Patient

View this article online at: patient.in/doctor/nocardia

Nocardia

What is nocardia?[1]

Nocardia is a genus of aerobic actinomycetes found ubiquitously in soil and water. Nocardia can cause multiple illnesses and also disseminated (or invasive) disease, known as nocardiosis.

- Opportunistic infections caused by Nocardia often afflict immunocompromised individuals like cancer patients receiving chemotherapy, individuals with AIDS, and organ transplant recipients.
- Nocardia is interesting because it releases virulence factors, allowing it to evade the normal human defence mechanisms. Examples of the virulence factors include:
    - Release of **cord factor**, which prevents nocardia from being phagocytosed by macrophages.
    - Catalase production, which inactivates oxygen metabolites which would normally be toxic to bacteria.[2] [3]

Nocardia infection in humans

Disseminated nocardiosis is most commonly caused by *Nocardia asteroides*. *Nocardia brasiliensis* is found in the tropics and causes skin infection (30% of cases are in the immunocompetent).[4] Other human pathogens include *Nocardia otitidiscaviarum* and *Nocardia transvalensis*.

How common is nocardia? (Epidemiology)

- Nocardial infections are rare in the UK but their prevalence is increasing in the USA and countries such as Africa and India. This may in part be due to improved detection techniques.

- Nocardial infections are usually acquired by:
    - Inhalation of the bacteria with either lung infection and/or haematological spread (this accounts for the majority of human cases).
    - Direct inoculation via traumatised skin.
- Adults are most commonly affected, especially males. There is no seasonality and outbreaks are rare.

Nocardia symptoms (presentation)

Risk of infection with nocardia is increased in the immunocompromised including:

- Pre-existing lung disease - eg, chronic obstructive pulmonary disease (COPD), alveolar proteinosis.[2]
- Chronic steroid use or use of azathioprine and methotrexate.[5]
- Transplant recipients - eg, kidney transplant.[6]
- HIV/AIDS.

Nocardia can affect any organ in the body but mostly leads to five types of illnesses:

- Pneumonia.
- Involvement of the skin.
- Disseminated nocardiosis.
- Involvement of the central nervous system.
- Involvement of the eyes.

Pneumonia

Pneumonia caused by nocardia may be indistinguishable from other pneumonias. It is usually subacute, developing over weeks but may be acute in the very immunocompromised.[7] Nocardia should be suspected in any prolonged pneumonia that does not respond to empirical antibiotics.[8]

The features of a nocardial pneumonia can include:

- Cough.
- Fever, malaise and anorexia.
- Night sweats.
- Weight loss.
- Haemoptysis, chest pain and difficulty in breathing - may also be present but are usually less prominent.

CXR may show infiltrates or nodules which may be multiple and can be mistaken for pulmonary metastases. In fact, some cases of nocardial lung disease have appeared as an endobronchial mass rather than pneumonia. [9]

30% of patients may also have a pleural effusion which is usually an empyema.

There may be local spread from the pneumonia - eg, pericarditis or mediastinitis.

It has been noted that some patients with chronic lung disorders may have positive sputum cultures for nocardia although they do not display any other clinical features to suggest active infection. Nocardia can also cause tracheitis, laryngitis and sinusitis; however, these are more rare.

Skin

Nocardial infection of the skin can present in any of the following ways:

- **Ulcers**.
- **Nodules**.

- **Actinomycetoma or mycetoma** - this is a mass that consists of granulomas, which continues to progress with eventual fibrosis and necrosis. It is commonly seen on the hands and feet but may also affect the neck, head and back. The mycetoma can lead to sinus and fistula formation which can discharge pus. These lesions may continue to be infected for months and can lead to deformity or involve deeper structures that may even be fatal, especially if the original mycetoma is on the head or neck. Mycetomas are common in Mexico, Central and South America and Africa. *N. brasiliensis* is the most common pathogen; other species implicated are *N. transvalensis*. It is a serious illness, as infection can pass on to surrounding or deeper structures - eg, bone, joints and muscles.
- **Lymphocutaneous disease** - this presents with a lesion at the inoculation site, which develops a central ulcer that drains pus. There may also be enlargement of local lymph nodes.
- **Cellulitis** - this can take up to one month to develop and is clinically indistinguishable from other causes of cellulitis. Dissemination is usually rare but patients need to be reviewed for signs of local spread - eg, into the muscle. The most common nocardia involved are *N. brasiliensis* and *N. asteroides*.
- **Subcutaneous abscesses**.
- **Madura foot** - this is seen in North Africa, Sudan and India in inhabitants who walk barefoot. It has also been described in Australia. It is a chronic infection and, like mycetoma, the infection can pass to other structures. Madura foot usually results in gross deformity of the foot.

