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INTERNATIONAL JOURNAL OF ADVANCED RESEARCH

## **RESEARCH ARTICLE**

### NOCARDIA IN BRONCHIECTASIS - AN UNUSUAL ASSOCIATION.

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Manuscript Info Abstrac	et
Manuscovint History	Dromobiostosis is a common condition of lungs abarratorized by abnormal
manuscript History:	permanent dilatation of airways .Structural abnormalities will lead to abnormal accumulation of secretions, colonization of organisms and repeated infectious exacerbations. Common organisms include Pseudomonas, Pneumococci and Hemophilus.Sometimes unusual organisms like Nocardia can lead to infectious exacerbations in these patients. Prompt recognition of organism and accurate antibiotic coverage will lead to complete recovery. We present 3 bronchiectasis patients who had infectious exacerbation with
Received: 14 January 2016 Final Accepted: 22 February 2016 Published Online: March 2016	
<i>Key words:</i> Bronchiectasis, Nocardia	
	Nocardia with variable outcomes.
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## **Introduction:-**

Nocardiosis is an unusual infection occurring in immune compromised and patients with chronic lung disease like Chronic Obstructive Pulmonary Disease (COPD)& bronchiectasis. Unless recognized and treated early it may lead to fatal consequences. Hereby we present 3 cases of bronchiectasis with secondary infection due to Nocardia. Out of 3 patients, one patient died, indicating importance of high degree of suspicion in early diagnosis and treatment.

## **Case Reports:-**

### Case 1:-

An 80 year old male patient presented with cough and breathlessness of 1 month duration. He was an ex-smoker and using inhaled bronchodilator and inhaled steroids on & off. On clinical examination crepitations are heard on right chest. Imaging showed extensive cystic bronchiectatic changes in right lower lobe, dense consolidation in right middle lobe, diffuse centrilobular nodules in right upper lobe (Fig 1). Bronchial washings grown Nocardia spp. He was started on cotrimoxazole and improved clinically.

#### Case 2:-

A 49 year old male patient, known case of bronchiectasis, using on & off bronchodilators and inhaled steroids presented with fever of 3 months duration, cough with minimal sputum since 1 month, progressive breathlessness of 20 days duration. On examination he was conscious, coherent & hypoxic. Bilateral crepitations were heard on chest auscultation. There was neutrophilic leukocytosis arterial blood gases showed hypoxia, chest X ray and CT thorax showed dense consolidation in right lower lobe, ground glass opacities, multiple nodules in both lungs, bronchiectatic changes in right middle lobe, left lower lobe(Fig2). CT guided FNAC showed extensive Nocardia organisms. He was started on cotrimoxazole, carbapenems. Inspite of antibiotic therapy patient deteriorated needed mechanical ventilation and died of respiratory failure.

## Case 3:-

A 50 year old male patient presented with cough, fever and occasional hemoptysis of 45 days duration. Clinically he had bilateral coarse crepitations & clubbing. He had mild anemia, mild leukocytosis. Imaging showed left lingual and lower lobe, right upper lobe cystic bronchiectatic changes. Infiltrations were seen in lingula and left lower lobe (Fig 3). Sputum examination showed Nocardia species and the same was grown in bronchial washings. He was

started on cotrimoxazole and symptoms improved. Cotrimoxazole was stopped after 6 months and he is under follow up.

# **Discussion:-**

Nocardia is an aerobic, gram positive, weak acid fast, branching, filamentous bacterium. It belongs to Genus Nocardia, family Nocardiaceae and order Actinomycetales. It is a ubiquitous organism found in soil, water and decaying vegetative matter. It becomes aerosolized and reaches the lungs of humans. Although inhalation is common not all persons will develop disease .Immunodeficiency commonly predisposes to the development of disease, but many studies reported in immunocompetent patients also (1, 2, 3, 4). High index of suspicion is necessary in predicting the organism. Nearly 86 species have been identified and half of these are pathogenic to humans (5).

