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

Dr. Ali Khan[1], Dr Noha Elsakka[2]
(1) Infectious Diseases Registrar, Aberdeen Royal Infirmary, UK
(2) Consultant Medical Microbiology and Virology, Aberdeen Royal Infirmary, UK

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

Diagnosis and Management

Definitive Diagnosis

- Demonstration of JCV in blood and CSF along with the clinical picture and MRI changes point towards a diagnosis of PML
- There was no obvious immunocompromise, except for slightly low IgM and IgG levels, and the only intervention made was to stop Carbamazepine
- In the next few weeks to months, our patient noticed improvement in her symptoms, so much so that she was once again able to dress, toilet and mobilise independently, no longer needing assistance
- Her most recent MRI shows slight improvement in the cerebellar changes that explained her symptoms.
- Follow up LP and blood tests has shown clearance of JC virus in both CSF and blood.
- Her immunophenotyping shows no abnormality in her white cell populations.

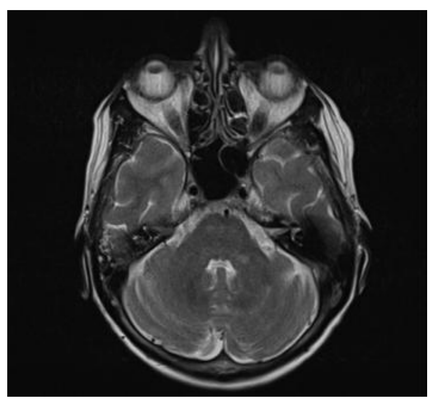

Fig. 1

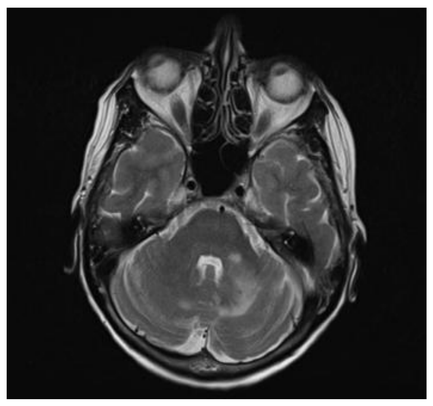

Fig. 2

Figure 1: Inflammatory change in left cerebellar hemisphere (February 2018)

Figure 2: Worsening left cerebellar changes, in keeping with patient deterioration (March 2018)

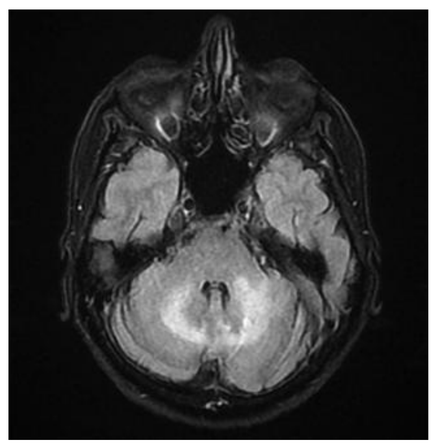

Fig. 3

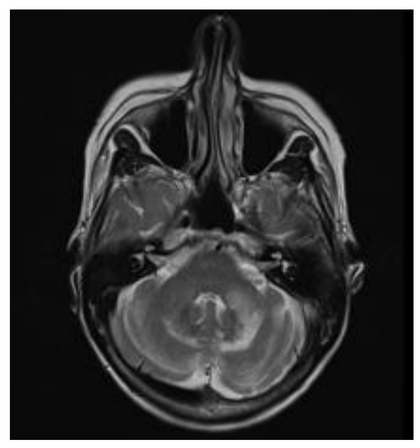

Fig. 4

Figure 3: Inflammatory changes now in both cerebellar hemispheres (April 2018)

Figure 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

1. *Journal of Neurology, Neurosurgery & Psychiatry 2010;81:247-254*
2. *Seizure. 2012 Apr;21(3):229-31*