Spinal Cord Neurosarcoidosis

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Abstract: *Background:* Spinal cord neurosarcoidosis (SN) is problematic to diagnose because it mimics other inflammatory neurologic diseases. The authors report the clinical features of 29 SN cases. *Methods:* They retrospectively reviewed the medical records of 29 histologically proven sarcoidosis patients with spinal cord involvement seen at 3 university medical centers. They collected clinical data including laboratory and radiological findings. Clinical outcomes were assessed retrospectively using the modified Rankin scale. *Results:* The cohort included high number of African Americans (16/29, 55%). The lung and intrathoracic lymph nodes were the most common confirmatory biopsy sites (18/29, 62%), whereas the spinal cord was a relatively uncommon one (4/29, 14%). The most common presenting symptoms were lower extremity weakness and paresthesias. Thoracic segment was most frequently involved (21/27, 78%). Lesions were mostly intramedullary (22/27, 81%), although nearly half involved the leptomeninges (13/27, 48%). The average size of a lesion spanned 3.9 spine segments (range, 1–9); 17 of 22 (77%) intramedullary patients had ≥3 spine segments involved. Angiotensin-converting enzyme levels in cerebrospinal fluid were elevated in only 2 of 11 (18%) patients. All patients received glucocorticosteroids. Additional immune-modulating agents were used in 24 of 29 (83%) patients. Scores on the modified Rankin scale at the final follow-up visit were improved. *Conclusions:* Most SN cases were diagnosed indirectly based on extraneural tissue biopsy. Extended spinal cord lesion (≥3 spine segments) may be useful to distinguish SN from multiple sclerosis. Cerebrospinal fluid analysis was of limited value. Most patients experienced clinical improvement with immunosuppressive treatment, but many required combination therapy.

Key Indexing Terms: Neurosarcoidosis; Spinal cord; Magnetic resonance imaging; Cerebral spinal fluid; Immunosuppresive treatment.
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Sarcoidosis is a multisystem granulomatous disorder of unknown etiology.[1] Neurosarcoidosis, which represents involvement of the central and peripheral nervous system, is estimated to occur in approximately 5% to 16% of sarcoidosis patients.[2–4] Neurosarcoidosis is most commonly associated with granulomatous infiltrates involving the leptomeninges, dura, hypothalamus, pituitary gland and cranial nerves.[5] Spinal cord neurosarcoidosis (SN) is rare with an incidence estimated at 0.43% to 1% of all sarcoidosis patients.[6–10] Patients with SN are considered to be at high risk for severe neurological sequelae without prompt diagnosis and management.[11] SN is problematic to diagnose because it mimics other inflammatory neurologic diseases such as multiple sclerosis (MS), neuromyelitis optica and spinal cord tumor.[12]

We report 29 cases of SN from 3 institutions with a special focus on the magnetic resonance imaging (MRI) and laboratory findings. The goal of this study is to describe the clinical and radiographic manifestations of SN, which may provide guidance in terms of diagnosis and treatment for this condition.

METHODS

We retrospectively reviewed the medical records of patients with neurosarcoidosis identified at (a) the Medical University of South Carolina (MUSC) (between January 1997 and July 2011); (b) the Cleveland Clinic Foundation (CCF) (between August 2005 and March 2010); and (c) Allegheny General Hospital (AGH) (between January 1995 and December 2010). We defined SN as (1) histological evidence of sarcoidosis in the spinal cord, including dura and leptomeninges or (2) histological evidence of sarcoidosis in the extra-spinal cord organ and an MRI abnormality in the spinal cord, including dura and leptomeninges, which was consistent with SN and no alternative clinical cause of the MRI abnormality was identified or likely. We excluded patients with disease strictly limited to the vertebral bodies.

We collected data including sex, race, age at the onset of neurologic symptoms or spinal cord lesion identification, neurological manifestations, biopsied organ(s), laboratory findings including cerebrospinal fluid (CSF) analyses and spinal MR findings. We also inventoried the SN treatment regimens. Clinical outcome was assessed using the modified Rankin Scale (mRS)[13] at the initial and final evaluations and further categorized based on the presence of leptomeningeal disease, length of spinal lesions and treatment with infliximab. The mRS was not prospectively collected but was abstracted by chart review. The modified Wilcoxon rank sum test was used for bivariate analysis of noncontinuous data. The Spearman correlation coefficient was used for statistical dependence between 2 variables. Differences were considered significant if $P < 0.05$. This study was approved by the Institutional Review Boards of MUSC, CCF and AGH.

RESULTS

We identified 29 patients with histologically proven SN: 10 patients were identified at MUSC, 17 patients at CCF and 2 patients at AGH. Seventeen patients were men (17/29, 59%), and 16 patients were African American (16/29, 55%). The mean age of the initial neurologic manifestations was 43 years (22–63 years). The most common initial neurologic manifestations were lower extremity weakness and paresthesia (Table 1).

