Journal of the Turkish Academy of Dermatology
eISSN 1307-394X

Case Report

Disseminated Nocardiosis: A Case Report with Review of the Literature

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Published:
J Turk Acad Dermatol 2009; **3 (4)**: 93402c
This article is available from: http://www.jtad.org/2009/4/jtad93402c.pdf
Key Words: Nocardia, actinomycetes, immunosuppression suppurative disease, trimehoprim-sulphmethoxazole

Abstract

Observations: A 70 years- old farmer who presented with three months' history of fever with chills, productive sputum, pleuritic chest pain, exertional breathlessness, anorexia and three days history of altered sensorium was found to have signs of pleural effusion clinically on the right side. Aspiration revealed frank pus which was drained by an intercostal tube. Subsequently the patient developed multiple abscesses in the right costal area which were drained surgically. Gram staining of the purulent material revealed Gram positive and acid fast bacilli which had branching and fragmented morphology, suggestive of Nocardia. Thorax CT revealed a resolving consolidation with pleural effusion on the right side. Cranial CT with contrast revealed multiple ring enhancing lesions with vasogenic edema in the right fronto-parietal and left occipital area. CSF did not show any abnormality. A diagnosis of disseminated Nocardiosis was made. Patient was started a treatment with Trimethoprim-Sulphmethoxazole and is on regular follow up. The case is highlighted because of the rarity of the disease and the patient in question did not have an underlying immune compromise or any other systemic disease.

Introduction

Nocardiosis refers to the disease associated with members of the genus *Nocardia*. *Nocardiae* are saphrophytic aerobic actinomycetes that are common worldwide in soil and contribute to the decay of organic matter. Nine species have been associated with human disease (*N.asteroides, N.brasiliensis, N.otitidiscaviarum, N.farcinica, N.abscessus, N.nova, N.transvalensis, N.pseudobrasiliensis and N.africana*) [1]. *N.asteroides* is the species commonly associated with invasive disease. Nocardiosis is a systemic disease commonly occuring as an acute, subacute or chronic infectious disease in cutaneous, pulmonary and disseminated forms.It occurs at all ages, in all races with a male:female ratio of 3:1 (probabaly related to exposure difference with an underlying immune compromise in 60% cases). *N. asteroides* is commonly associated with invasive disease and *N. brasiliensis* with localised skin disease.They are branching, beaded filamentous Gram (+) , weakly acid fast bacteria causing suppurative necrosis and frequent abscess formation. Cell mediated immunity is important for control and the organisms survive inside of macrophages for long periods of time. Route of entry may be inoculation due to trauma (in cutaneous, lymphocutaneous and subacute form), inhalational exposure in pulmonary and brain disease and wounds after surgery. Knees, eyes, bones, kidneys and muscles are rarely infected. Conditions associated with increased risk are pulmonary alveolar protinosis, cirrhosis, renal failure, SLE, systemic vasculitis,

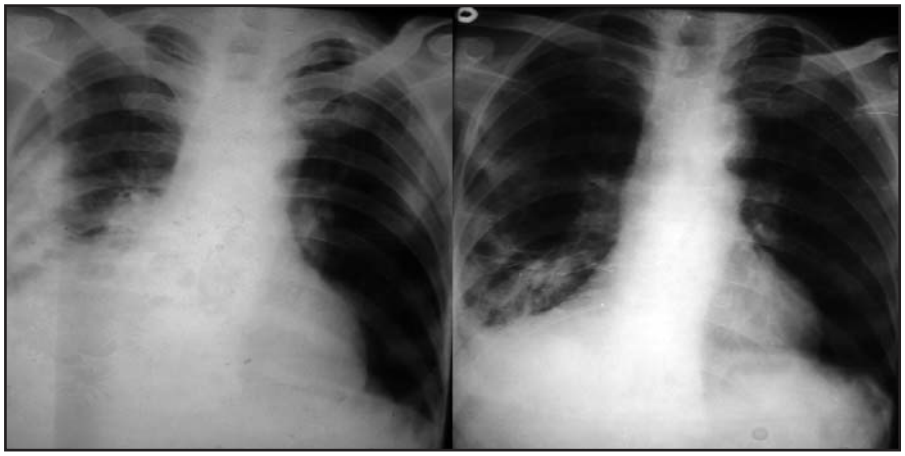

Figure 1. X-ray chest of the patient showing a right sided pleural effusion

ulcerative colitis, sarcoidosis, *Whipple*'s disease, hypogammaglobenemia, *Cushing*'s syndrome, lymphoreticular malignancies, bone marrow/stem cell/organ transplant patients, HIV with CD4 <50 and immunocompromised people on corticosteroid therapy. Prognosis is good and depends upon the stage of presentation, concomitant disorders and the immune status of the patient.

