LB-CAS-001

Herpes Zoster Virus Infection Triggering Neuromyelitis Optica Spectrum Disorder: Two case reports

Alex Tanoto LIM[1 2] Gareth LIM Zigui[3] Tianrong YEO [345] Sapna P SADARANGANI [124]

[1]Department of Infectious Diseases, Tan Tock Seng Hospital, Singapore.

[2]National Centre for Infectious Diseases, Singapore.

[3] Department of Neurology, National Neuroscience Institute (Tan Tock Seng Hospital Campus), Singapore.

[4] Lee Kong Chian School of Medicine, Nanyang Technological University, Singapore

[5] Duke-NUS Medical School, Singapore

Introduction

Herpes-zoster (shingles) is caused by reactivation of the varicella-zoster virus (VZV). Shingles itself has been associated with various neurological manifestations from direct viral invasion into the central nervous system. However, there is growing evidence for the role of VZV in triggering neuromyelitis optica spectrum disorder (NMSOD), an immune-mediated neuroinflammatory disorder.

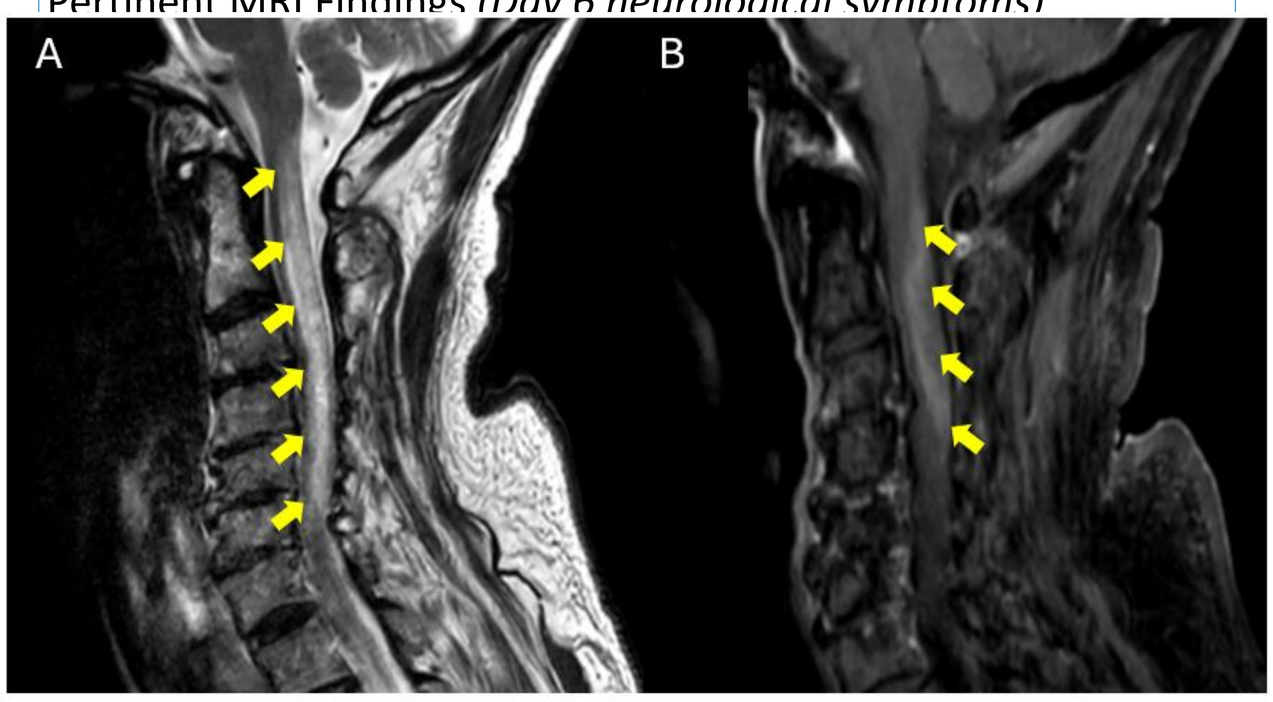
NMSOD, when compared to VZV myelitis, has a much higher relapse rate, worse prognosis and requires aggressive treatment modalities such as plasmapheresis and long-term immunosuppression, which are not included in the treatment of VZV myelitis.

