

Dementia, gait disturbance, and urinary incontinence in a patient with pulmonary sarcoidosis

Gonzalo Labarca¹, Romina Ramirez², Ximena Monsalve³ & Isabel Mira-Avendano⁴

¹Department of Internal Medicine, Complejo Asistencial Víctor Ríos Ruiz, Los Ángeles, Chile.

²Department of Internal Medicine, Pontifical Catholic University, Santiago, Chile.

³Department of Internal Medicine, Hospital Sotero del Río, Santiago, Chile.

⁴Department of Pulmonary Medicine, Mayo Clinic, Jacksonville, Florida, USA.

Keywords

Sarcoidosis, dementia, neurosarcoidosis, hydrocephalus.

Correspondence

Gonzalo Labarca, Department of Internal Medicine, Hospital Víctor Ríos Ruiz, Ricardo Vicuña 147, Los Angeles 4451055, Chile. E-mail: glabarcat@gmail.com

Received: 18 May 2016; Revised: 18 July 2016;

Accepted: 19 July 2016.

Respirology Case Reports, 4 (5), 2016, e00182

doi: 10.1002/rcr2.182

Abstract

Hydrocephalus is an uncommon presentation of neurosarcoidosis. We discuss the case of a 67-year-old woman with a prior diagnosis of hypothyroidism, systemic hypertension, and lung sarcoidosis who presented with a 1-month history of progressive impairment of consciousness leading to prostration and loss of sphincter control. At admission, patient was febrile with altered speech and without focalization. Laboratory results showed leucocytosis and mild anaemia. Cerebrospinal fluid (CSF) analysis was characterized by mild elevated protein level, increased cell count, normal glucose and adenosine deaminase (ADA), negative cytology, and no bacterial isolations. Electroencephalogram showed toxic-metabolic encephalopathy. Computed tomography (CT) of the brain revealed hydrocephalus without structural damage, and magnetic resonance imaging of the brain demonstrated non-specific diffuse meningeal enhancement and periventricular changes supporting normal pressure hydrocephalus. Chest X-ray showed mediastinal adenopathy and parenchymatous lesions, consistent with stage II lung sarcoidosis. A ventriculoperitoneal shunt was installed, and the patient experienced rapid improvement in her symptoms. Neurological involvement in association with lung sarcoidosis should be suspected in patients with known history of sarcoidosis. Neurosarcoidosis needs to be treated promptly.

Introduction

Sarcoidosis is a multisystem syndrome of unknown aetiology, characterized by the formation of multiple non-caseating granulomas that alter the affected tissue. There are no Chilean studies of prevalence. In North America, incidences of 35.5 cases per 1,000,000 in African American and 10.9 cases per 1,000,000 in Caucasian populations have been reported. The lungs are affected in approximately 90% of patients. Other commonly involved tissues include the skin, eyes, and lymph nodes [1,2]. Only 5%–10% of patients with sarcoidosis suffer neurological involvement, with positive symptomatology present in half of them [2].

We report the case of a woman with a prior diagnosis of lung sarcoidosis who developed rapidly progressing dementia, secondary to normal pressure hydrocephalus (NPH), explained by neurological involvement in this disease.

Case Report

A 67-year-old Hispanic woman with a past medical history of hypothyroidism, hypertension, and recently diagnosed stage II pulmonary sarcoidosis (confirmed through trans-bronchial biopsy 2 months prior) presented with a 1-month history of progressive impairment of

consciousness that was associated with decreased strength and progressed to prostration and loss of sphincter control. At initial evaluation in the emergency department, she was found to be haemodynamically stable, febrile (39°C), somnolent, with non-comprehensible speech, and with no signs of neurological focalization. The rest of her physical examination was unremarkable. Cerebrospinal fluid (CSF) showed protein levels of 0.66 g/L (normal value < 0.5 g/L), 70 cells (mostly mononuclear), glucose levels of 45 mg/dL (normal value > 60 mg/dL), and adenosine deaminase (ADA) levels of 3.3 U/L (normal value < 7 U/L). Gram stain was negative for bacteria and the bacterial and fungus cultures were negative. Computed tomography (CT) of the brain revealed hydrocephalus without structural lesions. The study was complemented with magnetic resonance imaging (MRI) that revealed non-specific periventricular changes and diffuse meningeal enhancement, quadriventricular hydrocephalus, and diffuse leucoencephalopathy. The image was compatible with NPH (Figs. 1, 2).

