# Pleuropulmonary and soft tissue *Nocardia cyriacigeorgici* infection in a patient with Behcet's disease

*Ugur Arslan,* MD, *Inci Tuncer,* PhD, *Elif B. Uysal,* MD, *Ramazan Inci,* MD.

## ABSTRACT

Infections with *Nocardia* species are generally seen in immunocompromised subjects. In this report, we present a case of pleuropulmonary and skin *Nocardia cyriacigeorgici* infection in a male patient with Behcet's disease who used corticosteroids and immunosupressives for a long period of time. He died before the diagnosis of *Nocardia* infection was made.

*Saudi Med J 2007; Vol. 28 (9): 1435-1437*

*From the Department of Microbiology, (Arslan, Tuncer, Uysal), Selcuk University, Meram School of Medicine, Konya, Turkey, and the Department of Microbiology, (Inci), Ege University School of Medicine, Izmir, Turkey.*

*Received 13th September 2006. Accepted 20th December 2006.*

*Address correspondence and reprint request to: Dr. Ugur Arslan, Department of Clinical Microbiology, Selcuk University, Meram Faculty of Medicine, Konya 42080, Turkey. Tel. +90 (33) 22237260. Fax. +90 (332) 2236184. E-mail: arslan_ugur40@yahoo.com*

Behcet's disease is an inflammatory disease of unknown cause, characterized by recurrent oral aphthous and genital ulcers, uveitis, and skin lesions. These symptoms might necessitate the use of high dose of corticosteroids and immunosupressive agents.[1] Pathogenic species of *Nocardia* are commonly found in soil worldwide, but infection in humans and animals is rare, complicating both immunodepressive states and previous diseases. Nocardial infection is a localized, or deep granulomatous, or pus-forming infection. It is an opportunistic disease, affecting immunodepressed subjects, or more rarely, a true nosocomial infection. Its mortality ranges from 30-56%. Secondary cutaneous nocardiosis results from dissemination via the bloodstream from the lungs. It is primarily seen in immunosuppressed people (10-15% of cases), where multiple subcutaneous abscesses in the skin are described. They can be fistulous. Disseminated nocardiosis is characterized by a pulmonary contamination, with propagation via the lymphatic system, or the bloodstream to other tissues such as the central nervous system (50%), skin and subcutaneous tissues (in 10%), pleura and thoracic wall (in 10%), lymph nodes from the eye, liver, kidney, and bones (3% each).[2] We present pleuropulmonary and skin *Nocardia cyriacigeorgici* infection in a patient with Behcet's disease who used corticosteroids and immunosuppressives for a long time, and died few days before the diagnosis of *Nocardia* infection was made. In order to prevent delay in diagnosis we want to impress the importance of *Nocardia* infections in immunosuppressive patients.

**Case Report.** A 25-year-old male, presented with a history of cough with sputum, and thoracic pain, for 2 months duration. He was admitted to our hospital with the diagnosis of pneumonia. On physical examination, the axillary temperature was 37.5°C, with blood pressure of 160/100 mm Hg. He had a cushingoid appearance. The lung auscultation revealed sibilant rhonchus on the right, and rale on the left inferior. The rest of the physical examination was normal. Laboratory tests results showed sedimentation rate of 134 mm/hr, white blood cells 22.300/mm$^3$, glucose 205 gr/dl, urea 95 mg/dl, creatinine 5.4 mg/dl, uric acid 4.5 mg/dl, lactate dehydrogenase 1075 U/l, total protein 5.04 gr/dl, albumin 2.01 gr/dl, and C reactive protein 399 mg/l. On microbiological examination of sputum, the Gram and Ziehl Neelsen stained smears, or film results were negative. He was on prednisone for 2 years for his Behcet's disease. Treatment started with 16 mg/day methylprednisolone, azathioprine 50 mg x3/day, and cyclosporin 100 mg x3/day. On the 10th day of cyclosporin therapy, it became necessary to carry out hemodialysis due to acute renal failure. Sputum culture taken during this time grew *Candida*, and fluconazole 200 x 2 mg/day was given. After 5 days of treatment, the patient was discharged on his own request. He went to other hospital, and was discharged after 7 sessions of hemodialysis. He was again admitted to our hospital after 45 days from the first admission, with symptoms of severe pneumonitis. The laboratory tests results showed white blood cells 24,200/mm$^3$, (78% polymorphonuclear leukocytes), hemoglobin 4 gr/dl, and sedimentation rate 127 mm/hr. He started treatment with meropenem 500 mg/day intravenous (iv) for 10 days, clarithromycin 500 mg/day iv for 10 days, vancomycin 1 gr/weekly, and amphotericin B 1 gr/iv for 5 days. After no response was received, he was