Case Report

A 70 years- old smoker male farmer presented with three months' history of intermittent fever with chills, right sided pleuritic chest pain and productive purulent sputum, one month history of exertional breathlessness and altered sensation with loss of appetite of three days duration. There was

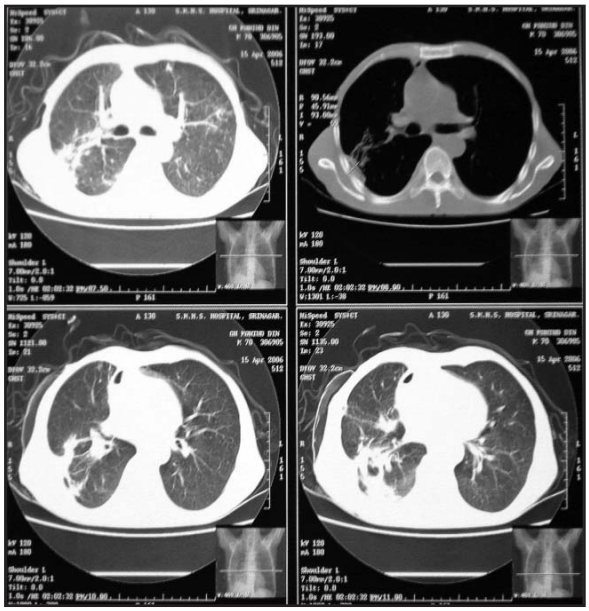

Figure 2. CT scan chest of the patient showing a right sided resolving consolidation with cavitation and pleural effusion

no history of haemoptysis, palpitations, paroxysmal nocturnal dyspnoea, orthopnoea, skin rash, joint pain, vomitting, convulsions, loss of conciousness, weakness of any part of the body or alteration in bowel motility. No significant past history of diabetes, tuberculosis, jaundice, blood transfusion, peneterating injury, drug intake (steroids) or high risk behaviour was seen. Personal history was non-contributory. Examination revealed a febrile, emaciated pale person of lean and thin build without lymphadenopathy, clubbing, cyanosis or icterus. BP was 120/70 mm Hg, pulse 100/mt. regular, temperature 100º F and a respiratory rate of 24/mt. Chest exam revealed a diffuse bulge in the right infra-scapular area posteriorly, decreased movements of the chest on the right side, decreased tactile vocal fremitus in the right infra-mammary and infra-scapular area, a stony dull percussion note in the right infra-scapular area and loss of breath sounds in the right infra-scapular and infra-mammary area. No adventitious sounds were heard. Cardiovascular and abdominal systems were normal. CNS examination revealed a confused, disoriented person with no meningeal signs, cranial nerve palsies or motor weakness. Fundus was normal. Investigations revealed :- Hb- 7.7g, TLC 6800/cmm, DLC (P-66%, L- 28%), ESR- 50 mm / hour, Platelets- 1.5 lac / cmm, PBF- hypochromic microcytic and Reticulocyte count- 1.5%. Serum iron- 20 mg%. Blood chemistry (Blood sugar, KFT, Electrolytes, LFT, ALP and ALT), Urine exam and ECG were normal. Sputum for AFB (3) was negative. Chest X-ray PA view (**Figure 1**) showed right sided pleural effusion. Analysis of pleural fluid revealed a straw colour, pH- 7.1, TLC- 5000, DLC (P-70%, L- 30%), Protein- 3 gm/dl, Sugar- 30 mg/dl, ADA- 30 iu/l and negative for malignant cells. *Gram*'s and AFB staining did not reveal any organisms or AFB. Cultures of pleural fluid, blood, urine and sputum were sterile. PCR and Bactec from pleural fluid were negative for AFB. CT scan (**Figure 2**) of the chest showed a resolving consolidation with cavitation (in the right lower lobe) and pleural effusion.