Nocardiosis is a disease of immunocompromised. Most common risk factor is steroid induced immunosuppression (6, 7) followed by Diabetes mellitus (1, 3), HIV (8, 9), alcoholism (10) post-transplant immunosuppression (11) autoimmune diseases (9), hypogammaglobulinemia (12), polymyalgia rheumatica (13). Compromise in Cell mediated immunity is the underlying process which allows organism to become pathogenic. Steroid doses as less as 0.5-1mg/kg for 3-6 wks is sufficient to predispose to disease (1). Patients with HIV with CD 4 count less than 100 are particularly prone to invasive disease (6). Of pulmonary disorders COPD (6,7,9,12,14,15,16,17) bronchiectasis (10,18,19,20,21) cystic fibrosis (22,23) and ABPA(24) are commonly associated. In transplant patients the incidence reported is 0.04-3.5% (11). Both solid organ transplantation and HSCT Hematopoietic Stem Cell Transplantation patients are at increased risk due to immunosuppressive therapy. Allogeneic HSCT patients are at more risk than autogenic patients due to more Graft versus Host Disease chances and more requirement of immunosuppression. Alcoholism has been related to CNS spread (6)

Inhalation is the most common method followed by inoculation. Cases following trauma have been reported (1, 25). Co-infection is observed in many studies (30-40%) and has influence on mortality in post-transplant infections (11). Other coexisting infections reported are tuberculosis, atypical mycobacterial infections, Stenotrophomonas, Klebsiella, Streptococcus pneumonia, Enterococcus, Aspergillus, Candida (1, 13 & 26).

Bronchiectasis, in view of its loss of ciliary function may give rise to colonization to nocardiae. Clinical features, imaging may be nonspecific and isolation of organism, inappropriate response to other antibiotics, high index of suspicion are important features in treating this entity. Various case reports have mentioned association of bronchiectasis in nocardiosis patients as in our case series (18,19& 20). Early recognition, prompt antibiotic therapy will improve outcomes.

Pulmonary nocardiosis is the most common form of nocardiosis followed by CNS, skin (6, 7, 12 & 25). Other organs involved are eye (27), urinary tract infection (28). Health care associated – post-sternotomy suture infections, peritonitis following CAPD catheter infection and central venous catheter related infections are also reported (30). Disseminated disease is defined by involvement of 2 noncontiguous organs involvement. Bacteremia has been reported in some studies (1, 30).

Clinically patients present with subacute to chronic form and rarely in acute form also. Symptoms like cough, chest pain, breathlessness, fever are common whereas others like fatigue, night sweats, diarrhea, and cellulitis have been described. Median time of presentation is 30-42 days for pulmonary Nocardiosis (1, 6 & 7), 45 days for disseminated disease and 55 days for CNS disease (6).

Common imaging findings are alveolar shadows, consolidation, nodules, masses, solitary nodule (7), cavitation (1, 10). Cavitation has been reported in 47% in one study (10). Pleural involvement is reported in 33% cases (6, 10). There was no statistically significant difference between imaging findings between immune compromised and immune competent (30). In a chest computerized tomography study done by A.Christie et al in pulmonary nocardiosis, bronchiectasis was the only abnormality in 17% of patients (31).

Sputum, bronchial washings, bronchoalveolar lavage, transthoracic fine needle aspiration cytology, biopsy will usually provide sufficient diagnostic material. Communication with microbiologist will enhance chances of identification. Microscopy with its classical description and cultures are confirmatory. Culture needs at least 2 weeks of incubation since Nocardia is a slow growing organism. Identification by biochemical methods, chemotaxonomic

methods are not specific. Serologic methods may not be sensitive as many patients are immune compromised and they may not elicit immune response. Newer molecular methods include DNA probes, PCR (32), PRA (PCR Restriction Fragment Length Polymorphism Analysis), gene sequencing, and ribotyping. Gene sequencing appears a promising method based on analysis of genes, coding for 16S rRNA and hsp 65, secA1. (33, 34). Availability at only reference centers is the limiting factor for these investigations. MALDI-TOF (Matrix Assisted Laser Desorption/Ionization –Time of Flight) is an excellent technique which detects mass spectral fingerprints which are unique to each organism based on protein structures. It has advantage of rapid (less than 1 hr) and reliable identification of organism (35, 36).

