Research Square

Preprints are preliminary reports that have not undergone peer review.
They should not be considered conclusive, used to inform clinical practice,
or referenced by the media as validated information.

Transverse myelitis and Guillain Barre Syndrome secondary to reactivation of viral hepatitis B

Wai Kin Su
Royal North Shore Hospital
Saad Shams Bin Shaheen
saad.shaheen@health.nsw.gov.au
Royal North Shore Hospital
Jacob George
Westmead Hospital
Natasha Gerbis
Royal North Shore Hospital
Simone I Strasser
Royal Prince Alfred Hospital
Salim Maher
Royal North Shore Hospital
Cameron Gofton
Royal North Shore Hospital

Case Report

Keywords:

Posted Date: July 10th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-10183658/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License.
Read Full License

Additional Declarations: No competing interests reported.

Abstract

Background

Hepatitis B virus (HBV) reactivation is a well-recognised complication of immunosuppressive therapy, particularly following B-cell-depleting agents such as rituximab. Although several extrahepatic neurological manifestations of HBV have been described, concurrent transverse myelitis and Guillain Barre syndrome (GBS) associated with HBV reactivation has not previously been reported.

Case Presentation

A 58-year-old man with a history of transformed diffuse large B-cell lymphoma developed HBV reactivation eight months after completing rituximab-based chemotherapy (R-CHOP) following premature cessation of antiviral prophylaxis. He presented with severe acute hepatitis, characterised by alanine aminotransferase 2,974 U/L, hepatitis B surface antigen seroreversion, hepatitis B e antigen positivity and detectable HBV DNA. Despite prompt recommencement of entecavir, he developed rapidly progressive lower limb weakness, paraesthesia, a T4 sensory level, neurogenic bladder and bowel dysfunction and absent lower limb reflexes. Magnetic resonance imaging demonstrated longitudinally extensive T2 hyperintensity extending from C4 to T10, consistent with transverse myelitis. Nerve conduction studies demonstrated a mixed axonal and demyelinating sensorimotor polyneuropathy consistent with Guillain Barre syndrome. Cerebrospinal fluid analysis excluded infectious, autoimmune and other inflammatory causes, including central nervous system HBV infection. The patient was treated with a five-day course of intravenous immunoglobulin alongside continued antiviral therapy. This resulted in progressive neurological recovery, complete radiological resolution of spinal cord abnormalities within three weeks, suppression of HBV viraemia, hepatitis B surface antigen clearance and normalisation of liver biochemistry by three months. Residual neurogenic bladder dysfunction persisted at follow-up.

Conclusions

This case represents, to our knowledge, the first reported association of concurrent transverse myelitis and Guillain Barre syndrome occurring during HBV reactivation. It expands the recognised neurological spectrum of HBV associated immune-mediated disease and highlights the importance of considering HBV reactivation in patients presenting with acute inflammatory neurological syndromes following immunosuppressive therapy. Early recognition, prompt antiviral treatment and immunomodulatory therapy may result in favourable neurological and virological outcomes.

Case

A 58-year-old man was admitted for evaluation of markedly abnormal liver biochemistry, discovered incidentally on routine laboratory testing. He was clinically well at presentation with no abdominal pain, fever or other systemic symptoms.

His past medical history was significant for transformed lymphoma from marginal zone to diffuse large B-cell lymphoma. Prior to the commencement of Rituximab, cyclophosphamide, doxorubicin, and vincristine (R-CHOP) chemotherapy for this condition, the patient underwent routine Hepatitis B Virus (HBV) serological testing. The baseline HBV serological results are summarised in Table 1.

Table 1
Baseline hepatitis B virus (HBV) serological profile obtained prior to commencement of R-CHOP chemotherapy.

Test	Result
Hepatitis B core antibody (anti-HBc)	Positive
Hepatitis B surface antibody (anti-HBs)	Negative
Hepatitis B surface antigen (HBsAg)	Negative
Hepatitis B e antibody (anti-HBe)	Negative
Hepatitis B DNA viral load	Negative

This testing was consistent with previous exposure to HBV. The route of acquisition was unclear and he was not born in a high prevalence country. There was also no history of chronic liver disease at the time of testing. He was commenced on Entecavir 0.5 mg daily for prophylaxis against HBV reactivation, prior to commencement of R-CHOP, for which he received 6 cycles in total. The patient continued Entecavir throughout the chemotherapy duration, however self-ceased at cessation of therapy. His medical history was also significant for ischaemic heart disease with previous percutaneous coronary intervention to the left anterior descending artery in 2015, dyslipidaemia and inflammatory arthritis.

