

# Central nervous system *Nocardia* infection in a lymphoma patient: a diagnostic challenge resolved by 16s PCR

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## Introduction

Central nervous system mass lesions in immunocompromised patients are a diagnostic challenge. Infection with the aerobic actinomycete *Nocardia* is a relatively rare but important cause that can mimic tumours or other mass lesions. Diagnosis requires a high clinical suspicion and is often difficult without biopsy material. Treatment options are limited, particularly for cephalosporin-resistant species such as *Nocardia farcinica* or in patients who develop side effects to established treatments such as co-trimoxazole hence establishing the species responsible can help guide management, even in the absence of sensitivity testing.

## Case presentation

A 74-year old lady with an aortic valve replacement in 2009 for degenerative valve disease was diagnosed with follicular lymphoma having presented in 2015 with lymphadenopathy and lung nodules. She underwent chemotherapy achieving complete remission in early 2016 and had been on rituximab maintenance for 10 months when she presented with diplopia, headache, confusion and hyponatraemia.

MRI showed a parietal mass lesion and she was started empirically on meropenem and vancomycin plus dexamethasone.

An open biopsy was performed and a small amount of yellowish pus-like fluid was aspirated. CSF and biopsy material were negative for organisms including TB, fungi and *Nocardia* on stains, culture and TB PCR.

Cryptococcal antigen, toxoplasma PCR and viral screen including polyoma and HHV8 were negative.

Histology results suggested infection and not lymphoma recurrence. Blood cultures and echocardiogram looking for vegetations were negative

Material from the first biopsy was not sent for 16s PCR

## *Nocardia farcinica*

The taxonomy of the *Nocardia* group is complex but has been resolved using genetic analysis. Prior to this isolates were grouped as *Nocardia asteroides* complex and recognised to fall into a defined set of antibiotic susceptibility profiles, classified by Wallace et al as 'susceptibility type I – VI'. Subsequently, *Nocardia farcinica* isolates have been shown to correspond to susceptibility type V with an antibiotic susceptibility profile that is predictable for many drugs (table 1)(1,2,3,4)

Highly likely to be sensitive	Uncertain	Highly likely to be resistant
Co-trimoxazole	Moxifloxacin	Ceftriaxone
Imipenem (+/- cilastatin)	Minocycline	Ampicillin
Meropenem	Ciprofloxacin	
Linezolid	Tigecycline	
Amikacin	Co-amoxiclav	

Table 1: Predicted sensitivity of *Nocardia farcinica* in the absence of susceptibility testing

## Management

Intravenous imipenem /cilastatin therapy once again achieved good clinical and radiological regression over three months and oral switch to co-trimoxazole was attempted. This resulted in pancytopenia, renal failure and nausea, which resolved on removal of co-trimoxazole. Re-challenge with co-trimoxazole caused recurrence of renal impairment suggesting interstitial nephritis as a mechanism. Repeat MRI appearances have been stable and oral therapy with combination minocycline 200mg BD and moxifloxacin 400mg OD was commenced; persistent pancytopenia following bendamustine chemotherapy has prevented the use of linezolid.

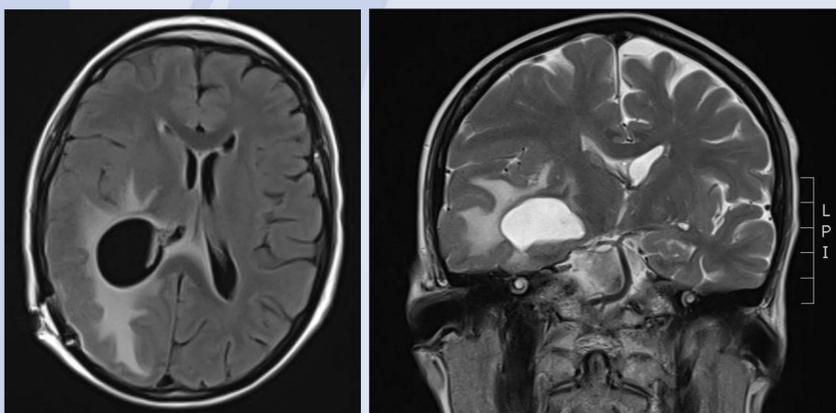


Figure 1: MRI appearances at presentation in January 2017

She received 8 weeks of meropenem and linezolid and on completion she underwent placement of an External Ventricular Device (EVD) followed by internalisation of a ventriculo-peritoneal (VP) shunt. However, symptoms recurred 3 weeks after stopping antibiotics with worsening MRI appearances involving abscess formation at the cranio-cervical junction, the posterior fossa and upper spinal cord. An urgent foramen magnum decompression with further biopsy was performed which once again suggested infection but was negative on repeat tests including bacterial and fungal culture as well as PCR for TB.

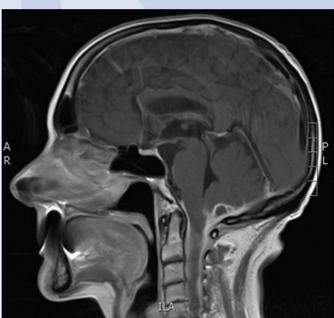


Figure 2: Recurrence of infection with abscess at cranio-cervical junction and widespread enhancement of upper spinal cord

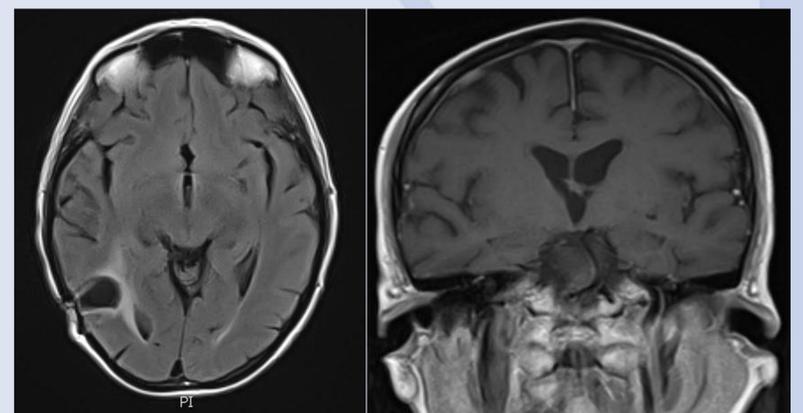


Figure 3: Improved MRI appearances in August 2017 following prolonged IV imipenem therapy

## Outcome

Following an improvement clinically and radiologically with further imipenem she was converted to a combination of oral minocycline 200mg BD and moxifloxacin 400mg OD with a plan for 1 year of treatment in total. This has been complicated by a further recurrence of pancytopenia and a mild elevation of ALT which is possibly linked to minocycline use at the dose given. This has since been withheld and she continues on monotherapy moxifloxacin until alternative causes of pancytopenia have been ruled out.

## Conclusion

- *Nocardia* can cause CNS mass lesions in immunocompromised patients and biopsy should be considered in all cases of uncertainty.
- 16s PCR can be helpful if routine recovery methods are negative; species-level identification can guide treatment.
- Treatment with co-trimoxazole remains prone to serious side effects, with alternative oral options being limited in patients with cytopenia
- Empirical therapy for brain infection may treat *Nocardia*, but cure requires prolonged therapy.

## Diagnosis

PCR of the 16s ribosomal RNA genes was however positive for *Nocardia*, with sequence homology suggesting *N. farcinica* and *N. kroppenstedtii* species.

## References

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