

Case Report

DISSEMINATED NOCARDIA OTITIDISCAVIARUM INFECTION IN AN IMMUNO COMPROMISED PATIENT

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ABSTRACT

Nocardiosis is a disease of protean manifestations and mimics other infectious diseases such as tuberculosis, fungal infection and malignancy. Immuno compromised state and impaired pulmonary defenses predispose to pulmonary nocardiosis particularly in patients with chronic obstructive pulmonary disease. Genus and species identification is necessary in the management and for epidemiological purpose. Identification of these organisms by conventional phenotypic assays is laborious, time consuming and needs expertise. We present a case of disseminated nocardiosis caused by *Nocardia otitidiscaviarum* in a patient with COPD, treated with long term, high dose corticosteroid therapy.

Keywords: *Nocardia Otitidiscaviarum*, Pulmonary/ Disseminated Nocardiosis, Immunocompromised

INTRODUCTION

Nocardiosis is a localized or disseminated, acute or chronic infection caused by aerobic soil inhabiting actinomycete of the *Nocardia* genus. Immunocompromised state and impaired pulmonary defenses predispose to pulmonary nocardiosis particularly in patients with chronic obstructive pulmonary disease (COPD) (Pelaez *et al.*, 2009). It is a disease of protean manifestations and mimics other infectious diseases such as tuberculosis, fungal infection and malignancy (Lerner, 1996). Genus and species identification is necessary in the management and for epidemiological purpose. Identification of these organisms by conventional phenotypic assays is laborious, time consuming and needs expertise. Here we present a case of pulmonary nocardiosis caused by *Nocardia otitidiscaviarum* in a patient with COPD, treated with long term, high dose corticosteroid therapy.

CASES

A 60 year old male farmer, known case of COPD for 20 years, treated with corticosteroids for 10 years, presented with breathlessness and cough with expectoration for 15 days. He had thick purulent sputum and grade IV dyspnoea, history of paroxysmal nocturnal dyspnoea and orthopnoea. He had high grade fever for 4 days associated with chills. He developed papules and vesicles all over the body below the neck four days before admission. He was a smoker and an alcoholic. Not a known diabetic /hypertensive. On examination, febrile (101° F), conscious, oriented, dehydrated, pulse 100/ mt, Bp 160/100 mm Hg, dyspnoeic and tachypnoeic, intercostal tenderness, stony dullness, diminished lung movement and breath sounds on left side, normal vesicular breath sound, crepitation and wheeze on right side were present. CVS- S1, S2 heard normally, no murmur. CNS- No focal deficit, Abdomen – soft, right hypochondrial and epigastric tenderness were present. The differential diagnosis on admission was COPD with left sided pyothorax / pleural effusion / tuberculosis and drug or insect bite allergy. He had hyponatremia 10 days after admission and improved. After 19 days, he developed left side shoulder pain. Final diagnosis was COPD with left sided pyothorax and cutaneous infection due to disseminated *Nocardia otitidiscaviarum*

Laboratory analysis yielded the following: Hb-11.2g/dl, Total count – 22,200cell/ mm³, platelet count- 4.2 lakhs/mm³, ESR- 30 mts- 7 mm, 1 hr- 15 mm, random blood sugar- 115 mg/dl, urea- 35mg/dl, creatinine- 1.1mg/dl, sodium- 137meq/L, potassium- 4.0meq/L, chloride- 96meq/L, bicarbonate- 22meq/L, total bilirubin- 22mg/dl, direct bilirubin- 0.5mg/dl, SGOT- 30U/L, SGPT- 32U/L, serum protein- 7.0g/dl,

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alkaline phosphatase- 71U/L, LDH- 121U/L, O₂ saturation – 99%, HIV, HBV and HCV- negative, widal test, malarial parasite and leptospira (IgM & IgG) - negative, RA factor- negative, ANA – negative, C reactive protein- 24 mg/L, X-ray chest- left homogenous opacity, ECG- sinus tachycardia, USG- Abdomen- mild cystitis, loculated L pleural effusion, Pleural tapping was done and 15 ml of pus was aspirated, gram stain showed gram negative thin filaments, AFB stain – thin, acid fast filaments were seen. Modified AFB also revealed the same, cell count- full of pus cells, malignant cells-negative, culture- dry, irregular, adherent, white colonies on nutrient and blood agar after 72 hours of aerobic incubation at 37°C which was identified as *Nocardia* spp and sensitive to amikacin, meropenem, linezolid, ciprofloxacin, trimethoprim- sulphamethoxazole, resistant to cefataxime, cefataxime + clavulanic acid. The growth was confirmed as *Nocardia otitidiscaviarum* by MALDI system. sputum AFB- negative, blood culture – No growth even after 30 days of aerobic incubation, sputum culture – No pathogen grown, pus swab from skin lesion revealed no organism on Gram stain and KOH preparation, No pathogen grown on culture, CT thorax- loculated abscess in left hemithorax, ? thick pus, CT brain-normal, sodium- 120meq/L 10 days after admission. X- ray shoulder showed C3- C4 disc narrowing, sclerosed supraspinatus at insertion suggestive of peri-arthritis.

