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Diagnosis of nocardia is very challenging due to limited literature and diagnostic tools

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Abstract

Infective endocarditis by Nocardia is a rare disease carrying very high morbidity and mortality. We report a 50 y/o male patient who was diagnosed with isolated nocardiosis endocarditis. All relevant radiological, microbiological and pathological investigations were done. Aortic valve replacement was performed post CAG and patient was started on TMP SMX and amikacin. This report discusses the challenges faced in the diagnosis of Isolated endocarditis by Nocardia and the treatment regimens, both surgical and medical to improve patient outcome. Patient recovered well and was discharged on long term oral antibiotics. This case report discusses the apt management and the approach to a case of infective endocarditis by Nocardia.

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Introduction

The diagnosis of Nocardia-related infective endocarditis is uncommon. Accurate laboratory identification of Nocardia species presents a significant obstacle, primarily arising from difficulties in differentiating it from other microorganisms and the extended incubation periods required for its isolation [1]. The optimal approach to Nocardia endocarditis combines extended treatment with a mix of antibiotics and surgical intervention to eliminate the infection's origin. We report a 50-year-old male who was diagnosed with infective endocarditis due to Nocardia spp. and treated with combination of antibiotics and aortic root replacement.

Case presentation

A 50 year old male patient presented with fever which was on and off associated with cough and expectoration, for which he was diagnosed with Right Lower Lobe Consolidation and Right sided Empyema - Status post (S/p) Inter Costal Drain (ICD) insertion on the right side 2 months ago. The patient also had history of shortness of breath which was associated with B/L Lower Limb (LL) swelling since 4 months to Emergency Room (ER). Patient is a known case of Pulmonary TB, on ATT since 3 months, Diabetes Mellitus since 7 years on oral antidiabetic drugs, history of Pancreatitis 7 years ago in 2019 with Atrophic Pancreatitis - pseudo cyst which was drained. The patient also has a history of fall with femur fracture for which dynamic hip screws were placed 4 months ago and he was bedridden since then. On arrival to ER the vitals were - Heart Rate (HR): 89 beats per min, Respiratory Rate: 21 breaths per min, SpO_2: 100% on room air, Bilateral (B/L) vesicular breath sounds, Mean Arterial Pressure (MAP): 60 mmHg, warm peripheries, Distal pulses felt, Cardiopulmonary Limited Ultrasound Examination (CLUE) showed Multiple Dense B lines, Left Basal consolidation, Mild B/L Effusion, IVC < 50% collapsing and Echocardiography (ECHO) done on 20/06/2023 showes aortic valve - three leaflets, thickened, 12x9 mm echolucent cavity at the left coronary sinus with 7x6 mm mobile mass with vegetation, Paradoxical movement seen in the interventricular septum, PASP-35 mmHg, with bilateral pleural effusion (41 mm on the right side and 59 mm on the left side). In suspicion of Aortic root abscess Computed Tomography (CT) Thorax was performed which reveled Aneurysmal out pouching at aortic sinus suggestive of aortic root abscess, Right Lower Lobe Empyema, B/L Pleural Effusion R>L, Atelectatic/consolidative changes in right middle and B/L Lower Lobe. USG abdomen and pelvis showed Ascites and B/L pleural effusion. The Patient was started on antibiotics empirically - Inj. Piperacillin and Tazobactam 4.5 g every 6^{th} hourly for 7 days, Inj. Doxycycline 100 mg and ATT was continued, Deep Vein Thrombosis (DVT) pump was started in view of Thromboprophylaxis, Pantoprazole 40 mg once daily was started in view of ulcer prophylaxis. 3 sets of Blood culture and urine culture were sent on 20/06/2023.

Central line: Right Internal Jugular Vein inserted on (20/6/23), **Peripheral line:** Right hand 20G and Foleys inserted on (20/6/23).