Antibiotic sensitivity testing is advised in all cases. Invitro synergistic activity is demonstrated between combinations of imipenem, amikacin, cefotaxime and this can be choice of initial therapy in serious infections. Linezolid appears a promising drug since it covers all species and available in oral form. Incidence of adverse reactions like thrombocytopenia can be limiting factor for long term treatment (37, 38). Duration of therapy is not described exactly but for localized disease 6 months and disseminated, immune compromised and neurological involvement will be benefitted by 1 year treatment.

Prophylaxis with cotrimoxazole in the setup of post transplantation has not shown promising results since breakout infections have been reported (11).

Mortality has been 18%-41% for pulmonary nocardiosis, 64% for disseminated and 100% for CNS involvement (7, 39).

In a recent case series from India, Aggarwal D et al reported nocardiosis in patients with COPD and hydropneumothorax (40) whereas our case series consists of bronchiectasis cases exclusively.

The main drawback in our case series is nonavailability of species identification methods. Finally we would like to impress importance of this organism in bronchiectasis patients as this can have an impact on mortality and outcomes.



Fig 1:- showing Right lower lobe bronchiectatic changes and middle lobe consolidation.



Fig 2:- Right lower lobe and left lobe dense consolidation and bronchiectatic changes



Fig 3:- Right middle lobe bronchiectasis ,Left lingula and lower lobe bronchiectasis.



Fig 4:- Thin branching filamentous occasionally beaded Nocardia organism (May GrunwaldGiemsa stain)

# **References:-**

- 1. Yang M, Xu M, Wei W, Gao H, Zhang X, Zhao H, Hu J, Dong H, Xu L, Li L. Clinical findings of 40 patients with Nocardiosis: A retrospective analysis in a tertiary hospital. Exp Ther Med. 2014 Jul; 8(1):25-30. Epub 2014 May 14. PubMed PMID: 24944592; PubMed Central PMCID: PMC4061227.
- Singh I, West FM, Sanders A, Hartman B, Zappetti D. Pulmonary Nocardiosis in the Immunocompetent Host: Case Series. Case Rep Pulmonol. 2015; 2015:314831. doi: 10.1155/2015/314831. Epub 2015 Sep 30. PubMed PMID: 26491594; PubMed Central PMCID: PMC4605260
- Alavi Darazam I, Shamaei M, Mobarhan M, Ghasemi S, Tabarsi P, Motavasseli M, Mansouri D. Nocardiosis: risk factors, clinical characteristics and outcome. Iran Red Crescent Med J. 2013 May; 15(5):436-9. doi: 10.5812/ircmj.2384. Epub 2013 May 5. PubMed PMID: 24349735; PubMed Central PMCID: PMC3838657.
- 4. Okawa S, Sonobe K, Nakamura Y, Nei T, Kamio K, Gemma A. Pulmonary Nocardiosis due to Nocardia asiatica in an Immunocompetent Host. J Nippon Med Sch. 2015; 82(3):159-62. doi: 10.1272/jnms.82.159. PubMed PMID: 26156671.
- 5. Brown-Elliott, Barbara A. et al. Current Status of Nocardia Taxonomy and Recommended Identification Methods. Clinical Microbiology Newsletter 2015 Feb 15; 37 (4), p25 32.
- Martínez Tomás R, Menéndez Villanueva R, Reyes Calzada S, Santos Durantez M, VallésTarazona JM, Modesto Alapont M, Gobernado Serrano M. Pulmonary Nocardiosis: risk factors and outcomes. Respirology. 2007 May; 12(3):394-400. PubMed PMID: 17539844.
- Zhang 7. Chen J. Zhou H, Xu P. P. Ma S, Zhou J. Clinical and radiographic characteristics of pulmonary Nocardiosis: clues diagnosis. PLoS to earlier One. 2014 Mar 3: 9(3):e90724. doi: 10.1371/journal.pone.0090724. eCollection 2014. PubMed PMID: 24594890; PubMed Central PMCID: PMC3940923.
- 8. Mootsikapun P, Intarapoka B, Liawnoraset W. Nocardiosis in Srinagarind Hospital, Thailand: review of 70 cases from 1996-2001. Int J Infect Dis. 2005 May; 9(3):154-8. Review. PubMed PMID: 15840456.
- Minero MV, Marín M, Cercenado E, Rabadán PM, Bouza E, Muñoz P. Nocardiosis at the turn of the century. Medicine (Baltimore). 2009 Jul; 88(4):250-61. doi: 10.1097/MD.0b013e3181afa1c8. PubMed PMID: 19593231.
- 10. Menéndez R, Cordero PJ, Santos M, Gobernado M, Marco V. Pulmonary infection with Nocardia species: a report of 10 cases and review. Eur Respir J. 1997 Jul; 10(7):1542-6. Review. PubMed PMID: 9230244.
- Lebeaux D, Morelon E, Suarez F, Lanternier F, Scemla A, Frange P, Mainardi JL, Lecuit M, Lortholary O. Nocardiosis in transplant recipients. Eur J Clin Microbiol Infect Dis. 2014 May; 33(5):689-702. doi: 10.1007/s10096-013-2015-5. Epub 2013 Nov 23. Review. PubMed PMID: 24272063.

