IDCases 27 (2022) e01444

Contents lists available at ScienceDirect

IDCases

journal homepage: www.elsevier.com/locate/idcases

Case report

Spinal nocardiosis: A rare tuberculosis mimic in an HIV infected patient

Monique Knoetzen[a,*], Pieter-Paul Straus Robbertse[b], Arifa Parker[c]

[a] Department of Internal Medicine, Karl Bremer Hospital, Cape Town 7530, South Africa
[b] Division of Cardiology, Department of Medicine, Stellenbosch University and Tygerberg Hospital, Cape Town 7505, South Africa
[c] Division of General Internal Medicine and Infectious Diseases, Department of Medicine, Stellenbosch University and Tygerberg Hospital, Cape Town 7505, South Africa

ARTICLE INFO

Article history:
Received 12 December 2021
Received in revised form 3 February 2022
Accepted 3 February 2022

Keywords:
HIV
Nocardia
Spinal tuberculosis

ABSTRACT

Despite advances in treatment, human immunodeficiency virus/tuberculosis (HIV/TB) coinfection remains highly prevalent in selected low- and middle income countries. The diagnosis of tuberculosis frequently proves challenging in the setting of advanced HIV, as patients may present with atypical features. A high index of suspicion must be maintained for TB in this setting, but it is critical that alternative diagnoses are considered. A myriad of opportunistic infections may mimic TB and a definitive microbiological diagnosis prior to TB treatment should always be sought. We report on a case of a young, HIV positive male who presented with a delayed diagnosis of nocardiosis that was thought to be TB of the spine. Despite extensive laboratory and radiological investigations, the diagnosis was only made after tissue was cultured. Earlier diagnosis of this mimic would have led to appropriate therapy and may have improved the outcome for this patient.

Case

A 37-year-old HIV positive male from a rural area presented to the emergency department with a 3-week history of pathological back pain and constitutional symptoms. He complained of severe pain located at his mid thoracic spine (T-spine). The pain resulted in difficulty completing activities of daily living and nocturnal wakening. He also experienced night sweats, loss of appetite and weight loss. No fever or cough was reported. There was no history of recent or prior injuries. His medical history included Rifampicin and Isoniazid sensitive pulmonary TB which was successfully treated with a standard regimen of Rifampicin, Isoniazid, Ethambutol and Pyrazinamide 2 years prior. His latest CD4 count was 47 cells/μL. He was reinitiated on first line antiretroviral therapy (Tenofovir, Lamivudine, Efavirenz) 3 months prior to presentation following a treatment interruption of 2 years.

Clinical examination revealed generalised wasting and lymphadenopathy. No bony tenderness was present over his spinal column and no sensory or motor fallout was present. His chest radiograph was unremarkable. The thoracic spine radiographs raised the suspicion of T8 and T9 vertebral collapse (Fig. 1a).

A week later, the patient reported worsening pain and constitutional symptoms. His clinical examination now revealed central T-spine tenderness. No deformity or neurological fallout was noted. His blood results showed an elevated C –reactive protein of 266 mg/L (normal range < 10 mg/L), a mildly elevated white cell count of 11100/μL (normal range 3920 – 10400/μL), normal creatinine, negative serum cryptococcal latex antigen test and a unsuppressed HIV viral load of 3636 copies/mL. In light of his poor quality spine x-rays, a normal chest radiograph and the absence of neurological fallout, repeat imaging and out-patient follow-up was arranged.

His symptoms progressively worsened. A week later he had fever, tachycardia and a T-spine gibbus was evident. While awaiting magnetic resonance imaging (MRI) (Fig. 1b), he remained systemically unwell and developed focal neurological deficits in the form of decreased power and sensation involving the 1st lumbar (L1) to 1st sacral (S1) spinal roots. His urine lipoarabinomannan antigen and sputum TB polymerase chain reaction (PCR) was negative. Empiric TB treatment was initiated as resources for spinal biopsy was limited. Additional sputa, blood and urine cultures for TB were requested.

