ARTICLE OPEN ACCESS

Neurosarcoidosis

Longitudinal experience in a single-center, academic healthcare system

Jennifer Lord, MD, M. Mateo Paz Soldan, MD, PhD, Jonathan Galli, MD, Karen L. Salzman, MD, Jacob Kresser, BS, Rae Bacharach, MD, L. Dana DeWitt, MD, Julia Klein, FNP-C, John Rose, MD, John Greenlee, MD, and Stacey L. Clardy, MD, PhD

Correspondence
Dr. Clardy
stacey.clardy@hsc.utah.edu

Neurol Neuroimmunol Neuroinflamm 2020;7:e743. doi:10.1212/NXI.0000000000000743

Abstract

Objective

To characterize patients with neurosarcoidosis within the University of Utah healthcare system, including demographics, clinical characteristics, treatment, and long-term outcomes.

Methods

We describe the clinical features and outcomes of patients with neurosarcoidosis within the University of Utah healthcare system (a large referral center for 10% of the continental United States by land mass). Patients were selected who met the following criteria: (1) at least one *International Classification of Diseases Clinical Modification*, 9th revision code 135 or *International Classification of Diseases Clinical Modification*, 10th revision code D86* (sarcoidosis) and (2) at least one outpatient visit with a University of Utah clinician in the Neurology Department within the University of Utah electronic health record.

Results

We identified 56 patients meeting the study criteria. Thirty-five patients (63%) were women, and most patients (84%) were white. Twelve patients (22%) met the criteria for definite neurosarcoidosis, 36 patients (64%) were diagnosed with probable neurosarcoidosis, and 8 patients (14%) were diagnosed with possible neurosarcoidosis. A total of 8 medications were used for the treatment of neurosarcoidosis. Prednisone was the first-line treatment in 51 patients (91%). Infliximab was the most effective therapy, with 87% of patients remaining stable or improving on infliximab. Treatment response for methotrexate and azathioprine was mixed, and mycophenolate mofetil and rituximab were the least effective treatments in this cohort.

Conclusions

This is a comprehensive characterization of neurosarcoidosis within a single healthcare system at the University of Utah that reports long-term response to treatment and outcomes of patients with neurosarcoidosis. Our results suggest the use of infliximab as a first-line therapy for neurosarcoidosis.

From the Department of Neurology (J.L., M.M.P.S., J. Galli, R.B., L.D.D., J. Klein, J.R., J. Greenlee, S.L.C.), University of Utah; George E. Wahlen Veterans Affairs Medical Center (J.L., M.M.P.S., J. Galli, S.L.C.); Department of Radiology and Imaging Sciences (K.L.S.), and Departments of Internal Medicine and Bioinformatics (J. Kresser), University of Utah, Salt Lake City.

Go to Neurology.org/NN for full disclosures. Funding information is provided at the end of the article.

The Article Processing Charge was funded by the authors.

GLOSSARY

ACE = angiotensin-converting enzyme; **CVID** = common variable immune deficiency; **PNS** = peripheral nervous system; **TNFα** = tumor necrosis factor-alpha.

Sarcoidosis is a rare systemic inflammatory disease characterized by the formation of noncaseating granulomas (and occasionally caseating granulomas, but in such cases, extra investigation must definitively rule out tuberculosis and other infectious etiologies of caseating granulomas). With an average age of onset from 20 to 40 years old, sarcoidosis affects men and women equally.[1,2] In the United States, the prevalence varies based on race, with a range of 3–10/100,000 in whites and up to 35–80/100,000 among African Americans.[3,4] Although sarcoidosis most commonly affects the lungs, skin, and eyes, nervous system involvement is seen in 5%–15% of patients.[2] Neurologic manifestations commonly include cranial neuropathies, aseptic meningitis, peripheral neuropathy, myelopathy, intraparenchymal mass lesions, and hydrocephalus, all of which can lead to significant morbidity and mortality.[1,5]

There are no FDA-approved therapies for the treatment of neurosarcoidosis. Historically, corticosteroids and immunosuppressants, such as azathioprine and methotrexate, have been used for treatment.[6–8] In recent years, biologic therapies have shown promise in the treatment of neurosarcoidosis, with class IV evidence supporting the use of infliximab, a chimeric monoclonal antibody biologic drug targeting tumor necrosis factor-alpha (TNFα).[9] Here, we review the long-term follow-up of a neurosarcoidosis patient population at a tertiary referral center, including a report of the various treatments used and the response to therapy.