- 12. Bruguera-Àvila N, Becker C, Garcia-Olivé I, Ruiz-Manzano J (2014) Pulmonary Nocardia: A Single-center Experience. J Pulm Respir Med 4:167. doi: 10.4172/2161-105X.1000167
- Mari B, Montón C, Mariscal D, Luján M, Sala M, Domingo C. Pulmonary Nocardiosis: clinical experience in ten cases. Respiration. 2001; 68(4):382-8. PubMed PMID: 11464085.
- Garcia-Bellmunt L, Sibila O, Solanes I, Sanchez-Reus F, Plaza V. Pulmonary Nocardiosis in patients with COPD: characteristics and prognostic factors. Arch Bronconeumol. 2012 Aug; 48(8):280-5. doi: 10.1016/j.arbres.2012.04.009. Epub 2012 May 30. English, Spanish. PubMed PMID: 22656187.
- Rivière F, Billhot M, Soler C, Vaylet F, Margery J. Pulmonary Nocardiosis in immunocompetent patients: can COPD be the only risk factor? Eur Respir Rev. 2011 Sep 1; 20(121):210-2. doi: 10.1183/09059180.00002211. PubMed PMID: 21881150
- Maggiorelli C, Di Pierro I, Manta C, Maccari U, Galanti I, Scala R. Nocardia and Lungs in COPD: Beyond Immuno-deficiencies. COPD. 2015 Jun; 12(3):315-9. doi: 10.3109/15412555.2014.933951. Epub 2014 Aug 5. PubMed PMID: 25093624.
- 17. M.J. Diez-Garcia, A.L. Andreu, and E.Chiner. Bronchopneumonia Due to Nocardia asteroides in a man with Chronic Obstructive Pulmonary Disease. Arch Bronchopneumol.2005;41(11):641-3.
- 18. NabinShrestha ,N.K.Shrestha, AnishSharda, Geraldine Hall, J Tomford , Nocardia –Bronchiectasis Syndrome ,poster- L 689,The World of Community Acquired Pneumonia,IDSA.
- 19. Cremades MJ, Menéndez R, Santos M, Gobernado M. Repeated pulmonary infection by Nocardia asteroides complex in a patient with bronchiectasis. Respiration. 1998;65(3):211-3. PubMed PMID: 9670306.
- Aidê MA, Lourenço SS, Marchiori E, Zanetti G, Mondino PJ. Pulmonary Nocardiosis in a patient with chronic obstructive pulmonary disease and bronchiectasis. J Bras Pneumol. 2008 Nov; 34(11):985-8. English, Portuguese. PubMed PMID: 19099108.
- Sanyal K, Sabanathan K. Nocardia Opportunistic chest infection in elderly: A case report. Cases J. 2008 Aug 21; 1(1):122. doi: 10.1186/1757-1626-1-122. PubMed PMID: 18718020; PubMed Central PMCID: PMC2542347.
- 22. Aravantagi A, Patra KP, Broussard M, Jones K. A case of Nocardia transvalensis pneumonia in a 19-year-old cystic fibrosis patient. Lung India. 2012 Jul; 29(3):283-5. doi: 10.4103/0970-2113.99121. PubMed PMID: 22919172; PubMed Central PMCID: PMC3424872.