Despite receiving TB treatment, the patient gradually became confused, developed cerebellar signs and unilateral gaze palsy. Computed tomography (CT) of his brain and chest were requested (Fig. 2).

With neurological deficits worsening and inflammatory markers rising despite broad spectrum antibiotics and anti-tuberculous agents, the differential diagnosis broadened to include drug resistant

* Corresponding author.
E-mail address: monique.knoetzen@gmail.com (M. Knoetzen).

https://doi.org/10.1016/j.idcr.2022.e01444
2214-2509/

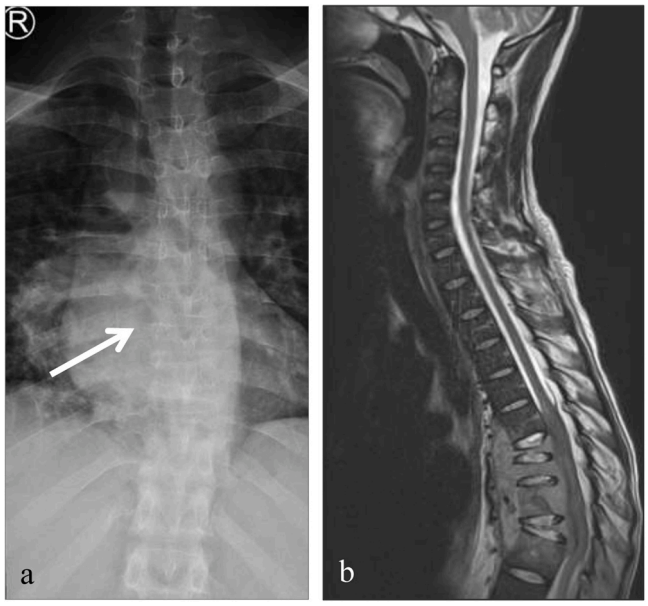

Fig. 1. Spinal x-ray (a) and MRI (b) of the thoracic spine. Fig. 1a: The spinal x-ray taken between the first and second presentation raised the suspicion of 8th and 9th thoracic vertebra (white arrow) collapse. Interpretation was limited by the quality of the original x-ray and the absence of a lateral radiograph. Fig. 1b: Sagittal, T2 weighted MRI demonstrating infiltration at T6 –T11 with spinal cord involvement and sparing of the intervertebral discs. Extensive mediastinal and subcarinal lymphadenopathy with a right para-hilar mass nodal complex with central breakdown was visualised (not shown). An adjacent right pleural collection and a small right sided pleural effusion were present. Although not classic, TB spondylodiscitis was considered as cause for the findings. Lymphoma was on the list differential diagnoses.

TB, lymphoma, toxoplasmosis, cryptococcosis or another granulomatous infection with an atypical organism. Sputum, blood cultures, lymph node aspirates and bronchial washings for TB remained negative.

A transthoracic needle aspiration of the paravertebral collection showed inflammation with occasional granulomas and atypical cells on histology. Auramine staining and mycobacterial culture were negative. One week later, the bacterial culture confirmed the diagnosis of a *Nocardia* species (Fig. 3). Using PCR and DNA sequencing of the 16SrRNA, the specific species could be identified as *Nocardia beijingensis*.

Case management

By the time the diagnosis of disseminated nocardiosis was made, the patient was confused with cranial nerve 6 fallout, visual impairment and bilateral sensory- and motor fallout most severely affecting his right leg and left hand.

High dose oral cotrimoxazole (800/160 milligram 8 hourly) with intravenous (IV) imipenem 1 g (g) 6 hourly for four weeks was initiated. TB treatment was discontinued. After four weeks of cotrimoxazole and imipenem, the patient had made a slow but steady recovery. His clinical condition stabilized, he remained apyrexial and his pain improved. He became fully orientated and he had regained some neurological function in his limbs. His cranial nerve fallout persisted. A repeat CT brain revealed no change in the intracranial lesions.