The Patient was shifted to CCU in view of Acute pulmonary edema and tachypnea requiring NIV support and plan for Aortic surgery in view of Aortic root abscess. The patient during hospital stay developed shock with reducing urine output for which Inj. Noradrenaline was started to maintain a MAP of 65 mmHg. Antibiotics were escalated to Inj. Vancomycin 500 mg every 8th hourly from on 23/06/2023 for a period of 5 days. Diagnostic Pleural tapping was done on 23/06/2023 by Interventional Radiologist where 700 ml of serous fluid was aspirated from the left pleural cavity and significant right sided pleural thickening with associated pleural effusion was seen on the right side. Pleural fluid was sent for cytology which showed no malignant cells, few polymorphs, scattered foamy histiocytes and lymphocytes. Blood culture and sensitivity done using MALDI TOF MS method showed growth of Nocardia cyriacigeorgica on 26/06/2023. Antibiotics were escalated to Inj. Imipenem 500 mg every 8th hourly for 26 days and Tab. Sulfamethoxazole and Trimethoprim 800 for 5 days and another Blood culture was sent which later showed no growth. Fiber Optic Bronchoscopy and BAL was done on 28/06/2023 which was reported to be normal and samples were sent for Gram stain and culture, Fungal stain and Fungal culture, Gene Xpert and AFB culture. BAL showed growth of Candida albicans. Coronary Angiography was done which showed Aortic root abscess, moderate AR, Normal epicardial coronaries. Homograft Aortic root replacement was done on 10/7/23 which was uneventful and intraoperatively patient was transfused with 2 pints of PRBC, 4 pints of FFP and Cryoprecipitate. Patient is sedated with Fentanyl infusion and also requiring Dobutamine support. Patient was also intubated and had mediastinal drains placed. Tissue was sent during Surgery in suspicion of Nocardia. Echocardiogram done post aortic root replacement showed well functioning aortic homograft, trivial AR, PASP of 45 mmHg, 3 mm pericardial effusion, 102 mm left sides pleural effusion and 20 mm right sided pleural effusion. The Patient was taken up for gastroscopy following which he was diagnosed to have gastroparesis for which patient was started on Esomeprazole and levosulpiride. The Patient was extubated on 11/7/23. TEE was done which showed minimal pericardial effusion. ICD Drains and arterial line where removed on 13/7/23. Temporary pacemaker was removed on 15/7/23. Vasopressor supports was titrated and stopped on 20/7/23. Patient was transfused with 1 pint PRBC on 25/7/23. Patient was discharged on 2/8/23 initially to continue IV antibiotics and later switched to oral antibiotics. Pre discharge ECHO showed well functioning aortic homograft with no pericardial effusion, PASP of 28 mmHg and 30 mm left sided pleural effusion.

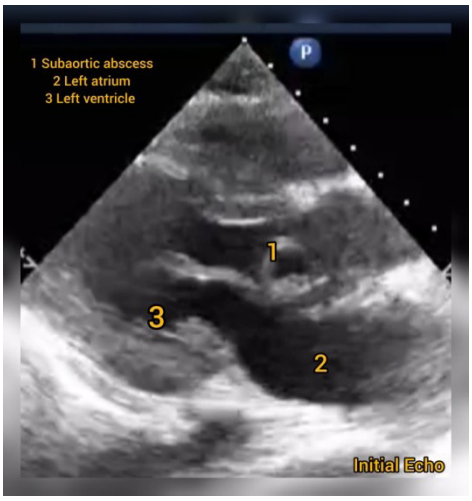

Figure 1: Initial Echo (TTE) done on 21/06/2023 showed dynamic subaortic root abscess most likely involving the non coronary cusp (parasternal long axis view), with possible left ventricular outflow tract obstruction and hypertrophied left ventricle.

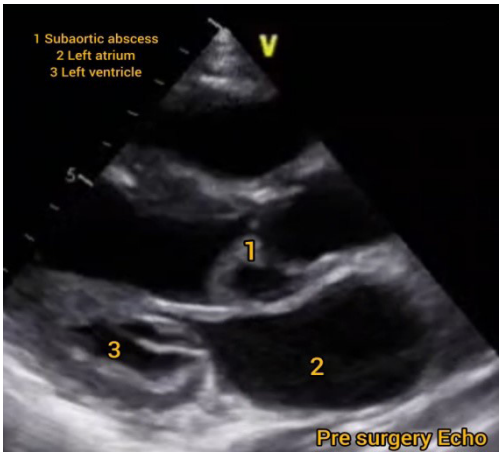

Figure 2: TTE done before surgery; parasteranal long axis view showing similar findings as initial Echo inspite of starting IV antibiotics.

