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CASE REPORT

Stroke and Guillain-Barre syndrome secondary to spotted fever – A case report

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Abstract

Rickettsial infection is an important differential diagnosis in prolonged febrile illness and in returned travellers.

We report a 44-year-old male from Deraniyagala, Sri Lanka, with spotted fever Rickettsiosis presenting with stroke and Guillain-Barre syndrome. He presented with dysarthria, reduced sensorium, and acute renal failure on the background of a prolonged febrile illness over two weeks. Following admission there was rapid deterioration of consciousness due to renal failure requiring intubation and repeated haemodialysis. On brain imaging, there were bilateral basal ganglia and internal and external capsule infarctions. His serology was positive for spotted fever Rickettsial infection and there was rapid improvement following treatment with doxycycline. However, difficulty in weaning off from the ventilator due to poor respiratory effort and symmetrical flaccid quadriparesis with areflexia raised concerns of concomitant Guillain-Barre syndrome. Serial cerebrospinal fluid (CSF) studies showed the development of elevated CSF protein with cytoalbuminologic dissociation during his stay in the intensive care unit (ICU). A diagnosis of co-existing Guillain-Barre syndrome was supported by the neuro-physiological findings and marked motor improvement following therapeutic plasmapheresis. This unmasked the right-sided mild residual hemiparesis he suffered due to stroke.

KEYWORDS

Rickettsial infections, Neurorickettsioses, Sri Lanka

CASE REPORT

A 44-year-old grocery shop owner from Deraniyagala, Sri Lanka, with type 2 diabetes mellitus, presented to a local hospital with dizziness, dysarthria, and generalized body weakness. He had intermittent low-grade fever for two weeks with arthralgia, myalgia, and frontal headache. Following admission to the local hospital, his consciousness level deteriorated over a short period requiring intubation and ventilation. There was concomitant acute renal failure requiring haemodialysis and he was transferred to the tertiary centre. The fever persisted for two weeks without response to empirical antibiotics. A transient erythematous macular rash over the medial surface of the right elbow was noted at the initial period of the stay and a healed eschar on the right lower leg was found on targeted examination. The patient underwent a tracheostomy on day nine of the intensive care unit (ICU) admission due to prolonged intubation.

The full blood count showed a rising white cell count with neutrophil predominance and an elevated C-reactive protein (CRP) (201mg/dl). Serum creatinine was elevated (814 micromoles/L) and urine full report (UFR) revealed a few red cells with 25 leucocytes and a trace of protein. A 2D echocardiogram was performed. It showed no embolic focus, and the ultrasound scan of the abdomen was normal. His cerebrospinal fluid (CSF) evaluation on admission showed elevated red cells, normal CSF protein, and one polymorph with no definite indication of central nervous system (CNS) infection. There was no electroencephalogram (EEG) performed

at the initial stage. The non-contrast computed tomography (NCCT) brain scan showed bilateral basal ganglia infarctions.

With the clinical suspicion of rickettsial infection, oral doxycycline was commenced on day 20 in the ICU. There was a rapid improvement with control of temperature and normal conscious level. His renal function normalised following repeated haemodialysis, and he became dialysis-independent.

Despite becoming hemodynamically stable with a normal conscious level, repeated attempts to wean off from the ventilator failed. He demonstrated flaccid quadriparesis with absent limb power and poor neck power, with global areflexia. This could not be explained by the infarctions seen on the NCCT.

The nerve conduction study confirmed a clinical suspicion of concomitant Guillain-Barre syndrome and a repeat CSF evaluation showed a significant increase in the CSF protein level with a cytoalbuminologic dissociation. The patient was managed with plasmapheresis resulting in significant improvement and was weaned from the ventilator after a single 5-day cycle. At this point of illness, a clear right hemiplegia was noted. He demonstrated good recovery with rehabilitation to a modified Rankin scale of 1.