The broth dilution minimum inhibitory concentration (MIC) antibiogram proved sensitivity to amikacin, ceftriaxone, clarithromycin, imipenem, cotrimoxazole and linezolid. Based on the antibiotic sensitivity profile and poor clinical response, high dose IV ceftriaxone (2 g IV 12 hourly) was added while continuing oral cotrimoxazole and IV imipenem for another 4 weeks. This combination resulted in improvement of global neurological functioning and vision. He received multi-disciplinary rehabilitation. He regained his ability to sit up and eat independently. Significant improvements in gross motor function were obtained but his fine motor function was still affected.

He was discharged with a walking frame, thoracic spinal brace and moderate assistance to complete activities of daily living. Outpatient rehabilitation continued. Even though he made a remarkable recovery, he remains unemployed and is receiving a disability grant due to irreversible neurological damage.

Discussion

Nocardiosis is an uncommon and potentially life threatening infection caused by soil borne aerobic bacteria. They are recognized as gram positive, beading and branching filaments on microscopy. Nocardia is an opportunistic pathogen but infection in immune competent individuals do account for about one third of cases [1].

Authors report an incidence rate of 500–1000 cases per year in the United States [1,2] while a recent review found the prevalence varied between 0.4% and 3.6% among immunosuppressed patients [3].

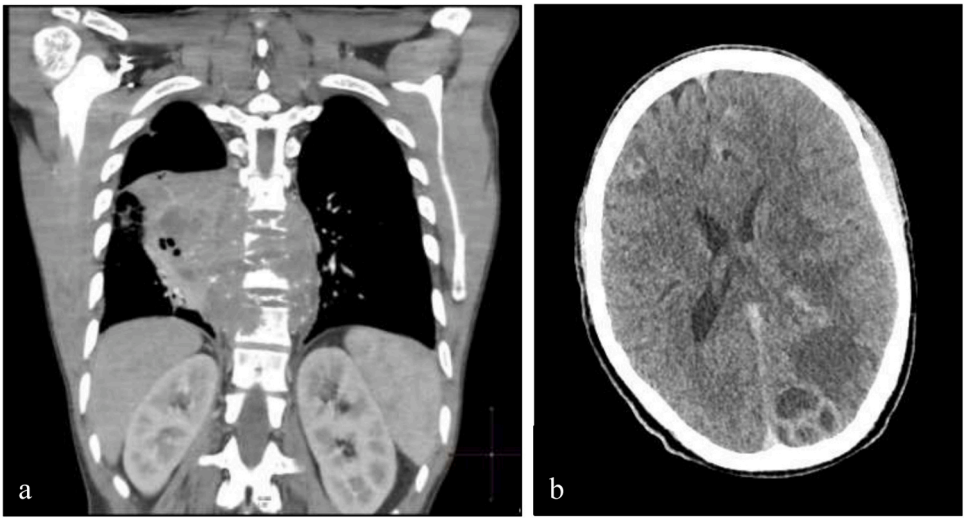

Fig. 2. Computed tomogram (CT) of the chest (a) and brain (b). Fig. 2a: CT chest, coronal reconstruction, demonstrating a paravertebral collection extending into the apex of the right lower lobe with dense consolidation, cavitation and pulmonary nodules. Bilateral pleural effusions and extensive lymphadenopathy (not shown) were present. Fig. 2b: Post contrast CT of the brain shows multiple abscesses with surrounding oedema in bilateral hemispheres, the midbrain and pons.