Methods

We performed a retrospective chart review of patients seen at the University of Utah between July 1, 2010, and August 24, 2018. Patients were included if they fulfilled both the following criteria: (1) at least one instance of a diagnostic code for sarcoidosis in their medical record (*International Classification of Diseases Clinical Modification*, 9th revision code 135 or *International Classification of Diseases Clinical Modification*, 10th revision code D86*) and (2) at least one outpatient visit with a University of Utah clinician in the Neurology Department within the University of Utah electronic health record. A total of 135 charts were reviewed. Demographics, medical history, laboratory data, imaging, biopsy results, and response to treatment were collected for each patient.

Definite, probable, and possible neurosarcoidosis designations were determined using the consensus diagnostic criteria.[10] Per these criteria, a "possible" neurosarcoidosis diagnosis requires a clinical presentation and diagnostic evaluation suggestive of neurosarcoidosis *without* pathologic evidence. A "probable" neurosarcoidosis diagnosis requires pathologic confirmation of *systemic* granulomatous disease consistent with sarcoidosis, and "definite" neurosarcoidosis criteria require *nervous system* pathology consistent with sarcoidosis.[10] Sarcoidosis is identified histologically by the presence of noncaseating granulomas, but rarely caseating granulomas may be present. We excluded patients who were subsequently diagnosed with common variable immune deficiency (CVID) based on pretreatment immunoglobulin levels because they are diagnosed as "CVID-associated granulomatous disease" and should be treated differently than patients with neurosarcoidosis (given underlying immunodeficiency), although the granulomas in CVID are pathologically indistinguishable from sarcoid granulomas.[11]

Seventy-six charts did not meet the diagnostic criteria as outlined, and 4 charts were excluded for insufficient data. Patient response to treatment was characterized as "improved," "stable," "failed," and "unknown." Response to treatment was determined based on clinical symptoms and MRI. An initial improvement or stabilization of disease followed by disease progression was deemed a treatment failure. The presence of medication side effects did not play a role in determining the treatment success or failure. Owing to the variety of clinicians and long duration of follow-up for many patients, there was not a uniform interval of time to determine treatment response. We report descriptive statistics, including count and percentage, for patients in our cohort.

Standard protocol approvals, registrations, and patient consents

The study was approved by the institutional review board.

Data availability

The corresponding author has full access to all the data in the study. She takes full responsibility for the integrity of the data, the accuracy of the data analysis and interpretation, and the conduct of the research. The authors have the right to publish any and all data, separate and apart from the guidance of any sponsor.

Results

Fifty-six patients met the diagnostic criteria for definite, probable, or possible neurosarcoidosis. Patients were followed between 1 month and 19 years, with a median duration of 3 years and 1 month. Table 1 summarizes the patient population demographics. Thirty-five patients (63%) were women, and most patients (84%) were white. Of the 15 patients with only peripheral nervous system (PNS) involvement, all patients were Caucasian. The mean age at presentation of the first neurologic symptom was 49 years (range 22–77). Six patients (11%) had a family history of sarcoidosis, and 15 patients (27%) had a family history of an

Table 1 Patient characteristics

Characteristic	N (%)
Male	21 (37)
Female	35 (63)
Mean age at symptom onset, y	49
Neurologic symptoms first	36 (64)
Ethnicity	
Caucasian	47 (84)
African Descent	5 (9)
Hispanic	3 (5)
Asian	1 (2)
Deceased	2 (4)
Family history	
Autoimmunity	15 (27)
Sarcoidosis	6 (11)
Diagnosis	
Definite	12 (22)
Probable	36 (64)
Possible	8 (14)
Neurologic involvement	
CNS	45 (80)
PNS	15 (27)
Systemic involvement	
Pulmonary	28 (50)
Lymphadenopathy	25 (45)
Joint	15 (27)
Ocular	8 (14)
Cutaneous	4 (7)
Liver	2 (4)
Cardiac	2 (4)
Bone	1 (2)

Abbreviation: PNS = peripheral nervous system.

