Introduction

Sarcoidosis is a granulomatous disorder of unknown origin that can affect multiple organ systems. Most commonly, it affects the lungs, skin, and lymphatic system. It typically presents in young adults. Central nervous system (CNS) involvement occurs in only 5%-10% of cases and increases morbidity and mortality significantly.\(^1\) The most common neurologic finding in neurosarcoidosis is cranial neuropathies, predominantly peripheral facial palsy (occurring in 50% of patients), and optic neuritis followed by palate dysfunction, hearing abnormalities, and vertigo.\(^2\)-\(^4\) Other manifestations include hypothalamic and pituitary abnormalities, chronic aseptic meningitis, mass-lesion effect, and seizures.\(^1\)

**FIGURE 1** Dilation of third and lateral ventricles with FLAIR sequence (A, B). Enlargement of the third and fourth ventricles with patent cerebral aqueduct on T1 sagittal sequence (C)
Hydrocephalus occurs in only 6% of cases of sarcoidosis, but of all manifestations of CNS involvement, it has been reported to confer the worst long-term prognosis.5-7 In most reported cases of neurosarcoidosis with hydrocephalus, the patient had a previous diagnosis of systemic sarcoidosis. Hydrocephalus as the presenting symptom of sarcoidosis in a previously healthy patient is an atypical presentation that is exceedingly rare and challenging to diagnose.1,6 We present the case of a previously healthy 52-year-old woman with significant hydrocephalus of all four ventricles as the presenting manifestation of sarcoidosis.

2 | CASE PRESENTATION

A 53-year-old African-American woman with no past medical history visited the emergency department due to progressive nausea and vomiting. She had a month-long course of fatigue, headaches, intermittent vertigo, tinnitus, and ataxia. Review of systems revealed she had an unintentional weight loss of 30 pounds over the last 4 months. Neurologic examination showed right gaze-evoked nystagmus, postural instability, and an unsteady shuffling gait. Fundoscopic examination showed no papilledema or other abnormalities. Respiratory examination was normal. Her complete blood count and routine biochemistry were normal. C-reactive protein and erythrocyte sedimentation rate (ESR) were within normal limits. Serum level of angiotensin-converting enzyme (ACE) was 51 U/L (normal range: 12-60 U/L). Brain computed tomography (CT) revealed remarkable hydrocephalus with dilation of all four ventricles. Magnetic resonance imaging (MRI) showed patency of the cerebral aqueduct and ruled out cerebral or subarachnoid mass lesions, consistent with communicating hydrocephalus (Figure 1). Lumbar puncture was performed in light of clinical and radiographic findings. Cerebrospinal fluid (CSF) was transparent and showed lymphodominant pleocytosis with increased protein level (104 mg/dL), markedly decreased glucose (21 mg/dL), and normal opening pressure. Chest CT showed bilateral lymphadenopathy, and biopsy revealed noncaseating granulomas admixed with giant cells without evidence of malignancy or infection (Figure 2). A diagnosis of neurosarcoidosis with hydrocephalus was made, and the patient was started on 1 g of intravenous solumedrol for 5 days with a subsequent oral prednisone taper with methotrexate. Three months later, she received a ventricular shunt for persistent severe gait disturbance. She returned to walking independently within one month of the procedure and has since shown marked improvement in all neurologic symptoms.

