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Fatal Superadded Nocardia Infection in a Case of Pulmonary Aspergillosis

R. K. Mahajan[1], Shweta Sharma[1*], Shukla Das[2], Arun Wilson[1] and R. S. Tonk[3]

[1]Department of Microbiology, Dr Ram Manohar Lohia Hospital & PGIMER, India.
[2]Department of Microbiology, UCMS & GTB Hospital, Delhi, India.
[3]Department of Medicine, Dr Ram Manohar Lohia Hospital & PGIMER, India.

Authors' contributions

This work was carried out in collaboration between all authors. Authors RKM and SS wrote the first draft of the manuscript and managed the literature searches. Author SD corrected the final manuscript. Authors AW and RST analysed the history of patient and managed the case. All authors read and approved the final manuscript.

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Case Report

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ABSTRACT

Pulmonary nocardiosis is a severe opportunistic infection in which chronic lung disease along with long term steroid therapy is the most significant predisposing factor. Demonstration of Nocardia in even potentially contaminated sample like sputum, warrant strong warning signal of association of the organism with the clinical condition because Nocardia are rarely encountered as laboratory contaminants. Immediate initiation of appropriate treatment is absolutely essential since any delay in diagnosis or treatment may prove detrimental to the extent of complete fatal outcome.

Keywords: Pulmonary nocardiosis; aspergillosis; fatal.

**Corresponding author: E-mail: drshwetamicro@gmail.com;*

1. INTRODUCTION

Genus Nocardia is a constituent of aerobic actinomycetes and includes organisms that are gram positive, acid fast and grow as thin branching filaments that fragment into coccobacillary forms. Acid fastness is due to the presence of short chain [40-60 Carbon] mycolic acids. Nocardia are ubiquitous and may be recovered from water, soil, dust, decomposing organic matter etc. [1]. Nocardia usually attack patients with some degree of compromised immune function. Clinical nocardia infections range from cutaneous lesions following trauma in healthy to serious pulmonary, extra pulmonary or CNS disease in immunocompromised patients.

First case of human nocardiosis was reported by Eppinger in 1890 [2]. In the last couple of decades, there has been significant increase in the number of human cases. This amplification in numbers could be attributed to ever expanding population of immune compromised hosts coupled with markedly improved methods of detection and identification of Nocardia. Presently, more than 80 species of Nocardia have been identified using 16srRNA typing and about 30 have been implicated in human pathologies [3]. Major pathogenic Nocardia comprise N asteroids complex, N otitidiscaviarum and N brasiliensis. N asteroids is responsible for about 80% of pulmonary, systemic and CNS infections while the most important cause of cutaneous lesions remains N brasiliensis [4]. We report here a case of fatal pulmonary nocardia infection in a case of pre-existing aspergillus infection.

2. CASE REPORT

A 46 yrs old asthmatic, diabetic female presented in the emergency department of our hospital with complaints of severe breathlessness and chest pain. She was also coughing out thick, rusty sputum for the last five days. She was febrile with temperature of 101ºF; pulse rate was 120/minute, blood pressure 140/80 mmHg and respiratory rate 22/min. There was exaggerated use of accessory respiratory muscles and her oxygen saturation was 98%. On respiratory examination, bilateral diffuse ronchi were present along with right sided crepts. Rest of the systemic examination appeared normal. Patient was put on ventilator on synchronized intermittent mandatory ventilation (SIMV) mode after collecting sputum sample. She was evaluated for productive cough with breathlessness a month back and was diagnosed as a case of broncho-pulmonary aspergillosis as evident by observing dichotomously branching septate hyphae in direct microscopic examination of broncho-alveolar lavage. She also had raised levels of Aspergillus fumigates specific IgG Abs [77.4 KUA/L against reference range of <0.35] and IgE antibodies [7243 KUA/L] with FEIA (Fluorescent enzyme immunoassay). She was on steroids and itraconazole [200 mg OD] for her respiratory complaints as advised by the treating physician.

