CASE REPORT

Central and peripheral nervous system involvement in neuromelioidosis

Muhammad A Arif,¹ Muhammad H Abid,² Radhakrishnan Renganathan,¹ Khurram A Siddiqui¹

¹Department of Neurology, Medical Institute, Al Ain Hospital, Al Ain, UAE

²Department of Internal Medicine/Academic Affairs, Al Ain Hospital, Al Ain, UAE

Correspondence to
Dr Radhakrishnan Renganathan,
jandumbo@yahoo.com

Accepted 8 October 2015

SUMMARY

We report a case of a 33-year-old Sri Lankan man who presented with flaccid quadriparesis with brainstem signs and acute motor axonal polyneuropathy. MRI of the brain showed multiple abscesses with ring enhancement seen predominantly in the brainstem and upper cervical cord. The patient was initially treated with intravenous immunoglobulin, considering this to be a form of Guillain-Barré syndrome. Cerebrospinal fluid, however, showed lymphocytic pleocytosis with raised protein. Tests for *Brucella*, tuberculosis, toxoplasmosis, syphilis and HIV were negative. Chest X-ray revealed a cavity in the left lung, which, on bronchoscopy, showed a collection of purulent secretions. Culture of these secretions grew *Burkholderia pseudomallei*. The patient was treated with two courses of intravenous antibiotics, with resultant radiological improvement; however, with significant morbidity.

BACKGROUND

Neuromelioidosis is a rare infection of the nervous system. It is caused by *Burkholderia pseudomallei*, and carries a high rate of mortality and morbidity. The most common presentation is outside the nervous system and manifests as pneumonia. Neurological manifestations of melioidosis, although rare, have been described. Neuromelioidosis accounts for approximately 4% of all melioidosis cases. It is associated with a significant debilitating morbidity and mortality rate reaching as high as 25%. What was interesting about this case was the presentation: the patient had initial peripheral nervous system involvement followed by central nervous system (CNS) involvement. He also had multiple ring-enhancing lesions, with progressive findings on brain neuroimaging, which made the diagnosis challenging. He developed a lung lesion, which, on culture of bronchoscopic lavage, grew *B. pseudomallei*.

CASE PRESENTATION

A 33-year-old Sri Lankan man, a zoo worker with no known medical conditions, presented to the emergency department, after a 3-day history of nausea, vomiting and difficulty walking. On his third inpatient day, he developed dysphagia and loss of protective reflexes, for which he was mechanically ventilated. His wife gave a travel history of a recent trip to Sri Lanka. There was also a history of a recent epidural injection, which he had received for back pain about a month earlier. At

the zoo, he took care of primarily healthy lions and tigers.

At presentation, he was diaphoretic. His temperature was normal, heart rate was 96 bpm, blood pressure was 131/98 mm Hg and his respiratory rate was 18 breaths/min. There was no dysautonomia. Neurological examination showed flaccid quadriparesis with 3/5 power in both upper and lower extremities, and absent reflexes. While intubated, he was able to follow one-step commands. His initial investigations showed leucocytosis and raised C reactive protein of 165 mg/L. His initial MRI of the brain with gadolinium, showed multiple small abscesses with ring enhancement seen in the posteroinferior brainstem and upper cervical cord (figure 1A). Nerve conduction studies (NCS) showed symmetrical motor axonal polyneuropathy.

The day after admission, the patient deteriorated further and his consciousness level worsened; his neurological examination showed bilateral pinpoint pupils with absent corneal reflexes. He had gaze paresis in horizontal directions bilaterally with preserved vertical gaze on oculoccephalic reflex testing. Motor power deteriorated to 1/5 in upper and lower limbs. All deep tendon reflexes were absent

Figure 1 (A) Brain MRI fluid-attenuated inversion recovery showing a hyperintense lesion involving the posterior brainstem, extending from midbrain to medulla at diagnosis. (B–F) Brain MRIT1 with gadolinium showing multiple ring-enhancing lesions in the posterior brainstem with worsening and extension of lesions into the corticospinal tract with enhancement. (G) Brain MRIT1 with gadolinium showing significant resolution of the lesions.

CrossMark

To cite: Arif MA, Abid MH, Renganathan R, et al. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2015-211001

Figure 1 Continued

and plantars were flexor. Cerebrospinal fluid (CSF) examination showed lymphocytic pleocytosis with 129 lymphocytes with raised protein at 2080 mg/L. CSF glucose was normal. The patient was started on a combination of ampicillin, ceftriaxone, vancomycin, antituberculosis (TB) medicines (isoniazid, rifampicin, pyrazinamide and ethambutol) and intravenous immunoglobulin (IVIG).

There was no improvement in the patient's condition for a week. Follow-up MRI of the brain with gadolinium showed worsening and extension of the lesions, with involvement of the bilateral thalamus and internal capsule extending up to the corona radiata along the corticospinal tract, with enhancement (figure 1B–F). There were more extensive ring-enhancing lesions seen in the medulla oblongata and cerebellum. CSF was negative for acid-fast bacilli (AFB), TB PCR, Quantiferon TB, antitoxoplasma antibodies, herpes simplex virus PCR and bacterial antigen. Fungal culture was negative. *Listeria* antibodies were negative. CSF cytology was negative for malignant cells. Serum ACE levels were normal. Autoimmune and HIV screens were negative. Follow-up chest X-ray showed a cavitory lesion in the left mid-lung zone at the end of his 2-week treatment. CT of the thorax showed bilateral lower lobe consolidation, with a left lobe cavity lesion.