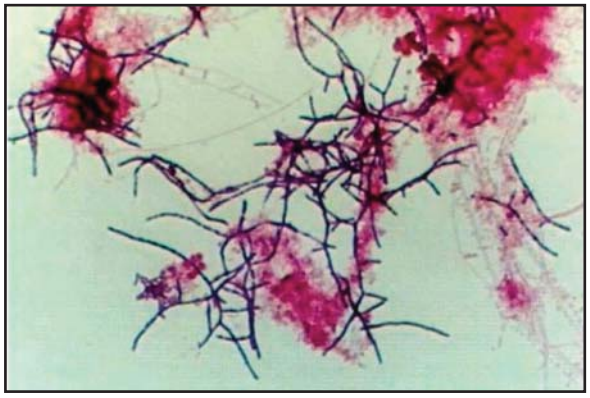

Figure 3. Photomicrograph of the isolate of *Nocardia asteroids* showing thin, slender, acid fast branching filamentous rods (Modified *Kinyoun* stain)

A thoracic drain was employed. Three days later multiple abscesses appeared in the right costal margin around the chest tube. These abscesses were drained surgically and pus was sent afresh for Gram's staining and culture. Gram's staining revealed Gram (+) branching, fragmented acid fast bacilli suggestive of *Nocardia* (**Figure 3**). Fresh pus culture done reported growth of *Nocardia asteroides* species after 2 weeks of aerobic incubation in *Sabouraud*'s dextrose agar at 37°C and the modified *Kinyoun* staining of cultured *Nocardia* showed acid fast branching filamentous rods later identified as *Nocardia asteroides*. In view of these findings the patient was vigourously investigated for immune compromising conditions. An Elisa for HIV infection was negative. Immunoglobulin assay and CD4 count were normal. CSF examination including culture and assay for malignant cells was

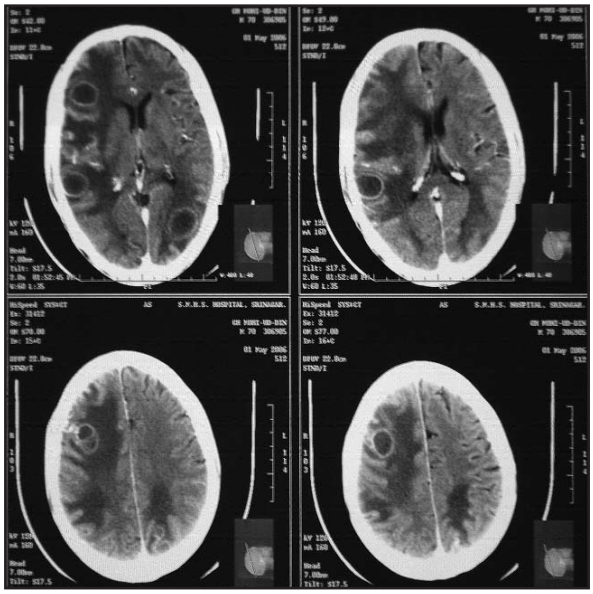

Figure 4. CT Scan brain of the patient with contrast revealed multiple ring enhancing lesions in the right fronto-parietal and left occipital lobes with compression of the lateral ventricle

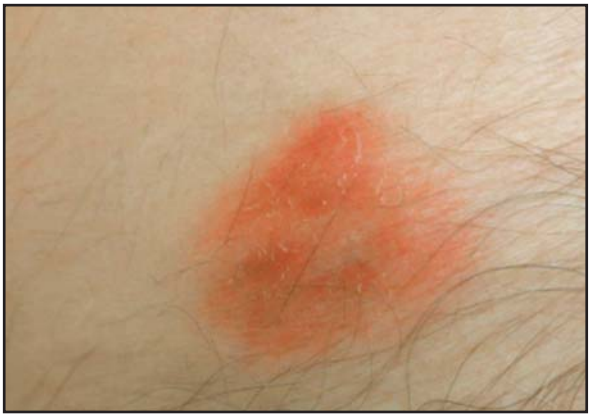

Figure 5. Reveals the skin lesions on the lateral wall of the chest in the patient.

negative. CT scan of the brain with contrast revealed multiple ring enhancing lesions in the right fronto-parietal and left occipital lobes with compression of the lateral ventricle (**Figure 4**). In view of the examination and investigations a diagnosis of "Disseminated Nocardiosis" was made (**Figure 5**) and the most significant aspect of this problem was that the patient did not have an underlying immune compromise.The patient was accordingly managed with trimethoprim-sulphmethoxazole and is doing well on regular follow up.