Below we describe two cases with poor neurological outcome despite appropriate treatment, highlighting the high morbidity of this disease and thus the need for early recognition with a view towards implementation of appropriate treatment.

Patient A

A 96-year-old Chinese man with a history of hypertension, hyperlipidaemia, type 2 diabetes mellitus with chronic kidney disease and atrial fibrillation presented with a 4-day history of progressive right-sided weakness and numbness which occurred 3 days after onset of right C5-C6 shingles infection despite treatment with oral steroids and valacyclovir. On examination there was noted crusted over vesicles at right C5-6, right hemiplegia and hemisensory loss, along with pseudo-athetosis from sensory ataxia. He was started on IV acyclovir however developed worsening right hemiparesis and new acute urinary retention.

Pertinent MRI Findings *(Day 6 neurological symptoms)*

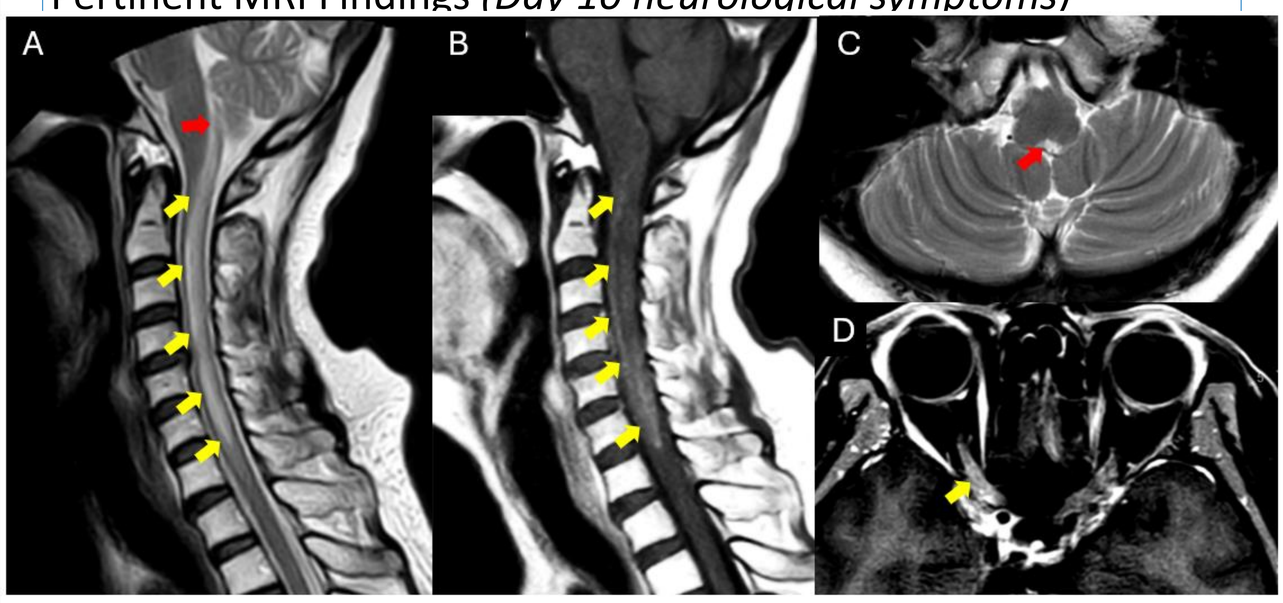


A: Sagittal T2 MRI of the cervical spine showed a longitudinally extensive T2 hyperintense lesion extending from C2 to C7 with cord oedema (arrows)
B: Sagittal STIR (Short Tau Inversion Recovery) MRI of the cervical spine with contrast showed patchy enhancement over the cord lesion (arrows)

