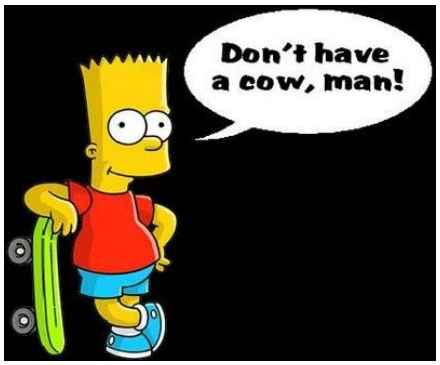


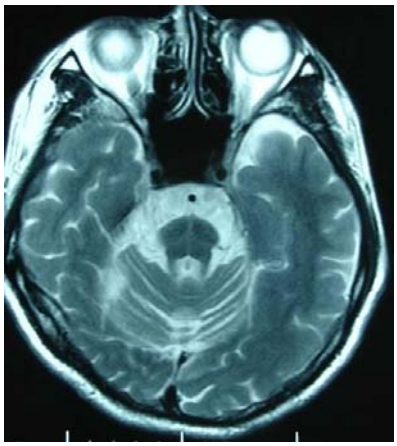
HOLY C.O.W.!

IT'S...

Clinical Question of the Week #10
September 1st, 2008 through September 8th, 2008

Please e-mail your answers to Kuo, Tim, Wendy, and Kevin (klian@mednet.ucla.edu; tprovias@mednet.ucla.edu; wsimon@mednet.ucla.edu; kbreger@mednet.ucla.edu) by 0800 on Monday, September 8th, 2008. The resident or intern with the most correct answers at the end of each month will receive a prize!

Case: A 51-year-old Hispanic truck driver is brought in by his family after developing progressively worsening loss of control of his limbs, wobbly gait, and inability to maintain a stable seated position over the past several weeks. These have now limited his ability to work. Over the past few months, they have also noticed that his verbal output has been less and he seems to have less expression when engaging members of the family, although his mentation appears to be only mildly decreased during the same period of time. Last week, the family also began noticing that he had one or two episodes of choking on his food. He does not have a tremor, but additional features noted on examination include nystagmus and hyperreflexia. Laboratory tests including thiamine, thyroid function tests, and ceruloplasmin are within normal range. He does not take any medications. A T2-weighted MRI image is shown below.



Questions:

1. **What is the diagnosis?**
   Multiple system atrophy, with cerebellar variant, or MSA-C. One of the Parkinson's-plus syndromes, multiple system atrophy is a rare disorder which presents often with clinical features similar to idiopathic Parkinson's disease, however with additional constellations of neurologic symptoms which may have different variations. Average age of onset is usually in the 50s, and incidence is estimated at 3 in 100,000. Some suggest a mild male predominance. There is no known genetic or environmental cause.

Symptoms of MSA in early stage include the typical akinetic-rigid symptoms of idiopathic Parkinson's disease, making it difficult to distinguish. Diagnosis depends on the development of additional distinct neurologic signs and symptoms, as well as biopsy. (1)

2. **What are the three clinical subgroups of this syndrome?**
   The three different subgroups of MSA are Parkinsonism (MSA-P), Cerebellar (MSA-C), and autonomic (MSA-A, also known as Shy-Drager syndrome, SDS). MSA-P, or striatonigral degeneration, typically presents with parkinsonian features (bradykinesia, rigidity, postural instability, and/or resting tremor). While it may be transiently responsive to dopaminergic agents, it is notable for development of virtual resistance to dopaminergic therapy.

   MSA-C, or olivopontocerebellar atrophy (sOPCA, say that three times fast) presents initially with parkinsonian features as well as either concomitant or subsequent cerebellar features including ataxia of limbs, gait and speech, dysrhythmia, dysdiadochokinesis (inability to perform rapid alternating movements), titubation (impaired truncal coordination), and nystagmus. Bulbar symptoms may also develop including dysphagia.

   MSA-A, or Shy-Drager Syndrome, usually presents parkinsonian features and concomitant autonomic dysfunction including orthostatic hypotension without compensatory tachycardia, urinary retention or incontinence, male impotence, and may also include anhydrosis, constipation, and decreased pupillary reactivity. Typically, parkinsonian symptoms in MSA-C and MSA-A may initially respond to dopaminergic therapy, but are not sustained over time. (1)

3. **What is the finding shown in the image?**
   The Hot Cross Bun sign in the pons (see below). Brain MR imaging may reveal hypointensity or atrophy in the putamen, or alternatively hyperintensity or atrophy in the cerebellum and brainstem. Functional imaging such as PET or SPECT scanning using markers for neuronal activity, dopaminergic terminals and dopaminergic recepters may distinguish MSA from IDA, but does not distinguish MSA from other Parkinson's-plus syndromes such as PSP. Cardiac imaging using SPECT with a ligand targeted to the autonomic innervation has been shown to distinguish MSA-A from IPD with autonomic involvement. (0.5)

Hot Cross Buns (yum!)

4. **What is the diagnostic pathologic finding on biopsy?**
   Neuropathologic changes that occur include neurodegeneration and glial cytoplasmic inclusions (GCIs) in multiple subcortical structures, which are composed of α-synuclein. This finding, however, is not necessarily diagnostic but suggestive only. Interestingly, α-synuclein deposits are also observed in the Lewy bodies of idiopathic Parkinson's disease and diffuse Lewy body disease, suggesting a possible common pathophysiologic pathway. (0.5)