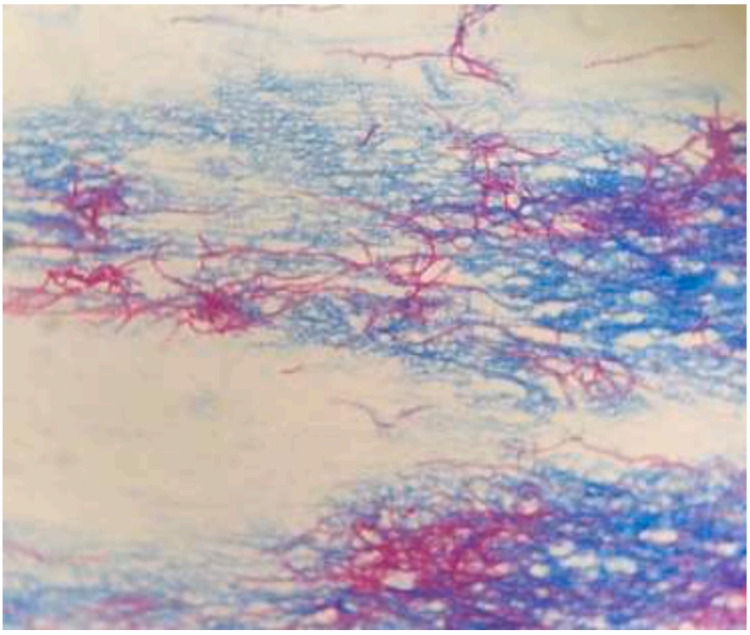

Fig. 3. Kinyoun stain. Nocardia seen as pink beaded branching filaments.

N. beijingensis was first described in 2001 in China. Although it has become more prevalent in the last decade, only two cases of spinal infection due to *N. beijingensis* have been documented in prior literature [4,5]. *N. asteroides* appears to be the predominant organism responsible for spinal nocardiosis [2,4–6].

Nocardiosis presents in one of four clinical forms: Primary cutaneous, pulmonary (most common), central nervous system (CNS) or disseminated disease. Presentation is variable and depends on its clinical form and severity [1,7,8]. Dissemination can occur to any organ but CNS involvement, usually in the form of cerebral abscesses, is most common [1,3,8,9]. In contrast, primary spinal nocardiosis is exceedingly rare with less than thirty cases reported in the literature up to 2020 [2,6,10,11].

Low awareness, poor access to diagnostic tests and the slow growing nature of nocardia often leads to a delay in diagnosis and treatment initiation [2,6,10,12]. Nocardiosis is difficult to diagnose as symptoms are non-specific with no pathognomonic clinical features. Pathology can mimic other granulomatous infections and malignancies [2,6,13,14]. The definitive diagnosis relies on invasive sampling that requires additional culture time [7,9,12]. Treatment is challenging as new molecular techniques are identifying additional species, each with its own antimicrobial sensitivity profile [7,12]. Data regarding best treatment guidelines are limited and largely based on expert opinion therefore sensitivity testing remains the gold standard [1,2,7,8]. In general, an extended course of a sulfonamide based regime, commonly cotrimoxazole, is the rule. Treatment duration remains uncertain and varies according to host immunity and extent of the disease. Combination therapy is indicated in severe disease [4,10,11,14].

TB may prove challenging to confirm in the immunocompromised host, leading to empiric TB treatment in many cases. TB and nocardiosis may be similar in their non-specific presentation with symptoms that are dependent on many factors. Both have a predilection for the lungs and they tend to disseminate more frequently in immunosuppressed patients. CNS involvement is encountered in both TB infection and nocardiosis. Radiological findings are similar and it is difficult to differentiate vertebral osteomyelitis caused by either of these granulomatous infections from one another on MRI alone. Whether Spinal TB or spinal nocardiosis, prompt bacteriological diagnosis is essential to appropriate early treatment to limit morbidity and mortality [13–15].

Conclusion

In settings with a high TB prevalence, clinicians should be aware of infections that may mimic common TB presentations. In this regard, awareness of nocardiosis, especially in the immunocompromised patient, is important. Once spinal tuberculosis is suspected, early microbiological sampling is crucial to provide an accurate diagnosis and guide appropriate therapy.

Ethical approval

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Funding resources

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

CRediT authorship contribution statement

Monique Knoetzen: Conception and design, Acquisition of data, Analysis and interpretation of data, Writing, drafting and revision, Final approval. **Pieter-Paul Straus Robbertse:** Conception and design, Analysis and interpretation of data, Writing, drafting and revision, Final approval. **Arifa Parker:** Design, Analysis and interpretation of data, Drafting and revision, Final approval.

Conflict of interest

None.

Acknowledgements

We would like to thank the microbiology and radiology department at Tygerberg Hospital for providing us with the images used in this article.

