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Case Report

Post-infectious dengue cerebellitis in a patient with transfusion-dependent β-thalassaemia major: A case report

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ABSTRACT

Dengue fever is endemic in Sri Lanka and can rarely cause neurological complications, including post-infectious cerebellitis. Although patients with β-thalassaemia major have altered immune profiles, the intersection of expanded dengue syndrome with underlying haematological disorders is poorly documented. We report a 22-year-old woman with optimally managed, transfusion-dependent β-thalassaemia major who developed progressive cerebellar dysfunction eleven days after the onset of dengue haemorrhagic fever. Neurological examination revealed characteristic cerebellar signs, and the magnetic resonance imaging of the brain was normal. A clinical diagnosis of post-infectious dengue cerebellitis was made. Intravenous methylprednisolone led to rapid and complete resolution of symptoms.

This case highlights a rare neurological sequela of dengue and underscores the need for vigilance for post-infectious autoimmune complications in multiply transfused patients, even when iron overload is minimal. We propose that chronic alloantigen exposure from lifelong transfusions establishes a constitutively dysregulated adaptive immune state, characterised by expanded Tregs and elevated IL-6, IL-10, and TGF-β, which may amplify post-viral autoimmune responses irrespective of iron overload status. This case emphasises the importance of early recognition and immunosuppressive treatment of immune-mediated neurological complications in optimally managed, multiply transfused patients.

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Introduction

Dengue is a mosquito-borne viral infection endemic in Sri Lanka, and a major public health concern. The neurological manifestations of dengue are increasingly recognised as part of the "expanded dengue syndrome," affecting up to 4% of patients. These complications encompass both direct viral invasion and post-infectious immune-mediated processes.[1] Among these, dengue cerebellitis is exceptionally rare, with fewer than 20 cases reported globally.[2-6] In post-infectious conditions, pathogenesis is believed to involve autoimmune mechanisms triggered by molecular mimicry between viral antigens and cerebellar tissue, typically occurring 2–14 days after the acute phase.[1]

In Sri Lanka, β-thalassaemia major is one of the most prevalent inherited haemolytic anaemias.[8] Patients with transfusion-dependent β-thalassaemia require lifelong regular blood transfusions and strict iron chelation therapy to prevent complications of chronic iron overload. These patients show altered immune function, which has historically been attributed to severe iron overload, oxidative stress, and functional hyposplenism.[9]

However, emerging evidence suggests that even among optimally chelated transfusion-dependent thalassaemia (TDT) patients, a constitutively activated adaptive immune state is maintained, driven by chronic alloantigen exposure from repeated transfusions. This state is characterised by expanded regulatory T cells (Tregs) and chronically elevated pro-inflammatory and immunoregulatory cytokines, including IL-6, IL-10, and TGF-β.[9] This persistently primed immune environment may lower the threshold for aberrant post-viral autoimmune responses, irrespective of the degree of iron overload.

Although dengue haemorrhagic fever has been reported in patients with thalassaemia, the intersection of dengue neurological complications with underlying haematological disorders remains poorly characterised. This case highlights the potential for atypical post-viral complications in patients with chronic antigenic exposure.

Case presentation

A 22-year-old woman with transfusion-dependent β-thalassaemia major, from a dengue-endemic region, presented with an acute febrile illness. She had been maintained on optimal transfusion therapy (target haemoglobin 9–10 g/dL) with twice-weekly red cell transfusions. Her iron chelation was well managed, with a serum ferritin of 484 ng/mL (target ≤1,500 ng/mL). Cardiac and hepatic iron levels, assessed by T2* Magnetic Resonance Imaging (T2* MRI), showed normal myocardial iron concentration (0.82 mg/g dry weight) and mild hepatic iron concentration (5.01 mg/g dry weight). Notably, she had not undergone splenectomy.

The patient initially presented on Day 1 with an acute onset of fever accompanied by arthralgia and myalgia, without any identifiable focus of infection. By Day 2, the diagnosis of dengue was confirmed with a positive NS1 antigen test. On Day 5, she entered the critical phase of dengue haemorrhagic fever, during which significant thrombocytopenia was noted (platelet count reaching a nadir of 25×10^9/L), along with ultrasonographic evidence of free fluid in the hepatorenal pouch; however, she remained hemodynamically stable without features of shock. By Day 7, she transitioned into the recovery phase, with resolution of fever and continued clinical stability. Subsequently, on Day 11, she developed a subacute onset of neurological symptoms, including progressive unsteadiness, impaired coordination of the hands, and vertigo.

Over the subsequent week, the neurological examination revealed classic cerebellar signs, including horizontal nystagmus, dysdiadochokinesia, ataxic gait, and intention tremor. Muscle tone, power, reflexes, and sensation were normal. Cranial nerve examination was unremarkable, with no evidence of encephalopathy.

