Short reports

Mixed pulmonary infection with *Nocardia*, *Candida*, methicillin-resistant *Staphylococcus aureus*, and group D *Streptococcus* species

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Summary

A 67-year-old man on prednisolone and azathioprine for ulcerative colitis, developed severe pneumonia due to *Nocardia otitidis cavium*, methicillin-resistant *Staphylococcus aureus*, a group D *Streptococcus* and *Candida albicans*. The patient responded well to aggressive antimicrobial therapy.

Keywords: pneumonia, *Nocardia otitidis cavium*, *Staphylococcus aureus*, *Streptococcus*, *Candida albicans*

A 67-year-old man with a long-standing history of ulcerative colitis, on azathioprine and high dose prednisolone, was admitted with a one-week history of fever and productive cough. His general practitioner had previously given him a course of oral cefuroxime axetil, 250 mg bid, with no effect.

On admission he had clinical and radiological features of left lower lobe pneumonia. His initial white cell count was 10.1×10^9 cells/l. He was started on intravenous ceftazidime, 2 g 8 hourly, and gentamicin, 80 mg 8 hourly, without any response and his clinical and radiological condition continued to deteriorate. A direct Gram stain, a Ziehl–Neelsen and a modified Ziehl–Neelsen stain, performed on freshly expectorated sputum, yielded packed fields of Gram-positive cocci, numerous yeasts and hyphae, and weakly acid-fast, Gram-positive, branching filaments. A presumptive diagnosis of a mixed infection due to *Nocardia*, *Candida* and *Staphylococcus* and/or *Streptococcus* was made and the antimicrobial therapy was changed to intravenous imipenem 500 mg 6 hourly, co-trimoxazole, 120 mg/kg daily in four divided doses, and fluconazole, 50 mg bid. The azathioprine was discontinued and the dose of prednisolone was gradually tapered down. His condition improved but sputum culture yielded a methicillin-resistant *Staphylococcus aureus* (MRSA) which was resistant to cloxacillin, gentamicin, erythromycin, co-trimoxazole, ciprofloxacin and imipenem, but sensitive to vancomycin, fusidic acid, clindamycin and netilmicin. The sputum specimens were all cultured without significant delays and were rapidly digested at room temperature with *N*-acetyl cysteine, to a final dilution of 1 in 200 before culture, effectively diluting out commensals.

A group D *Streptococcus* which was sensitive

to vancomycin, fusidic acid and ampicillin was cultured. The latter organism is increasingly being identified as a pathogen in immunocompromised patients. *Candida albicans* and *Nocardia* species were also cultured. The latter was later identified as *Nocardia otitidis cavium*.

Subsequently the patient was started on additional parenteral vancomycin and fusidic acid and his condition improved markedly as assessed by repeated clinical and radiological examinations and laboratory investigation. The latter included regular Gram staining and culturing of the sputum. The *Nocardia* organisms were detectable in the sputum on direct Gram stains for up to 10 days after starting effective therapy. Vancomycin was stopped after eight days of therapy. Fluconazole, fusidic acid, imipenem and intravenous co-trimoxazole were given for 14 days, while the latter preparation was changed to oral form and continued for a further eight weeks at a dose of 960 mg bid. The patient has remained asymptomatic since then.

Discussion

To our knowledge this is the first reported case of multiple pulmonary infection of such magnitude involving *Nocardia otitidis cavium*, and having a favourable outcome. We believe that all the organisms cultured, played a pathogenic role. The presence of large numbers of fungal hyphae support a pathogenic role for *Candida*, while the presence of large numbers of MRSA and group D *Streptococcus* similarly supports a pathogenic role for these organisms. The clinical condition of the patient indicated aggressive antimicrobial therapy against all these organisms. We believe that this contributed to the rapid improvement in the patient's condition, as did the early discontinuation of azathioprine.

Nocardia species are a group of aerobic Gram-positive branching, filamentous organisms which cause an acute or chronic, often disseminated disease. They are important members of the soil microflora worldwide. *Nocardia* can infect any individual but is much more common in patients with impaired immunity (box 1). It is not a rare condition, though it is not given prominent attention in the medical literature. It can be easily missed if the index of suspicion is low as it can resemble more common diseases, such as tumours and

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Nocardiosis: predisposing factors
<ul style="list-style-type: none">● cytotoxic chemotherapy● immunosuppressants including corticosteroids● post-splenectomy● haematological malignancies● AIDS● diabetes● alcoholism● underlying lung disease, eg, cancer, bronchiectasis

Box 1

other granulomatous diseases.¹ Most cases begin as pulmonary infection and disseminate haematogenously, with abscess formation in the brain, kidneys, bones, etc. Infection may also start as skin or subcutaneous abscess.

Several species have been documented to be pathogenic in man. These are *N asteroides*, *N brasiliensis*, *N farcinica*, *N otitidis caviarum*, *N nova* and *N transvalensis*.² The diagnosis is made by culture of the organism. However, as this can take weeks, therapy should be started on microscopic morphology. A chest X-ray is useful in narrowing the differential diagnosis but is nonspecific (box 2).³

Sputum examination is diagnostic in only a third of cases, and although oropharyngeal colonisation can occur, isolation of *Nocardia* from the sputum of an immunocompromised host should be regarded as pathogenic. It is imperative that in immunocompromised patients with lung infiltrates of uncertain causation, bronchoscopy should be performed in conjunction with BAL or even open lung biopsy to get a diagnosis. The organism can also sometimes be isolated from blood cultures.

Nocardiosis: chest X-ray findings
<ul style="list-style-type: none">● solitary pulmonary mass● pulmonary infiltrates● pleural thickening● chest wall involvement

Box 2

In vitro they show susceptibility to several antibiotics including sulphonamides, co-trimoxazole, imipenem, amikacin, minocycline, fusidic acid, ceftriaxone, cefotaxime, and co-amoxycylav.⁴ Resistance is, however, common, especially with *N farcinica*.

The standard therapy for nocardiosis is co-trimoxazole; the combination of amikacin and imipenem is usually reserved for resistant strains or for patients allergic to sulpha drugs. Minocycline and co-amoxycylav are alternative medications.⁵ It is usually recommended that treatment be continued for three to six months in mild infections and for six to 12 months in severe infections, because of the risk of relapse. Patients who are on steroids or other immunosuppressants should have the dose of the steroid tapered and the immunosuppressant drug should be stopped if possible. In this case 10 weeks of treatment proved adequate. This could possibly be due to the intensive initial therapy; imipenem, co-trimoxazole and fusidic acid all show activity against *Nocardia*. Further investigations to study the efficacy of short-course therapy is warranted. This would improve patient compliance and reduce toxicity.

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5 Thomas CF Jr, Jones TK, Edson RS. A 74-year-old woman with dyspnoea, fever, and cough. *Mayo Clin Proc* 1995; **70**: 397–400.