolve. Empyema is present in one-third of cases. Other radiographic variants include solitary or multiple nodules or abscesses, miliary infiltrate, subpleural plaques and pleural effusion[3].

Diagnosis:

Examination of sputum after gram and modified acid-fast stains is the first step when pulmonary nocardiosis is suspected. Sputum smears are often negative. Sputum cultures are positive more often, but growth may not be apparent for 3 to 21 days. If nocardia is suspected. Cultures should be kept for at least 1 month before the possibility is excluded[3]. Fungal culture media often contain antibiotics that inhibit nocardia and the sputum digestive procedures used in the isolation of mycobacteria render nocardia nonviable[11]. If sputum examinations do not yield the diagnosis in a suspected case and the diagnosis cannot be made easily from lesions elsewhere in the body, more invasive diagnostic procedures should be performed. Bronchoscopy, needle aspiration, and open lung biopsy are all useful[9].

Nocardia are aerobic gram-positive bacilli that appear as beaded, branching filaments[2]. Most nocardia in clinical specimens are acid-fast if a weak acid is used for depolarization as with the modified kinyoun, ziehl-Neelsen, and fite-foraco methods[9]. Demonstration of the gram-positive and acid-fast branching filaments, with or without their bacillar or coccal form

in the clinical material from a patient with pulmonary lesion, should be sufficient for the diagnosis and institution of specific therapy. Nocardiosis should be borne in mind especially in suspected cases of tuberculosis not responding to anti-tubercular therapy and showing no tubercle bacilli either in the direct smears or cultures[12].

Treatment:

Sulfonamides are the antimicrobials of choice[9]. 6 to 8 grams of sulfisoxazole or sulfadiezine should be given daily in 4 to 6 divided doses. In difficult cases, sulfonamide levels should be measured and dosages should be adjusted to keep serum levels between 100 and 150 mg/ml. Many patients have been treated with the combination of sulfamethoxazole and trimethoprim, but it is unclear whether the combinations is superior to the use of sulfonamides alone. If the combination is selected, 5 to 20 mg/kg per day of trimethoprime and 25 to 100mg/kg per day of sulfamethoxazole should be given in 2 to 3 divided doses[9]. After the disease is brought under control, doses can be reduced to approximately 4 gram per day of sulfonamides alone or to 5mg/kg per day of trimethoprim and 25mg/kg per day of sulfomethoxazole for the remainder of therapy.

In the case of sulfonamide allergy or a sulfanamide-resistant organism, minocycline, amikacin, cefotaxime, ceftriaxone and imipenem might be useful but choices should always be guided by results of in vitro susceptibility testing. Minocycline (100mg to 200mg twice a day) is very effective in the treatment of pulmonary nocardiosis in the severely immuno compromised patient and appears to be the most effective orally administered alternative to sulfonamides[13]. Amikacin (15mg/kg per day in single or divided doses) appears to be the must reliable parentral drug[9].

Therapy must be prolonged to prevent relapses. The duration of treatment for nocardiosis depends on disease site. For pulmonary involvement, therapy is usually continued for 6 to 12 months or for 2 to 3 months after disease resolution[14].

Mortality was mostly related to the presence of disseminated or pulmonary nocardiosis and/or the progression of underlying conditions such as pulmonary disease or immunosuppression. A mortality ranging from 3-44% has been reported and the outcome of the infection has been related with some prognostic factors such as corticosteroid therapy, immunosupplession, disseminated disease and nocardia species[15].

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