He last received Rituximab 8 months prior to his presentation to hospital. On initial investigation, there was a marked hepatocellular pattern of liver enzyme derangement with evidence of HBV reactivation. The biochemical and virological findings at presentation are summarised in Table 2.

Table 2
Liver biochemistry and HBV serological and virological findings at presentation, consistent with HBV reactivation.

Test	Result
Bilirubin	14 umol/L
Alkaline Phosphatase ALP)	121 unit/L
Gamma Glutamyl Transferase (GGT)	119 unit/L
Alanine Aminotransferase (ALT)	2974 unit/L
Aspartate Aminotransferase (AST)	1446 unit/L
(anti-HBc)	Positive
(HBsAg)	Positive
HBeAg	Positive
HBV Viral Load	3.23×10^3 IU/mL

In light of these results, treatment with Entecavir 0.5 mg daily was commenced immediately. On day 7 of admission, the patient began to experience acute lower limb paraesthesia and proximal muscle weakness with absent knee and ankle reflexes. He demonstrated reduced sensation to pain and temperature to a sensory level at T4 bilaterally as well as a neurogenic bladder requiring an indwelling urinary catheterisation and a neurogenic bowel. Magnetic Resonance Imaging (MRI) of his thoracic and lumbar spine showed longitudinally extensive T2 hyperintense abnormalities involving the central cord from C4 to T10 with minimal expansion. The signal abnormality is mostly contiguous; however the changes appeared more patchy at the lower cervical and cervico-thoracic junction. An MRI of the brain did not reveal any intracranial enhancement or mass to suggest an inflammatory or infective disease or demyelination process.

Nerve conduction studies demonstrated electrophysiological evidence of a length-dependent sensorimotor polyneuropathy with mixed axonal and demyelinating features, as summarised in Table 3.

Table 3. Nerve conduction study findings demonstrating a length-dependent sensorimotor polyneuropathy with mixed axonal and demyelinating features.

Sensory Nerve Conduction

Nerve / Sites	Rec. Site	Onset Lat ms	Peak Lat ms	Amp. µV	Segments	Distance mm	Velocity m/s
L Median, Ulnar - Dig II Dig V							
Median Digit II	Wrist	3.5	4.1	7.6	Median Digit II - Wrist	120	34
Ulnar Digit V	Wrist	3.5	4.3	2.8	Ulnar Digit V - Wrist	90	25
R Median, Ulnar - Dig II Dig V							
Median Digit II	Wrist	3.2	3.9	3.6	Median Digit II - Wrist	130	40
Ulnar Digit V	Wrist	3.2	4.1	2.4	Ulnar Digit V - Wrist	100	31
R Sural, Superficial peroneal - Ankle							
Sural Lower Leg	Ankle	3.9	5.3	6.3	Sural Lower Leg - Ankle	110	28
Superficial peroneal Lower Leg	Ankle	3.4	4.6	2.7	Superficial peroneal Lower Leg - Ankle	100	29
L Sural, Superficial peroneal - Ankle							
Sural Lower Leg	Ankle	4.4	5.5	4.1	Sural Lower Leg - Ankle	100	23
Superficial peroneal Lower Leg	Ankle	3.6	4.5	2.1	Superficial peroneal Lower Leg - Ankle	110	30
R Radial - Anatomical snuff box (Forearm)							
Forearm	Snuff Box	2.4	3.1	19.0	Forearm - Snuff Box	100	42

Motor Nerve Conduction

Nerve / Sites	Muscle	Latency ms	Amplitude mV	Duration ms	Segments	Distance mm	Lat Diff ms	Velocity m/s
R Median - APB								
Wrist	APB	5.5	5.6	8.1	Wrist - APB	70		
Elbow	APB	10.5	5.4	8.6	Elbow - Wrist	230	5.1	45
L Median - APB								

