

# JC Virus-Associated Progressive Multifocal Leukoencephalopathy with Transverse Myelitis Successfully Treated Using Mirtazapine

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## ABSTRACT

*Progressive multifocal leukoencephalopathy (PML) is a demyelinating disease secondary to JC polyomavirus which rarely involves the spinal cord. Limited evidence suggest mirtazapine<sup>™</sup> may be effective treatment. We present a 38 year-old man on natalizumab for multiple sclerosis presenting with acute asymmetrical lower limb weakness, who was subsequently diagnosed with PML with transverse myelitis and successfully treated with mirtazapine.*

## Keywords

Progressive multifocal leukoencephalopathy, Multiple sclerosis, Polyomavirus.

## Introduction

Progressive multifocal leukoencephalopathy (PML) is a multifocal white matter demyelinating disease secondary to JC polyomavirus (JCV) infection [1]. PML typically arises from JCV reactivation in the setting of impaired cellular immunity from haematological malignancy, Acquired Immunodeficiency syndrome, and immunosuppressive monoclonal antibody treatment – most notably natalizumab for treatment of multiple sclerosis [1].

Due to the rarity of the disease, PML treatment is guided by very limited evidence and involves immune reconstitution and direct antiviral therapy [1]. Mirtazapine, a serotonergic 5-hydroxytryptamine 2A receptor (5-HT<sub>2A</sub>) antagonist, has been proposed as a potential treatment for PML, with benefit described in a few case reports [2-5].

PML tends to affect supratentorial and infratentorial white matter structures and present with progressively worsening multifocal neurological symptoms [1]. PML with spinal cord involvement is a very rare entity described in only a few case reports [6-8], with no previous cases of successfully-treated PML with spinal cord involvement. We present a case of a patient with natalizumab-associated PML presenting with transverse myelitis, successfully

treated with Mirtazapine.

## Case Presentation

A 38-year-old gentleman presented to hospital with a 6 hour history of progressive lower limb weakness. He also noted a recent decline in short-term memory but no issues with long term memory. He did not have bladder or bowel incontinence or retention. He did not have visual disturbance, loss of consciousness nor constitutional symptoms.

His medical history was significant for relapsing remitting multiple sclerosis diagnosed when he was 18 years-old and was well controlled without flares since commencing natalizumab therapy three years prior. He also diet-controlled type 2 diabetes mellitus without complications. He did not take any other regular medications. He never smoked and does not drink alcohol nor use illicit drugs.

On examination he was hemodynamic stable, afebrile, alert and oriented to time, place and person. However, he had difficulty with counting in reverse order. Lower limb neurological examination revealed severe asymmetrical distal weakness with 1/5 dorsiflexion and knee extension on the right side and lesser weakness on the left. There was loss of pain sensation, light touch, vibration and joint position sense at the ankles and knees worse on the right. Babinski sign was positive on the right. Lower limb reflexes were brisk and more hyperreflexic on the right. His cranial nerve examination was

normal. His upper limb neurological examination was normal for tone, power, reflexes and sensation. There was no truncal ataxia or other cerebellar signs. His cardiorespiratory and abdominal examination was unremarkable. There was no active tenosynovitis or abnormal rash.

Investigations revealed a high-normal C-reactive protein, but otherwise an unremarkable full blood count, electrolytes, creatinine, liver function tests, haematinic studies and coagulation profile.

Antinuclear antibodies, extractable nuclear antigen antibody screen, Anti-dsDNA antibodies, Anti-neutrophil cytoplasmic antibodies, complement studies, serum immunoglobulins and rheumatoid factor were all normal/negative. Blood and urine cultures were negative.

Serum anti-aquaporin antibodies and anti-myelin oligodendrocyte glycoprotein antibodies were negative. Serum copper level was normal.

Cerebral spinal fluid analysis revealed lymphocytic pleocytosis with a lymphocyte count of 30 cells/mm. JC virus was detected by polymerase chain reaction (PCR) with 300 copies DNA/ml. PCR was otherwise negative for other pathogens. Cytology was negative. Oligoclonal bands were detected in cerebrospinal fluid and serum in keeping with known multiple sclerosis.