Her Hb was 10.1 g%, total leucoycte count of 16400 cu/mm with 84% neutrophils. Neutrophils showed toxic granulation. Liver function, renal function and serum electrolyte values were within reference ranges. Random blood sugar was 299 mg/dl and HbA1c was 8.5%. X-ray chest showed bilateral diffuse shadowing. HRCT (high resolution computed tomography) scan of chest revealed multiple areas of peribronchial consolidation with surrounding ground glass opacity in bilateral lung fields, cylindrical and varicose bronchiectasis and multiple cavitary lesions in the posterior segment of right upper lobe. Patient was HIV seronegative.

A repeat bronchopulmonary lavage was undertaken and washings forwarded to the department, for microbiological investigation. The bronchial washings were negative for acid fast bacilli but gram stain revealed gram positive thin, branching filaments resembling actinomycetes infection. As per operating protocols, to complement the gram stain findings, modified acid fast staining (1% sulphuric acid is used as a decoloriser) was done. In modified ZN stain, acid fast thin, branching, beaded, filamentous bacilli were seen [Fig. 1]. Sample was inoculated on Blood agar, MacConkey agar and Sabouraud dextrose agar. On Blood agar, after 72 hrs of aerobic incubation, there was growth of colonies 2-3 mm in size, dry, convex, white and adherent to the medium. On Sabouraud dextrose agar, colonies were dry and yellowish orange in colour [Fig. 2]. Gram stain of the colonies showed, gram positive thin, branching filaments; while in modified ZN stain, acid fast thin, branching, beaded, filamentous bacilli were seen. The isolate was subjected to biochemical reactions and identified as Nocardia asteroides complexes (urea hydrolysis, decomposition of hypoxanthine and adenine, nitrate reductase etc.) [5].

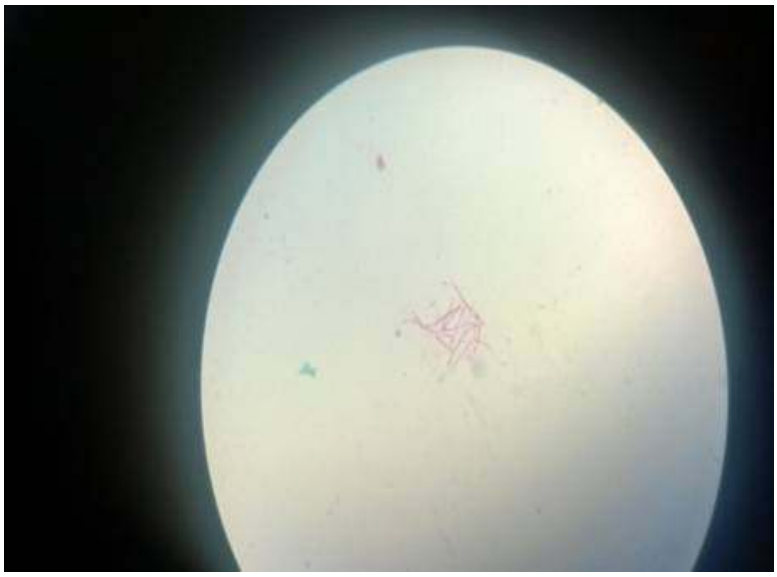

Fig. 1. Modified ZN stain showing acid fast thin, branching, beaded, filamentous bacilli

Fig. 2. Sabouraud dextrose agar showing dry yellowish orange colonies of *Nocardia asteroids*

Following detection of nocardia, the patient was started on tablet cotrimoxazole in dose of sulphamethoxazole 2400 mg and trimethoprim 480 mg (double strength two tablets twice daily) per day in divided doses along with intravenous amikacin and imipenem and for control of diabetes patient was switched to Insulin. The endotracheal aspirate sent after 4 days of broncho-alveolar lavage, also grew the same organism. The blood and urine cultures were sterile. However patient condition deteriorated and succumbed to her illness after 12 days of admission in the hospital.

3. DISCUSSION

The present case highlights the relentless course that an organism like nocardia can follow in a patient of COPD especially when pre existing co-morbid conditions like; aspergillus infection, diabetes, steroid usage etc. provide all the necessary prolific impetus to the infecting organism.