Contrast-enhanced brain MRI performed on Day 12 of the illness showed no evidence of cerebellitis, infarction, haemorrhage, or space-occupying lesions. Mild prominence of the pituitary gland was noted, consistent with physiological hyperplasia. Electroencephalogram (EEG) and magnetic resonance angiography/venography (MRA/MRV) were normal. Cerebrospinal fluid (CSF) analysis was deferred given the patient's clinical stability and the absence of encephalopathy.

Throughout the course of dengue haemorrhagic fever, laboratory findings were consistent with the typical disease course (Table 1). An initial leucopenia was observed, followed by gradual recovery. Neutropenia was evident early in the illness, while a relative lymphocytosis emerged during the recovery phase. The platelet count

Table 1
Laboratory parameters during the disease course.

Parameter	Day 1	Day 3	Day 5	Day 7	Day 9	Day 12
WBC (×10^9/L)	5.58	1.38	3.57	5.63	5.61	6.23
Neutrophils (×10^9/L)	4.03	0.71	1.56	2.12	1.94	3.56
Lymphocytes (×10^9/L)	1.35	0.63	1.93	3.28	3.40	2.61
Haemoglobin (g/dL)	10.6	11.8	11.2	11.2	10.8	10.2
Platelets (×10^9/L)	183	95	25	45	68	212
CRP (mg/L)*	12	–	21	–	–	0.2
AST (U/L)*	36	54	69	63	57	52
ALT (U/L)*	41	48	48	48	44	42

*(normal values: AST 0–40 U/L, ALT 0–41 U/L, CRP < 5 mg/L)

declined significantly, reaching a nadir of 25 × 10^9/L on Day 5 (normal: 150–400 × 10^9/L), coinciding with the critical phase and then recovered to normal by Day 12. Haemoglobin levels remained relatively stable throughout. These laboratory changes are in keeping with the natural course of dengue infection and preceded the onset of neurological manifestations.

Given the classic temporal relationship to the acute viral phase and the absence of alternative aetiologies, a clinical diagnosis of post-dengue cerebellitis was made. The patient was treated with intravenous methylprednisolone pulse therapy (1 g daily for 5 days), followed by a gradual taper of oral prednisolone (1 mg/kg daily for 2 weeks). The response to corticosteroid treatment was remarkable, with marked improvement of cerebellar symptoms within days of treatment initiation. At the one-month follow-up, the patient showed complete resolution of neurological symptoms with no residual sequelae.

Discussion

This case represents a rare clinical intersection between post-infectious cerebellitis following dengue fever and the underlying immune milieu in transfusion-dependent β-thalassaemia major.

The pathogenesis of dengue-related neurological complications involves both direct viral invasion and immune-mediated inflammatory mechanisms.[1] Post-dengue cerebellitis typically occurs during the convalescent phase of infection,[2] aligning with the day 11 onset observed in our patient. Neuroimaging in such cases is notoriously variable; while some patients show cerebellar hyperintensities, many have completely normal imaging despite profound cerebellar signs.[2,5] This suggests that the pathology often reflects immune-mediated neuronal dysfunction – possibly autoimmune responses targeting cerebellar Purkinje cells – rather than gross structural injury.

The presence of β-thalassaemia major adds complexity to this pathophysiology. Historically, immune dysfunction in thalassaemia has been attributed to severe iron overload, oxidative stress, and hyposplenism.[8] However, our patient had not undergone splenectomy, was well chelated, with a ferritin level well below 1000 ng/mL and minimal hepatic iron. Ehsanipour et al. demonstrated that innate immune components, such as complement factors C3 and C4, are generally preserved unless severe iron overload occurs.[7] This suggests that innate immunodeficiency did not drive our patient's pathology.

Instead, the exaggerated post-viral inflammatory response observed in this patient is more likely linked

Table 2
Summary of reported post-dengue cerebellitis cases from the literature (Weeratunga[2], Withana[4], Khoo[5], Sathees[3], Khan[6]).

