# 62nd ANNUAL DIAGNOSTIC SLIDE SESSION 2021

## CASE 2021-7

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Clinical History:

This 65-year-old woman presented in 2010 with a 2 year history of intermittent headaches, a 6-month history of worsening ataxia, word-finding difficulties, tremor, confusion, and hallucinations followed by a more rapid onset of confusion and disturbed spatial perception and progressive left visual field loss. Cerebrospinal fluid (CSF) studies, cerebral angiogram, and an electroenceophalogram were unrevealing. MRI demonstrated abnormal T2 signal centered in right temporoparietal cortex and subcortical white matter, and minimal cortical enhancement on postcontrast images, which was overall concerning for vasculitis or mitochondrial encephalopathy.

In 2015, she subsequently underwent a right parieto-occipital brain biopsy, which did not render a specific diagnosis. Following her surgery, she had a comprehensive mitochondrial DNA analysis and MRI spectroscopy performed, both of which were unrevealing. In 2016, she had multiple episodes, lasting up to 3 days, in which she developed severe headache, slurred speech, arm heaviness and numbness, decrease in vision, and mild confusion. Head imaging studies did not demonstrate evidence of disease progression. She underwent whole exome sequencing, which identified a variant of unknown significance in *MACF1*. In 2016, her brother began experiencing stroke-like and encephalitis-like episodes similar to his sister. In 2017, both siblings underwent skin biopsy which further directed clinical work-up.

Autopsy findings:

At the time of autopsy, the brain appeared normally developed with mild hydrocephalus ex vacuo with a brain weight of 1026.4 grams (fixed). There was evidence of a right parietooccipital biopsy site defect and a right inferior parietal lobe laminar necrosis with associated softening. Mild depigmentation of the substantia nigra was present.

Material submitted:

1. H&E section of amygdala
2. H&E section of midbrain
3. H&E section of right leg skin

Points for discussion:

1. Differential diagnosis
2. Ancillary immunohistochemical/additional stains
3. Useful ante-mortem tests