Patient B

A 61-year-old Chinese female with a history of hyperlipidaemia and resected stage 2 breast cancer, now on anti-HER cyclin dependent kinase inhibitor (Abemaciclib), presented with a 1-day history of blurring of vision and involuntary hand movements along with 1-week of worsening centrifugal numbness starting 4 days after onset of right C4-C8 shingles. The shingles had been treated with oral Valaciclovir and oral Prednisolone. On examination there were crusted over vesicles at right C4-C8 with no active lesions, upper limb sensory ataxia with pseudo-athetosis, and a right rapid afferent pupillary defect. She was started on IV acyclovir, but her vision loss progressed, and she developed new acute urinary retention.

Pertinent MRI Findings *(Day 10 neurological symptoms)*



A: Sagittal T2 MRI of the cervical spine showed a longitudinally extensive T2 hyperintense lesion extending from the dorsal medulla to C7 with cord oedema (arrows)
B: Sagittal T1 MRI of the cervical spine with contrast showed patchy enhancement over the cord lesion (arrows)
C: Axial T2 MRI of the brain showed that the T2 hyperintense lesion involved the area postrema (red arrows on panel C, and on sagittal MRI in panel A)
D: Axial T2 MRI of the orbits showed equivocal right intracanalicular optic nerve hyperintensity (arrow)

Lumbar Puncture Results	Patient A (Day 7 CNS Symptoms)	Patient B (Day 9 CNS Symptoms)
Nucleated cells (Normal 0 – 5 cells/uL)	3	7 (lymphocytes predominant 46%)
Protein (Normal 0.10 – 0.40 g/L)	0.69	0.45
Glucose	Normal	Normal
Microbiological Results	CSF microbiology for a range of bacteria, mycobacteria, fungi and viruses including VZV DNA PCR was negative via multiplex PCR and relevant cultures. CSF VZV IgG negative.	
Serum Aquaporin-4 (AQP-4)	Detected (Day 11 CNS Symptoms)	Detected (Day 10 CNS Symptoms)

Post-Diagnosis Progress

Treatment

- Both received 5 days of intravenous methylprednisolone at 1g per day followed by a slow oral prednisolone taper
- Patient A underwent 5 cycles of plasmapheresis before maintenance therapy with mycophenolate mofetil
- Patient B underwent 7 cycles of plasmapheresis before maintenance therapy with 6-monthly Rituximab.

Outcomes

Both cases neurologically plateaued following plasmapheresis.

- Patient A at 3 months has persistent dense right hemiplegia and hemisensory loss and requires a long-term indwelling urinary catheter.
- Patient B at 1 year has bilateral complete vision loss, persistent altered sensation with allodynia and hyperaesthesia. She can stand with assistance but needs assistance with most activities of daily living.

Discussion

Post-VZV/HZV NMOSD is an increasingly recognized phenomenon with 9 cases reported in the literature between 2009 and 2020, excluding our patients.

Diagnostic clues are

1. Concurrent myelitis and brainstem involvement such as optic neuritis, cerebellar signs or area postrema syndrome
2. Relapsing or refractory disease despite anti-viral therapy

These cases demonstrate the need to be vigilant for alternative diagnosis and to consider testing for serum AQP-4 for patients with “VZV myelitis” for early diagnosis and appropriate management of this fulminant disease.

References

1) Xiaolin Wang et al. Long term outcomes of varicella zoster virus infection-related myelitis in 10 immunocompetent patients

2) H Eguchi et al. Herpes Zoster Radiculomyelitis with Aquaporin-4 Antibodies: A Case Report and Literature Review

3) EC Turco et al. Herpes zoster preceding neuromyelitis optica spectrum disorder: casual or causal relationship? A systematic literature review.