Complementary studies, including HIV and venereal disease research laboratory (VDRL) tests, were negative. Electroencephalogram (EEG) showed non-specific changes suggesting diffuse encephalopathy due to metabolic abnormalities, and the patient had normal thyroid panel, complement and B12 levels, with negative connective tissue serologies. Chest X-ray showed grade II pulmonary sarcoidosis (Fig. 3).

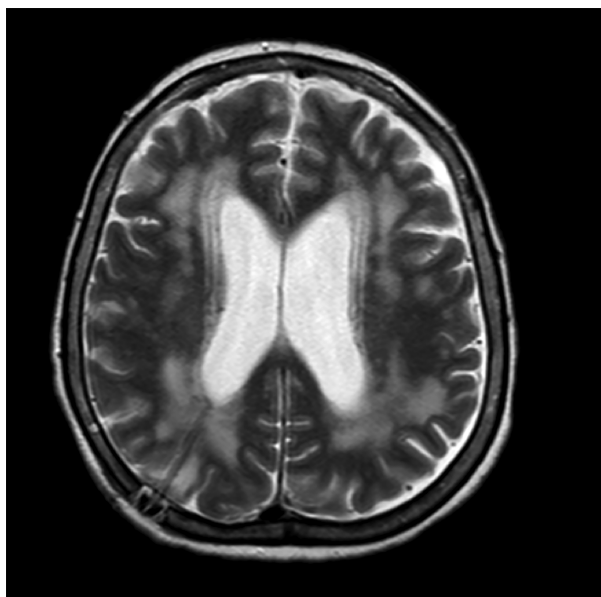


Figure 1. Magnetic resonance imaging revealing quadriventricular hydrocephalus, non-specific periventricular change, and diffuse meningeal enhancement.

After a multidisciplinary evaluation, a ventriculoperitoneal (VP) shunt was installed without complications, and the patient was started on steroid therapy with prednisone of 0.5 mg per kg, with rapid improvement in her symptoms. After 2 years of follow-up, patient recovery was successful, without fever or evidence of infection. Current medication includes prednisone of 5 mg per day and azathioprine of 100 mg per day.

Discussion

We report an unusual cause of neurosarcoidosis in association with pulmonary involvement. Neurosarcoidosis is a severe disease condition and the most common

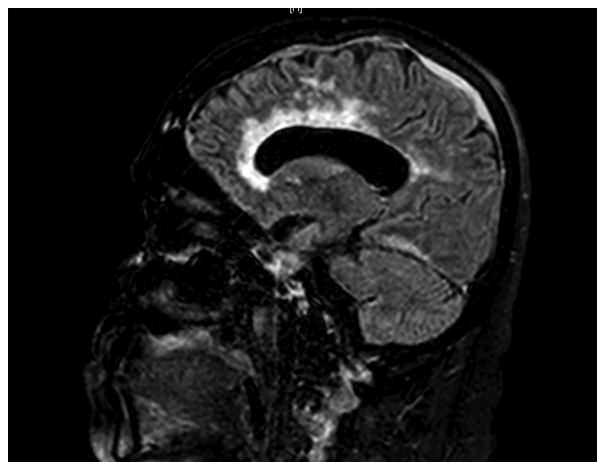


Figure 2. Magnetic resonance imaging revealing diffuse leucoencephalopathy and meningeal enhancement (occipital predominance).

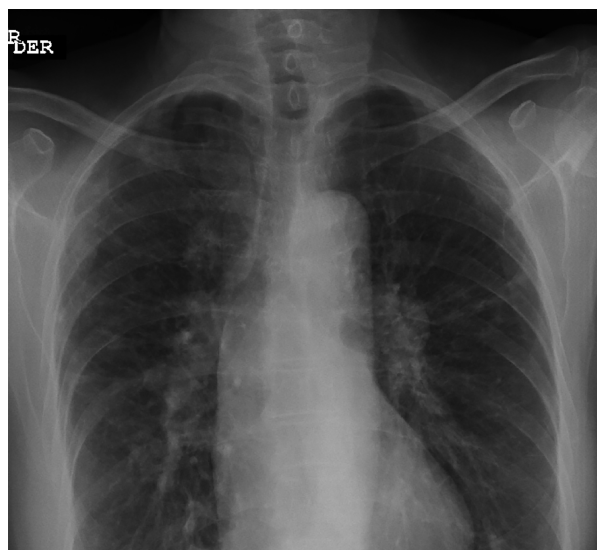


Figure 3. Chest X-ray showing pulmonary sarcoidosis.