Bronchoscopy performed by the pulmonologist revealed severely inflamed bronchial mucosa in the entire right lower lobe and left middle lobe, with a large amount of purulent secretion obstructing several ostia. Bronchial biopsy was suggestive of bronchitis of the left middle lobe. Culture of bronchoalveolar lavage grew *B. pseudomallei*. Diagnosis of neuromelioidosis with brainstem abscesses and meningoencephalitis was considered, and a course of sulfamethoxazole-trimethoprim and meropenem was given for 4 weeks.

In the following weeks, the patient's neurological examination showed improvement; his pupils were equal at 3 mm and reacting to light. Corneal reflex was present in the right and absent in the left eye. He had a gag/tracheal reflex on suctioning. He still had flaccid quadriplegia and absent reflexes. Postantibiotic course, CSF analysis showed lymphocytic pleocytosis and raised protein of 1604 mg/L. Repeat MRI scan with contrast showed enlarged cerebral lesions with enhancement. There was perilesional oedema of the previously noticed ring-enhancing lesions, which was progressing. There was no evidence to suggest regression. While there were no significant changes in the clinical neurological examination, the patient developed palatal myoclonus along with opsoclonus, which resolved spontaneously over a few days. As there was no clinical improvement and as

imaging showed persistent lesions on follow-up MRI, the patient underwent a neuronavigation-guided wedge-shaped brain and meningeal biopsy. The biopsy report showed an oedematous pale-stained area with patchy myelin loss (H&E)/Luxol Fast Blue (LFB)) and gliosis. Scattered CD68+ macrophages were present; axons (neurofilament protein) were depleted but some remained. The nature of the lesion was not clear; no neoplasms or granulomas were identified. Anti-TB treatment was stopped after the CSF TB cultures were found to be negative. Repeat CSF analysis showed lymphocytic pleocytosis and protein of 969 mg/L. After consultation with the infectious disease team, the patient was given a further course of meropenem for 2 weeks. He was also advised to continue a combination of doxycycline and sulfamethoxazole-trimethoprim for 3 months. The patient underwent an extensive neurorehabilitation programme and was repatriated to Sri Lanka. MRI of the brain at discharge showed improvement and regression in the size of abscesses (figure 1G).

DIFFERENTIAL DIAGNOSIS

- Guillain-Barré syndrome with Bickerstaff's encephalitis was considered based on the clinical presentation and findings of acute motor axonal polyneuropathy in NCS. The patient was treated with IVIG.
- CNS TB was considered as the patient was from southeast Asia. He was treated empirically with anti-TB medication; but this was stopped as results of an AFB smear, TB PCR and TB cultures came back negative.
- *Listeria* brainstem encephalitis was considered. The patient was empirically treated for this until the titres for *listeria* came back negative.
- Cerebral toxoplasmosis was considered in view of the ring-enhancing lesions seen on brain MRI and also because of the patient's close contact with lions. However, antitoxoplasma antibodies were negative.
- Neurosarcoidosis was considered. Serum ACE levels were, however, normal.
- CNS demyelination was less likely as the lesions were limited to the brainstem, and ring enhancement was non-suggestive.
- CNS neoplasia was less likely as the presentation was acute and the lesions were spreading in a corticospinal tract distribution; brain biopsy was negative.
- CNS lymphoma (primary or secondary) was less likely as there was no response to steroid therapy and there were no malignant cells in the CSF cytology.

- ▶ Cryptococcal meningoencephalitis was again less likely as there was no hydrocephalus or basal ganglia involvement on imaging.
- ▶ Herpes simplex encephalitis was considered, however, there was no preferential involvement of the temporal lobes.

TREATMENT

On the basis of differential diagnosis, the patient was initially treated with IVIG and later treated with a combination of antibiotics and anti-TB medication. These medications were gradually withdrawn as negative results for most of these infectious aetiologies were obtained. The patient had partial response to antibiotics. His neuroimaging and CSF continued to show abnormalities. So, he was offered further courses of intravenous followed by long-term oral antibiotics.

OUTCOME AND FOLLOW-UP

At discharge, the patient had spastic quadriplegia. He was on a tracheostomy tube with speaking cap along with a percutaneous endoscopic gastrostomy tube in-situ. Neuroimaging showed regression in the size of the lesions. He was repatriated to his country of origin and had significant morbidity at the time of discharge.

