CASE REPORT

A NEW ASSOCIATION OF GUILLAIN BARRE SYNDROME IN A PATIENT WITH CENTRAL NERVOUS SYSTEM MELIOIDOSIS

Ewe Jin Koh[1], Kah Nian Tan[1], Zhi Wei Chan[1], Hoy Yan Candice Wong[1], Ming Lee Chin[2], Tiong Chan Lee[3]

[1]Department of Internal Medicine, [2]Department of Medicine and Paediatrics, Hospital Taiping, Perak-Malaysia
[3]Jeffrey Cheah School of Medicine and Health Sciences, Monash University Malaysia, Johor Bahru, Johor-Malaysia

Burkholderia pseudomallei affecting the central nervous system has been extensively reported in the literature. However, combined central nervous system and peripheral nervous system involvement in melioidosis has never been reported. We report a 66-year-old man with diabetes mellitus who was diagnosed to have central nervous system melioidosis and developed acute flaccid quadriplegia. Nerve conduction studies and anti-ganglioside antibodies were consistent with Guillain-Barre syndrome. This case report highlights the importance to recognise the possibility of Guillain Barre syndrome complicating central nervous system melioidosis and stresses the urgency of early consideration of this complication, as early immunomodulatory therapy may hasten neurological recovery.

Keywords: Melioidosis; Peripheral nervous system; Acute flaccid paralysis; Guillain barre syndrome

Citation: Koh EJ, Tan KN, Chan ZW, Wong HYC, Chin ML, Lee TC. A new association of Guillain barre syndrome in a patient with central nervous system melioidosis. J Ayub Med Coll Abbottabad 2023;35(2):334–6.

DOI: 10.55519/JAMC-02-11470

INTRODUCTION

Melioidosis is an infectious disease caused by the gram-negative bacterium *Burkholderia pseudomallei*, which is endemic in South Asia, Southeast Asia, and Northern Australia. The hallmark of the disease is the formation of microabscesses in internal organs. In the 20-year Darwin prospective study, the largest cohort to date reported that the principal presentation was pneumonia followed by genitourinary, intra-abdominal, skin, bone, and joint infections.[1]

There have also been reports of melioidosis affecting the eye presenting as periorbital cellulitis and eyelid abscesses.[2]

Neurological melioidosis (Neuromelioidosis) is exceedingly rare, with an incidence of only 1.5–5%; however, the mortality rate may be as high as 20–25% if untreated.[3]

Guillain Barre syndrome has classically been associated with Campylobacter jejuni infections, viral infections and possibly post-vaccination. Guillain barre syndrome classically presents as an acute motor polyneuropathy, however, there have also been variants presenting as acute motor and sensory polyneuropathy as in our patient.[4]

The association of Guillain Barre syndrome complicating central nervous system melioidosis has only been very scarcely reported which may lead to a low index of suspicion.[5]

CASE REPORT

A 66-year-old gentleman presented to a Malaysian district general hospital with a 10-day history of high grade fevers, lethargy, malaise, and reduced oral intake. He had long-standing poorly controlled Type 2 diabetes mellitus and was a rural palm oil estate worker. Upon presentation, he was lethargic to the point of needing assistance to sit up; however, he had remained hemodynamically stable and did not require oxygen support. There was no focal neurology on admission. Blood cultures taken on admission grew Burkholderia pseudomallei, for which he was started on IV Ceftazidime.

His fever persisted over the next five days, and he subsequently developed left-sided hemiparesis. A contrasted computed tomography of the brain demonstrated a right frontal ill-defined hypodensity which suggested active central nervous system infection. Magnetic resonance imaging of the brain was suggestive of cerebral fronto-parietal abscesses. A Contrast-enhanced computed tomography of the Thorax, Abdomen and Pelvis did not reveal any other foci of infection. His antibiotics were changed to intravenous meropenem 2g every 8 hours and oral Sulphamethoxazole-Trimethoprim 320/1600 mg orally every 12 hours. The diagnosis at that juncture was central nervous system melioidosis. His fever had resolved within five days of IV meropenem and had demonstrated blood culture clearance within the first week.

Surprisingly, on day 14 of admission, he developed acute flaccid quadriplegia with absent deep tendon reflexes and bilateral plantar responses. He was also unable to communicate or verbalise by his third week of hospitalization. Cranial nerve examination was otherwise unremarkable. A repeat magnetic resonance imaging of the brain and brainstem did not reveal any brainstem involvement. An electro-encephalogram (EEG) demonstrated moderate diffuse cortical dysfunction with no epileptiform discharges. Sepsis-associated encephalopathy was considered, and the treating team opted to continue the current antibiotics with watchful waiting. Nevertheless, the flaccid quadriplegia persisted despite treatment with appropriate antibiotics.