Table 2 Presenting symptoms

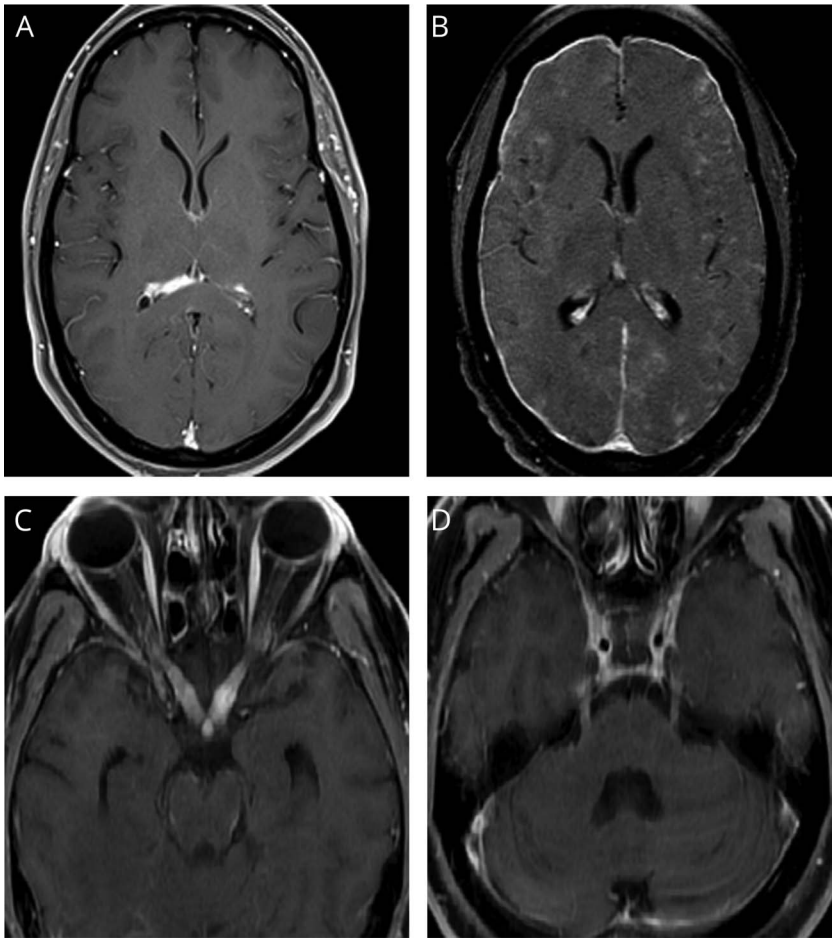
Symptom	N (%)
Limb sensory disturbance	19 (34)
Cranial neuropathies	17 (30)
CN 2	5 (9)
CN 3	1 (2)
CN 4	2 (4)
CN 5	5 (9)
CN 6	5 (9)
CN 7	3 (5)
CN 8	4 (7)
CN 9	1 (2)
CN 10	0
CN 11	0
CN 12	1 (2)
Headache	12 (21)
Peripheral neuropathy	12 (21)
Imbalance	11 (20)
Weakness	8 (14)
Vertigo	4 (7)
Memory/cognitive deficits	3 (5)
Tremor	3 (5)
Aseptic meningitis	2 (4)
Seizures	2 (4)

autoimmune disorder. Pulmonary involvement was the most common non-neurological manifestation of sarcoidosis, followed by lymphadenopathy, arthropathy, and ocular involvement. Ocular sarcoidosis in our cohort was characterized by panuveitis (4 patients), posterior uveitis (3 patients), and anterior uveitis (1 patient).

