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Authors

Bourgeois, James A., O.D., M.D.
Maddock, R J
Rogers, L
et al.

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Case Reports

Neurosarcoidosis and Delirium

JAMES A. BOURGEOIS, O.D., M.D., RICHARD J. MADDOCK, M.D.
LORI ROGERS, M.D., CLAUDIA M. GRECO, M.D.
RAJESH S. MANGRULKAR, M.D., SANJAY SAINT, M.D., M.P.H.

Sarcoidosis is a systemic inflammatory disease with characteristic noncaseating granulomas. There may be involvement of multiple organ systems, including the lungs, lymph nodes, liver, skin, muscles, bones, and eyes.[1] Involvement of the nervous system (neurosarcoidosis) is seen in less than 10% of cases; psychiatric symptoms infrequently herald disease onset.[1–3]

Case Report

Ms. A, a 39-year-old African American woman, came to a psychiatric hospital with incoherent speech, auditory hallucinations, and distractibility that had begun months earlier and worsened over 2 weeks. She had increased her long-term cocaine use and had unintentionally lost 70 kg in the last year. She was also a regular user of alcohol. She had no previous history of psychosis. After admission, she received oral risperidone, 2 mg b.i.d., without improvement. Four days later, she fell and suffered a right periorbital hematoma. For 2 days, she was nonverbal and refused food and drink.

Ms. A was then sent to a university medical center, where computed tomography (CT) revealed a low-density area in her right frontal white matter. Subsequent magnetic resonance imaging (MRI) revealed a right frontal lobe enhancing mass of 1.5 cm in diameter with surrounding edema, multiple small enhancing lesions, and areas of edema within both cerebral hemispheres and posterior fossa structures and diffuse meningeal enhancement in both cerebral hemispheres, the cerebellum, and the brainstem (Figure 1).

Ms. A was admitted to the neurology service, and a psychiatric consultation was obtained. Psychiatric examination findings included delusions; auditory hallucinations; thought disorganization; disorientation to person, place, and time; and stereotypical movements. Her risperidone dosage was increased to 1.5 mg q.i.d. CSF analysis revealed a glucose level of 27 mg/dl, a protein level of 166 mg/dl, 12 WBC/mm^3, 1 RBC/mm^3, and a negative Gram's stain. Chest radiography and a CT showed bilateral hilar adenopathy and nodular pulmonary infiltrates.

Intravenous dexamethasone and acyclovir were started for possible herpes simplex encephalitis. Tests for angiotensin-converting enzyme, antinuclear antibody, human immunodeficiency virus, hepatitis B surface antigen, hepatitis C antibody, and urinary histoplasmosis antigen were normal, as were VDRL results. A test for tuberculin-purified protein derivative without controls was nonreactive. Polymerase chain reaction on CSF for mycobacterium tuberculosis and herpes simplex virus types 1 and 2 were negative. Acyclovir was then discontinued.

Tests for CSF cryptococcal antigen titer and acid-fast bacillus smear were negative, as were tests for CSF mycobacterium, bacterial, and fungal cultures. Rifampin, ethambutol, isoniazid, pyrazinamide, and vitamin B6 were started for possible CNS tuberculosis. Psychiatry re-evaluation on the eighth hospital day revealed full alertness and intact orientation but continued blunted affect and auditory hallucinations. Ms. A scored 14 on the Folstein Mini-Mental State Exam (MMSE). Her risperidone dosage was decreased to 2 mg b.i.d.

An open brain biopsy of the frontal lobe mass showed pale white, rubbery soft tissue that histologically revealed noncaseating granulomas with multinucleated giant cells

Received March 12, 2004; revision received April 27, 2004; accepted June 15, 2004. From the Department of Psychiatry and Behavioral Sciences and the Department of Pathology/Neuropathology, University of California–Davis Medical Center; the Department of Veterans Affairs Health Services Research and Development Center of Excellence and the Department of Internal Medicine, University of Michigan, Ann Arbor. Address correspondence and reprint requests to Dr. Bourgeois, Department of Psychiatry and Behavioral Sciences, University of California–Davis Medical Center, 2230 Stockton Blvd., Sacramento, CA 95817; james.bourgeois@ucdmc.ucdavis.edu (e-mail).

and a mixed mononuclear inflammatory infiltrate interpreted as classic for neurosarcoidosis. Special stains for organisms, including bacteria, fungi, and acid-fast bacilli were negative. Samples of dura overlying the mass showed only focal macrophage infiltrates. Polymerase chain reaction and an acid-fast bacillus smear from the biopsy were negative for tuberculosis.

Ms. A was cognitively improved by her 16th hospital day. Her MMSE score was 27 of 27 items tested. She had no further hallucinations or delusions but did exhibit mild affective blunting and abulia. Repeated MRI showed an interval decrease in the number and degree of parenchymal lesions and in the intensity of the meningeal enhancement. After 6 weeks, antitubercular medications were discontinued when cultures from the biopsy were negative.