TABLE 1 Findings of serial blood investigations

	Day 14 of illness (ICU Day 1 at the tertiary unit)	Day 24 of illness (ICU Day 10 at the tertiary unit)	Day 30 of illness (ICU Day 16) (Oral Doxycycline was started on day 26 of illness/ ICU Day 13)
White Blood Cells (per L)	9.92	18.1	15.9
Neutrophils (per L)	78	88	80.8
Lymphocytes (per L)	14	5.3	8.5
Haemoglobin (g/dL)	15.5	10.2	8.1
Platelets (per L)	178	438	482
C-reactive protein (mg/L)	201	84.7	9.7
Serum creatinine (micromoles/L)	314	814	593
Serum sodium (mmol/L)	136	135	136
Serum potassium (mmol/L)	3.1	5.6	4.0
Aspartate transaminase (U/L)		55	
Alanine transaminase (U/L)		58	

TABLE 2 Findings from the repeated cerebrospinal fluid analysis

	Day 15 of illness (ICU Day 2 at tertiary centre)	Day 21 of illness (ICU Day 8)	Day 30 of illness ICU Day 17)
Appearance Clear/ no colour	Clear/ no colour	Clear/ no colour	
Protein (mg/dL)	32.3	86	112
Polymorphs (per mm^3)	1	1	Nil
Lymphocytes (per mm^3)	1	2	Nil
Red blood cells (per mm^3)	240	8	10
Sugar (mg/dL)	141	113	90

Random blood sugar (mg/dL) values at each CSF analysis respectively – 241, 240, 178

On admission, non-contrast imaging of the brain revealed bilateral basal ganglia infarctions later confirmed by Magnetic Resonance Imaging (MRI).

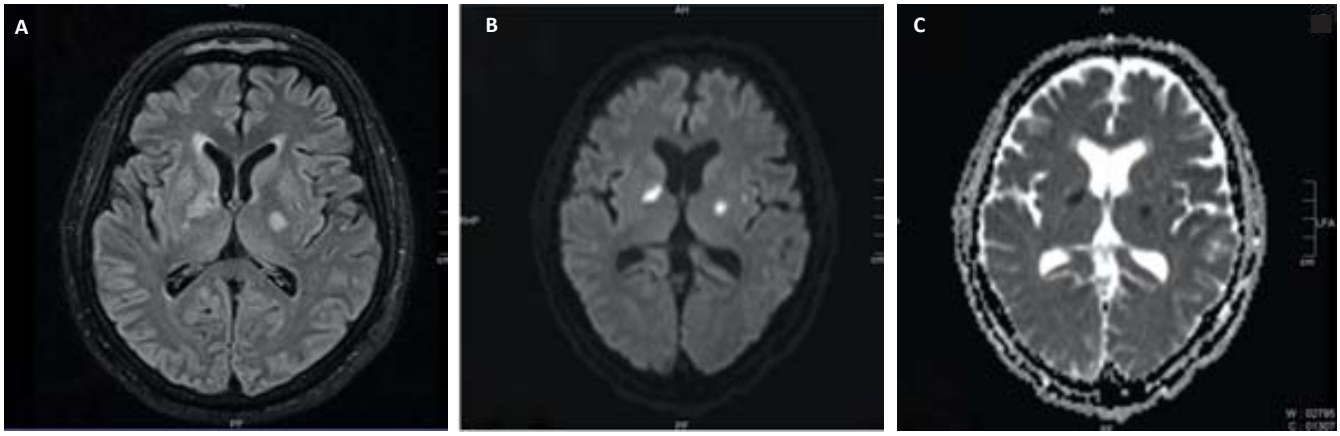

FIGURE 1 **A. T2 FLAIR, B. DWI, and C. ADC images demonstrate bilateral T2 FLAIR high signal intensities involving the left internal capsule, right globus pallidus, and bilateral external capsules. This shows diffusion restriction suggesting acute infarcts.**

The nerve conduction study showed features of a sensory-motor axonal polyneuropathy, suggesting a diagnosis of acute motor and sensory axonal neuropathy (AMSAN) type Guillain Barre syndrome.

Immuno-fluorescent assay for spotted fever, which was the standard serological test for Rickettsial infection, performed on day 34 of illness was positive with a titre >1:128. The convalescent serum result was not available due to a sampling error.