Twelve patients (22%) met the criteria for definite neurosarcoidosis, whereas 36 patients (64%) were diagnosed with probable neurosarcoidosis and 8 patients (14%) with possible neurosarcoidosis. CNS involvement was common, affecting 80% of patients, compared with 27% exhibiting evidence of PNS involvement. Of the patients with PNS involvement, 2 were diagnosed with definite neurosarcoidosis, 12 met the criteria for probable neurosarcoidosis, and 1 person met the criteria for possible neurosarcoidosis. Eight patients (14%) developed only neurosarcoidosis *without* evidence of systemic sarcoidosis. Thirty-six patients (64%) presented with neurologic involvement as their initial symptom of sarcoidosis, as summarized in table 2. Limb sensory changes were the most common symptom, followed by cranial neuropathies, headache, and peripheral neuropathy. Only 1 patient had a documented optic nerve granuloma of the 5 patients with CN 2 neuropathy. Fatigue was the most common associated symptom, affecting 57% of patients.

Diagnosis was achieved by a combination of history, examination, MRI, CSF analysis, and biopsy. Evidence of neurosarcoidosis was seen on 63% of brain MRIs, 23% of cervical spine MRIs, 27% of thoracic spine MRIs, and 7% of lumbar spine MRIs. MRI findings include leptomeningeal

Figure 1 Leptomeningeal and cranial nerve involvement on MRI



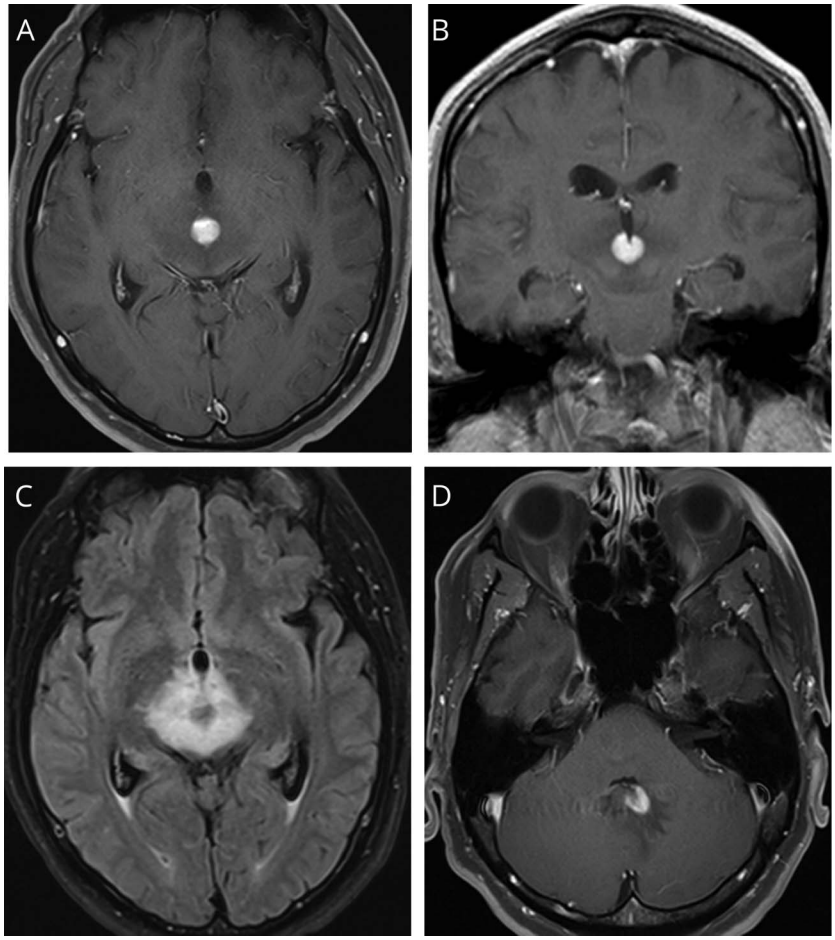
(A) Axial contrast-enhanced T1-weighted MRI at the level of the lateral ventricles shows abnormal enhancement in the right lateral ventricle posteriorly and along the anterior margin of the left lateral ventricle atrium in a 52-year-old woman with probable neurosarcoidosis. (B) Axial contrast-enhanced T1-weighted MRI shows diffuse leptomeningeal enhancement in a 37-year-old woman with probable neurosarcoidosis. Diffuse pachymeningeal (dural) enhancement is also present. Images (C) and (D) of a 50-year-old man with definite neurosarcoidosis and cranial neuropathies. (C) Axial postcontrast T1-weighted image at the level of the optic nerves shows marked enhancement and enlargement of the prechiasmatic optic nerves. (D) Axial postcontrast T1-weighted image at the level of the pons shows marked enhancement of the cisternal portions of the trigeminal nerves bilaterally.