Disseminated nocardiosis

- Nocardia can be inhaled and may result in pneumonia which can then be disseminated to the blood and other organs. Up to 50% of nocardial pneumonias will disseminate.
- Alternatively, 20% of patients will inhale nocardia and not have an ensuing lung illness but the nocardia spreads into the bloodstream and causes illness elsewhere. Once nocardia is in the blood, the kidneys, skin, gastrointestinal tract and central nervous system can be infected.

- The pathology of the illness is usually the formation of suppurative abscesses leading to organ dysfunction. However, the central nervous system is the organ most commonly affected in nocardiosis.

Central nervous system

The central nervous system is affected in more than 30% of cases of nocardial infection. Infection usually results in abscess formation and presenting features include:

- Headache.
- Fever.
- Focal neurological deficits: depending on which area of the brain is affected - eg, seizures, cranial nerve palsies.[10]
- Some patients may be asymptomatic.

The abscesses are usually supratentorial and may be multiple and loculated. They can drain into the subarachnoid space, although examination of the cerebrospinal fluid does not usually reveal nocardial organisms.

Eyes

Nocardial infection of the eyes, leading to keratitis, is rare and usually follows a traumatic injury to the eye - eg, surgery.[11] However, it is potentially reversible with treatment.

Diagnosis

- Diagnosis is confirmed by the growth of nocardia from tissue samples sent for staining and culture. Nocardia is a strict aerobe and, on culture, colonies are seen with hyphae. There may also be a mildew odour. No serological methods are presently available for diagnosis.[2]
- Examples of specimens that can be sent are sputum, bronchoscopy specimens and skin or brain biopsies.
- Nocardia is very slow-growing and it can take up to four weeks for a positive culture. The microbiology laboratory needs to be informed if nocardia is suspected so that samples can be incubated for a longer period of time than usual.

- Nocardia is a Gram-positive rod; however, the appearances on Gram staining can be misleading. For example, patients are usually treated with routine antibiotics to begin with and these cannot only slow the growth of the nocardia but also lead to wall changes, meaning that the nocardia is unable to keep the Gram stain and thus appears as a Gram-negative species.[2]
- Nocardia isolates can now be identified by multilocus sequence analysis (MLSA) and their antimicrobial susceptibility determined.[3] [12]

Nocardia treatment and management[1]

- Treatment of nocardiosis is usually prolonged because of the risk of relapse. Six to 12 months of antimicrobial therapy for immunocompetent patients and a minimum of 12 months of treatment for immunocompromised patients or those with CNS dissemination is often recommended.
- Trimethoprim–sulfamethoxazole is the treatment of choice for nocardial infections. Imipenem, amikacin, and third-generation cephalosporins are also used; combination therapy can yield better results.
- Resistance within the nocardial species has been described - eg, resistance to erythromycin and some of the third-generation cephalosporins.
- Abscesses may require drainage either surgically or radiologically if appropriate. Empyemas should be drained to dryness. Good wound care management will also be needed. Keratitis has been successfully treated with cefazolin eye drops; these, however, are not available in the UK.[13]
- Patients who are at risk, or who have previously been infected, may need long-term prophylactic therapy - eg, sulfamethoxazole with trimethoprim in HIV patients with a CD4 count less than 250 cells/µL or in transplant recipients.

Complications

- Involvement of the lungs may lead to fibrosis and long-term difficulty in breathing.

- Scarring of areas of the skin that have been infected may lead to disfigurement and deformity that may lead to malfunction.
- Abscesses in the brain may lead to long-term neurological deficits.