Nerve / Sites	Muscle	Latency ms	Amplitude mV	Duration ms	Segments	Distance mm	Lat Diff ms	Velocity m/s
Wrist	APB	5.3	7.4	6.7	Wrist - APB	70		
Elbow	APB	10.6	7.4	8.8	Elbow - Wrist	240	5.3	46
R Ulnar - ADM								
Wrist	ADM	3.5	8.6	7.5	Wrist - ADM	60		
B.Elbow	ADM	9.1	8.8	8.4	B.Elbow - Wrist	250	5.6	45
L Ulnar - ADM								
Wrist	ADM	3.8	11.0	7.6	Wrist - ADM	60		
B.Elbow	ADM	10.1	9.1	8.1	B.Elbow - Wrist	240	6.3	38
R Peroneal - EDB								
Ankle	EDB	7.4	1.6	5.7	Ankle - EDB	85		
Fib head	EDB	15.5	1.7	6.8	Fib head - Ankle	260	8.1	32
L Peroneal - EDB								
Ankle	EDB	7.2	1.9	6.5	Ankle - EDB	85		
Fib head	EDB	16.5	1.6	7.4	Fib head - Ankle	270	9.3	29
R Tibial - AH								
Ankle	AH	7.8	9.7	6.5	Ankle - AH	80		
Pop fossa	AH	18.9	7.5	6.8	Pop fossa - Ankle	330	11.0	30
L Tibial - AH								
Ankle	AH	8.8	4.6	7.7	Ankle - AH	80		
Pop fossa	AH	18.9	3.7	9.9	Pop fossa - Ankle	320	10.1	32

F Wave

Nerve	F Lat ms	M Lat ms	F-M Lat ms	Min F Lat ms	Min M Lat ms	Min F-M ms
R Tibial - AH	66.3	8.5	57.7	44.0	8.5	35.4
L Tibial - AH	76.3	9.9	66.3	26.1	9.9	16.1
R Ulnar - ADM	34.1	4.4	29.6	24.8	4.4	20.4
L Ulnar - ADM	35.4	4.4	31.0	31.3	4.4	26.8

A lumbar puncture was subsequently performed to evaluate for infective, autoimmune and inflammatory causes of myelopathy, including central nervous system involvement by HBV. Cerebrospinal fluid (CSF) showed protein of 0.67 g/L (0.20–0.62 g/L) and Glucose 3.9 mmol/L (2.8–4.5 mmol/L). CSF microscopy and culture was negative and oligoclonal bands were absent. CSF autoimmune panel for NMDA

Receptor Ab, CASPR2 Ab, LGI-1 Ab, GABA-B Ab, DPPX Ab, IgLON5 Ab were all negative. Further CSF testing was conducted including HBV DNA PCR (negative), HBsAg (negative), HBeAg (negative), and HBeAb (positive, 0.91 s/co).

His neurological and laboratory findings were consistent with transverse myelitis as well as concurrent Guillain Barre Syndrome in light of both upper and lower motor neurone clinical findings. The patient was managed with intravenous immunoglobulin (IVIG, total of 125g in 5 separate daily doses of 25g). Following the 5-day course IVIG there was improvement in his neurological symptoms with return of his lower limb strength and return of sensation in his thoracic area with a sensory level now at T10 / T11. There remained absent knee and ankle reflexes bilaterally. He had an ongoing neurogenic bladder which required ongoing intermittent self-catheterisation.

Subsequent MRI Cervical, thoracic, and lumbar spine performed 3 weeks later showed resolution of the abnormal signals within the spinal cord and vertebral body. Specifically, the previously demonstrated T2 hyperintense abnormality involving the central cord from C4 to T10 was no longer present. On long term follow up at 3 months the patient had once again achieved HBV seroconversion, losing their HbsAg, an absence of HBV viraemia and complete resolution of liver enzyme derangement.

Literature review

HBV is a global health issue and patients who receive immunosuppressive therapy are at increased risk of HBV flare (in those who are HBsAg positive) or reactivation (in those who are HBsAg negative, but anti-HBc positive). HBV reactivation is characterised by the reappearance or a marked increase in HBV replication, typically defined as de novo detectable HBV DNA in a patient with previously undetectable HBV DNA or a 10-fold increase in HBV DNA from baseline, often accompanied by HBsAg seroconversion and hepatitis.[1] An episode of acute hepatitis is characterised by 2- to 3- fold increase in ALT above the patient's baseline level.[2] Patients who are at greatest risk of HBV reactivation are those with HBsAg positive or HBsAg negative/anti-HBc positive who receive B cell-depleting therapy such as rituximab, anthracycline derivatives, or high dose corticosteroid therapy for 4 or more weeks.[1,2]

Extrahepatic manifestations of HBV have been described including glomerulonephritis, polyarteritis nodosa, cryoglobulinemia, serum sickness-like syndrome, and Guillain-Barre syndrome.[3] Neurological complications of HBV that have been described include encephalitis, meningitis, myelitis, CNS haemorrhage, Meniere's disease, pyramidal and extrapyramidal tract dysfunction psychiatric disturbances, seizures, mononeuritis, plexitis and dermatomyositis.[4] Guillain-Barre syndrome is a rare extrahepatic manifestation of acute or chronic HBV infection. It is unclear whether it is the virus itself, immune-mediated injury or vascular related injury to the myelin sheath that is responsible.[4]