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TABLE 1. Initial clinical presentations of SN patients (n = 29)

Presenting symptom	n (%)
Leg weakness	21 (72)
Leg paresthesia	21 (72)
Back pain	8 (28)
Arm paresthesia	6 (21)
Urinary incontinence	6 (21)
Arm weakness	4 (14)
Neck pain	3 (10)
Bowel incontinence	3 (10)

SN, spinal cord neurosarcoidosis.

Histological evidence was obtained in all 29 patients. The lung and intrathoracic lymph nodes were the most common confirmatory biopsy sites (18/29, 62%), whereas the spinal cord was a relatively uncommon one (4/29, 14%) (Table 2). CSF study results were available in 20 patients (Table 3). No CSF parameter [elevated protein, elevated IgG index, lymphocytic pleocytosis, oligoclonal bands and angiotensin-converting enzyme (ACE)] occurred frequently enough to be a useful diagnostic test for SN. In particular, the CSF ACE level was elevated in only 2 of 11 patients who underwent the test (2/11, 18%).

All 29 patients underwent spine MRIs. Because detailed MRI data were not available for 2 patients, further analysis was performed on the data of the remaining 27 patients (Table 4). Most patients (22/27, 81%) had intramedullary lesions and nearly half (13/27, 48%) had leptomeningeal involvement. Thoracic segments were most commonly affected (21/27, 78%), followed by cervical (18/27, 67%). These lesions almost always demonstrated gadolinium enhancement (26/27, 96%). The SN lesions spanned 3.9 (range, 1–9) spinal segments on average, and 77% (17/22) of intramedullary patients had ≥3 spine segments. We also obtained brain MRI data in 26 patients, and intracranial involvement was noted in 15 patients (15/26, 58%).

All 29 patients received corticosteroids as the initial treatment, either intravenous high-dose corticosteroids or oral prednisone followed by maintenance prednisone. Additional immunosuppressive treatments were required in 24 patients (24/29, 83%) owing to refractory disease or corticosteroid-induced complications, with infliximab as the most commonly used in 69% (20/29) patients (Table 5).

Clinical information was available to assess mRS at initial and final visits in all patients. The mRS score at the final visit was significantly improved compared with that at the initial visit (initial visit: 2.5 ± 1.0 versus final visit: 1.8 ± 1.4; $P = 0.0012$, n = 29). However, there was no statistically significant difference in outcomes based on leptomeningeal disease, number of involved segments or treatment with infliximab (data not shown).

TABLE 2. Organ in which a histological diagnosis of sarcoidosis was established

Organ	n (%)
Lung and intrathoracic LNs	18/29 (62)
Spinal cord	4/29 (14)
Nerve roots	2/29 (7)
Extrathoracic LNs	2/29 (7)
Vertebral body	1/29 (3)
Liver	1/29 (3)
None[a]	1/29 (3)

[a] Presumptive diagnosis although confirmed on autopsy.
LN, lymph node.

TABLE 3. CSF analyses of SN patients

	n (%)
Elevated protein	16/20 (80)
Elevated IgG index	8/11 (73)
Elevated cell count	14/20 (70)
Positive oligoclonal bands	5/12 (42)
Elevated ACE	2/11 (18)

ACE, angiotensin-converting enzyme; CSF, cerebrospinal fluid; IgG, immunoglobulin G; SN, spinal cord neurosarcoidosis.

DISCUSSION

In this multicenter study, we analyzed the clinical presentation, radiographic and laboratory findings and treatment response of 29 patients with SN, a rare complication of sarcoidosis. To our knowledge, our cohort contains the largest number of African American SN patients. As reported in other studies, SN was found to be more common in men in our study.[4,14] The clinical presentation of SN is similar to other myelopathies with paraparesis, quadriparesis, paresthesias and bladder and bowel dysfunction.[4,11,12] Therefore, the diagnosis of SN is problematic in patients without a history of sarcoidosis. An evaluation for the presence of extraneural sarcoidosis should be performed even in patients without evidence of extraneural disease because biopsy of neural tissue is highly invasive. In most of our patients, the diagnosis of sarcoidosis was established by histological evidence obtained from extraneural organs.

Spinal cord MRIs in SN show high signal intensity on T2-weighted images, low signal on T1-weighted images and patchy/nodular contrast enhancement.[4,15,16] Junger et al described 4 progressive phases of spinal neurosarcoidosis: linear leptomeningeal enhancement, cord expansion, focal or multiple intramedullary involvement with minimal enhancement and resolution of the inflammatory process often associated with cord atrophy.[10,17] In

TABLE 4. Spinal cord MRI characteristics of SN patients

	n (%)
(A) Level of lesion	
Thoracic	21/27 (78)
Cervical	18/27 (67)
Lumbosacral	10/27 (37)
(B) Location	
Intramedullary	22/27 (81)
Leptomeningeal	13/27 (48)
Dura	4/27 (15)
Roots	5/27 (19)
(C) Intramedullary lesion	
Single lesion	15/22 (68)
Multiple lesion	7/22 (32)
≥3 spinal segments	17/22 (77)
(D) Gadolinium enhancement	26/27 (96)

MRI, magnetic resonance imaging; SN, spinal cord neurosarcoidosis.