Author	Age	Sex	Phase of Presentation	Cerebellar Signs	Dengue Serology	Brain MRI	CSF Analysis	Recovery Duration
Weeratunga (Sri Lanka) et al.	40	F	Critical	Dysarthria, Bilateral nystagmus, Bilateral limb and gait ataxia	IgM + (Serum and CSF)	Normal	Normal	2 Months
Weeratunga et al.	28	M	Post-recovery	Bilateral vertical and horizontal nystagmus, Gait ataxia	IgM + (Serum and CSF)	Normal	Normal	1 Week
Weeratunga et al.	25	M	Febrile	Bilateral nystagmus, Dysmetria, Severe ataxia	IgM + (Serum and CSF)	Bilateral cerebellar T2 lesions	Normal	2 Weeks
Withana (Sri Lanka) et al.	45	F	Febrile	Scanning dysarthria, Horizontal nystagmus, Dysmetria, Dysdiadochokinesia, Ataxia	NS1 +, IgM + (Serum)	Normal	Not done	17 days
Khoo (Malaysia)	60	M	Recovery	Nystagmus, Bilateral dysmetria, Ataxia	IgM + (Serum), CSF PCR Negative	Old Stroke: Right corona radiata and Left frontal lesion	Normal	34 days
Sathees (Sri Lanka) et al.	20	F	Febrile	Scanning dysarthria, Nystagmus, Dysmetria, Ataxic gait	NS1 +, IgM + (Serum)	Normal	Normal	20 days
Khan (Pakistan) et al.	56	M	Post-recovery	Marked ataxia, Past pointing, Nystagmus, Walking difficulty	IgM + (Serum), NS1 +	Bilateral cerebellar peduncle T2 signals	Normal	1 Week *(With IV steroids)*

to adaptive immune mechanisms and chronic antigenic stimulation.[10] Patients requiring lifelong transfusions face constant alloantigen exposure. Recent studies have demonstrated increased regulatory T-cell (Treg) levels, along with elevated levels of cytokines such as IL-6, IL-10, and TGF-β, in transfusion-dependent β-thalassaemia patients, reflecting an altered and persistently activated immune regulatory state associated with chronic transfusion exposure.[9]

Similarly, Amin et al. demonstrated elevated levels of immunoglobulins (IgG, IgM, and IgE), reflecting chronic antigenic stimulation.[10] Even when optimally managed, this persistent immune activation creates a pro-inflammatory environment that may prime the host for exaggerated autoimmune responses triggered by viral infections, such as molecular mimicry following dengue infection.

We therefore propose a two-hit immunological model to explain the development of cerebellitis in this patient. The first hit is the persistent, low-grade immune dysregulation imposed by chronic transfusion-mediated alloantigen exposure in TDT. The second hit is dengue infection, which, through molecular mimicry between viral epitopes and cerebellar Purkinje cell antigens, triggers an acute, targeted autoimmune response in the already-primed immune system. This mechanism operates independently of iron overload, explaining why even an optimally chelated patient remains vulnerable. The prompt, complete response to corticosteroids further supports this immune-mediated pathogenesis and suggests that TDT, even when optimally managed, confers a distinct and under-recognised immunological risk for post-viral neurological complications.

While some cases of dengue viral cerebellitis present during the febrile phase, suggesting a para-infectious process, others occur in the post-recovery phase, 1–2 weeks after the initial illness, consistent with a post-infectious immune-mediated sequela. Overall, these cases typically show normal CSF findings and unremarkable MRI findings, which are consistent with our clinical presentation.

Consistent with the epidemiology of this complication, a retrospective observational cohort of 23 dengue patients with neurological manifestations from a tertiary centre in South India identified cerebellitis in 4 cases (17%), all of whom made complete recovery within 5–20 days. No statistically significant association was found between thrombocytopenia, dengue serotype, or metabolic derangements and the type of neurological manifestation, highlighting that cerebellitis may occur across a spectrum of dengue severity.[11] Another recently published case report has further expanded the documented global case series of dengue cerebellitis, reinforcing the importance of awareness of this complication across dengue-endemic regions.[12]

Acute disseminated encephalomyelitis (ADEM) was considered unlikely given the normal brain MRI and the absence of encephalopathy or multifocal white-matter lesions. Although many cases of dengue cerebellitis are managed conservatively, Khan et al. reported accelerated recovery (within one week) with intravenous steroids, mirroring the dramatic response observed in our patient.[6]

Conclusions

The development of post-dengue cerebellitis in an optimally chelated, non-splenectomised patient suggests that chronic antigenic exposure from repeated transfusions may foster an immune milieu highly susceptible to post-viral autoimmune phenomena. The excellent response to corticosteroid therapy highlights the importance of early recognition and immunosuppressive treatment for suspected post-infectious neurological sequelae in this vulnerable population. The proposed two-hit model, transfusion-driven adaptive immune priming followed by dengue-triggered molecular mimicry, provides a mechanistic framework for understanding why even optimally managed TDT patients may be at elevated risk of post-viral autoimmune complications. Clinicians should maintain a low threshold for investigating and treating immune-mediated neurological manifestations in multiply transfused patients presenting after dengue or other viral infections.

Author Declaration

Conflicts of Interest

The authors declare no conflicts of interest.

Author Contributions

Conception: SDS, AP, GR; literature review and initial manuscript: GR; editing of manuscript: SDS, AP; revisions: GR; supervision and final revision: SDS, AP. All authors read and approved the final version.

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Informed Consent

Written informed consent was obtained from the patient for publication of this case report.

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