Prior to admission, he was started on ATT, Piperacillin plus Tazobactam, anti pyretics, parenteral bronchodilator, and cortocosteroids with oxygen therapy for four days. After admission in IMCU, he was continued with same antibiotic for another 4days with other supportive therapy. Intercostal drainage was done on the second day of admission. After receiving microscopy report, ATT was discontinued and started on Inj. Amikacin and T. Levofloxacin and Tab. Trimethoprim- Suphamethaxazole. Fifth day he developed diarrhoea followed by vomiting, giddiness accompanied with sweating on seventh day. His urine output decreased. Serum sodium level was 120 meq/L. From 8th day Inj. Amikacin and T. Levoflox were withdrawn and T. Linezolid was added. Skin lesion treated with steroid and antibiotic cream. His condition improved and serum sodium level returned to normal. He was stable, fever and skin lesions subsided after 15 days, it was dry and eczema around healed lesions. Repeat x-ray chest revealed progressive improvement. Patient discharged with the advice to continue T. Linezolid 600 mg- and Tab. Trimethoprim- Suphamethaxazole - with bronchodilators. He was on follow up.

DISCUSSION

Nocardiosis predominantly affects lungs, central nervous system, and subcutaneous tissues and other organs like kidney, liver and heart may also be involved. Nocardiae were misclassified as fungi many years because they branch into filaments, sometimes incorrectly referred as hyphae (Lerner, 1996). The genus *Nocardia* consists of gram or acid fast variable, filaments. On aging, they fragment into pleomorphic rods or coccoid forms (Koneman *et al.*, 1997). They are slow growing, difficult to cultivate routinely. Colony morphology and filamentation depends on the composition of medium, temperature of incubation and other conditions of culture. Hence, the laboratory must be informed when nocardiosis is suspected (Lerner, 1996).

Multiple clinical specimens should be submitted for culture since smears and cultures are positive only in one third of cases. Gram staining is the highly sensitive method, presence of gram positive, branching filaments with many polymorphonuclear leukocytes is suggestive of nocardiosis. Use of modified acid fast stain with clinical samples is unreliable and should be used to confirm acid fastness of organism detected in Gram stain. Smear results should be used in conjunction with other laboratory tests and clinical history (Sorrell *et al.*, 2000). The diagnosis of nocardiosis is difficult based on the clinical, radiological, or histological findings. Isolation of *Nocardia* sp. remains the mainstay in the diagnosis (Boiron *et al.*, 1992). But it is often difficult to identify from sputum cultures. The organism can be highly elusive unless pus from discharging sinus or abscess is studied or invasive diagnostic techniques such as transbronchial biopsy, percutaneous aspiration, needle biopsy and open lung biopsy are performed. Currently no serological tests are available for quick identification. Because they lack sensitivity, specificity and high degree of cross reactions due to antigenic sharing (Brown- Elliott *et al.*, 2006).