Transverse myelitis is characterised by acute or subacute, motor, sensory and autonomic spinal cord dysfunction.[5] This syndrome often arises as an autoimmune phenomenon following an infection or

vaccination, or in those with underlying autoimmune disease, or an acquired demyelinating disease such as multiple sclerosis or neuromyelitis optica spectrum disorders.[6]

In this case, our patient presented with signs, symptoms and investigations which were consistent with concurrent transverse myelitis as well as Guillain-Barre syndrome. Prompt initiation of treatment with antiviral therapy and intravenous immunoglobulin resulted in serological response with suppression of HBV DNA, improvement of liver enzymes and resolution of radiological findings. To our knowledge, this is the first case in the literature detailing transverse myelitis and Guillain-Barre syndrome associated with HBV reactivation. It is reasonable to consider testing for HBV in those patients who present with evidence of neurological phenomenon with a known association with immune-mediated injury.

Abbreviations

- ALP – Alkaline phosphatase
- ALT – Alanine aminotransferase
- AST – Aspartate aminotransferase
- anti-HBc – Hepatitis B core antibody
- anti-HBe – Hepatitis B e antibody
- anti-HBs – Hepatitis B surface antibody
- CSF – Cerebrospinal fluid
- GBS – Guillain-Barré syndrome
- GGT – Gamma-glutamyl transferase=
- HBeAg – Hepatitis B e antigen
- HBsAg – Hepatitis B surface antigen
- HBV – Hepatitis B virus
- IVIG – Intravenous immunoglobulin
- MRI – Magnetic resonance imaging
- PCR – Polymerase chain reaction
- R-CHOP – Rituximab, cyclophosphamide, doxorubicin, vincristine and prednisone

Declarations

Ethics approval and consent to participate

Ethics approval was not required for this single-patient case report according to institutional policy. Written informed consent was obtained from the patient for publication.

Consent for publication

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

Funding

No, this research did not receive funding.

Author Contribution

W.S. conceived the case report, collected the clinical data and drafted the initial manuscript. S.S. revised and edited the manuscript and coordinated the submission process. J.G., N.G., S.S., S.M. and C.G. critically reviewed the manuscript, provided expert clinical input and contributed to manuscript revisions. All authors read and approved the final manuscript.

Acknowledgements

Nil acknowledgements

Availability of data and materials

No or not applicable. This manuscript does not report data generation or analysis.

Competing Interests

No, I declare that the authors have no competing interests as defined by BMC, or other interests that might be perceived to influence the results and/or discussion reported in this paper.

References

1. Lubel JS, Strasser SI, Thompson AJ, Cowie BC, MacLachlan J, Allard NL, et al. Australian consensus recommendations for the management of hepatitis B. Med J Aust. 2022;216(9):478–486. doi:10.5694/mja2.51430.
2. Perrillo RP, Gish R, Falck-Ytter YT. American Gastroenterological Association Institute technical review on prevention and treatment of hepatitis B virus reactivation during immunosuppressive drug therapy. Gastroenterology. 2015;148(1):221–244.e3. doi:10.1053/j.gastro.2014.10.038.
3. Sarin SK, Kumar M, Lau GK, Abbas Z, Chan HLY, Chen CJ, et al. Asian-Pacific clinical practice guidelines on the management of hepatitis B: a 2015 update. Hepatol Int. 2016;10(1):1–98. doi:10.1007/s12072-015-9675-4.

4. Sonavane AD, Saigal S, Kathuria A, Choudhary NS, Saraf N. Guillain-Barré syndrome: rare extra-intestinal manifestation of hepatitis B. Clin J Gastroenterol. 2018;11(4):312–314. doi:10.1007/s12328-018-0847-3.
5. Frohman EM, Wingerchuk DM. Transverse myelitis. N Engl J Med. 2010;363(6):564–572. doi:10.1056/NEJMcp1001112.
6. Matsui M, Kakigi R, Watanabe S, Kuroda Y. Recurrent demyelinating transverse myelitis in a high titer HBs-antigen carrier. J Neurol Sci. 1996;139(2):235–237.

Figures



Figure 1

Image 1. Initial MRI T2 weighted sagittal images of cervical and thoracic spine showing T2 hyperintense abnormality involving the central cord.



Figure 2

Image 2. Repeat MRI T2 Weighted sagittal images of cervical and thoracic spine.