enhancement (figure 1, A and B), cranial nerve enhancement (figure 1, C and D), enhancing supratentorial masses (figure 2), and spinal cord enhancement (figure 3). Twenty patients (36%) had spinal cord involvement on MRI. Of these 20 patients, 6 patients (30%) had discrete solitary lesions, 5 patients (25%) displayed a patchy multifocal lesion pattern, and 8 patients (40%) demonstrated a tumefactive pattern. Five patients exhibited more than 1 pattern on imaging. Fourteen of these 20 patients (70%) displayed gadolinium enhancement of the spinal cord, and 6 of these patients (30%) showed leptomeningeal enhancement.

CSF analysis was performed on 29 patients, but chart documentation of these laboratory values was incomplete. A pleocytosis (>5 white blood cells) was present in 13 of 26 patients (50%), with a lymphocyte predominance in 17 of 19 patients (89%) for whom a differential cell count was available. Low CSF glucose (<50 mg/dL) was found in 8 of 26 patients (31%); however, the lack of contemporaneous serum glucose values limits the interpretation of these data. An elevated CSF protein level (>50 mg/dL) was present in 16 of 29 patients (55%), and oligoclonal bands were present in 6 of 21 patients (29%). IgG index was elevated (ratio >0.66) in 2 of 13 patients (15%). CSF angiotensin-converting enzyme (ACE) was elevated (>2.5 U/L) in 4 of 16 patients (25%). Biopsy tissue consistent with sarcoidosis was obtained in 49 patients, with the most commonly biopsied sites, including lymph nodes (28 patients), brain (8 patients), and lung (7 patients).

Over the nearly 2 decades covered in this study, numerous medications were tried for treatment of neurosarcoidosis. Prednisone monotherapy was the first-line treatment in 51 patients (91%), followed by methotrexate (2 patients), azathioprine (1 patient), and infliximab (1 patient). Of the 51 patients started on prednisone monotherapy, 7 patients began the initial prednisone monotherapy as planned lead-in for infliximab. One patient with probable neurosarcoidosis presenting as peripheral neuropathy chose not to receive treatment. Prednisone monotherapy resulted in improvement in 19 of 51 patients and stabilization of 13 patients. Eight patients required long-term adjunctive steroids in addition to immunosuppressants to stabilize their disease. Two of the 3 medically significant side effects (Common Toxicity Criteria grade 3) were seen in patients on 60 mg prednisone tapers. One patient developed sepsis due to cellulitis, and another patient was hospitalized with diabetic ketoacidosis. The third

Figure 2 Thalamic and cerebellar masses in a patient with neurosarcoidosis



A 48-year-old man with probable neurosarcoidosis and parenchymal involvement on MRI. (A) Axial contrast-enhanced T1-weighted MRI shows an enhancing lesion in the thalamus along the inferior third ventricle. (B) Coronal contrast-enhanced T1-weighted MRI shows the same enhancing lesion along the inferior third ventricle. (C) Axial fluid-attenuated inversion recovery MRI at the level of the thalamus shows marked bilateral edema surrounding the enhancing lesion. (D) Axial contrast-enhanced T1-weighted MRI in the same patient shows an additional enhancing lesion in the left cerebellar hemisphere along the posterior fourth ventricle.

medically significant side effect was osteomyelitis/septic joint in a patient on infliximab. There were no life-threatening side effects in any treatment group.