References

[1] Deepa Rawat, Venkat Rajasurya, Rebanta K, Chakraborty SS. Nocardiosis [Internet]. StatPearls (Internet). Treasure Island: StatPearls Publishing. Treasure Island. StatPearls Publishing,; 2020 [cited 2020 Jun 16]. Available from. ⟨https://www.ncbi.nlm.nih.gov/books/NBK526075⟩.

[2] Ma F, Kang M, Liao YH, Lee GZ, Tang Q, Tang C, et al. Nocardial spinal epidural abscess with lumbar disc herniation A case report and review of literature. Med (U S) 2018;97(49):2–7.

[3] Minero MV, Marín M, Cercenado E, Rabadán PM, Bouza E, Muñoz P. Nocardiosis at the turn of the century. Med (Baltim) 2009;88(4):250–61.

[4] Tanaka H, Kiko K, Watanabe Y, Yaguchi T, Oya S, Shiojiri T. Miliary cerebrospinal lesions caused by Nocardia beijingensis in an immunocompetent patient. IDCases 2020;20:00737. https://doi.org/10.1016/j.idcr.2020.e00737

[5] Rigotti S, Marocco S, Angheben A, Screpis D, Piovan G, Zorzi C. The first case of Nocardia beijingensis isolated infection to lumbar spine. J Neurosci Rural Pr 2015;6(3):462–3.

[6] Johnson P, Ammar H. Nocardia brasiliensis vertebral osteomyelitis and epidural abscess. Case Rep 2013;2013. bcr2012008400–bcr2012008400.

[7] Saubolle MA, Sussland D. Nocardiosis: Review of clinical and laboratory experience. J Clin Microbiol 2003;41(10):4497–501.

[8] D. Spelman, Clinical manifestations and diagnosis of nocardiosis [Internet]. uptodate. 2020 [cited 2020 Jun 18]. Available from: https://www.uptodate.com/contents/clinical-manifestations-and-diagnosis-of-nocardiosis.

[9] Anagnostou T, Arvanitis M, Kourkoumpetis TK, Desalermos A, Carneiro HA, Mylonakis E. Nocardiosis of the central nervous system: Experience from a general hospital and review of 84 cases from the literature. Med (U S) 2014;93(1):19–32.

[10] Hamdad F, Vidal B, Douadi Y, Laurans G, Canarelli B, Choukroun G, et al. Nocardia nova as the causative agent in spondylodiscitis and psoas abscess. J Clin Microbiol 2007;45(1):262–5.

[11] Peeters I, Casselman JW, Vandecasteele SJ, Janssen A, Regaert B, Vantomme N, Vanopdenbosch LJ. Multiple nocardial abscesses of the brainstem and spinal cord diagnosed after an open biopsy through a cervical partial central corpectomy: Case report. J Neurosurg Spine 2015;23(3):290–3.

[12] Conville PS, Brown-Elliott BA, Smith T, Zelazny AM. The complexities of nocardia taxonomy and identification. In: Kraft CS, editor. J Clin Microbiol [Internet], 56. 2017 8. p. 1–10. (Available from). ⟨https://jcm.asm.org/content/56/1/e01419-17⟩.

[13] Bertrán-López J, Abbott A, Archibald LK, Benninger L, Lascano J, Kalyatanda G. Disseminated nocardia beijingensis masquerading as pulmonary tuberculosis in a patient with human immunodeficiency virus/acquired immune deficiency syndrome. Open Forum Infect Dis 2020;7(6):1–5.

[14] Steinbrink J, Leavens J, Kauffman CA, Miceli MH. Manifestations and outcomes of nocardia infections Comparison of immunocompromised and non-immunocompromised adult patients. Med (U S) 2018;97(40).

[15] Galloway KM, Parker R. Could an increase in vigilance for spinal tuberculosis at primary health care level, enable earlier diagnosis at district level in a tuberculosis endemic country? Afr J Prim Heal Care Fam Med [Internet] 2018;10(1):1–9. (Available from). ⟨https://phcfm.org/index.php/phcfm/article/view/1666⟩.