Discussion

Disseminated nocardiosis is defined as lesions containing nocardia found at more than one body location [**1**]. Nocardia is an opportunistic pathogen and most of all nocardia infections occur in persons with some degree of immunosuppression. The most common predisposing factors (conditions) leading to nocardia infection is organ transplantation and diabetes [**2, 3, 4, 5, 6**]. Disseminated nocardiosis can occur in various rheumatologic diseases including SLE, temporal arteritis, polyarteritis nodosa, intermittent hydarthrosis, vasculitis, uveitis and pulmonary alveolar protinosis [**7, 8, 9**]. A high number of cases are reported in individuals with acquired immune deficiency syndrome (AIDS), and malignancy particularly hematologic malignancy [**2, 10**]. *Nocardia* have been isolated on culture of pus from a thyroid abscess in a patient evaluated for pyrexia of unknown origin who was ultimately found to have disseminated nocardiosis of the brain, lungs and abdomen [**11**]. Disseminated nocardiosis can occur from direct inoculation due to trauma or erosion of a primary focus into a blood vessel. The disseminated nocardia have the potential

to invade any body organ system commom being the lungs, central nervous system, eyes, kidneys, skin, subcutaneous tissue and bone. Disseminated nocardia tend to behave as pyogenic bacteria and the result is typically a suppurative abscess at the embolic end point. The abscess tends to progress or enlarge into the surrounding tissue by filamentous extension and self limitation of the disease is rare [**2**]. As described in literature almost every organ system can be infected [**12**].

The lungs are the most frequent primary site of systemic nocardiosis (60-80% of cases) with a variety of clinical presentations including cough, dyspnoea, fever, night sweats, weight loss and pleuritic chest pain. Roentgenographic studies are nonspecific with multifocal airspace opacities, lobar consolidation, nodules with or without cavitation, reticulonodular interstitial lung disease, pleural effusion or empyema. Granulomas mimicking tuberculosis though rare have also been reported. The central nervous system has been shown to be involved in 20-44% of patients with disseminated nocardiosis. Abscesses occur in any region of the brain similar to pulmonary nocardiosis with non specific clinical presentation including headaches, seizures, focal neurological deficits or meningismus [**2, 6**]. Typical radiological features in a cerebral abscess include a hyperintense lesion on diffuse weighted imaging and ring enhancing lesions encircling a central necrotic focus. Occasionally multiple concentric rings are seen that vary with intensity.13 Rarely nocardia may invade native heart valves but invasion of prosthetic heart valves to cause nocardia endocarditis have been documented in literature with high mortality. Valve replacement is required in these circumstances to prevent mortality [**14**].

Due to the relative rarity of disseminated nocardiosis it is infrequently included in differential diagnosis particularly in patients with no evidence of immunosuppression, comorbid illness or malignancy as has been highlighted by the case under discussion where none of these factors was present. Nevertheless a high index of suspicion should be maintained where the patient symptomatolgy and chronicity of the disease suggest or point towards an alternative diagnosis of nocardiosis. Diagnosis of the disease requires a full body imaging apart from the usual diagnostic modalities which may include evaluation to rule out underlying immunosuppression, malignancies, collagen vascular diseases, diabetes, interstitial lung disease, cirrhosis of the liver, renal disease, *Whipple*'s disease, ulcerative colitis, AIDS and lymphoreticular malignancies, cultures of blood, urine, body fluids including pus, pleural fluid, cerebrospinal fluid and bone marrow. CD4 and CD8 counts are imperative in diagnosis. Recent molecular techniques like PCR restriction enzyme analysis and 16S rRNA have revolutionized the identification of nocardia [**15**].

Most cases of disseminated nocardiosis have fatal outcome. Therapy is initiated with parenteral treatment with Trimethoprim/Sulphmethoxazole (TMP/SMZ) and continued with oral therapy using one double strength tablet twice a day in adults [**16, 17**]. In cases where allergy/resistance to TMP/SMZ is present the best alternative oral drug available is Minocycline [**18**] given in a dose of 100-200 mg twice daily. Amikacin, imipenem and ceftriaxone [**13**] are other alternative parenteral drugs used in patients who are resistant or allergic to TMP/SMZ. Treatment may be given from six months to one year depending upon the response of the patient as evidenced by clinical improvement and radiological clearing of the lesions. Surgical treatment of nocardiosis includes drainage of pus from the pleural cavity by aspiration or insertion of an intercostal tube. Successful surgical management of cerebral nocardiosis is problematic. Image directed sterotactic aspiration, craniotomy and total excision of the nocardial abscesses which are occasionally multiloculated is undertaken [**6**].

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