Table 1. Neurological involvement in sarcoidosis.

	Frequency	Clinical finding	Comments
Cranial neuropathies	25%–50%	<ul style="list-style-type: none"> • Unilateral facial palsy • Optic neuropathy • Eight nerve palsy • Multiple cranial nerve 	Bilateral neuropathy, bad prognosis. Bilateral eighth neuropathy involvement is highly suggestive of neurosarcoidosis.
Meningeal involvement	40%	<ul style="list-style-type: none"> • Aseptic meningitis • Chronic meningitis (>4 weeks) • Hydrocephalus 	Treatment includes steroids and prognosis is good. Treatment for chronic meningitis includes long-term therapy.
Granulomatous involvement		<ul style="list-style-type: none"> • Partial or generalized seizures • Encephalopathy/vasculopathy • Focal cerebral infarction 	Patients can present with cognitive or behavioural problems and/or focal neurological deficits referable to the anatomic area involved.
Neuroendocrine dysfunction		<ul style="list-style-type: none"> • Hypothalamic dysfunction • Diabetes insipidus • Adenopituitary failure • Amenorrhea-galactorrhea syndrome 	Polyuria and polydipsia are the more common presentations, due to either diabetes insipidus or disturbances of thirst. Other clinical symptoms include disorders in sleep, appetite, temperature, or libido.
Myelopathy/radiculopathy	16%–43%	<ul style="list-style-type: none"> • Spinal cord compression • Mononeuritis multiplex • Caudal equine • Guillain–Barre syndrome • Longitudinally extensive myelitis 	Clinical involvement includes paraesthesia, muscular weakness, and paraplegia of lower limbs in patients with severe disease.

manifestation is cranial nerve compromise, most often presenting as peripheral seventh nerve palsy. Other possible manifestations are hydrocephalus, myopathy, peripheral neuropathy, meningitis, and seizures [3–7]. But the rates of asymptomatic involvement may be higher, with positive autopsy findings in up to 15% of patients [8]. When neurological manifestations occur, it usually happens during the first two years of diagnosis, corresponding to isolated manifestation of the disease in only 1% of the cases [1,9], and three-fifths of neurosarcoidosis cases are characterized by lesions at different levels (brain, leptomeningeal, or peripheral nerve) [3,10–12]. A summary of clinical manifestations of neurosarcoidosis is shown in Table 1.

Our patient developed hydrocephalus, an uncommon presentation of neurosarcoidosis, with few previously reported cases [7,13]. This manifestation is likely secondary to pathological granulation of arachnoids. Normal pressure hydrocephalus refers to a ventricular enlargement with normal opening pressures on lumbar puncture. Normal pressure hydrocephalus is characterized by the classic triad of dementia, gait disturbance, and urinary incontinence. Prognosis in these cases is poor, with mortality within 1 year for about 75% of patients [8,14] and it is important to recognize these cases because they can be reversed by the placement of a VP shunt. The most

probable mechanism in these cases is the impaired absorption of CSF secondary to chronic granuloma or pachymeningitis.

Laboratory evaluations in neurosarcoidosis include general exams and lumbar puncture. Although they have low diagnosis yields, lumbar puncture and CSF analysis should always be considered because some abnormalities such as elevated immunoglobulin (Ig)G index, oligoclonal bands, and high levels of elevated angiotensin enzyme can aid in the diagnosis [8]. In addition, elevated protein levels and CSF opening pressure, along with pleocytosis (predominantly mononuclear cell), are characteristic of NPH.

In regard to neuroimaging, MRI is considered the most sensitive non-invasive test for neurosarcoidosis [5], but a normal result does not exclude the diagnosis. The most common MRI finding is leptomeningeal involvement, with nodules or plaques seen when contrast is used [8,15]. Damage to the spinal cord, cauda equina, and the cranial nerves can also be seen. In a series of 30 cases in patients diagnosed with neurosarcoidosis, 40% presented with positive MRI findings, such as meningeal enhancement and/or multiple white matter lesions [16]. Our patient presented a hydrocephalus and diffuse meningeal enhancement, changes suggestive of neurosarcoidosis.