3 | DISCUSSION

Hydrocephalus is a very rare complication of sarcoidosis, especially as the presenting symptom.3 We present one such case in this report. To the best of our knowledge, only 21 others exist in the literature, of which we were able to include 19 in this report (Table 1).7-22 Hydrocephalus typically presents
| Author        | ESR/CRP         | Serum ACE | CSF Findings                                      | Diagnosis                                      | Type                  | Treatment                                           | Outcome          |
|--------------|-----------------|-----------|--------------------------------------------------|-----------------------------------------------|-----------------------|-----------------------------------------------------|------------------|
| This report  | ESR: Normal, CRP: Normal | Normal    | Lymphodominant pleocytosis, elevated protein, hypoglycorrhachia | Lymphadenopathy on chest CT | Communicating | Corticosteroids + methotrexate, followed by VP months later | Partial recovery |
| Brouwer 2009 | Normal          | Normal    | Lymphodominant pleocytosis, elevated protein | Lymphadenopathy on FDG-PET | Communicating | Corticosteroids                                      | Complete recovery |
| Muayqil 2006 | ESR: Normal     | Normal    | Lymphodominant pleocytosis | Lymphadenopathy on CXR and chest CT; meningeal and hypothalamic enhancement in brain MRI | Communicating | VP shunt + corticosteroids | Partial recovery |
| Muniesa 2006 | Elevated        | Leukocytic pleocytosis | Cutaneous lesions | Increased ACE in CSF | Communicating | VP shunt + corticosteroids | Died from nosocomial pneumonia |
| Onoda 2004   | Elevated        | Normal    | Lymphodominant pleocytosis, elevated protein, hypoglycorrhachia | Lymphadenopathy on chest CT | Communicating | VP shunt + corticosteroids + Methotrexate + Infliximab | Partial recovery |
| Sano 2015    | Elevated, CRP: Normal | Normal    | Lymphodominant pleocytosis, protein elevated protein, hypoglycorrhachia, ACE normal | Lymphadenopathy on chest CT; meningeal lesions in basal cistems | Communicating | VP shunt + corticosteroids | Partial recovery |
| Sugiyama 2016 | ESR: Elevated, CRP: Normal | Normal    | Leukocytic pleocytosis, elevated protein | Lymphadenopathy on whole body contrast CT and FDG-PET | Communicating | VP shunt + corticosteroids | Partial recovery |
| Zoja 2012    |                 | Autopsy   |                                   | Autopsy                                        | Communicating | Death                                               |                  |
| Benzagmout 2007 | Elevated        | Elevated opening pressure, lymphodominant pleocytosis, elevated protein, hypoglycorrhachia | Cervical and submandibular lymphadenopathy | Noncommunicating | External Ventricular Drain + Corticosteroids | Partial recovery |
| Benhouma 2009 |                 | Brain MRI with temporal trapped horn and multiple enhancing lesions in subarachnoid space | Noncommunicating | Right temporal tip lobectomy + corticosteroids | Complete recovery |

(Continues)
| Author        | ESR/CRP       | Serum ACE | CSF Findings                          | Diagnosis                                     | Type               | Treatment                                                                 | Outcome       |
|---------------|---------------|-----------|---------------------------------------|-----------------------------------------------|--------------------|---------------------------------------------------------------------------|---------------|
| Brouwer 2009  | Normal        | Normal    | Lymphodominant pleocytosis, elevated protein | Lymphadenopathy on FDG-PET                     | Noncommunicating   | Ventriculopexy assisted fenestration of lateral ventricle cyst             | Complete recovery |
| Chandna 2015  | Normal        | Normal    | Lymphadenopathy on CXR                | Noncommunicating                              | VP shunt + corticosteroids | Death                                                                    |               |
| Chiang 2002   | Elevated      | Normal    | Cutaneous lesions                     | Noncommunicating                              | VP shunt + corticosteroids |               |
| Hitti 2015    | Normal        | Normal    | Leptomeningeal enhancement in brain and spine MRI months later | Noncommunicating                              | VP shunt + corticosteroids + Mycophenolate mofetil |               |
| Kim 2012      | Elevated      | Leukocytic pleocytosis, elevated protein | Lymphadenopathy on CXR | Noncommunicating                              | VP shunt + corticosteroids | Complete recovery |
| Matsuda 2015  | Normal        | Normal    | Lymphodominant pleocytosis, hypoglycorrhachia | Neuroendoscopic biopsy of enhancing ventricular lesions | Noncommunicating | Venticulostomy, followed by VP shunt + corticosteroids | Complete recovery |
| McKeever 2019 | Normal        | Normal    | Nodular lesions in brain MRI years later | Noncommunicating                              | Endoscopic third ventriculostomy, years later recurred and required shunt | Complete recovery first episode |
| Tabuchi 2013  | ESR: Elevated, CRP: Normal | Normal    | Pleocytosis, elevated protein | Lymphadenopathy on CXR | Noncommunicating                              | VP shunt + corticosteroids | Partial recovery |
| Westhout 2008 | ESR: Elevated | Elevated protein | Biopsy of temporal lobe lesion | Noncommunicating                              | VP shunt + corticosteroids | Complete recovery |
| Yoshitomi 2015 | CRP: Elevated | Elevated opening pressure, hypoglycorrhachia | Diffuse leptomeningeal enhancement in brain MRI and mass lesions in third and fourth ventricles | Noncommunicating | Endoscopic fenestration foramen of Magendie, followed by VP shunt + corticosteroids | Complete recovery |
with nonspecific symptoms, and the diagnosis is made based on imaging. The differential diagnosis is extensive (Table 2) making the correct attribution difficult due to a lack of definitive diagnostic testing for neurosarcoidosis. As such, a high degree of clinical suspicion must be maintained.