Prognosis

Prognosis varies with the site of infection of nocardia. Involvement of the central nervous system increases the mortality and morbidity. Furthermore, the presence of disseminated nocardiosis or involvement of more than one site also carries a poorer prognosis.

Nocardia prevention

- Avoid walking barefoot in high-risk areas and also ensure that cuts and grazes are appropriately covered.
- A high index of suspicion is required for the detection of cases of nocardia.

Genetics of nocardia

With the advent of molecular methodologies, specifically gene sequencing, a huge number of new Nocardia species have been identified. Even previously recognised species have undergone evaluation, reassessment, and inclusion into various groups and complexes. [14]

Further reading

- Rathish B, Zito PM; Nocardia. StatPearls, Jan 2023.

References

1. Mehta HH, Shamoo Y; Pathogenic Nocardia: A diverse genus of emerging pathogens or just poorly recognized? PLoS Pathog. 2020 Mar 5;16(3):e1008280. doi: 10.1371/journal.ppat.1008280. eCollection 2020 Mar.
2. Saubolle MA, Sussland D; Nocardiosis: review of clinical and laboratory experience.; J Clin Microbiol. 2003 Oct;41(10):4497-501.

3. Komaki H, Ichikawa N, Hosoyama A, et al; Genome based analysis of type-I polyketide synthase and nonribosomal peptide synthetase gene clusters in seven strains of five representative Nocardia species. BMC Genomics. 2014 Apr 30;15:323. doi: 10.1186/1471-2164-15-323.
4. Lai KW, Brodell LA, Lambert E, et al; Primary cutaneous Nocardia brasiliensis infection isolated in an immunosuppressed patient: a case report. Cutis. 2012 Feb;89(2):75-7.
5. Warnatz K, Peter HH, Schumacher M, et al; Infectious CNS disease as a differential diagnosis in systemic rheumatic diseases: three case reports and a review of the literature.; Ann Rheum Dis. 2003 Jan;62(1):50-7.
6. Lebeaux D, Morelon E, Suarez F, et al; 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.
7. Aggarwal D, Garg K, Chander J, et al; Pulmonary nocardiosis revisited: A case series. Lung India. 2015 Mar-Apr;32(2):165-8. doi: 10.4103/0970-2113.152638.
8. Lederman ER, Crum NF; A case series and focused review of nocardiosis: clinical and microbiologic aspects. Medicine (Baltimore). 2004 Sep;83(5):300-13.
9. Kumar N, Ayinla R; Endobronchial pulmonary nocardiosis.; Mt Sinai J Med. 2006 May;73(3):617-9.
10. Ponticelli C, Campise MR; Neurological complications in kidney transplant recipients.; J Nephrol. 2005 Sep-Oct;18(5):521-8.
11. Rao SK, Madhavan HN, Sitalakshmi G, et al; Nocardia Asteroides keratitis: report of seven patients and literature review.; Indian J Ophthalmol. 2000 Sep;48(3):217-21.
12. Baio PV, Ramos JN, dos Santos LS, et al; Molecular identification of nocardia isolates from clinical samples and an overview of human nocardiosis in Brazil. PLoS Negl Trop Dis. 2013 Dec 5;7(12):e2573. doi: 10.1371/journal.pntd.0002573. eCollection 2013.
13. Faramarzi A, Feizi S, Javadi MA, et al; Bilateral nocardia keratitis after photorefractive keratectomy. J Ophthalmic Vis Res. 2012 Apr;7(2):162-6.
14. Conville PS, Brown-Elliott BA, Smith T, et al; The Complexities of Nocardia Taxonomy and Identification. J Clin Microbiol. 2017 Dec 26;56(1):e01419-17. doi: 10.1128/JCM.01419-17. Print 2018 Jan.

Authored by:	Peer Reviewed by: Dr Hayley Willacy, FRCGP	
Originally Published: 20/11/2023	Next review date: 20/09/2023	Document ID: doc_1655

View this article online at: patient.in/doctor/nocardia

Discuss Nocardia and find more trusted resources at Patient.