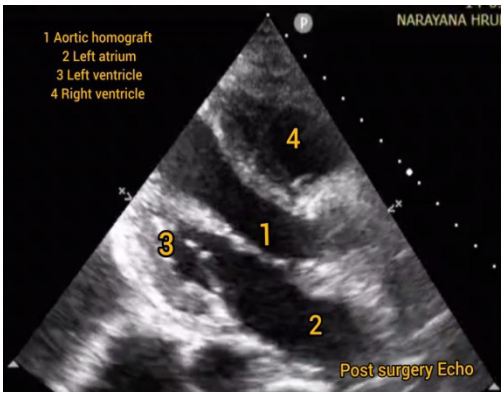

Figure 3: TTE done post surgery with a well functioning aortic homograft and no evidence of abscess.

Discussion

We report a 50 years old male with Aortic root abscess/ Aortic valve endocarditis due to Nocardia cyriacigeorgica. This intricate case sheds light on the diagnostic maze and optimal treatment roadmap for Nocardia endocarditis, offering valuable insights into the effectiveness of combining antibiotics and surgery. The source of infection was likely due to community acquired infection affecting the endocardium causing Aortic root abscess. Nocardia spp. are globally identified as saprophytes occurring in soil, organic matter, and aquatic habitats [1]. The slow-growing nature of some Nocardia strains renders traditional blood cultures ineffective in timely diagnosis, highlighting the need for alternative approaches. Nocardia spp. are often wrongly identified as other gram-positive rods [1]. Disseminated Nocardia infection is most often a diagnosis of patients with some underlying immunocompromised condition and usually have a high mortality rate [1]. The risk factors present in this case was the patient having a history of pulmonary tuberculosis and long term history of diabetes mellitus. Other risk factors usually associated with disease would be patients on steroids, HIV patients, COPD, malignancies, alcoholism, cigarette use and

injecton drug use. Nocardia exhibits a predilection for targeting the respiratory system, the brain and spinal cord, the skin, and the subcutaneous tissue. The joints, bone, and heart are less commonly involved [1]. Patients usually presented with the symptoms of fever (56.8%), cough (35.1%), pleuritic chest pain (24.3%), and headache (13.5%). On clinical examination the following clinical signs have been commonly noted; hyperventilation (21.6%), skin lesions (16.2%), altered consciousness (13.5%), and central nervous system (CNS) involvement (8.1%) [2]. However, studies have shown that >50% of pulmonary nocardiosis cause disseminated infection. Some of them cause empyema, pleural effusion, pericarditis, SVC syndrome. Chest X-ray showed infiltrates in 59.5% of cases, nodules in 35.1%, cavitations in 13.5%, and pleural effusion in 13.5%. Bilateral lung lesions were seen in 54.1% of patients. Fifteen patients (40.5%) underwent thoracic Computed Tomography (CT) scan, which revealed signs of disease in 12 (32.4%) [2]. CNS infections are most likely due to disseminated infections which present as brain abscess. Usual modality of investigation is MRI brain which may show lesion with or without mass effect. Investigations that lead to sooner diagnosis and subsequent faster treatment leads to reduced morbidity and mortality. High suspecion is required in order to conduct the right microbiological and molecular testing. Alterations in the regular culture methods are also necessary in quicker diagnosis. Microbiologically Nocardia spp. are identified based on their morphology using standard staining techniques as gram positive branched bacilli and the presence of aerial hyphae. Further tests can be run and classification can be made based on their ability to grow in lysozyme broth, urease production. Species level identification needs further testing. Once identified, antibiotic susceptibility testing can be performed by disk diffusion with various antibiotics. Chart 1 highlights the various antibiotics tested against Nocardia and their MIC.