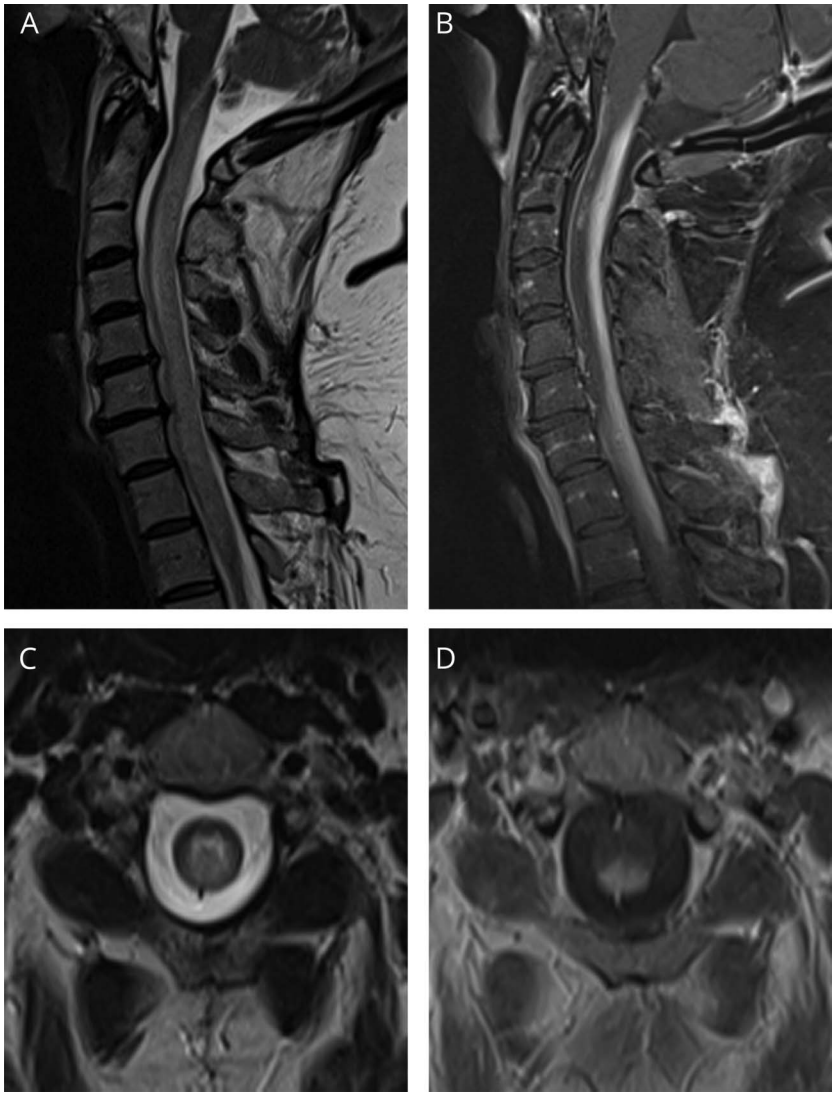
As summarized in table 3, infliximab was the most effective treatment, with 11 of 23 patients experiencing improvement and 9 patients with stabilization of symptoms. Infliximab was overall tolerated well in our cohort; however, 4 of 23 patients (17%) developed infusion reactions, and 2 of 23 patients (9%) developed increased frequency of infections, including osteomyelitis/septic joint. Methotrexate and azathioprine monotherapy led to more treatment failures than successes. None of the patients in this series improved on rituximab or mycophenolate mofetil. Cyclophosphamide and hydroxychloroquine sulfate were the least used medications. Overall, peripheral neuropathy was the clinical presentation most responsive to treatment, whereas thoracic cord lesions tended to be the least responsive.

