Progressive Multifocal Leukoencephalopathy (PML) in Immunocompetent Patient Secondary to Carbamazepine

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**Introduction**

Progressive Multifocal Leukoencephalopathy (PML) is a deadly demyelinating disease of the brain that is caused by reactivation of the polyomavirus JC (JCV) and is typically seen in patients with profound cellular immunosuppression, HIV infection, haematological malignancies and organ transplant.(1) We describe a case of PML in an immunocompetent 65 year-old lady, who improved clinically following cessation of her Carbamazepine, with demonstration of clearance of JCV from CSF and blood, and improving appearances on MRI.

**History and Presentation**

Female (65 years) referred to Neurology for review

**Presenting Complaint**
- New onset discoordination
- Left hand weakness and dragging of left leg

**History of Presenting Complaint**
- Brief non specific viral illness (diarrhoea, lethargy, dizziness)
- Left-sided cerebellar manifestations in the following weeks
- Unable to perform daily activities independently.

**Past Medical History**
- Epilepsy (well-controlled over many years)

**Drug History**
- Carbamazepine and Levetiracetam

**Social History**
- Lives with husband and works on farm

**Initial Assessment**
- Left-sided cerebellar signs: Past-pointing, intention tremor, ataxia, slow and narrow gait
- Reduced power in left hip flexion

**Investigations**
- CT Brain: Generalised atrophy, no focal abnormality
- MRI Brain: Left cerebellar inflammatory changes
- LP: Normal CSF with negative PCR and no oligoclonal bands
- Negative HIV, syphilis and Borrelia serology and vasculitis screen

**Differential Diagnosis**
- Post-infective cerebellitis
- Started on steroids

**Follow-up**

The patient continued to deteriorate clinically, and required hospital admission due to falls, worsening ataxia and dysarthria.

**Further Investigations & Management**
- Repeat MRI Brain showed deteriorating cerebellar change
- CT Body and PET-CT showed no evidence of malignancy
- Repeat LP: showed now elevated proteins (331)
- Discussed at MDT, biopsy deemed too risky
- Single blood culture grew gram positive bacilli. Treated for possible Listeria infection with IV amoxicillin and gentamicin, however she continued to deteriorate

**Clinical Progress over the next month:**
- Symptoms continued to worsen
- Repeat MRI: Worsening cerebellar changes now affecting right hemisphere
- Carbamazepine was stopped as this is associated with ataxia
- Hypogammaglobulinaemia noted (low IgM and IgG, no paraprotein band)
- Repeat LP showed no new biochemical change
- CSF virus PCR was positive for JCV (1635 copies/ml) with raised JC virus antibody.
- Detectable JCV virus in blood: Positive PCR and JCV antibodies

**Fig. 1**
- Inflammatory change in left cerebellar hemisphere

**Fig. 2**
- Worsening left cerebellar changes, in keeping with patient deterioration (March 2018)

**Fig. 3**
- Inflammatory changes now in both cerebellar hemispheres (February 2018)

**Fig. 4**
- Slight improvement in inflammatory changes, particularly in the right cerebellar hemisphere (August 2018)

**Discussion**

- The clinical presentation of our patient, along with demonstration of JCV in blood and CSF and her MRI changes, confirms the diagnosis of PML.
- After stopping Carbamazepine she improved clinically, with JCV now cleared from CSF and MRI changes beginning to resolve. This suggests a link between PML and Carbamazepine in her case.
- Carbamazepine is rarely known to cause hypogammaglobulinaemia,(2) as seen in our patient. Whether this was enough to cause JCV reactivation is unclear.
- PML can be seen in patients who do not have any clear immunocompromise.

**References**

2. Seizure. 2012 Apr;21(3):229-31