started on Cefoperazone 1 mg x2/day, and a pleural biopsy was carried out. Cultures from the biopsy material were carried out on 5% sheep blood agar and Eosin Methylene Blue agar, and incubated at 35ºC, aerobically. The results of these cultures were negative. After 5 days, an abscess of 10 x 7cm size, inferior to his left clavicula on the place of biopsy occurred. He died as the cause of pulmonary embolism, after 2 days. A sample taken from the abscess was cultured, and Gram stain was carried out. On examination of Gram stain, a Gram-positive branched, bacterial filaments were seen. On the 3rd day of culture, white, soft rough colonies were visible. On Gram stain from these colonies, Gram-positive filamentous bacilli were seen. The colonies were sent for bacterial identification with 16S rRNA gene sequence analyses, to a mycologist from our hospital. After which, the colonies were sent to a mycologist from France, for further identification. The bacteria was identified as *Nocardia cyriacigeorgici* (*N.cyriacigeorgici*). The bacteria, *N.cyriacigeorgici* was found susceptible for amoxicillin+clavulanic acid, imipenem, cefotaxime, cefepime, gentamicin, linezolid, amikacin, minocycline, tobramycin, trimethoprim+sulphamethoxa zole, and resistant to ampicillin, amoxicillin, piperacillin, piperacillin+tazobactam, ticarcillin, ticarcillin+clavulanic acid, ceftazidime, erythromycin, vancomycin, trimethoprim, ciprofloxacin, and rifampin, by the disk diffusion method. Posterior anterior thorax radiography, and axial CT image during his hospitalization at our hospital are shown (**Figures 1 & 2**).

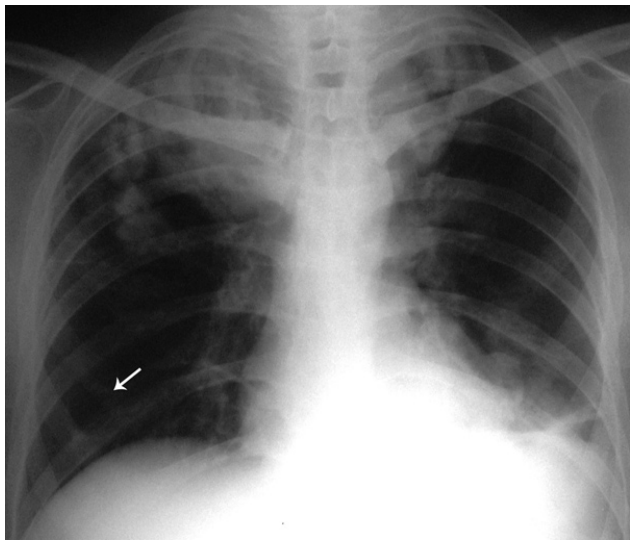

**Figure 1 -** Posteroanterior thorax radiography. The first radiography of the patient: non-homogenous consolidations, especially in the right, are seen bilaterally in the upper lobes of the lungs. A cavity (arrow) is seen in the right lower zone.