Therefore, this prompted a new set of investigations for flaccid quadriparesis only after a month of admission. MRI of the spine revealed no spinal cord compression of nerve root impingement. Of particular interest, his lumbar puncture showed a CSF protein count of 0.43 g/l, and glucose of 4mmol/L, consistent with albumino-cytological dissociation. His nerve conduction study was consistent with diffuse axonal sensorimotor polyneuropathy. This was followed up with a ganglioside antibody panel, which revealed positive anti-Sulfatide IgM and GM3-ganglioside IgG antibodies. The diagnosis of Guillain-Barre syndrome was postulated based on his clinical presentation, electrodiagnostic findings, and cerebrospinal fluid analysis results.

No immunomodulatory therapy was given as the patient had already reached the nadir of the disease, and it had already been 1 month since the flaccid quadriplegia was noticed.

By day 41 of antibiotics, the patient showed gradual improvement in neurological function and was able to start swallowing and moving his distal right upper and lower limbs.

On assessment prior to discharge, the patient showed significant improvement neurologically. He was able to move his right upper limb spontaneously with a motor power of at least 3/5 on the Medical Research Council (MRC) scale, comprehend and communicate in full sentences, albeit still with significant morbidity. Hence, he was discharged with maintenance oral Sulphamethoxazole-Trimethoprim for another 24 weeks. A serial MRI of the brain over the ensuing 2 months after discharge revealed that the brain abscesses were regressing, indicating a good response to the antibiotics.

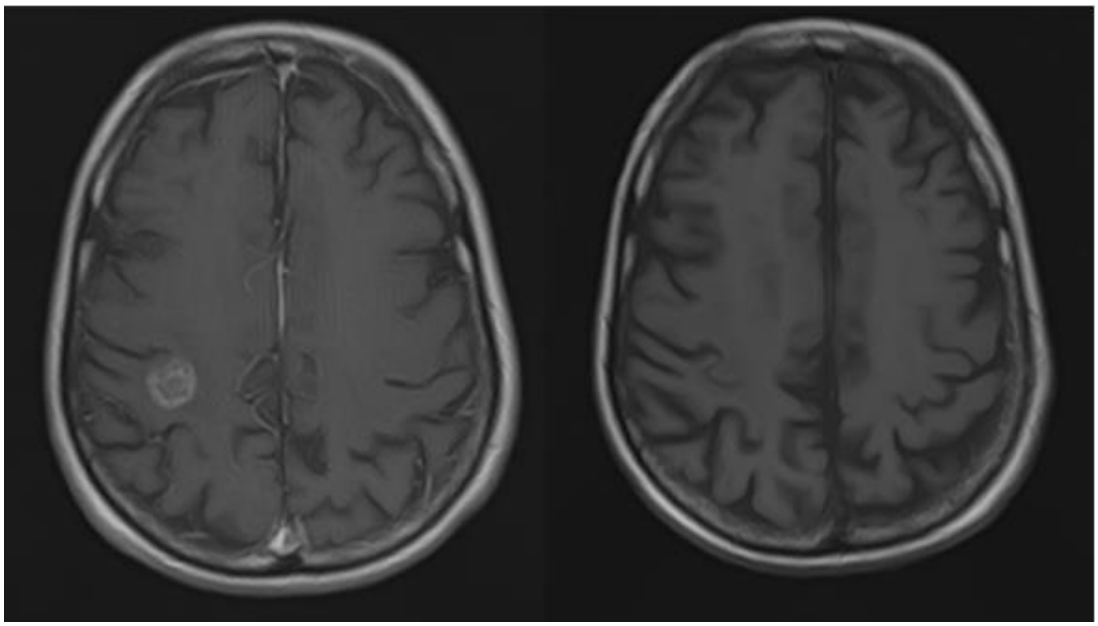

Figure-1 MRI Brain: Left: small rounded hyperdensity measuring 1cmx1.5cm x 1cm at the right parietal lobe suggestive of brain abscess. Right: Resolution of the brain abscess after Day 40 of antibiotics.

DISCUSSION

The term ‘neuro melioidosis’ generally refers to bacterial invasion of the central nervous system. Typical clinical features include high fever, headaches, cranial nerve palsies, encephalitis, and unilateral limb weakness. Common neuroimaging findings are brain abscesses with a predilection for the frontal and parietal lobe cortex that may involve the corona radiata, basal ganglia, and brainstem as the disease progresses.[5] A review of the literature has revealed that, although rare, central nervous system melioidosis alone has been extensively reported. Melioidosis with pure peripheral

nervous system involvement has only been reported in two case studies in recent years.[6,7]

Our case interestingly demonstrates melioidosis with an initial presentation of central nervous system involvement followed by peripheral nervous system involvement.