Serology for Epstein-Barr virus, Cytomegalovirus, Human immunodeficiency virus, Human T cell virus type 1, Mycoplasma, and Syphilis was negative. Nasopharyngeal PCR was negative for respiratory viral pathogens.

Computerised tomography of the brain did not reveal any lesions, hemorrhage or infarct. Magnetic resonance imaging (MRI) brain and whole spine revealed a hyperintense signal on T2 fluid attenuated inversion recovery (FLAIR) sequence in the right lateral spinal cord at the L4-L5 level, along with hyperintense lesions in left thalamus. There was no vessel occlusion on MRI angiography.

### Outcome and Follow-up

The patient was diagnosed with transverse myelitis on the basis of the radiological findings and clinical presentation, along with PML on the basis of detected JC virus in CSF in the setting of natalizumab immunosuppressive therapy.

The diagnosis and treatment options were discussed with the patient. He declined steroid therapy due to concern regarding hyperglycaemia and other adverse effects, but was agreeable to other options. He was subsequently commenced on mirtazapine 15 mg once daily and started inpatient rehabilitation.

The patient continued to improve to the point where after 6 weeks, he was able to walk independently and had no residual neurologic deficit. Repeat CSF PCR for JC virus was negative. MRI brain and whole spine showed resolution of the thalamus and spinal cord

lesions. Natalizumab was ceased.

### Discussion

PML with spinal cord involvement is an exceedingly rare entity with only a few case reports [6-8], and no previous reports of successful treatment. We present a case of natalizumab-associated PML with spinal cord involvement that was successfully treated with mirtazapine. Mirtazapine is thought to prevent viral entry into glial cells by antagonizing 5-HT<sub>2A</sub>R [1]. There is a small body of evidence suggesting that mirtazapine may be an effective treatment for PML – particularly PML associated with natalizumab [2-5].

To the best of our knowledge, this case represents the first case of PML with spinal cord involvement successfully treated with mirtazapine. Future research could involve larger-scale interventional studies to further elucidate the efficacy of mirtazapine for treating PML.

### Conclusion

In summary, we present a case of natalizumab-associated PML with spinal cord involvement successfully treated with mirtazapine. PML should be considered as a rare differential diagnosis for patients presenting with neurological compromise in the setting of impaired cellular immunity. Mirtazapine may be considered as a potential therapeutic agent for PML.

### References

1. Cortese I, Reich DS, Nath A. Progressive multifocal leukoencephalopathy and the spectrum of JC virus-related disease. *Nat Rev Neurol*. 2021; 17: 37-51.
2. Jamilloux Y, Kerever S, Ferry T, et al. Treatment of Progressive Multifocal Leukoencephalopathy With Mirtazapine. *Clin Drug Investig*. 2016; 36: 783-789.
3. Mullins C, Miranda J, Sandoval H, et al. The Benefit of Mirtazapine in the Treatment of Progressive Multifocal Leukoencephalopathy in a Young HIV-positive Patient: A Case Report. *Innov Clin Neurosci*. 2018; 15: 33-35.
4. Takashi Matsudaira KA, Wataru Oishi, Akira Sugiura, et al. Mirtazapine treatment ceased the progression of progressive multifocal leukoencephalopathy associated with systemic sarcoidosis. *Neurology and Clinical Neuroscience*. 2014; 2: 158-160.
5. Verma S, Cikurel K, Korolnik IJ, et al. Mirtazapine in progressive multifocal leukoencephalopathy associated with polycythemia vera. *J Infect Dis*. 2007; 196: 709-711.
6. Bernal-Cano F, Joseph JT, Korolnik IJ. Spinal cord lesions of progressive multifocal leukoencephalopathy in an acquired immunodeficiency syndrome patient. *J Neurovirol*. 2007; 13: 474-476.
7. Mohamed GA eDOG, Abd el Nour H, Neuman D, et al. Case report: JC virus induced Longitudinally Extensive Transverse Myelitis in immunocompromised patient. *Case reports*. 2019; 56.
8. Takeda S, Yamazaki K, Miyakawa T, et al. Progressive multifocal leukoencephalopathy showing extensive spinal cord involvement in a patient with lymphocytopenia. *Neuropathology*. 2009; 29: 485-493.