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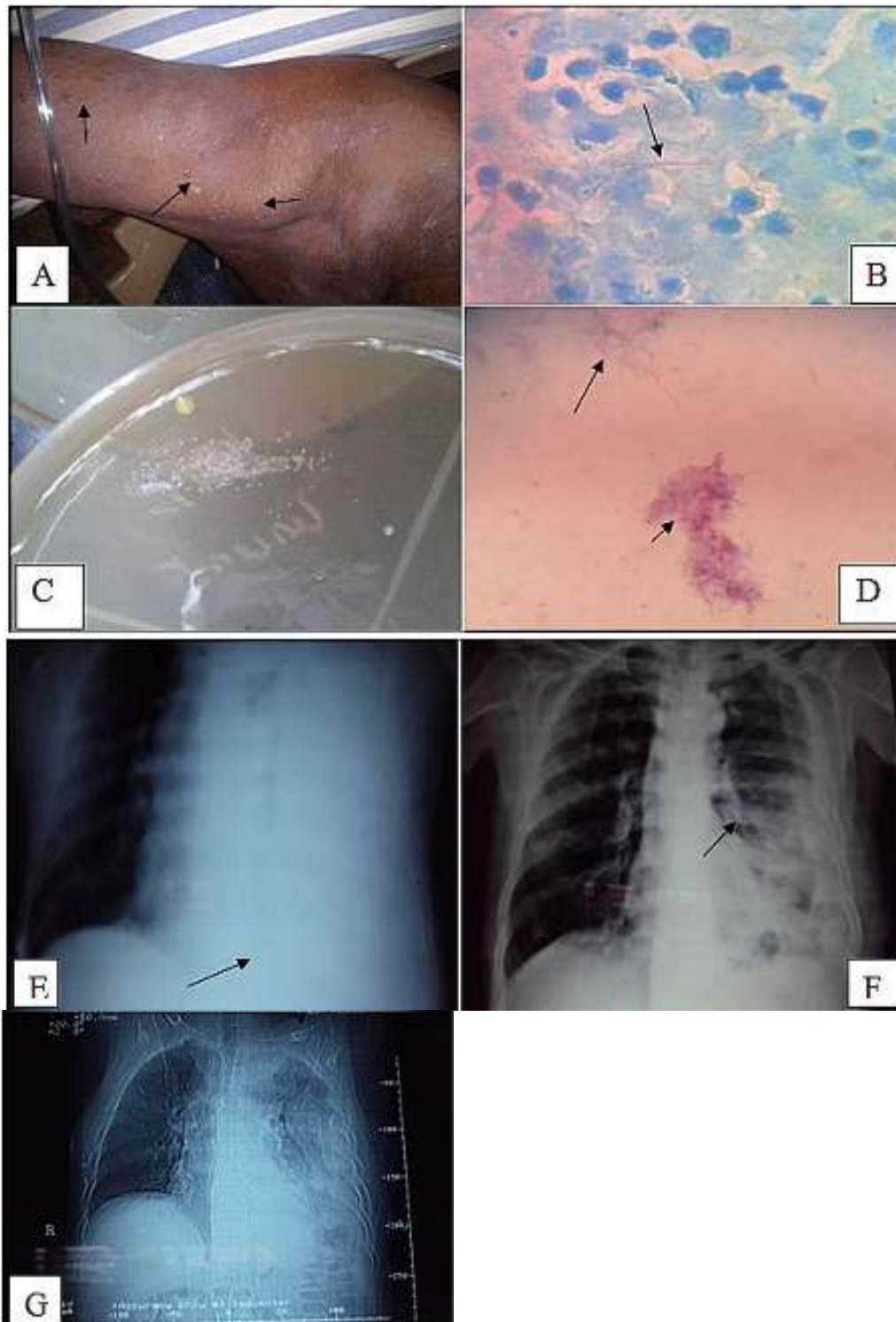


Figure 1: Disseminated *Nocardia Otitidiscavlarum* Infection

A. Papules, vesicles, pustules & healing skin lesions over Rt shoulder **B.** Pl.fluid smear-modified AFB –Acid fast filaments **C.** Colonies on Nutrient agar **D.** Gram stain- Pleural fluid culture – branching filaments **E.** X Ray Chest on 01/12/2013 – Pyothorax – Lt Side **F.** X Ray Chest - 28/12/2013- clearance after therapy **G.** CTscan Chest on 05/12/2013 – Pyothorax Lt Side

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N. otitidiscaviarum was first described by Snijders in 1924 from a Sumatran cavy or guinea pig with ear disease hence named so. Infections due to this species appear to be rare compared to other species because of reduced pathogenicity or low prevalence in soil (Duran *et al.*, 2001).

Pulmonary nocardiosis may present as subacute disease with symptoms such as cough, thick purulent sputum, fever, weight loss and malaise. Infiltrates are seen in x-ray with single or multiple nodules appear smooth and round (Brown- Elliott *et al.*, 2006). Primary cutaneous or subcutaneous nocardiosis can occur following traumatic introduction of soil organisms. This may provoke cellulitis, pustules, pyoderma, paronychia, or localized abscess mimicking infections due to other pyogenic bacteria, except that nocardial infection tends to be more indolent (Sorrell *et al.*, 2000). Secondary cutaneous infection due to disseminated disease also occurs (Grossman *et al.*, 2012). Smears and cultures from skin lesions are often negative unless skin biopsy is taken (Lerner, 1996). Routine blood cultures are not usually positive, unless biphasic blood culture systems incubated aerobically up to 6 weeks with frequent subculturing is done (Koneman *et al.*, 1997).

Suppression of cell mediated immune response, particularly macrophages and T cells, plays an important role in nocardiosis (Koneman *et al.*, 1997; Beaman and Beaman, 1994). Hence, in the present study, long term corticosteroid therapy was considered to be the major contributor for immunosuppression. All immunosuppressed patients, whatever their presentation should receive a minimum of 12 months therapy because nocardial infection tends to relapse. *N.otitidiscaviarum* is mostly resistant to beta lactams and imipenem. The mainstay of therapy has been TMP-SMX, treatment failure has been reported when used alone in disseminated infections. Amikacin and fluroquinolones are drug of choice as well. Hence, a combination therapy with these bactericidal agents is recommended (Sorrell *et al.*, 2000; Brown- Elliott *et al.*, 2006).

In most of the patients with pulmonary nocardiosis, early diagnosis and prompt treatment gives successful clinical outcome. Further, it requires high level of clinical suspicion in patients with risk factors, because infections due to *N. otitidiscaviarum* are common if properly diagnosed. Hence, microbiologist must be alerted to include stains and specific cultures incubated for a longer duration.

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