

## CASE REPORT

# Progressive multifocal leukoencephalopathy masquerading as cerebellar infarction

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## Abstract

Progressive neurological signs and symptoms, in immunocompromised individuals, could be due to progressive multifocal leukoencephalopathy (PML). We report the case of a patient who present a stroke unit with symptoms that were consistent initially with a posterior circulation stroke. Prior chemotherapy with Rituximab, for a lymphoma, had predisposed the patient to infection with the JC virus. Physicians need to be aware of the condition, and patients need to aware of these risks of chemotherapy.

**Keywords:** stroke, progressive multifocal leukoencephalopathy, brain infarction, posterior circulation, rituximab, ataxia, older people

## Introduction

A 79-year-old man presented with recent onset of falls, ataxia and diplopia. A brain MRI scan showed a focal lesion in the middle cerebellar peduncle leading to a diagnosis of ischaemic stroke. Two months later, he was readmitted with progressive ataxia and feeling ‘sea-sick’. The MRI scan showed progression of the signal abnormality (Figure 1), crossing the midline and sparing the dentate nucleus. The possibility of PML was raised. Over the preceding 16 months, he had been treated for Non-Hodgkin’s Lymphoma with radiotherapy and three doses of chemotherapy (fludarabine, cyclophosphamide and rituximab), the last dose 6 months prior to initial presentation. In addition, he had been given prophylactic IV immunoglobulin for repeated admissions with neutropenic sepsis. Laboratory investigations revealed normal blood counts, urea, creatinine, glucose; negative serology for HIV, Toxoplasma, Varicella zoster and CMV. Anti-neuronal antibodies were negative, and oligoclonal bands were weakly positive. PCR for JC virus was positive confirming a diagnosis of PML. He deteriorated subsequently and died peacefully.

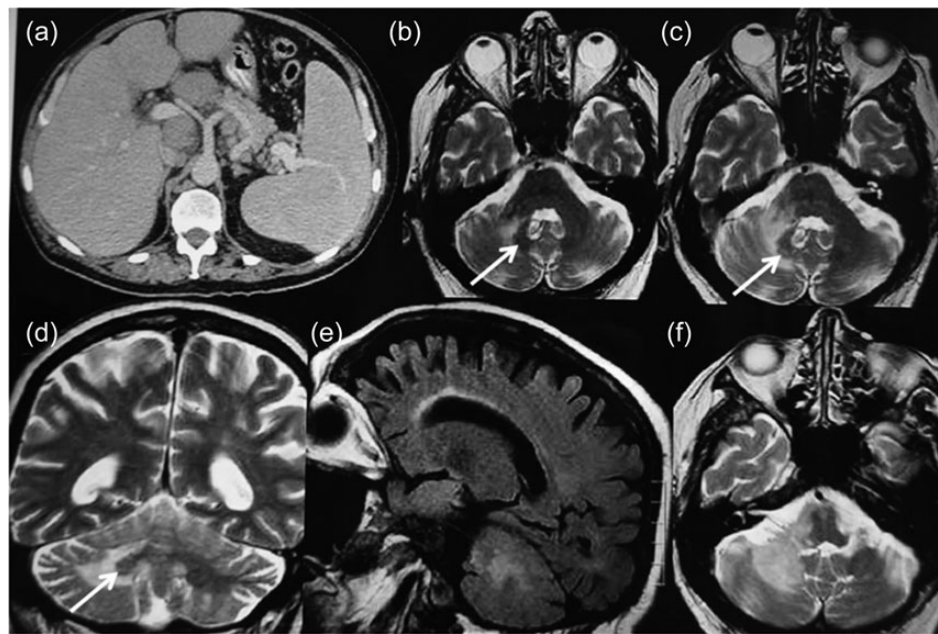
## Discussion

PML is a demyelinating disease of the CNS that occurs as an opportunistic infection in the setting of immunosuppression

[1, 2]. A productive infection of oligodendrocytes (and to a lesser extent astrocytes) results in cell death [2, 3]. PML was rare until the mid-1980s, but is now an AIDS-defining illness, affecting ~3% of HIV-seropositive patients [3]. A second important group of patients, notably those patients who have suffered haematological malignancies constitute 8% of PML cases [2].

The virus causing PML, JC virus, belongs to polyoma-virus family. Within the population, JC virus is ubiquitous as demonstrated by antibodies to the viral capsid found in 70–80% of adults [4]. The mode of transmission remains unclear, but the tonsils are a prime initial site of a childhood infection. A viraemia, followed by seeding and latency occurs. The JC virus has a narrow host cell range, affecting the tonsillar stromal cells, kidney uroepithelium, CD20+ B lymphocytes and CD34+ haemopoietic stem cells. During immunosuppression, a mutation and expansion of a non-coding control region of DNA occurs allowing the virus to become neurotrophic, infecting oligodendrocytes and astrocytes [4, 5].

Common signs and symptoms are motor dysfunctions (e.g. a lack of coordination, gait disturbances, ataxia and hemiparesis), cognitive impairments (e.g. subcortical dementia, disorientation and behavioural changes) and visual defects—these are enshrined within the literature as a classical triad [3]. Radiological findings of PML do not correspond



**Figure 1.** (a) CT abdomen showing splenomegaly and lymph nodes. (b to f) MRI head showing gradually increasing lesion in the right middle cerebellar peduncle with sparing of the dentate nucleus.

with specific vascular territories [1]. A brain biopsy is the gold standard to confirm a diagnosis of PML, but this is both invasive and risky, consequently CSF testing using a qPCR is the current diagnostic.

Rituximab is a chimeric IgG1 monoclonal antibody that targets CD20 on B lymphocytes and causing their depletion by a complement-mediated cytotoxicity. It is used in the treatment of lymphoproliferative disease, rheumatoid arthritis and SLE [2–4]. The mechanism by which rituximab may pre-dispose to PML appears to be more complex than simply one of B-cell depletion and reduced immune surveillance: if the Rituximab failed to eliminate some of the B cells that are latently infected, these cells could traffic to the brain and initiate an infection in the oligodendrocyte—a ‘Trojan horse’ hypothesis [3, 4].

Treatment for PML is rarely successful without immune reconstitution

Lessons for the clinician:

- (1) In immunocompromised patients, neurological symptoms may be due to opportunistic infections including PML.
- (2) If the lesion does not conform to a vascular territory, ischaemia is an unlikely cause.
- (3) PML involves white matter and spares the grey matter.
- (4) The temporal profile of the disease is important in neurological diagnoses.
- (5) Patients receiving Rituximab should be informed of the risk of opportunistic infections, including PML.
- (6) The median time to onset of clinical disease after administration of Rituximab is over 6 months.

## Key points

- In immunocompromised patients, neurological symptoms may be due to opportunistic infections including PML.
- Ischaemia is unlikely to be the cause if the lesion does not conform to a vascular territory.
- The temporal profile of the disease is important in neurological diagnoses.
- Patients receiving Rituximab should be informed of the risk of opportunistic infections, including PML.
- The median time to onset of clinical disease after administration of Rituximab is over 6 months.

## Conflicts of interest

None declared.

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