49th ANNUAL DIAGNOSTIC SLIDE SESSION 2008

CASE 2008 - 1

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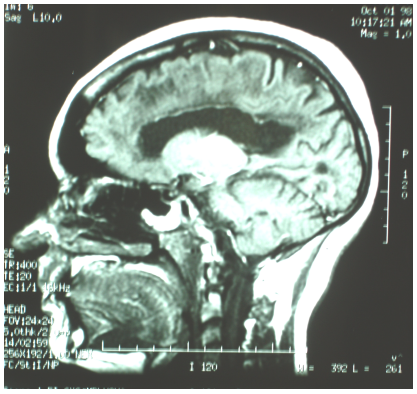
Clinical History: The patient is 36-year-old woman whose neurological history began in 1988 at age 17 when a head CT was performed for post traumatic headaches following a motor vehicle accident and revealed bilateral diffuse white matter disease of unknown etiology.

Over the following 1-2 years she had several episodes that lasted up to 1 hour in duration and were characterized by a variety of neurological symptoms including headaches, blurred vision, hemianopia, expressive aphasias, seizure-like activity, and extremity numbness and weakness.

These "episodes" were diagnosed as complex migraines. The "episodes" continued to increase in frequency over the ensuing years and included additional symptoms such as bizarre behavior, wrist drop, facial drooping, and clonus. These episodes could last from 12-48 hours.

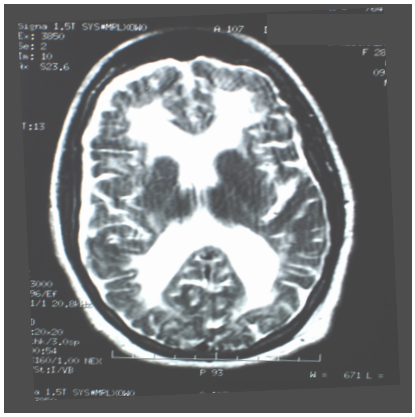
At age 27, following a fall she had an acute neurologic event requiring hospitalization which left her lethargic and unable to carry out her activities of daily living. MRI revealed diffuse white matter abnormalities in the centrum semiovale and periventricular region with marked ventricular dilation.

Extensive metabolic workup was negative. She was subsequently diagnosed with cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL), despite negative skin, nerve, and muscle biopsies.



In 1999 at age 29, she experienced sudden unresponsiveness and status epilepticus requiring hospitalization. This event left her in a persistent vegetative state with facial grimacing, crying, moaning, occasional seizures, hand twitching, myoclonc jerks, and no purposeful movement. She was discharged to a skilled nursing facility. Over the ensuing years, she had a stepwise progressive deterioration. She died in May 2007 at the age of 36.

Pertinent negative laboratory results included: absence of NOTCH3 mutations, with sequencing of exons 3, 4, 11, 18, and 19 plus 28 other exons, and absence of mutations in the mitochondrial genome.



Necropsy findings: General autopsy revealed the immediate cause of death to be bilateral acute pneumonia. The brain weighed 890 grams. There was dramatic cystic degeneration of the corona radiata bilaterally with relative sparing of the basal ganglia. The cerebellum and brainstem were unremarkable.

Material submitted:

1. CT and MRI images performed in 1999.
2. H&E section of basal ganglia and temporal cortex.

Points for discussion:

1. Diagnosis
2. Genetics