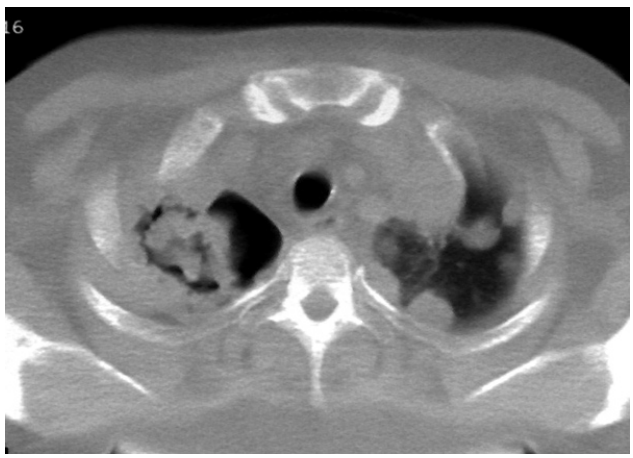

**Figure 2 -** Axial CT image; there is a big cavity of the apical segment of the right lung, and also loculated pleural effusions are shown in the apical part of the left lung.

**Discussion.** The *Nocardia spp.* are comprised of a group of Gram-positive, aerobic, and weakly acid-fast bacteria that form into branching filaments, likely to fragment into rods or coccoid elements. Nocardiosis is usually an opportunistic infection, and most commonly present as pulmonary disease. The majority of patients with clinically recognized disease have underlying debilitating factors. Arguably, the most common condition predisposing the patient to nocardiosis is an underlying chronic lung disease, often in association with long-term corticosteroid therapy. The majority of primary cases present as pulmonary disease, although traumatically induced local abscesses occur as well. Dissemination from the lungs may be manifested as bacteremia, empyema, brain abscess, pericarditis, synovitis, and soft tissue infection.[1,3,4] The clinical diagnosis of nocardiosis is difficult. The radiological signs are often nonspecific. The only formally, accepted criteria for diagnosis is the evidence of the presence of microorganisms in multiple repeated specimens, because of difficulty in visualizing nocardiae due to their low number.[1] As a species, *Nocardia asteoides (N.asteoides)* is distributed evenly throughout the United States, and *Nocardia farcinica* (*N.farcinica)* is also found, but less prevalent than *N.asteroides*. The distribution of other species (*Nocardia nova, Nocardia otitidiscaviarum*, and so forth) varies regionally.[4] In this report, we describe a case of soft tissue and pulmonary nocardiosis in a patient with Behcet's disease, who was using corticosteroids and immunosuppressives for a long period of time. The first case report of nocardiosis in patients with Behcet's disease was described by Kormaz et al.[3] They reported 2 cases of nocardiosis, and from the first patient they isolated *N.asteroides*, and from the second, *N.farcinica*. In the same year, Pamuk et al[5] and

Auzary et al[6] reported cases of nocardiosis in patients with Behcet's disease. Auzary et al[6] isolated the bacteria from subcutaneous fine-needle aspirate, and identified as *N.asteroides*. In 2001, Yassin et al[7] from Germany, described a new species that differs from previously described members of the genus by biochemical tests, and basing on phylogenetic and phenotypic evidence, the name *N.cyriacigeorgici sp. novel isolate* was proposed for this isolate. Only 2 cases of *N.cyriacigeorgici* cases have been reported to date. The first report of invasive human infection with *N.cyriacigeorgici* was reported by Fux et al[8] in 2003, and the second, by van Dam et al[9] in 2005. In our case, the bacteria isolated from the abscess was identified as *N.cyriacigeorgici*.

The diagnosis of nocardiosis can be difficult for several reasons, and this problem often leads to a delayed diagnosis. We believe that due to this delay, our patient had been lost. We conclude that in a patient with Behcet's disease, opportunistic infections should be considered, and a special diagnostic approach be started.

**Acknowledgments.** *We would like to thank Mr. P. Boiron, Universite Claude Bernard Laboratoire de Mycologie Fondamentale et Appliquee aux Biotechnologies Industrielles, Lyon, France, for identification of N.cyriacigeorgici, and Mr. Serdar Karakose, Radiology Deparment, Selcuk University Meram School of Medicine, Konya, Turkey, for his valuable assistance with the radiology images.*

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## Ethical Consent

All manuscripts reporting the results of experimental investigations involving human subjects should include a statement confirming that informed consent was obtained from each subject or subject's guardian, after receiving approval of the experimental protocol by a local human ethics committee, or institutional review board. When reporting experiments on animals, authors should indicate whether the institutional and national guide for the care and use of laboratory animals was followed.