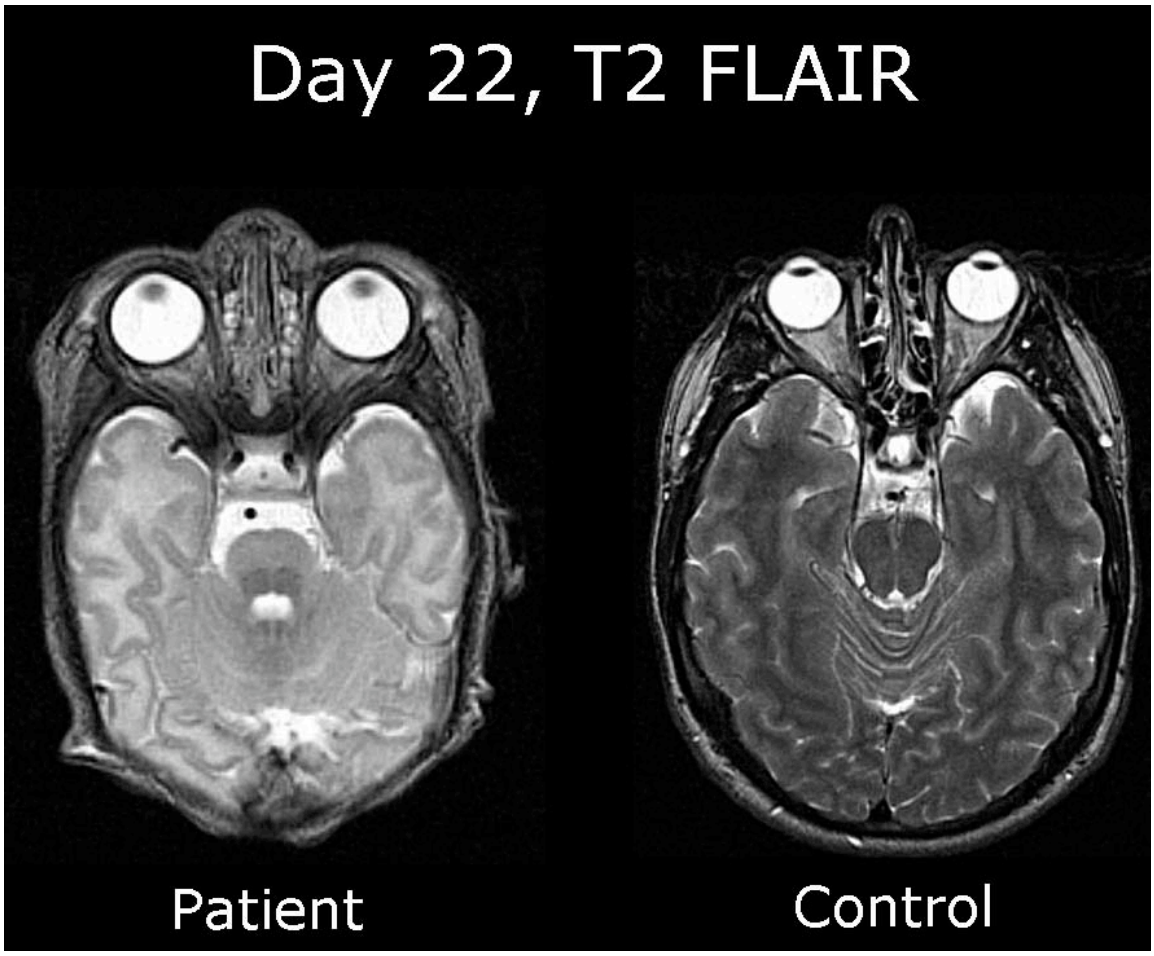
50th ANNUAL DIAGNOSTIC SLIDE SESSION, 2009
DIAGNOSES AND REFERENCES
MODERATOR: Anthony T. Yachnis, M.D.
EDITOR: Leroy R. Sharer, M.D.