Notably, this patient came with a history of fever, cough, lung consolidation, empyema since 2 months and presented with shortness of breath associated with b/l lower limb edema. In suspicion of heart failure, initial ECHO was done which revealed pericardial effusion, aortic root vegetation. Further CT thorax confirmed the presence of aortic root abscess along with lung consolidation, right sided empyema, b/l pleural effusion. The latest guidelines for diagnosis of IE by the Duke-ISCVID criteria, emphasizes the use of cardiac CT. Compared to echocardiography, CCT is less adept at detecting vegetations. However, its superior spatial resolution makes it more sensitive to identifying paravalvular leaks or abscesses [3]. For example, CCT had a better sensitivity than TEE to diagnose pseudoaneurysm or abscess (78% vs 69%), while TEE identified vegetations (94% vs 64%), valvular perforation (81% vs 41%) and paravalvular leakage (69% vs 44%) better [3]. It has been noticed that, using both CCT and TEE together gives us better chances at identifying valvular and paravalvular lesions [3]. As a result, the ISCVID Working Group consider both the imaging modalities as complementary in patients with suspected IE. Furthermore, CCT may be a better adjunct when TEE is contraindicated, or when TEE images are suboptimal [3]. Further, coronary angiography can be used as definitive diagnostic procedure in cases of aortic root abscess, as performed in this case. The dearth of clinical data on Nocardia endocarditis poses a substantial challenge for physicians, potentially leading to delayed diagnoses, less effective treatment strategies, and prolonged durations of therapy. Studies have shown that valvular surgery is of vital importance for source control as well as patient outcome. Think of a tick-

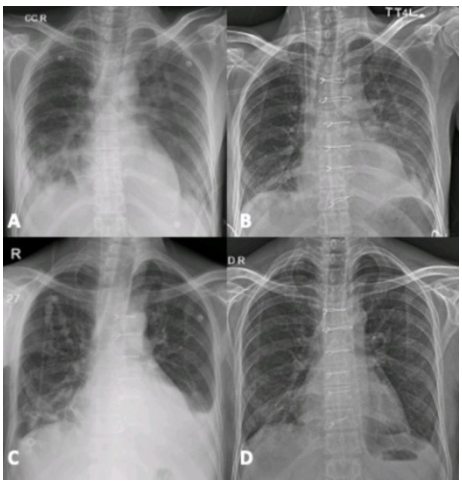

Figure 4: Serial chest radiographs (CXR's) of the patient at admission **(A)**, immediate post op **(B)**, post operative period **(C)** and at discharge. This shows the presentation with bilateral effusions with consolidations in the lower lobes with resolution of parenchymal changes at discharge.

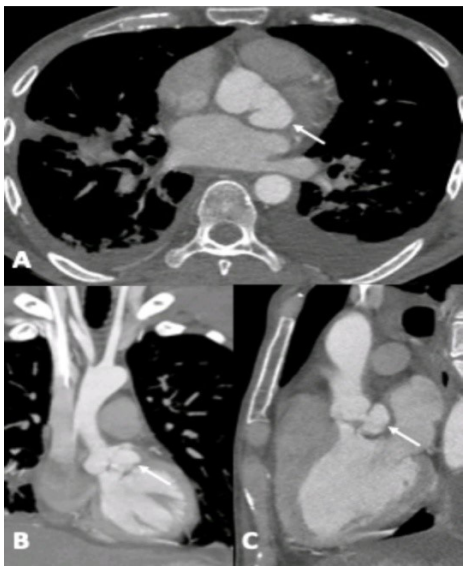

Figure 5: Computed Tomography (CT) images of the chest post contrast in axial **(A)**, coronal **(B)** and sagittal **(c)** planes. The para-aortic root collection/ abscess is seen (white arrow) closely related to the sinus of Valsalva. Bilateral pleural effusions can also been in the lung bases.

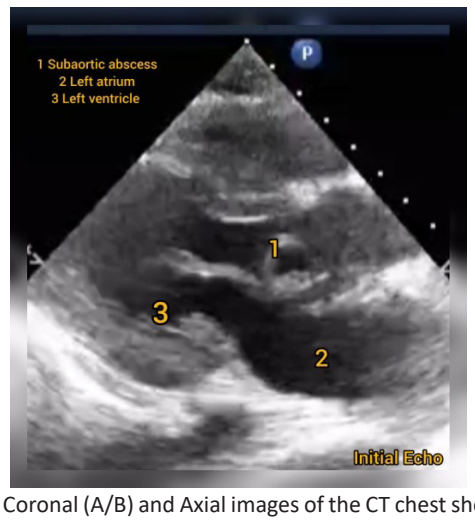

Figure 6: Coronal (A/B) and Axial images of the CT chest showing bilateral pleural effusions with underlying consolidation (right worse than left).

ing time bomb strapped to a patient's heart. Leaving serious valve problems untreated, like skipping valvular surgery, is akin to letting that bomb detonate. Research indicates that mortality rates soar in such cases (Chart 2). This emphasizes the life-saving potential of valvular surgery in terms of source control.

