THE JOURNAL OF FAMILY PRACTICE

A stroke—or something else?

The patient—who'd had a CVA the year before—was experiencing numbness and weakness in her right leg and foot, and had an increasingly unsteady gait. Initial lab work provided no clues.

Hillary R. Mount, MD; Jeffrey D. Schlaudecker, MD
The Christ Hospital/University of Cincinnati Family Medicine Residency Program (Drs. Mount and Schlaudecker); the University of Cincinnati, Department of Family and Community Medicine (Dr. Schlaudecker)

hillary.mount@thechristhospital.com

The authors reported no potential conflict of interest relevant to this article.

A 54-year-old white woman with a history of a cerebrovascular accident (CVA) a year earlier sought care at the local emergency department for numbness and weakness in her right foot. She reported no other neurologic symptoms. She had mild weakness in her right leg and a mildly unsteady gait. Her neurologic examination was otherwise normal.

Initial testing included a complete blood count (CBC), renal profile, and thyroid-stimulating hormone measurement. All results were normal. A noncontrast computed tomography (CT) scan of the head was normal. We admitted her for further evaluation of probable acute ischemic stroke.

By the following day, the patient's leg weakness and unsteadiness had worsened. A magnetic resonance imaging (MRI) scan of her head showed a prior left pontine infarct, but no new findings. She developed right arm weakness, and an MRI scan of her spine (**FIGURE 1**) showed multiple intradural lesions. A lumbar puncture showed elevated protein and oligoclonal bands. CT scans of the chest, abdomen, and pelvis were unremarkable. Two lumbar punctures for cytology and culture evaluations yielded negative results. A full-body positron-emission tomography (PET) scan showed diffuse small inguinal adenopathy bilaterally, suggestive of metastatic disease or lymphoma.

FIGURE 1
MRI of the spine

IMAGES COURTESY OF: THE CHRIST HOSPITAL, CINCINNATI, OHIO

This MRI scan with contrast of the patient's spine shows diffuse thoracic extramedullary, intradural lesions.

WHAT IS YOUR PRESUMPTIVE DIAGNOSIS?

Diagnosis: Sarcoidosis

Findings from the full-body PET scan (**FIGURE 2**) prompted a biopsy of a right inguinal node, which showed a noncaseating granuloma—a hallmark finding of sarcoidosis.

Sarcoidosis is a multisystem disease of unknown cause. The exact prevalence in the general population is estimated at 10 to 20 cases per 100,000.[1] A higher incidence occurs in blacks in the United States, with a 2.4% lifetime risk compared with 0.85% of whites.[2] Sarcoidosis usually appears in patients ages 20 to 40 years, and although this systemic disease usually affects the lungs, 5% to 10% of patients will have nervous system involvement.[3,4]

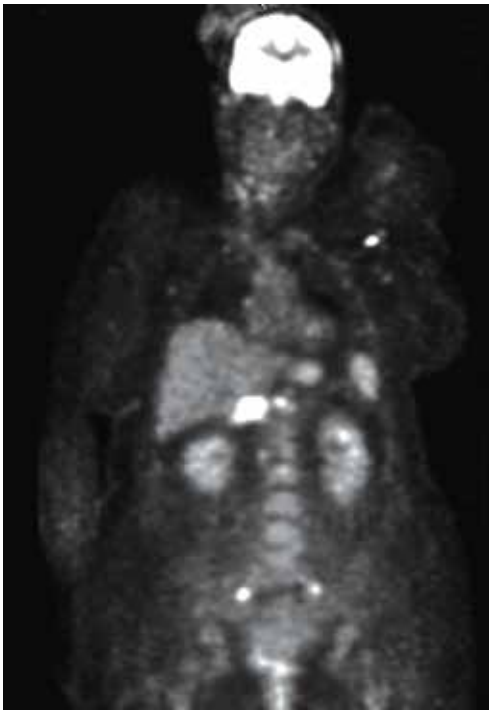
What you'll see

The most common presenting symptoms of systemic sarcoidosis are chronic cough, shortness of breath, and chest pain. Fatigue, weight loss, and myalgias are also frequently part of the initial presentation.

In the absence of systemic symptoms, the diagnosis of neurosarcoidosis is easily confused with a cerebrovascular accident.

FIGURE 2

Full-body PET scan



This PET scan shows diffuse hypermetabolic adenopathy with bilateral iliac adenopathy, small hypermetabolic bilateral cervical lymph nodes, a hypermetabolic left axillary node, and a large hypermetabolic portacaval node.

TABLE 1

Differential diagnosis of an acute neurologic event

Infectious
Encephalitis
Helminthic infection
HIV
Lyme disease
Meningitis
Progressive multifocal leukoencephalopathy
Syphilis
Tuberculosis
Neoplastic
CNS lymphoma
Meningioma/glioma
Metastatic disease
Neurologic
CNS vasculitis
Cranial nerve palsy
Ischemic or hemorrhagic stroke
Meningitis/encephalitis
Multiple sclerosis
Neurosarcoidosis
Peripheral neuropathy
Seizure
Psychiatric
Depression
Malingering
Pseudoseizures
Somatoform disorder
Rheumatologic
Lupus erythematosus

CNS, central nervous system; HIV, human immunodeficiency virus.

Patients with sarcoidosis can present with neurologic symptoms suggestive of many diseases (**TABLE 1**), and in the absence of systemic symptoms the diagnosis of neurosarcoidosis is easily confused with CVA. Most patients with neurosarcoidosis have cranial nerve involvement (50%-75%).[1] Other common presentations include seizures, meningitis, psychiatric symptoms, mass lesions, or endocrine abnormalities.

