Progressive multifocal leukoencephalopathy

Progressive multifocal leukoencephalopathy (PML) is a rare and often fatal viral disease characterized by progressive damage (-pathy) or inflammation of the white matter (leuko-) of the brain (-encephalo-) at multiple locations (multifocal). It is caused by the JC virus, which is normally present and kept under control by the immune system. The JC virus is harmless except in cases of weakened immune systems. In general, PML has a mortality rate of 30–50% in the first few months, and those who survive can be left with varying degrees of neurological disabilities.

PML occurs almost exclusively in patients with severe immune deficiency, most commonly among patients with acquired immune deficiency syndrome (AIDS), but people on chronic immunosuppressive medications including chemotherapy are also at increased risk of PML, such as patients with transplants, Hodgkin's lymphoma, multiple sclerosis, psoriasis, and other autoimmune diseases.

PML in HIV/AIDS

Progressive multifocal leukoencephalopathy (PML):

1. is caused by a ubiquitous polyomavirus (a subgroup of papova virus, small nonenveloped viruses with a closed circular double DNA-stranded genome) called “JC virus” (JCV, named after the initials of the patient in whom it was first discovered, not to be confused with Jakob-Creutzfeldt—a prion disease—nor with Jamestown Canyon virus, also confusingly called JC virus, a singlestranded RNA virus that occasionally causes encephalitis in humans). 60–80% of adults have antibodies to JCV

2. frequently manifests in patients with suppressed immune systems, including

a) AIDS: currently the most common underlying disease associated with PML

b) prior to AIDS, the most common associated diseases were chronic lymphocytic leukemia & lymphoma

c) allograft recipients: due to immunosuppression

d) chronic steroid therapy

e) PML also occurs with other malignancies, and with autoimmune disorders (e.g. SLE)

3. pathologic findings: focal myelin loss (demyelination, ∴ affects white matter) with sparing of axon cylinders, surrounded by enlarged astrocytes and bizarre oligodendroglial cells with eosinophilic intranuclear inclusion bodies. EM can detect the virus. Sometimes occurs in brainstem and cerebellum

4. clinical findings: mental status changes, blindness, aphasia, progressive cranial nerve, motor, or sensory deficits and ultimately coma. Seizures are rare

5. imaging findings:

6. clinical course: usually rapidly progressive to death within a few months, occasionally longer survival occurs inexplicably. There is no effective treatment. Some promise initially with anti-retroviral

therapy

Diagnosis

Definitive diagnosis requires brain biopsy (sensitivity: 40–96%), although it is infrequently employed. JCV has been isolated from brain and urine. Polymerase chain reaction (PCR) of JCV DNA from CSF has been reported, and is specific but not sensitive for PML

Case reports

A 54-year-old woman with systemic lupus erythematosus and coexisting autoimmune hepatitis who presented with progressive cognitive decline, right hemiparesis, and ataxia was found to have PML. She had severe CD4 lymphopenia. She was managed with low-dose prednisolone and plasmapheresis after which she showed significant clinical improvement. This case highlights the diagnostic and therapeutic challenges encountered in managing a case of Progressive multifocal leukoencephalopathy in the setting of autoimmune conditions with profound lymphopenia [1].

1)
Gomathy S, Panigrahi B, Tirlangi PK, Wig N, Brijwal M, Sharma MC, Garg A, Tripathi M, Mohta S, Doddamani R, Vibha D, Singh RK, Yadav R, Sahu S, Suri V, Kaur K, Tripathi M, Rohatgi A, Elavarasi A. Progressive multifocal leukoencephalopathy in a patient with systemic lupus erythematosus and autoimmune hepatitis. Int J Rheum Dis. 2022 May 10. doi: 10.1111/1756-185X.14331. Epub ahead of print. PMID: 35535671.