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## **CASE OF THE MONTH**

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A 79 year old Caucasian female was transferred to University Hospital from an outside facility due to progressive weakness in her extremities over several weeks, spreading from her legs to her arms; at the time of admission, she was unable to walk, She also complained of urinary incontinence over the past week and reported an intermittent pounding headache, associated with photophobia and phonophobia. The patient denied any history of trauma and had not experienced back pain, spinal problems, visual problems, sensory deficits, speech disturbance or dysphagia. Her husband reported that she had been confused at times and that her memory had recently become impaired.

There was no history of recent fever, chills, night sweats or acute infection. No new medications were recently started and she did not recall any insect bites. There were no known sick contacts and no family history of similar musculoskeletal problems. Recent travel had been limited to Texas where she and her husband have a winter home.

The patient's past medical history was remarkable for hypertension, hyperlipidemia and two episodes of pneumonia in the past four months. She was diagnosed with colon cancer in 2002 which was treated with a partial colon resection; a follow-up colonoscopy in 2005 was normal and no other signs of recurrence had been documented. Other past surgeries included a hysterectomy, cataracts and a cholecystectomy. The patient is a former smoker but quit 20 years ago; alcohol use is limited to a glass of wine with her evening meal and she denied illicit drug use. She had been very active prior to the onset of her weakness and was still playing golf several months prior to admission. She lives with her husband; they have a summer home in Missouri and a winter home in Texas.

Admission vitals revealed T 36.2, P 87, R 18, BP 129/70, O2 sat 92% on RA. No rash or jaundice were noted and no meningeal signs were present. Her chest was clear, cardiovascular exam was normal and the abdomen was unremarkable. She was alert and cooperative; her speech was normal and cranial nerve function was intact bilaterally. Muscle strength was 3/5 in her proximal extremities and 4/5 distally; DTRs were diminished bilaterally but sensation, including vibration, was intact. Finger-nose testing was normal but her response was slow. Gait could not be assessed since she was unable to stand or walk.

Admission labs revealed WBC 10.3 (75 G, 13 L, 6 M, 4 E, 1 Baso), Hgb 13.3, MCV 88.2, Platelet Count 341, serum Na 125 (plasma osmolality 262, urine 744), K 4.1, glucose 102, BUN 15, Cr 0.45, Ca 9.7, normal LFTs, serum albumin of 4.0 and normal B12 and folate. CEA, AFP and CA-19 were normal. A lumbar puncture was performed which returned a WBC of 1050 (72 L, 3 E), RBC 200, Prot 338, G 21; the CSF was negative for HSV by PCR and AFB; India ink stain was negative and no fungal organisms were seen. Histoplasmosis antigen and VDRL were negative and her drug screen was unremarkable.

A PET/CT demonstrated nonspecific FDG uptake corresponding to a nodular lesion in the posterior aspect of the left lower lobe and the presence of multiple mediastinal and left hilar lymph nodes. An MRI of the brain did not show any restricted diffusions or abnormal enhancement; chronic small vessel disease and tiny, old infarcts in the basal ganglia and thalamic area were noted. An MRI of the spine revealed cervical spondylosis at C5-6 but no evidence of cord compression. A CT of the abdomen-pelvis was normal except for possible wall thickening in one area of the sigmoid, thought to be consistent with under-distention. Finally, a CT-guided biopsy of the pulmonary nodule revealed Cocciodes immitis.

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Infectious Disease was consulted and they agreed that her symptoms and clinical findings were consistent with Coccidiomycosis meningitis. They recommended that she be started on fluconazole, initially 400 mg BID and then 400 mg daily for life. The patient was discharged to a skilled nursing facility for recuperation and rehabilitation and she was scheduled for follow up by both Neurology and Infectious Disease.

**DISCUSSION:** Coccidioidomycosis is an infection caused by dimorphic fungi, either Coccidioides immitis or Coccidioides posadasii. Endemic to the Southwest U.S., from California to West Texas, this fungus is known for causing "Valley Fever" and "Desert Rheumatism." Infection with Coccidioides is via inhalation of spores; while most patients remain asymptomatic, some develop symptoms and clinical findings consistent with community acquired pneumonia. The pneumonia develops within 7-21 days of infection and may be associated with erythema nodosum or erythema multiforme; fatigue may persist for months. The primary infection may become disseminated, especially in immunocompromised patients, and can result in meningitis.

While Coccidioides causes more than 150,000 cases of symptomatic infection in the U.S. each year, less than 100 cases of Coccidioidal meningitis occur; if untreated, this CNS infection has a mortality rate of 95% within 2 years. The most common early symptom of Coccidioidal meningitis is a persistent headache and clinical findings may be absent early in the course; indeed, meningeal signs are uncommon. Over time, tremulousness, gait abnormalities and focal neurologic deficits may develop; the presence of papilledema suggests elevated intracranial pressure and/or hydrocephalus. Lab findings often include hyponatremia, secondary to SIADH, and nonspecific abnormalities such as a mild leukocytosis, peripheral eosinophilia and an elevated ESR. The CSF generally reveals the presence of leukocytes (predominantly lymphocytes), a low glucose and elevated protein; eosinophils may also be present. It is very difficult to isolate Coccidioides in the CSF and the diagnoses is often presumptive, based on the above findings and on the presence of anticoccidioidal antibodies.

Treatment of Coccidioidal meningitis is usually with fluconazole 400 mg per day; other options include itraconazole 200 mg BID or TID and intrathecal Amphotericin B (with or without an azole). The documentation of response to therapy is primarily based on a gradual improvement in symptoms. The CSF may be monitored after several weeks to demonstrate a gradual rise in glucose and follow-up serology can be helpful; a significant rise in antibody titer may correlate with progression of the disease. Serial MRIs of the brain and spine are recommended over the first two years to look for signs of focal infection or secondary complications and follow-up chest imaging should be performed to check for evidence of cavitation. In almost all cases, fatigue and weakness persist for weeks or months.

## **REFERENCES:**

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