Useful studies in the clinical evaluation

Consider a diagnosis of sarcoidosis involving the nervous system when an initial

TABLE 2

Treatment of neurosarcoidosis[3]

Medication*	Side effects	Comments
Methylprednisolone	Hyperglycemia	
Prednisone	Osteoporosis, hyperglycemia, hypertension, diabetes, glaucoma, cataracts, psychosis, Cushing's syndrome	Taper as able. Concomitant use of cytotoxic agents may facilitate taper. Monitor glucose and give calcium/vitamin D prophylaxis
Methotrexate	Anemia, neutropenia, liver damage	Weekly dosing well tolerated. Give folic acid 1 mg/d. Monitor liver function tests periodically
Cyclosporine	Renal insufficiency, hypertension	
Azathioprine	Anemia, neutropenia, liver damage	
Cyclophosphamide	Cystitis, neutropenia	Monitor urine monthly for microscopic hematuria
Hydroxychloroquine	Retinopathy, hypoglycemia, ototoxicity, myopathy, cardiomyopathy, neuropathy	Refer for eye exams every 3-6 months. May be useful to counteract hyperglycemic effect of steroids
Infliximab	Fever, headache, dizziness, flushing, abdominal pain, dyspepsia, myalgia, arthralgia, polyneuropathy	Screen for tuberculosis before starting treatment. Contraindicated in patients with congestive heart failure

*For dosing details, consult a neurologist or rheumatologist.

work-up for CVA is negative. In addition to asking about systemic symptoms, perform a complete neurologic exam and skin exam, search for lymphadenopathy, and conduct an ophthalmologic evaluation. After the initial evaluation, a neurology consult will likely be needed to guide further testing.

Choice of serum studies will vary depending on presenting symptoms, but they usually include tests for infection (CBC, cultures, Lyme titers, rapid plasma reagin, tuberculin skin test), rheumatologic disorders (antinuclear antibodies, erythrocyte sedimentation rate, C-reactive protein), and neoplastic diseases (lactate dehydrogenase, peripheral smear).[5] Serum angiotensin-converting enzyme (ACE) may be useful in the diagnosis of systemic sarcoidosis, with positive results seen in approximately 75% of cases.[3]

Examination of cerebrospinal fluid often reveals an elevated total protein with oligoclonal bands, normal to low glucose, and possibly mild pleocytosis of monocytic or lymphocytic predominance.[3] Spinal fluid ACE is neither sensitive nor specific for neurosarcoidosis, as it may be elevated in infectious or malignant processes.[3]

Imaging studies should include contrast-enhanced brain MRI, which may reveal multiple white matter lesions.[6] Although the specificity of PET for neurosarcoidosis is poor—with positive results being seen also in infectious and neoplastic processes—the scan may help in identifying extraneural sites for biopsy. Histology will generally show the classic noncaseating granuloma with surrounding lymphocytes, plasma cells, and mast cells.

Treat with high-dose steroids

The mainstay of treatment, based largely on expert opinion, is high-dose steroids that are gradually tapered over weeks (**TABLE 2**). Other agents may be added if the condition

is poorly controlled with steroids alone, or may be given if symptoms recur while tapering the steroid dose. Recurrence of sarcoidosis is common after doses of <10 to 20 mg/d. Prophylactic measures to counteract the adverse effects of long-term steroid use include weight-bearing exercise programs; administration of calcium, vitamin D, and bisphosphonates; and resorting to a stress-dose steroid regimen in times of illness.

The prognosis with sarcoidosis can vary widely. Case studies show that two-thirds of patients may have a nonrecurring illness. Among the remaining one-third, the disease course may be relapsing-remitting or progressive. When confronted with an acute neurologic event, consider recurrent sarcoidosis and coordinate care between specialists. Also, take steps to prevent complications related to prolonged steroid use.

Improvement for our patient

Based on cerebrospinal fluid study results, a positive peripheral lymph node biopsy, and the exclusion of other diagnoses, we regarded the diagnosis of sarcoidosis as highly probable and initiated high-dose intravenous corticosteroids. Over several weeks, our patient gradually improved with physical therapy and was walking unassisted at the time of discharge from a hospital-based rehabilitation unit. Repeat MRI scans showed a reduction in the size of her intradural lesions, and we slowly tapered her steroids. **JFP**

CORRESPONDENCE
Hillary R. Mount, MD, 2123 Auburn Avenue, #340, Cincinnati, OH 45219; hillary.mount@thechristhospital.com

References

1. Joseph FG, Scolding NJ. Sarcoidosis of the nervous system. *Pract Neurol*. 2007;7:234-244.
2. Burns TM. Neurosarcoidosis. *Arch Neurol*. 2003;60:1166-1168.
3. Hoitsma E, Drent M, Sharma OP. A pragmatic approach to diagnosing and treating neurosarcoidosis in the 21st century. *Curr Opin Pulm Med*. 2010;16:472-479.
4. Habersberger J, Manins V, Taylor AJ. Cardiac sarcoidosis. *Intern Med J*. 2008;38:270-277.
5. Vargas DL, Stern BJ. Neurosarcoidosis: diagnosis and management. *Semin Respir Crit Care Med*. 2010;31:419-427.
6. Cavazza A, Harari S, Caminati A, et al. The histology of pulmonary sarcoidosis: a review with particular emphasis on unusual and underrecognized features. *Int J Surg Pathol*. 2009;17:219-230.