More recently, the University of Utah providers have frequently increased the dosing interval of infliximab to every 3–4 weeks, rather than the more typical 6–8 weeks between maintenance infusions based on the half-life of infliximab for refractory patients and added low-dose methotrexate to (theoretically) prevent the development of antibodies against infliximab, as seen in the treatment of rheumatologic diseases.[12] However, these patients were not included given the short follow-up and relatively low numbers of patients on this dual therapy.

Discussion

Neurosarcoidosis is a heterogeneous disease capable of affecting all aspects of the nervous system. A previous meta-analysis reported average neurosarcoidosis patient population demographics as 62% Caucasians and 29% African-ancestry.[13] Owing to the demographics of our referral base, our patient population reflects the phenotype of a predominantly (83%) Caucasian population. Interestingly, only Caucasian patients in our cohort presented with PNS symptoms without CNS involvement. Manifestations of PNS involvement included distal sensorimotor polyneuropathy and mononeuropathies. Sixty-four percent of our patients presented with neurologic symptoms, similar to the 50%–70% reported in the existing literature.[8] Eight patients (14%) developed only neurosarcoidosis

Figure 3 Spinal cord involvement on MRI



A 52-year-old woman with probable neurosarcoidosis and extensive spinal cord involvement on MRI. (A) Sagittal T2-weighted image shows edema throughout the cervical spinal cord. (B) Sagittal postcontrast T1-weighted images shows enhancement along the entire dorsal aspect of the cervical spinal cord. Enhancement is also present along the posterior spinous processes at C7 and T1 related to sarcoid enthesopathy. (C) Axial T2-weighted image shows hyperintensity related to edema within the central cervical cord with relative sparing of the peripheral fibers. (D) Axial postcontrast T1-weighted image shows intramedullary enhancement along the dorsal aspect of the spinal cord.

without systemic disease, consistent with the 17% of patients reported in a previous study.[14] CNS involvement was significantly more common than PNS (80% vs 27%). The 27% of patients with PNS involvement in our patient population was somewhat higher than the 17% of patients with PNS symptoms reported in previous studies.[13] Although cranial neuropathies tend to be the most common presenting neurologic symptom in the existing literature, the most common presenting symptoms in our cohort were limb sensory changes, followed by cranial neuropathies, headache, and peripheral neuropathy.

Diagnosis of possible, probable, or definite neurosarcoidosis was achieved through a combination of history, physical examination, CSF analysis, imaging, and biopsy. Serum and CSF ACE levels were not routinely checked in our patients because of the limited utility in diagnosis, particularly when involvement outside the nervous system was absent or limited.[15] Previous studies have also used gallium-67 scintigraphy to identify the areas for possible biopsy.[13] These studies were not performed in our patients because of the high sensitivity and availability of CT and MRI as well as fluorodeoxyglucose PET when needed.

No established treatment guidelines exist for neurosarcoidosis. The general consensus among neurologists has been to initially treat with high-dose corticosteroids, often oral prednisone, followed by transition to immunosuppressants, such as methotrexate or azathioprine.[6–8] More recently, infliximab has been identified as an effective treatment option for patients, including those with disease previously refractory to other immunosuppresants.[9] In this study, infliximab was the most effective therapy with 87% of patients remaining stable or improving. This robust response is because of TNFα's critical role in the granuloma formation and supported by the high recurrence rate seen after stopping the medication.[9] The treatment response to monotherapy with either methotrexate or azathioprine was mixed but overall