Hydrocephalus secondary to sarcoidosis can present as communicating or noncommunicating. The latter scenario is the most common (60% of cases included in this report), and the presence of mass lesions in the CNS can raise the possibility of the diagnosis and even provide a site for biopsy. In the case of communicating hydrocephalus, when the differential diagnosis includes infectious or neoplastic pathologies of the leptomeninges, additional studies (including CSF analysis and chest imaging) usually provide the clues for diagnosis. In 50% of the patients, the diagnosis was suspected when lymphadenopathy was found, most commonly in chest imaging. Among patients with communicating hydrocephalus, this was the most common way to make the diagnosis (63%), including in our patient. In two of those patients, there were also abnormal findings in the contrast MRI (Table 1). In one patient, the diagnosis was made by biopsy of cutaneous lesions, in another, it was suggested by elevated ACE levels in CSF, and in the last case, the patient died suddenly from acute hydrocephalus and the diagnosis was made by pathological examination of the leptomeninges at autopsy.

Serum ACE levels were only reported in half of patients, with only 30% being elevated (25% of communicating and 33% of noncommunicating). All patients with communicating hydrocephalus in whom ESR was reported had normal values, while it was elevated in both patients with noncommunicating pathology in which it was reported. The most common abnormalities reported in CSF analysis include pleocytosis (100% of communicating and 63% of noncommunicating hydrocephalus) with a lymphocytic predominance in 75% of cases, and elevated protein (71% and 75% respectively). While the number of patients reported is low, the above findings suggest that serum ACE levels have limited sensitivity, but the specificity of the test might still make it valuable. Sarcoidosis should be a diagnostic consideration in patients with hydrocephalus with CSF pleocytosis or elevated protein levels in whom microbiological and cytology studies are negative.

While there has been no controlled trial for medical treatment of neurosarcoidosis, the consensus remains that corticosteroid therapy is first-line. Ventriculoperitoneal (VP) shunt placement should be considered for symptomatic hydrocephalus. Of the cases reported in the literature, only one case of communicating hydrocephalus in neurosarcoidosis was successfully treated with corticosteroids alone, all other cases required surgical management (VP shunt, ventriculostomy, or ventricle fenestration) which in many cases took place before a definite diagnosis in order to manage the hydrocephalus. In the present case, VP shunt placement was done after three months of persistent and severe gait disturbance despite corticosteroid treatment, with rapid improvement in neurologic symptoms. Obviously, in cases of acute hydrocephalus, ventriculostomy can be life-saving.

While most published reports of hydrocephalus in the context of sarcoidosis suggest a mortality rate as high as 75%, the great majority of those cases happened in patients with widespread disease that had not responded to treatment. In the current series of patients presenting with hydrocephalus, the reported mortality is 15%, with one patient dying suddenly from acute hydrocephalus, another from pulmonary embolism, and the last one from nosocomial pneumonia. The rest of the patients in whom outcomes were reported had either partial (35%) or complete (50%) recovery with treatment.

Nevertheless, long-term prognosis seems to depend more on the response of the underlying sarcoidosis to immunosuppressant treatment rather than the presence of hydrocephalus.

### Table 2: Differential diagnosis of acquired hydrocephalus in adults

| Subarachnoid/Intraventricular Hemorrhage | Trauma |
|----------------------------------------|--------|
| Tumor and metastases (including of the leptomeninges) | Meningitis/encephalitis |
| Bacterial (including syphilis) | Viral (including EBV and HIV) |
| Fungal | Infectious etiologies |
| Tuberculosis | Lyme disease |
| Toxoplasmosis | Neurocysticercosis |
| Whipple’s disease | Inflammatory etiologies |
| Sarcoidosis | Systemic lupus erythematosus (SLE) |
| Behçet's disease | Wegener's granulomatosis |

### CONCLUSION

We present a rare case of neurosarcoidosis manifesting as subacute communicating hydrocephalus in a previously healthy patient. Though this pathology may pose a diagnostic challenge, it responds well to treatment and prognosis is favorable.

### CONFLICT OF INTEREST

None of the authors have a financial interest in any of the products, devices, or drugs mentioned in this manuscript.
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**AUTHOR CONTRIBUTIONS**

Rachel J. Saban, BS, Meaghan M. Berns, BA, Mazen Al-Hakim, and MD Gustavo Patino, MD PhD: 1) substantially contributed to conception and design, or acquisition of data, or analysis and interpretation of data; 2) drafted and revised the article; 3) approved the final version; 4) involved in agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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