The successful management of Nocardia-related infective endocarditis underscores the paramount importance of prolonged antibiotic therapy, employing a polypharmacy approach. In this context, the extended duration of antimicrobial treatment is integral to eradicating the bacterial burden, while the utilization of multiple, synergistic agents mitigates the risk of resistance development and ensures comprehensive targeting of the infectious pathogen. Trimethoprim - Sulphamethoxazole (TMP-SMX) and amikacin, are the two frequently used agents but have been associated with nephrotoxic effects, which calls for rigorous surveillance of renal function and meticulous monitoring of therapeutic drug levels throughout the treatment course. Such stringent observation is crucial to ensure optimal clinical outcomes while minimizing potential iatrogenic complications. Due to the lack of randomised trials, there has been no effective treatment guidelines against nocardiosis yet. That said, current treatment plans depend on the severity of disease; TMP/SMX is the preferred initial treatment of choice [4]. In case of severe infection the combination of intravenous TMP/SMX and amikacin or imipenem is recommended [4]. The duration of therapy for nocardiosis depends on the severity of infection, but a typical regimen consists of 6-8 weeks of intravenous therapy followed by prolonged oral therapy for about 6-12 months or more.

Conclusion

Infective endocarditis caused by Nocardia, even though is of rare occurrence, timely identification and treatment can significantly improve patient outcome and reduce morbidity and mortality associated with it. The importance of various microbiological tests and longer periods of incubation in case of cultures need to be further emphasised. Also, sooner the surgery is done for source control better will be the response of the patient to medical treatment.

Our case is unique as Nocardiosis presents as isolated endocarditis lesion causing aortic root abscess and heart failure complication without classical presentation. The most common risk factors for Nocardiosis i.e. cancer, transplant, prosthetic valve, systemic steroid use, COPD were absent in our case. Our case highlights the importance of Nocardiosis as one of the importance differential diagnosis for early diagnosis leading to optimal outcomes.

Highlights

1. Infective endocarditis by Nocardia is a very rare illness carrying high mortality and morbidity.
2. Diagnosis of Nocardia is very challenging due to limited literature and diagnostic tools.
3. Improved patient outcome when surgical source control and medical management are started as soon as possible.

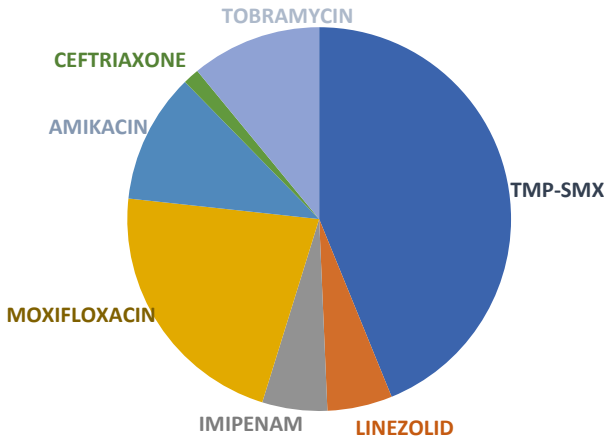

Chart 1: Chart showing the antibiotics that are maximally effective against Nocardia species [1].

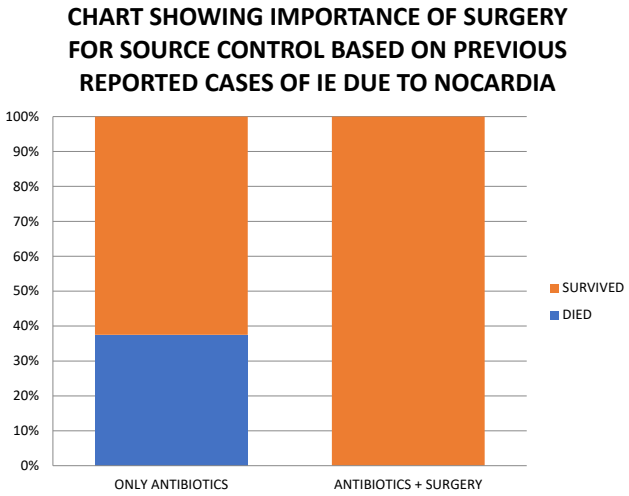

Chart 2: Chart showing importance of surgery for source for better patient outcome based on previous reported cases of endocarditis due to Nocardia species [1].

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