Screening for leptospirosis, mycoplasma, human immune deficiency virus, melioidosis, and hepatitis was normal. The blood and urine cultures were negative. CSF culture and repeated blood cultures showed no microbial growth. Anti-nuclear antibody (ANA), C3, C4 and Anti neutrophil cytoplasmic antibody tests (pANACA and cANCA) were negative. Other differentials encountered in a multiple territory febrile stroke with multi-organ involvement such as infective endocarditis, and CNS vasculitis were excluded.

Observed skin manifestations with a transient rash and a healed eschar, rapid response to doxycycline, positive serology for spotted fever infection, and negative screening for the other differentials led to the diagnosis of spotted fever infection and neurorickettsiosis. The altered sensorium at presentation could mainly be attributed to uraemia secondary to acute renal failure.

The recovery was complicated with Guillain Barre syndrome. The other possibility encountered was critical illness polyneuropathy and myopathy, with the prolonged ICU stay of 4 weeks. However, he had normal CSF protein and cells on admission to ICU and repeat CSF analysis showed a significant rise in CSF protein with cytoalbuminologic dissociation (32.3 to 112 mg /dL). The nerve conduction studies favoured the diagnosis of an acute motor sensory axonal neuropathy (AMSAN) type GBS. The strongest evidence was the marked improvement of weakness and the rapid weaning off from the ventilator following a single 5-day cycle of plasma exchange.

DISCUSSION

Clinical presentation of rickettsial infection

The type of spotted fever in Sri Lanka is thought to be Mediterranean spotted fever reported in the Mediterranean region and the Indian subcontinent, caused by *R conorii*, transmitted by the brown dog tick *Rhipicephalus sanguineus*.[1]

The clinical presentation is usually with fever accompanied by headache, and mental confusion due to meningo-encephalitis in severe cases. Myalgia, nausea, vomiting, and abdominal pain are common early symptoms. A macular rash which appears mainly on the trunk, with a small black scab or eschar at the site of the insect bite, with local or general lymphadenopathy can be present. In the spotted fever group, an eschar is rarely seen. Rickettsial infection can present as pyrexia of unknown origin leading to a diagnostic dilemma.[2]

The most severe complications may include acute kidney failure, thrombocytopenia, myocarditis, pneumonitis, and shock. Although higher rates have been observed, the current fatality rate is 3-7%, and the main risk factors for severe disease are advanced age, alcoholism, immunocompromised status, and diabetes.[3,4]

In making the diagnosis, the immuno-fluorescent assay (IFA) is the standard serological test for Rickettsial infection. The cut-off values depend on the background seroprevalence of the geographical region. An IgG titre of 1/128 is considered positive in regions in the Indian subcontinent. However, in Sri Lanka, the standard practice is to assess a convalescent titre, where a fourfold rise of antibody titre in acute and convalescent serum is diagnostic.[5,6]

Neurological manifestations of Rickettsial infection

In Sri Lanka, neurological manifestations have been reported with spotted fever and scrub typhus.[7] In a case series from

the central province including 134 patients with rickettsiosis, 17 were reported to have neurological manifestations. All these had positive serology for spotted fever. The predominant clinical manifestations were headache followed by extra-pyramidal features, rigidity, bradykinesia, and resting tremor, mainly in the elderly. These extrapyramidal features improved following antibiotic treatment. A few cases presented with an altered level of consciousness and headache with raised CSF protein and pleocytosis along with EEG changes suggestive of meningoencephalitis.[8] In this series, only 3 patients had NCCT brain, and one showed a cerebral infarction. Flaccid motor weakness suggestive of Guillain Barre syndrome and deafness were among other neurological manifestations.

Guillain Barre syndrome was reported following Rocky Mountain spotted fever (RMSF) and scrub typhus, in other case series, elsewhere in the world.[9,10] Stroke was reported secondary to scrub typhus and Mediterranean spotted fever (MSF). There are cases reported with brain lesions including a thalamic lesion that presented with hemisensory loss and encephalitis.[3]

CONCLUSION

Rickettsial infection is an important differential in febrile stroke with multi-system involvement. Later development of Guillain-Barre syndrome made the diagnosis further challenging with a favourable outcome at the end.

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