Submitted by:

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Clinical History:

The patient was a 67-year-old gentleman with a history of longstanding (39 years), debilitating multiple sclerosis (MS). He had been treated with Tysabri (Natalizumab) during the past 5 years. Due to new onset of neurological symptoms including bilateral arm dysmetria, slurred speech and choking, MRI was performed. FLAIR/T2 showed longstanding lesions in bilateral cerebral peri-ventricular regions (Fig. 1) and new hyperintense foci in bilateral cerebellar white matter extending into middle cerebellar peduncles (Fig. 2). The lesions had well-defined borders with no significant mass effect and minimal contrast enhancement. CSF analysis showed a normal differential count and glucose level with elevated protein level, elevated IgG index and oligoclonal bands. HHV6, HSV1, HSV2, and cytology studies were negative.

He was admitted for treatment of possible progressive multifocal leukoencephalopathy (PML). Tysabri was discontinued, and plasmapheresis and IV dexamethasone initiated. Despite treatment, his neurological condition continued to deteriorate. He was discharged to hospice and expired 8 days afterward.

Autopsy findings:

Autopsy revealed multiple grossly well-defined lesions in bilateral cerebral peri-ventricular areas (Fig. 3), cerebellar white matter (Fig 4), and gray and white matter of the spinal cord.

Material submitted:

H&E stains of deep cerebral white matter and cerebellar white matter lesions.

Points for discussion:

How have classical demyelinating lesions of MS changed with new therapies? What does the histopathology of these lesions suggest about the diagnosis, pathogenesis and treatment?