Case Studies

Isolated Central Nervous System Vasculitis as a Manifestation of Neurosarcoidosis

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A 62-year-old male presented to our clinic with recurrent fever, skin lesions (petechiae), scleral wounds, and hilar adenomegaly. A diagnosis of sarcoidosis was established, which resolved with corticosteroid treatment. After a few months, the patient developed confusion and behavioral changes, with few objective neurological deficits. Brain magnetic resonance imaging showed slight focal meningeal enhancement (prepontine region). The level of angiotensin-converting enzymes was normal in the serum and increased in the cerebrospinal fluid. The patient was diagnosed with neurosarcoidosis, and corticosteroid treatment was prescribed, yielding good clinical response. Nine months later, the patient presented with multiple ischemic strokes, and arteriography demonstrated multiple distal irregularities in all arterial territories, suggesting cerebral vasculitis. Even with corticosteroids, cyclophosphamide, and intravenous immunoglobulin, the patient died. Vasculitis is rarely seen in association with sarcoidosis, and in this case, no systemic manifestation was observed at the time that the patient developed vasculitis.
Key Words: Sarcoidosis—neurosarcoidosis—vasculitis—angiitis.

Sarcoidosis is a multisystemic, inflammatory and idiopathic disease characterized by the presence of noncaseus epithelioid granuloma, usually involving the lungs, uvea, lymph nodes, and skin.[1] In addition to specific organ symptomatology, nonspecific complaints (such as fatigue and general weakness) may also occur, which are usually related to the high levels of cytokines driven by granuloma formation.[2] Sarcoid granulomas produce angiotensin-converting enzymes (ACEs), with the serum levels of this enzyme increasing in more than half of the affected individuals.[1] Vasculitis associated with sarcoidosis is an unusual clinical feature, but various reported cases described the involvement of different organs (skin, lungs, and kidneys) and differently sized vessels, including large vessels such as the abdominal aorta.[3] The occurrence of cerebral vasculitis in the context of this granulomatous disorder is uncommon.[4]

Case Report

A 62-year-old male with a previous history of hypertension and chronic sinusitis had acute-onset fever, sweating, headache, and asthenia, raising the suspicion of dengue fever, which was ruled out after serology. One month later, the symptoms recurred in association with nonproductive cough, yielding a diagnosis of pneumonia.

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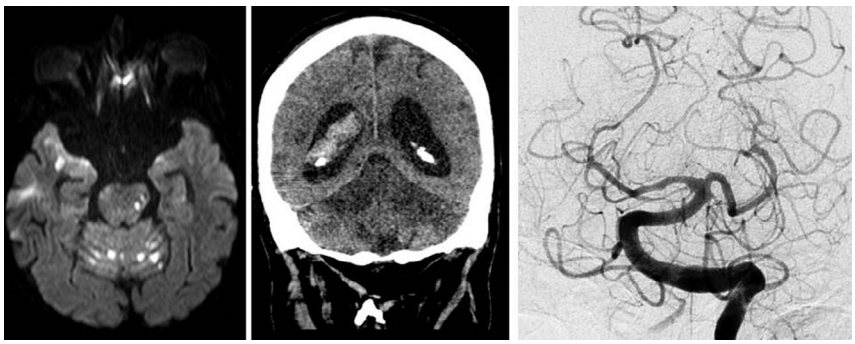

Figure 1. *Axial brain magnetic resonance imaging showing multiple infarctions in the brain stem, cerebellum, and cerebral hemispheres (left); computed tomography scan exhibiting extensive bilateral cerebellar infarction and hydrocephalus (center); and angiography showing arteriolar stenosis in the posterior cerebral artery (right).*

Despite a 10-day course of antibiotic therapy with amoxicillin–clavulanate and azithromycin, no clinical resolution was observed. Diffuse pustules then developed, as well as a scleral lesion on the right eye and lower limb edema; therefore, a skin biopsy was performed. Pathological analysis was compatible with annular granuloma. A corticosteroid regimen and allopurinol were started with good clinical response. Chest computed tomography (CT) exhibited isolated adenomegaly, which was confirmed by a positron emission tomography–CT scan, and lymph node biopsy showed only nonspecific inflammation without granulomas or any sign of malignancy or infection. Sarcoidosis was considered after the exclusion of other conditions and cloroquine was prescribed for 40 days with clinical improvement.

A few months later, the patient started to experience paroxysmal episodes of mental confusion, some of them with incoordination that lasted for hours, usually with full recovery. The patient was referred for neurological evaluation after incomplete resolution of one of these events. No history of cardiopathy, kidney diseases, smoking, or alcohol consumption was reported. Neurological examination showed only pain triggered by neck mobilization without nuchal rigidity and bradyphrenia, with no apparent cognitive dysfunction according to the Mini Mental Status Examination (score of 29/30). New chest and abdominal CT scans were normal. Brain magnetic resonance imaging showed slight focal meningeal enhancement (prepontine region), and angiography showed a 45% intracranial stenosis in the left internal carotid artery and mild proximal stenosis of the right vertebral artery.

Complete blood count, C-reactive protein, and erythrocyte sedimentation values were normal, while HLA-B51 and tuberculin skin tests were all negative. Cerebrospinal fluid (CSF) analysis showed pleocytosis (235 leukocytes/mm^3), elevated protein (265 mg/dL), low glucose (20 mg/dL), and high IgG index (2.58). Despite a positive IgG for Epstein–Barr virus in the CSF, other immune reactions (cysticercosis, syphilis, HIV, HTLV, cytomegalovirus, herpes simplex virus, and varicella zoster) were negative, as well as cultures (bacteria, fungi, and mycobacterium), polymerase chain reaction for *Mycobacterium tuberculosis*, and oncotic cytology. Serum ACE levels were normal (62 mg/dL), whereas high levels were found in the CSF (13.08—normal: <7). Based on these clinical features and laboratory findings, the patient was diagnosed with isolated neurosarcoidosis and a new corticosteroid course was prescribed with resolution of neurological symptoms.

Four months later, the patient was admitted to an emergency room due to the sudden onset of confusion, dysarthria, and left hemiparesis, achieving partial recovery. Brain CT scan was performed, showing 2 hypodense lesions in the left frontal deep white matter, whereas brain magnetic resonance imaging showed bilateral diffusion-weighted hyperintensity in the cortical and subcortical areas of the cerebellum, which was worse in the left hemisphere. After a few days, the patient abruptly presented with right internal ophthalmoplegia caused by a right-sided mesencephalic lesion (Fig 1). New CSF analysis showed the persistence of low glucose and elevated protein levels, but with lower cellular counts and normal IgG index. Positive IgG reactions for herpes simplex virus and Epstein–Barr virus were also found. Brain angiography results showed multiple distal irregularities over all vascular territories, which were suggestive of cerebral vasculitis, prompting corticosteroid therapy with 1 g of methylprednisolone daily for 5 days. Despite treatment, the patient experienced 4 new vascular events, developing intracranial hypertension due to hydrocephalus, as well as pneumonia. Antibiotic therapy, cyclophosphamide (1 g/m^2), and intravenous immunoglobulin (0.4 g/kg/day for 5 days) were prescribed, with no improvement. External ventriculostomy was performed, which caused intraventricular bleeding. The patient eventually died 1 month after admission due to the previously mentioned complications and septic shock.

Discussion

Central nervous system (CNS) involvement in sarcoidosis is rare, affecting 5%-10% of all patients according to retrospective studies; these symptoms are the presenting symptoms at clinical onset in half of these cases.[5] The most common neurological manifestation is cranial nerve neuropathy (bilateral involvement is not unusual), but