Discussion

The patient's presentation was consistent with subacute delirium following chronic symptoms of psychosis. Neuropsychiatric symptoms as the presenting feature for neurosarcoidosis are unusual. However, involvement of the nucleus accumbens bilaterally may have accounted for the auditory hallucinations, delusions, and disorganized thoughts in this instance. Dopaminergic systems in this nucleus have consistently been implicated in psychotic disorders.[4] Intracranial neurosarcoidosis can include meningeal, hypothalamic, pituitary, and brain parenchymal lesions.[2,3,5] Psychiatric manifestations may include psychosis, mood disturbances, cognitive impairment, and personality changes.[2,6]

Neuroimaging demonstrated an intracerebral mass with edema and diffuse meningeal involvement. The lumbar puncture results of hypoglycorrhachia, elevated CSF protein, and mild pleocytosis can be seen in neurosarcoidosis, fungal meningitis (specifically histoplasmosis or coccidioidosis), disseminated tuberculosis, meningeal carcinomatosis, cryptococcosis, and bacterial (e.g., nocardial) meningitis. The pulmonary radiographic findings make neurosyphilis unlikely but add to a suspicion of neurosarcoidosis, histoplasmosis, tuberculosis, or nocardiosis. One should also consider lymphoma with meningitis and hilar lymphadenopathy, but the nodular infiltrates would be atypical.

Meningeal thickening and nonenhancing diffuse or multifocal white matter lesions (hypointense on T_1 images but hyperintense on T_2 images) are the most common MRI findings in neurosarcoidosis.[5,7] Inflammatory infiltrates at times coalesce into parenchymal granulomatous masses. Leptomeningeal or enhancing parenchymal lesions may predict clinical relapses.[8] Biopsy results vary with clinical duration, as, eventually, granulomas and giant cells diminish and involved tissue becomes fibrotic and calcified.

FIGURE 1. Magnetic Resonance Imaging Studies of Ms. A's Brain Mass

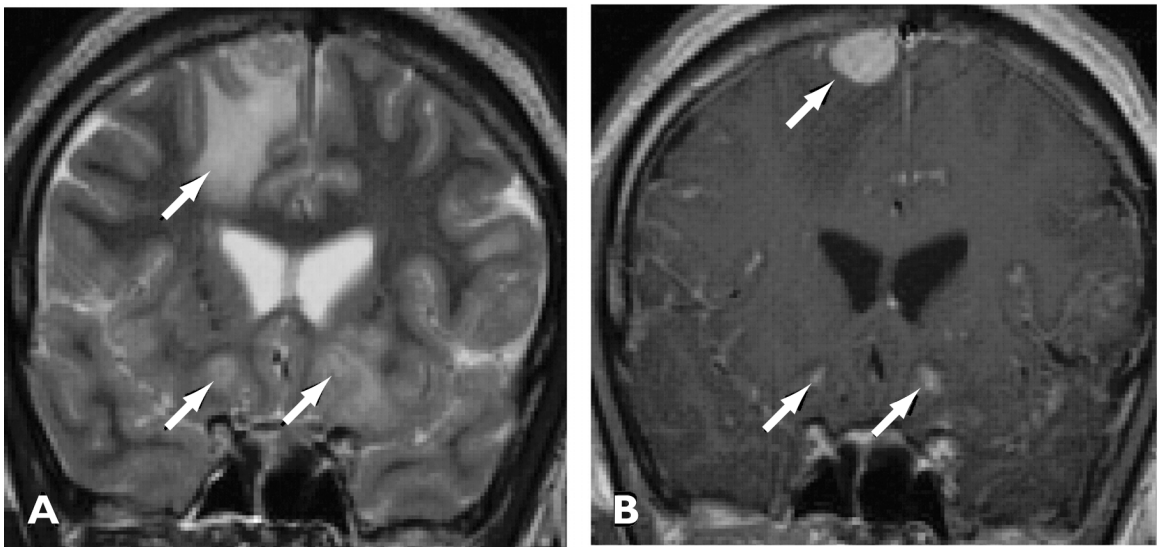

Image A is a T_2 coronal scan showing diffuse white matter hyperintensity consistent with edema in the right superior frontal gyrus (upper arrow) and bilaterally in the medial-basal region that includes the nuclei accumbens (lower arrows). In image B, a T_1 contrast image shows enhancing lesions in the right superior frontal cortex and bilaterally in the region of the nuclei accumbens, along with extensive meningeal enhancement.

The diagnostic yield of stereotactic brain biopsy has been reported as high as 96%, with a morbidity rate as high as 5% and a mortality rate less than 1%.[9,10] Bronchoscopy has been a major advance in the tissue diagnosis of systemic sarcoidosis, with diagnostic yields as high as 86% when endobronchial biopsy is combined with transbronchial biopsy, with major complication rates generally lower than those of brain biopsy.[11,12] The clinical team pursued biopsy of the right superior frontal gyrus of the brain, which is supported by a case series that emphasized the importance of demonstrating sarcoid pathology in neural tissue for a diagnosis of neurosarcoidosis.[13]

Treatment of sarcoidosis includes corticosteroids. One protocol for systemic sarcoidosis is 30 to 40 mg/day of prednisone for 8 to 12 weeks, with a gradual taper over 6 to 12 months.[1] For neurosarcoidosis, higher doses are recommended.[1,3] Cyclosporine, methotrexate, cranial irradiation, and neurosurgical intervention may also be indicated.[3]

Physicians encountering patients with psychotic symptoms and cognitive impairment are advised to maintain a high index of suspicion for active CNS illness and to have a low clinical threshold for early neuroimaging and systemic evaluation of these patients.

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