DISCUSSION

Melioidosis is a rare fatal infection caused by Gram-negative bacillus *B. pseudomallei*. *B. pseudomallei* is a wet soil saprophyte bacterium and Category B potential bioterrorism agent due to its high virulence. It is traditionally seen in endemic areas of southeast Asia and the Northern Territory of Australia with a peak incidence of disease during the rainy season.^{1 2} However, the disease is rarely seen in travellers returning from endemic areas.^{3 4} The commonest routes of infection are direct percutaneous inoculation, inhalation, or ingestion of contaminated dust, soil, or water as well occupational exposure to the surface water and mud.⁵ The risk factors present among the infected population, which include diabetes, heavy alcohol consumption, chronic lung and renal diseases, malignancies and intravenous drug abuse, suggest consideration of melioidosis as an opportunistic infection due to functional neutrophil defects playing a significant role in disease pathogenesis.⁶ Although the most common presentation of melioidosis is pneumonia, a varied clinical presentation of acute or chronic, localised or disseminated infection including neurological melioidosis has been described.⁷ In neuromelioidosis, there is predilection for involvement of the brainstem on imaging. This was seen in our patient, whose initial brain MRI fluid-attenuated inversion recovery sequence showed confluent lesions involving most of the brainstem. The ring enhancement seen on T1 with gadolinium appeared as multiple small abscesses. However, on subsequent imaging we saw these lesions ascending into thalami and, in addition, involving the corticospinal tract bilaterally. This radiological picture has not been described in any of the differential diagnoses we had considered. Neuromelioidosis accounts for approximately 4% of all melioidosis cases, with a significant debilitating morbidity and mortality rate reaching as high as 25%. A low degree of suspicion and awareness among healthcare providers delays and thus presents difficulties in diagnosis and treatment of infection; also, its unfamiliarity has led to the underdetection of melioidosis. At present, no vaccination against melioidosis exists. To reduce mortality and morbidity, the following antibiotic regimen is recommended.⁸ For melioidosis, initial therapy intravenously for 2 weeks with either ceftazidime

(50 mg/kg up to 2 g every 6 h) or meropenem (25 mg/kg up to 1 g every 8 h) or imipenem (25 mg/kg up to 1 g every 6 h) followed by eradication therapy orally for 3 months with trimethoprim-sulfamethoxazole (240/1200 mg (for adults weighing 60 kg or less) or 320/1600 mg (for adults weighing >60 kg) every 12 h) along with folic acid (0.1 mg/kg up to 5 mg once daily) is recommended. For neuromelioidosis, initial therapy intravenously for 4–8 weeks with meropenem (50 mg/kg up to 2 g every 8 h) along with trimethoprim-sulfamethoxazole (240/1200 mg (for adults weighing 60 kg or less)/320/1600 mg (for adults weighing >60 kg) every 12 h) along with folic acid (0.1 mg/kg up to 5 mg once daily) followed by eradication therapy orally for 6 months with trimethoprim-sulfamethoxazole and folic acid is recommended. We present an interesting case of a combination of initial peripheral nervous system followed by CNS involvement with significant morbidity as the outcome.

Learning points

- ▶ Neuromelioidosis is rare in the Middle East and, if suspected, should be treated early as it carries a high rate of mortality and morbidity.
- ▶ A combined peripheral nervous system presentation followed by central nervous system involvement is rarely reported with acute infectious aetiologies.
- ▶ Neuromelioidosis is a great mimicker of tuberculosis, with ring-enhancing lesions on brain MRI.
- ▶ Lesion progression with involvement of the corticospinal tract may be pathognomonic for this condition.
- ▶ Unresponsiveness to antibiotics warrants a further long-term course.
- ▶ This is a condition with devastating neurological consequences.

Twitter Follow Khurram Siddiqui at @kasidd

Acknowledgements The authors acknowledge Dr Ali Reza Dehdashtian, Consultant Neuroradiologist, Al Ain Hospital, Al Ain, UAE.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

- 1 Cheng AC, Currie BJ. Melioidosis: epidemiology, pathophysiology and management. *Clin Microbiol Rev* 2005;18:383–416.
- 2 Currie BJ, Ward L, Cheng A. The epidemiology and clinical spectrum of melioidosis: 540 cases from the 20 year Darwin Prospective study. *PLoS Negl Trop Dis* 2010;4:11.
- 3 Vestal ML, Wong EB, Milner D, et al. Cerebral melioidosis for the first time in the western hemisphere. *J Neurosurg* 2013;119:1591–5.
- 4 Peetermans WE, Van Wijngaerden E, Van Eldere J. Melioidosis brain and lung abscess after travel to Sri Lanka. *Clin Infect Dis* 1999;28:921–2.
- 5 Leelarasamee A, Bovornkitti S. Melioidosis: review and update. *Rev Infect Dis* 1989;2:413–25.
- 6 White NJ. Melioidosis. *Lancet* 2003;361:1715–22.
- 7 Currie B, Fisher DA, Howard DM, et al. Neurological melioidosis. *Acta Trop* 2000;74:145–51.
- 8 Writing Group. Melioidosis. In: *Therapeutic guidelines: antibiotic*. 14th edn. North Melbourne: Therapeutic Guidelines Ltd, 2010.

Copyright 2015 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.
BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- ▶ Submit as many cases as you like
- ▶ Enjoy fast sympathetic peer review and rapid publication of accepted articles
- ▶ Access all the published articles
- ▶ Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow