Diagnostic Slide Session, Case 2021-10

Thomas D. Zaikos, M.D., Ph.D.,¹ Peter Burger, M.D.,¹ Fausto Rodriguez, M.D.,¹
Jason Savell, M.D.,² and Meaghan Morris, M.D., Ph.D.¹

¹ The Johns Hopkins Hospital, Department of Pathology, Division of Neuropathology
² Morton Plant Hospital, Department of Pathology
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Clinical history

• 47-year-old female
• HIV-positive
• Presents with generalized weakness, dizziness, mild incoordination
Imaging

FLAIR

T1 post-contrast
Histology
Histology
Discussion

1) Differential diagnosis
2) Pathogenesis
Differential diagnosis

- JCV granule cell neuronopathy
- Progressive multifocal leukoencephalopathy (PML)
- Lymphoma
- Infectious/Inflammatory
Immunohistochemistry

- Inflammation is composed of B (CD20) and T (CD3) cells
- Rare p53 positive cells
Immunohistochemistry
In situ hybridization

Courtesy of Caterina Giannini, MD, PhD
Final Diagnosis

Chronic inflammation and JC virus granule cell neuronopathy.
Overview of JCV neuropathology

**JC virus infection**
- Ubiquitous human viral pathogen
- Impaired cellular immunity can lead to reactivation and pathology

**Spectrum of JCV-associated neuropathology**
- WM oligodendrocytes and astrocytes ➔ PML
- Cerebellar granule cell neurons ➔ JCV granule cell neuronopathy
- Cortical pyramidal neurons ➔ JCV encephalitis
- Leptomeninges ➔ JCV meningitis
**Clinical presentation**

- Immunocompromised
- Ataxia, dysarthria

**Typical MRI findings**

- T2/FLAIR: confluent hyperintensities in cerebellum and cerebellar peduncles
- Non-enhancing
- Bilateral, diffuse cerebellar atrophy

**Ancillary Studies**

- CSF viral genotyping

Koralnik IJ *et al.* Ann Neurol. 2005 Apr;57(4)
JCV granule cell neuronopathy (JCV GCN)

**Histology**
- Focal loss of internal granule cell neurons
- Enlarged, hypochromatic granule cell nuclei
- Spares Purkinje cells

Nath A. & Berger JR. Clinical Neurovirology (2nd ed.). 2020
The spectrum of JCV-associated neuropathology

Miskin DP and Koralnik IJ. Curr Opin Neurol. 2015;28(3)
Summary of JCV-GCN

- Immunosuppressed patients
- Clinical history of incoordination
- Radiographic evidence of cerebellar atrophy +/- T2/FLAIR hyperintensities
- Focal granule cell neuron loss with scattered granule cell neurons with enlarged nuclei
  - Confirmed with ancillary tests to demonstrate JCV infection of granule cell neurons
- May occur in isolation or concomitant with PML or other JCV-associated neuropathology
References


Thank you

JHH Neuropathology
- Charles Eberhart
- Meaghan Morris
- David Nauen
- Stephen Nix
- Fausto Rodriguez
- Juan Troncoso