

5-2019

Progressive Multifocal Leukoencephalopathy Presenting as Transverse Myelitis

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Recommended Citation

Onwubiko, Ifeoma; Taneja, Kanika; Gupta, Nilesh; and Mukherjee, Abir, "Progressive Multifocal Leukoencephalopathy Presenting as Transverse Myelitis" (2019). *Case Reports*. 65.
<https://scholarlycommons.henryford.com/merf2019caserpt/65>

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Introduction

Progressive multifocal leukoencephalopathy (PML) is a rare demyelinating disease caused by reactivation of JC virus affecting typically subcortical and periventricular white matter of immunocompromised hosts (HIV infection, hematologic malignancies). Cerebral hemispheric white matter are most commonly affected by lytic infection, leading to progressive damage to oligodendrocytes in the CNS. Neuroimaging usually highlights scattered foci of white matter hypodensity not attributable to contrast enhancement or mass effect. In contrast, we present an unusual case of PML predominantly affecting cervical spinal cord and brainstem in an immunocompetent host. This is a rare subset of PML case that can occur in association with connective tissue disorders (Sjögren in this case), SLE being the most common. PML should be considered in the differential diagnosis of spinal cord/brainstem lesions, particularly in the patients with connective tissue disorders.

Case Presentation and Management

A 65-year-old female with known history of Sjögren syndrome and liver cirrhosis presented to Emergency department with a broken ankle secondary to a four-month-old fall. She also reported a four-week history of vertigo, hemiparesis and right sided weakness.

On examination, she was minimally responsive and obtunded. Her speech was slurred with a right facial droop with no cough and gag reflex. There was absent and reduced muscle tone in the right extremities and left upper extremity respectively.

Laboratory test showed high ammonia levels (47umol/L), with abnormal liver enzymes and kidney function tests. Cerebrospinal analysis was suggestive of a traumatic tap. Immunoglobulin G antibodies to SSA/Ro, SSB/La were positive. Thyroglobulin antibodies and Anti-nuclear antibodies were elevated.

MRI of the spine without contrast showed T2 signal abnormality involving the medulla extending into the upper cervical cord to C2-C3 level with C3 medullary lesions. Patient continued to clinically deteriorate, expiring eight days later.

At autopsy, gross examination of the brain revealed unremarkable cerebral hemispheres, sinuses and spinal cord. Histological examination was suggestive of multifocal white matter lesions in the cervical spinal cord, pons, medulla, mid brain, cerebellum and basal ganglia. These lesions were characterized by pallor, edema, perivascular lymphocytic cuffing, microglial nodules, influx of activated microglial and numerous oligodendroglial nuclei with ground glass inclusions. The inclusions were immunoreactive with Simian virus-40 (SV-40), highlighted by P53 and MIB-1 immunostains. Other areas showed moderate hypoxic ischemic changes in the neocortex and hippocampus. These findings supported a diagnosis of PML with moderate hypoxic ischemic changes.

Imaging



Figure 1. MRI of the spine without contrast. Arrow shows T2 abnormality involving the medulla extending into the upper cervical cord to C2-C3 level.

Discussion

Progressive multifocal leukoencephalopathy is an opportunistic demyelinating disease of the central nervous system (CNS) caused by reactivation of the DNA viruses of the polyoma group. It is caused by one of two polyomavirus, John Cunningham virus (JCV). The disease predominantly affects immunocompromised hosts, including people with leukemia, HIV-1 infection, lymphomas and renal transplant.

JC virus seropositivity has been demonstrated in approximately 33%-90% of people depending on the study and geographical location. Inciting factors to the development of PML are the possibility of transformation of a large proportion of lymphocytes which become unable to participate in immune responses and therapy induced immunodeficiency.

Patient with autoimmune conditions such as systemic lupus erythematosus, sarcoidosis, rheumatoid arthritis and Sjögren's disease independent of immunotherapy could develop PML due to disease associated lymphopenia. Although 5.2% of Sjögren syndrome have CD4+ T-lymphocytopenia, to our knowledge, only one case of PML has been reported in a patient with known history of the disease.

The pathophysiology could be attributed to leukocyte sequestration in enlarged spleen arising from portal hypertension from hepatic cirrhosis leading to patients developing leucopenia. In addition, hypogammaglobulinemia sequel to liver cirrhosis contributes to decreased immunity.

This case highlights that although PML has been documented in immunocompromised patients, it has rarely been associated with connective tissue disorders. Awareness of this entity is crucial for pathologists as well as physicians to consider it as differential diagnosis of white matter lesions irrespective of the sites of neuraxial involvement.

Figures

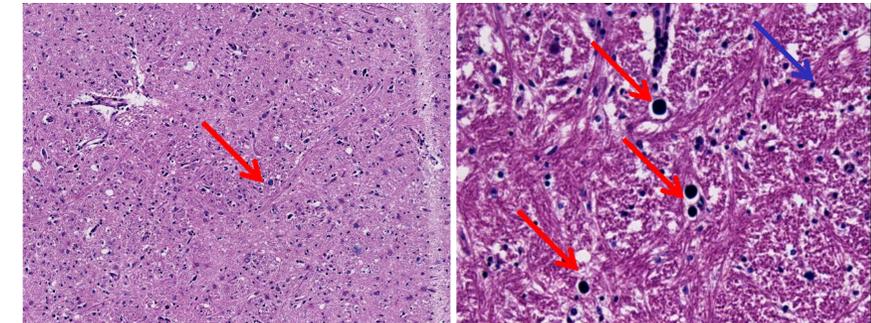


Figure 2: H&E stain x10

Figure 3: H&E stain x20

Figure 2 and 3. H&E stains highlighting JC virus inclusion s (red arrows) and unremarkable oligodendrocytes (blue arrow).

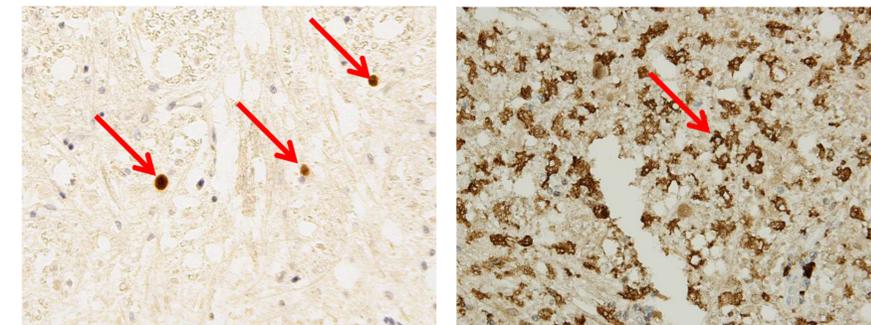


Figure 4: SV-40 highlighting JC virus inclusions

Figure 5: CD 163 highlighting perivascular monocyte/macrophage

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