- Schoen L, Santoro JD, Milla C, Bhargava S. Pulmonary Nocardiosis in an immunocompetent patient with cystic fibrosis. Case Rep Pulmonol. 2015; 2015:984171. doi: 10.1155/2015/984171. Epub 2015 Apr 15. PubMed PMID: 25960909; PubMed Central PMCID: PMC4414227.
- Sharma B, Ghosh G, Kamble U, Chaudhary K, Chauhan A, Lamba BM, Chowdhary A, Gupta BB. Allergic broncho pulmonary aspergillosis complicated by Nocardiosis. Case Rep Pulmonol. 2012; 2012:758630. doi: 10.1155/2012/758630. Epub 2012 Dec 25. PubMed PMID: 23320238; PubMed Central PMCID: PMC3540710.
- 25. Ambrosioni J, Lew D, Garbino J. Nocardiosis: updated clinical review and experience at a tertiary center. Infection. 2010 Apr; 38(2):89-97. doi: 10.1007/s15010-009-9193-9. Epub 2010 Mar 20. Review. PubMed PMID: 20306281.
- 26. Yagi K, Ishii M, Namkoong H, Asami T, Fujiwara H, Nishimura T, Saito F, Kimizuka Y, Asakura T, Suzuki S, Kamo T, Tasaka S, Gonoi T, Kamei K, Betsuyaku T, Hasegawa N. Pulmonary Nocardiosis caused by Nocardia cyriacigeorgica in patients with Mycobacterium avium complex lung disease: two case reports. BMC Infect Dis. 2014 Dec 10; 14:684. doi: 10.1186/s12879-014-0684-z. PubMed PMID: 25491030; PubMed Central PMCID: PMC4266951.
- Yu E, Laughlin S, Kassel EE, Messner HA, Yucel YH. Nocardialendophthalmitisandsubretinal abscess: CT and MR imaging features with pathologic correlation: a case report. AJNR Am J Neuroradiol. 2005 May; 26(5):1220-2. PubMed PMID: 15891188.
- Poisnel E, Roseau JB, Landais C, Rodriguez-Nava V, Bussy E, Gaillard T. Nocardia veterana: disseminated infection with urinary tract infection. Braz J Infect Dis. 2015 Mar-Apr; 19(2):216-9. doi: 10.1016/j.bjid.2014.11.003. Epub 2015 Jan 28. PubMed PMID: 25636185.
- Al Akhrass F, Hachem R, Mohamed JA, Tarrand J, Kontoyiannis DP, Chandra J, Ghannoum M, Haydoura S, Chaftari AM, Raad I. Central venous catheter-associated Nocardia bacteremia in cancer patients. EmergInfect Dis. 2011 Sep;17(9):1651-8. doi: 10.3201/eid1709.101810. PubMed PMID: 21888790; PubMed Central PMCID: PMC3322064.
- Mehrian P, Esfandiari E, Karimi MA, Memari B. Computed tomography features of pulmonary Nocardiosis in immunocompromised and immunocompetent patients. Pol J Radiol. 2015 Jan 7;80: 13-7. doi: 10.12659/PJR.892042. eCollection 2015. PubMed PMID: 25584096; PubMed Central PMCID: PMC4288394.