Pulmonary nocardiosis is well established in patients with malignancies, HIV and on long term steroids [3,6]. Nocardia co-infection aspergillosis is uncommon but markedly serious in patients with compromised immune function [7]. Both exist in the environment as soil saprophytes and pulmonary infections are most common, mostly caused by aerosol route. This patient was clinically and laboratory established case of Allergic Bronchial Aspergillosis. The radiological findings signaled features suggestive of tuberculosis, bronchopulmonary aspergillosis, nocardia infection etc. with pre-existing chronic obstructive lung disease. Since, clinical expression of pulmonary nocardia infections in the form of dysnoea, cough, fever etc. is largely non-specific; a great degree of clinical prudence is required to suspect these infections. Diagnosis in this case also was accidental since, after Itraconazole, antibiotics and systemic steroids being given for bronchial aspergillosis, failed completely to alleviate or mitigate the symptoms, a diagnostic bronchoscopy was planned to rework up this case. Gram positive thin branching hyphae observed in gram stain raised the suspicion of Nocardia infection. Modified acid fast staining and culture results confirmed the diagnosis. One of the shortcomings of this study was that antimicrobial sensitivity could not be undertaken on this isolate on grounds of lack of standardised operating procedure for AST of nocardia species.

This patient was a prototype of all the predisposing factors conducive to the establishment of nocardia infection. She was an old case of COPD, diabetic and on systemic steroids for last couple of months. Her bronchial aspergillosis was diagnosed just one month back and there was all the necessary laboratory evidence also in favour of this infection but it is postulated that nocardia infection could have been present at the previous episode also but predominance of aspergillus hyphae could have overshadowed the detection of nocardia at that point of time. During the present work up, no evidence of aspergillus infection could be found and presence of nocardia was so fulminant that the fine hyphae of nocardia could be seen in the wet mount of the sample also. The microscopic findings were communicated to the treating physician and patient was immediately started on cotrimoxazole, amikacin and imipenem but the treatment failed to contain this unrelenting organism and it grew profusely in endotracheal aspirations submitted after starting the treatment and within next 48 hours, patient succumbed to the fulminant nocardia infection. The aggressive course followed by this organism despite the initiation of comprehensive therapy, hints that there could have been delay in identifying this insult and warrants looking for this organism in all cases of pulmonary infection not responding to the conventional treatment protocols. There also appears urgent need to sensitise and raise awareness about the problem of this organism because the number of requests for investigation of nocardia hardly corroborate with the number of patients that would have reasonable chance to develop this kind of problem.

Culture and identification of nocardia from clinical sample remains the gold standard for diagnosing this infection but the culture results are usually not available before 48-72 hrs and identification of species would take its own course of time. And even this would be possible only when clinician has communicated his suspicion about this infection and appropriate culture efforts have been applied to optimize the recovery of the organism [8]. In light of the inherent gaps attached to this infection, this is suggested that due cognizance should be taken of the microscopic findings suggestive of nocardia infection and because most of the laboratories may not be having standardised facilities for culture and AST of nocardia, immediate empiric therapy commensurate with clinical condition of the patient should be initiated. Genotypic identification could be worthwhile for epidemiological and identifying the ecological existence of Nocardia species. Needless to say that rarely is nocardia species reported as laboratory contaminants in clinical samples.

4. CONCLUSION

Pulmonary nocardiosis is a serious respiratory tract infection which may prove disastrous in situations of pre-existing aspergillus bronchial infection. Physicians need to be more vigilant to entertain suspicion of nocardia infection in immunocompromised patients on long term steroids and should immediately notify the microbiologist to investigate for nocardia which would require prolonged incubation of cultures. Since nocardia may not grow before three days of incubation, a diligent examination of gram stain and acid fast stain may provide extremely relevant early signals for instituting appropriate empirical antimicrobial therapy. Though sulfonamides are the drugs of choice, serious infection would invariably require combination of sulphonamides with amikacin and ceftriaxone or

imipenem. It also needs to be emphasized that all delays in starting treatment would adversely affect the outcome of the disease.

CONSENT

All authors declare that 'written informed consent was obtained from the patient (or other approved parties) for publication of this case report and accompanying images.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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