Finally, pathology showing granulomatous lesions is the most specific diagnostic test for sarcoidosis, but because

biopsy of peripheral or central nerves carries high morbidity, it is usually supported with samples taken from other organs, particularly the lungs and lymph nodes [1,8,14,17]. We considered the clinical manifestation in association with imaging and differential diagnosis ruled out, in combination with a known history of pulmonary sarcoidosis as diagnostic in this case, and no pathological sample was needed in order to treat the patient.

In most cases, immunosuppressive therapy is needed for the control of neurosarcoidosis. Corticosteroids remain the first-line treatment [8,11,17].

Most patients respond to treatment and are able to tolerate steroid withdrawal after several months, although stronger immunosuppressants such as methotrexate, azathioprine, cyclophosphamide, cyclosporine, and more recently infliximab have also been used [17]. In some cases, such as ours, surgical intervention is indicated.

This case shows an uncommon clinical presentation of neurosarcoidosis with rapid progressive loss of consciousness secondary to hydrocephalus and emphasizes the importance of a timely diagnosis to ensure a good prognosis for the patient.

Disclosure Statements

No conflict of interest declared.

Appropriate written informed consent was obtained for publication of this case report and accompanying images.

References

- Baughman RP, Lower EE, and du Bois RM 2003. Sarcoidosis. *Lancet* 361:1111–1118.
- Burns TM 2003. Neurosarcoidosis. *Arch. Neurol.* 60:1166–1168.
- Stern BJ, Krumholz A, Johns C, et al. 1985. Sarcoidosis and its neurological manifestations. *Arch. Neurol.* 42:909–917.
- Joseph FG, and Scolding NJ 2007. Sarcoidosis of the nervous system. *Pract. Neurol.* 7:234–244.
- Terushkin V, Stern BJ, Judson MA, et al. 2010. Neurosarcoidosis: presentations and management. *Neurologist* 16:2–15.
- Scott TF 1993. Neurosarcoidosis: progress and clinical aspects. *Neurology* 43:8–12.
- Brouwer MC, de Gans J, Willemsse RB, et al. 2009. Neurological picture. Sarcoidosis presenting with hydrocephalus. *J. Neurol. Neurosurg. Psychiatry* 80:550–551.
- Tavee JO, and Stern BJ 2014. Neurosarcoidosis. *Continuum* 20:545–559. doi:10.1212/01.CON.0000450965.30710.e9.
- Ferriby D, de Seze J, Stojkovic T, et al. 2001. Long-term follow-up of neurosarcoidosis. *Neurology* 57:927–929.
- Allen RK, Sellars RE, and Sandstrom PA 2003. A prospective study of 32 patients with neurosarcoidosis. *Sarcoidosis Vasc. Diffuse Lung Dis.* 20:118–125.
- Nozaki K, and Judson MA 2012. Neurosarcoidosis: clinical manifestations, diagnosis and treatment. *Presse Med.* 41:e331–e348. doi:10.1016/j.lpm.2011.12.017.
- Vinas FC, and Rengachary S 2001. Diagnosis and management of neurosarcoidosis. *J. Clin. Neurosci.* 8:505–513.
- Benzagmout M, Boujraf S, Gongora-Rivera F, et al. 2007. Neurosarcoidosis which manifested as acute hydrocephalus: diagnosis and treatment. *Intern. Med.* 46:1601–1604.
- Hoyle JC, Jablonski C, and Newton HB 2014. Neurosarcoidosis: clinical review of a disorder with challenging inpatient presentations and diagnostic considerations. *Neurohospitalist* 4:94–101. doi:10.1177/1941874413519447.
- Bihan H, Christozova V, Dumas JL, et al. 2007. Sarcoidosis: clinical, hormonal, and magnetic resonance imaging (MRI) manifestations of hypothalamic-pituitary disease in 9 patients and review of the literature. *Medicine (Baltimore)* 86:259–268.
- Joseph FG, and Scolding NJ 2009. Neurosarcoidosis: a study of 30 new cases. *J. Neurol. Neurosurg. Psychiatry* 80:297–304. doi:10.1136/jnnp.2008.151977.
- Segal BM 2013. Neurosarcoidosis: diagnostic approaches and therapeutic strategies. *Curr. Opin. Neurol.* 26:307–313. doi:10.1097/WCO.0b013e3283608459.
- Sodhi M, Pearson K, White ES, et al. 2009. Infliximab therapy rescues cyclophosphamide failure in severe central nervous system sarcoidosis. *Respir. Med.* 103(2):268–273.