We postulate that the overwhelming infection and inflammatory response from the initial brain lesions triggered a cytokine storm and molecular mimicry targeted at ganglioside compounds in peripheral nerve tissues.[7] This eventually led to immune-mediated sensorimotor axonal polyneuropathy consistent with Guillain Barre syndrome. This diagnosis was supported by objective clinical improvement in motor function after 4 weeks from the nadir of illness, consistent with the natural history of Guillain Barre syndrome. His cerebrospinal fluid analysis revealed a classical albumin-cytological dissociation, further supporting the diagnosis. Hence, the patient fulfilled level I diagnostic criteria in all domains of Brighton criteria for diagnosis of Guillain Barre syndrome.[8]

Our suspicion was also supported by positive antiganglioside antibodies, specifically anti-sulfatide IgM. Sulfatide is a major acidic glycosphingolipid in myelin. Diseases with antibodies to sulfatide are most commonly associated with an axonal sensory predominant polyneuropathy, which is consistent with our patient. This indicates an immune-mediated neuropathic disorder.[9]

Our case highlights yet another atypical presentation of neuro melioidosis.

Unfortunately, no immunomodulatory therapy was given due to the low index of suspicion, and the peripheral nervous system involvement was only confirmed after 4 weeks from the onset of neuropathic symptoms.

The implications of this case for future use would be to recognize the possibility of combined central and peripheral nervous system involvement of melioidosis and consider initiation of immunomodulatory therapy or therapeutic plasma exchange as early treatment within 2 to 4 weeks from the onset of neuropathic symptoms, which has been shown to hasten recovery.[10]

CONCLUSION

Guillain Barre syndrome complicating central nervous system melioidosis is a rare but possible entity. Therefore, a high index of suspicion should be placed if the patient develops acute flaccid paralysis in the context of central nervous system melioidosis. Early recognition of this clinical syndrome is of the utmost importance as early administration of immunomodulatory therapy might accelerate neurological recovery.

Acknowledgements: The authors would like to thank Dr Chee Yik, Chang for providing suggestions and overseeing the write-up of this case report.

Conflict of Interest Statement: The authors declare no conflict of interest.

Financial Support: The authors declare no financial support during the write-up of this manuscript.

REFERENCES

1. Currie BJ, Ward L, Cheng AC. The epidemiology and clinical spectrum of melioidosis: 540 cases from the 20-year Darwin prospective study. PLoS Negl Trop Dis 2010;4(11):e900.
2. Chang CY. Periorbital cellulitis and eyelid abscess as ocular manifestations of melioidosis: A report of three cases in Sarawak, Malaysian Borneo. IDCases 2020;19(e00683):e00683.
3. Wongwandee M, Linasmita P. Central nervous system melioidosis: A systematic review of individual participant data of case reports and case series. PLoS Negl Trop Dis 2019;13(4):e0007320.
4. Leonhard SE, Mandarakas MR, Gondim FAA, Bateman K, Ferreira MLB, Cornblath DR, *et al*. Diagnosis and management of Guillain-Barré syndrome in ten steps. Nat Rev Neurol 2019;15(11), 671–83.
5. Zhan Y, Wu Y, Li Q, Yu A. Neuromelioidosis: a series of seven cases in Hainan province, China. J Int Med Res 2017;45(2):856–67.
6. Wijekoon PWMCSB, Bandara KAS, Kailainathan A, Chandrasiri NS, Hapuarachchi CT. Guillaine-barre syndrome; a rare complication of melioidosis. a case report. BMC Infect Dis 2016;16(1):1–4.
7. Krovvidi R, Mridula RK, Jabeen SA, Meena AK. Guillain Barre syndrome as a manifestation of neurological melioidosis. Ann Indian Acad Neurol 2013;16(4):681–3.
8. bc-coordinator. Guillain Barré and Miller Fisher Syndromes: Case definition Companion Guide [Internet]. Brighton Collaboration. 2021 [cited 2022 Oct 16]. Available from: https://brightoncollaboration.us/guillain-barre-and-miller-fisher-syndromes-case-definition-companion-guide
9. Dabby R, Weimer LH, Hays AP, Olarte M, Latov N. Antisulfatide antibodies in neuropathy: clinical and electrophysiologic correlates. Neurology 2000;54(7):1448–52.
10. Hughes RAC, Wijdicks EFM, Barohn R, Benson E, Cornblath DR, Hahn AF, *et al*. Practice parameter: immunotherapy for Guillain-Barré syndrome: report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology 2003;61(6):736–40.

Submitted: October 27, 2022	*Revised: January 31, 2023*	*Accepted: December 30, 2022*

Address for Correspondence:
Ewe Jin Koh, Hospital Taiping, Department of Internal Medicine, Taiping, Perak-Malaysia
Tel: +6017 2863880
Email: ewejinkoh@gmail.com