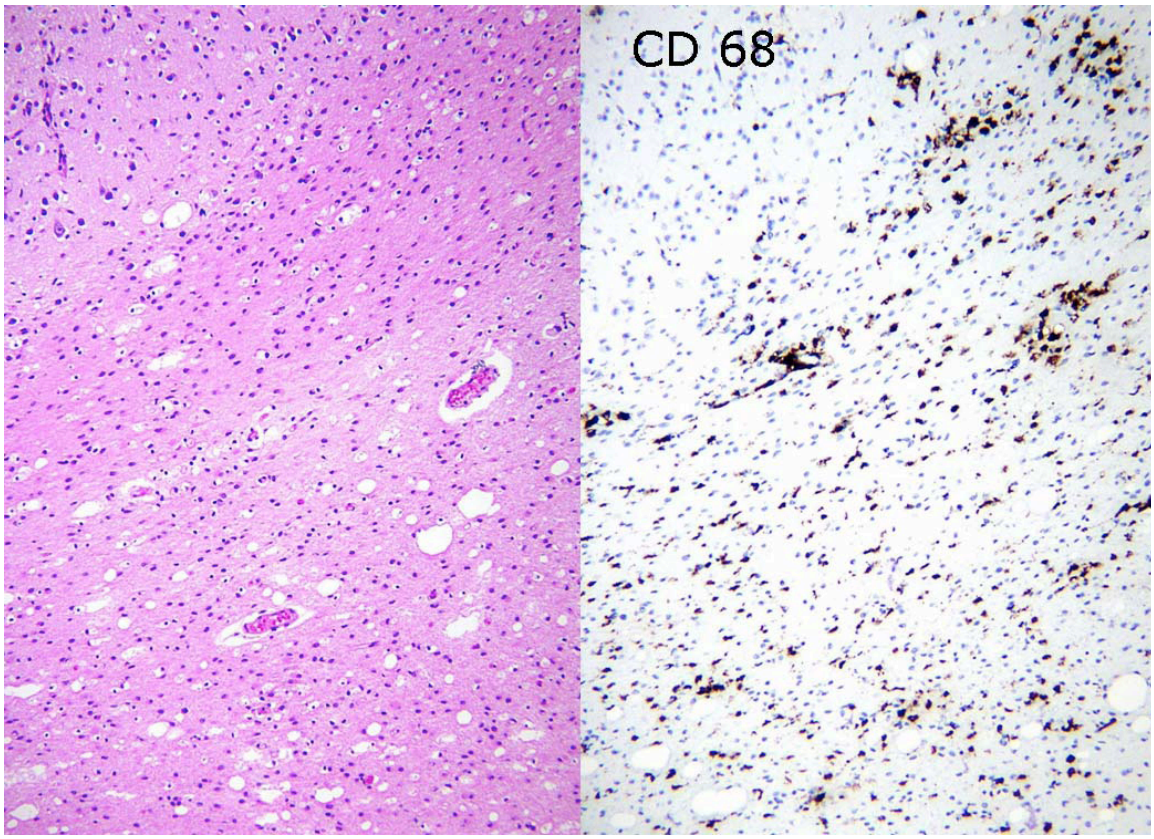
Case 2009-10

Submitted by: Pedro DSC Ciarlini, Alan E Siroy, Irina Mikolaenko and Mark L Cohen, University Hospitals of Cleveland, Cleveland, OH

The patient was a 4 month old male born at 38 weeks of gestation to an 18 year old G2P2002 mother by a vaginal delivery without complications. Birth weight was 2,895 grams (between 10th and 50th percentiles) and Apgar scores were 9(1) and 9(5). The mother was group B Streptococcus positive, treated with penicillin, and had a history of HSV without active lesions during delivery as well as negative HSV cultures. The infant was noted to be jittery after the delivery, which was attributed to maternal use of tobacco and marijuana. Two days after the delivery, he was evaluated for sepsis after 3 episodes of desaturation, apnea, and bradycardia. Four days after the delivery the patient began exhibiting frank seizure activity, including stiffening and extension of the extremities, head turning, and back arching. EEG showed status epilepticus. Initial MRI revealed abnormal diffusion restriction in the subcortical and periventricular white matter of the cerebral hemispheres, corpus callosum and basal ganglia bilaterally, extending into the cerebral peduncles bilaterally, as well as diffusely abnormal cerebral hemispheric white matter. He was started on antibiotic, antiviral, and antiseizure medications. His hospital course was characterized by intractable seizures, axial hypotonia, appendicular hypertonia, and hyperreflexia with clonus; feeding difficulties; autonomic symptoms including tachycardia; and repeated episodes of desaturation, respiratory distress with aspiration, and worsening neurological status. He developed anemia during the latter part of his hospital stay. A second MRI showed marked diffuse parenchymal volume loss with bilateral encephalomalacia (right more than left) involving both cerebral cortex and subcortical white matter. Interval development of abnormally increased T1 signal throughout the cerebral cortex bilaterally as well involving the right basal ganglia was noted. Abnormal diffusion restriction was seen within the splenium of the corpus callosum and frontal subcortical and periatrial white matter bilaterally. On day 121 of life, he went into ventricular fibrillation and expired.



General autopsy revealed pathologic features consistent with shock, hypertrophic pyloric stenosis, and hepatosplenomegaly. External examination of the head revealed dolichocephaly with microcephaly. The brain weighed 420 g (expected 516-540 g). Gross abnormalities included focal subdural hematoma, agenesis of the septum pellucidum, thinning of the corpus callosum, and decreased white matter volume. The white matter demonstrated focal gray discolorations and appeared sunken. Scattered small irregular areas of chalky-white discolorations consistent with infarctions were noted predominantly within white matter and focally within gray matter. The ventricles were dilated. The cortex was mildly atrophic, most obviously in the depths of the sulci. The thalami and basal ganglia were firm. The cerebellar folia and white matter were atrophic. Cross sections of the brainstem appeared unremarkable. The spinal cord was grossly normal.



Diagnosis: Molybdenum cofactor deficiency (OMIM #252150)

Comment: In addition to the findings mentioned in the protocol, there were bilateral lens subluxations, on MRI. Plasma uric acid levels in this child were undetectable, with elevated urinary levels of xanthine (574.6 mmol/mol Cr, normal up to 40 mmol/mol Cr) and hypoxanthine (40.5 mmol/mol Cr, normal up to 30 mmol/mol Cr), as well as a markedly elevated level of urinary S-sulfocysteine (452 mol / g Cr, normal up to 24 mol /g Cr). Mutational analysis revealed the patient to be compound heterozygous for two mutations in the MOCS1 gene: MOCS1A c.287Cdel and MOCS1B c.77G>A, at chromosome 6p21.3.

References:

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