- 31. Alexis Christie, MD<sup>1</sup>, Lewis Wesselius, MD<sup>2</sup> Chest Computed Tomography Evidence of Bronchiectasis in Patients with Pulmonary Nocardiosis Chapter DOI: 10.1164/ajrccm conference.2012.185.1\_MeetingAbstracts.A609510.1164/ajrccm\_conference.2012.185.1\_MeetingAbstracts.A6 095.
- Couble A, Rodríguez-Nava V, de Montclos MP, Boiron P, Laurent F. Direct detection of Nocardia spp. in clinical samples by a rapid molecular method. J Clin Microbiol. 2005 Apr; 43(4):1921-4. PubMed PMID: 15815019; PubMed Central PMCID: PMC1081390.
- Kong F, Wang H, Zhang E, et al. secA1 Gene Sequence Polymorphisms for Species Identification of Nocardia Species and Recognition of Intraspecies Genetic Diversity. Journal of Clinical Microbiology. 2010; 48(11):3928-3934. doi:10.1128/JCM.01113-10.
- 34. Conville PS, Zelazny AM, Witebsky FG. Analysis of secA1 Gene Sequences for Identification of Nocardia Species. Journal of Clinical Microbiology. 2006; 44(8):2760-2766. doi:10.1128/JCM.00155-06.
- 35. Segawa S, Nishimura M, Sogawa K, Tsuchida S, Murata S, Watanabe M, Matsushita K, Kamei K, Nomura F. Identification of Nocardia species using matrix-assisted laser desorption/ionization-time-of-flight mass spectrometry. Clin Proteomics. 2015 Mar 7; 12(1):6. doi: 10.1186/s12014-015-9078-5. eCollection 2015. PubMed PMID: 25931991; PubMed Central PMCID: PMC4409724.
- 36. Verroken A, Janssens M, Berhin C, Bogaerts P, Huang TD, Wauters G, Glupczynski Y. Evaluation of matrixassisted laser desorption ionization-time of flight mass spectrometry for identification of nocardia species. J Clin Microbiol. 2010 Nov; 48(11):4015-21. doi: 10.1128/JCM.01234-10. Epub 2010 Sep 22. PubMed PMID: 20861335; PubMed Central PMCID: PMC3020850.
- 37. Jodlowski TZ, Melnychuk I, Conry J. Linezolid for the treatment of Nocardia spp. infections. Ann Pharmacother. 2007 Oct; 41(10):1694-9. Epub 2007 Sep 4. Review. PubMed PMID: 17785610.
- Shen T, Wu L, Geng L, Wei Z, Zheng S. Successful treatment of pulmonary Nocardia farcinica infection with linezolid: case report and literature review. Braz J Infect Dis. 2011 Sep-Oct; 15(5):486-9. Review. PubMed PMID: 22230859.
- Martínez R, Reyes S, Menéndez R. Pulmonary Nocardiosis: risk factors, clinical features, diagnosis and prognosis. Curr Opin Pulm Med. 2008 May; 14(3):219-27. doi: 10.1097/MCP.0b013e3282f85dd3. Review. PubMed PMID: 18427245.
- 40. Aggarwal D, Garg K, Chander J, Saini V, Janmeja AK. Pulmonary nocardiosis revisited: A case series. *Lung India : Official Organ of Indian Chest Society*. 2015;32(2):165-168. doi:10.4103/0970-2113.152638.