Table 3 Treatments

Medication	Improved, N (%)	Stable, N (%)	Failed, N (%)
Prednisone	19 (37)	13 (26)	19 (37)
Methotrexate	5 (19)	9 (35)	12 (46)
Azathioprine	5 (38)	1 (8)	7 (54)
Infliximab	10 (45)	9 (41)	3 (14)
Rituximab	0	2 (50)	2 (50)
Mycophenolate mofetil	0	2 (25)	6 (75)
Hydroxychloroquine	1 (100)	0	0
Cyclophosphamide	1 (50)	0	1 (50)

suboptimal with 46% and 54% failing treatment, respectively. Mycophenolate mofetil (N = 8) and rituximab (N = 4) were the least effective treatments with no patients improving on these medications. The inferiority of mycophenolate mofetil to methotrexate has been reported previously, and our results support this conclusion.[16] No patients died due to neurosarcoidosis or systemic manifestations of sarcoidosis, but 2 patients died of causes not directly related to sarcoidosis (amyotrophic lateral sclerosis/bladder cancer and septic shock/disseminated intravascular coagulation).

In addition to expanding a very limited existing literature on neurosarcoidosis, strengths of this study include size, duration of time, followed after diagnosis and well-documented response to treatments. Owing to the retrospective nature of chart review, limitations of this study include incomplete medical chart documentation. Our study is the first to characterize the neurosarcoidosis patient population of the Mountain West and their response to treatment. With the overwhelming (albeit not prospective) improvement on infliximab, our patients' success supports the use of infliximab as maintenance therapy for neurosarcoidosis. Additional studies are needed to determine whether low-dose methotrexate in addition to infliximab improves outcomes and decreases the rate of antibodies against infliximab. Ultimately, this rare but frequently disabling condition would greatly benefit from a prospective, multicenter randomized treatment trial including infliximab.

Acknowledgment

The authors thank Barbara Steinmetz Gural and the Siegal Rare Neuroimmune Association for their continued support.

Study funding

No funding was received for this study.

Disclosure

The authors report no disclosures relevant to the manuscript. Go to Neurology.org/NN for full disclosures.

Publication history

Received by *Neurology: Neuroimmunology & Neuroinflammation* February 18, 2020. Accepted in final form April 13, 2020.

Appendix Authors

Name	Location	Contribution
Jennifer Lord, MD	University of Utah, Salt Lake City	Analysis and interpretation of the data and drafting the manuscript for intellectual content
M. Mateo Paz Soldan, MD, PhD	University of Utah, Salt Lake City	Revising the manuscript for intellectual content
Jonathan Galli, MD	University of Utah, Salt Lake City	Revising the manuscript for intellectual content
Karen Salzman, MD	University of Utah, Salt Lake City	Imaging acquisition and interpretation
Jacob Kresser, BS	University of Utah, Salt Lake City	Data acquisition
Rae Bacharach, MD	University of Utah, Salt Lake City	Revising the manuscript for intellectual content
L. Dana DeWitt, MD	University of Utah, Salt Lake City	Reviewing the manuscript
Julia Klein, FNP-C	University of Utah, Salt Lake City	Reviewing the manuscript
John Rose, MD	University of Utah, Salt Lake City	Revising the manuscript for intellectual content
John Greenlee, MD	University of Utah, Salt Lake City	Revising the manuscript for intellectual content
Stacey L. Clardy MD, PhD	University of Utah, Salt Lake City	Design and conceptualization of the study and revising the manuscript for intellectual content

References

1. Stern BJ, Krumholz A, Johns C, Scott P, Nissim J. Sarcoidosis and its neurological manifestations. Arch Neurol 1985;42:909–917.
2. Hoitsma E, Faber CG, Drent M, Sharma OP. Neurosarcoidosis: a clinical dilemma. Lancet Neurol 2004;3:397–407.
3. Rybicki BA, Major M, Popovich J, Maliarik MJ, Iannuzzi MC. Racial differences in sarcoidosis incidence: a 5-year study in a health maintenance organization. Am J Epidemiol 1997;145:234–241.
4. Pawate S, Moses H, Sriram S. Presentations and outcomes of neurosarcoidosis: a study of 54 cases. QJM 2009;102:449–460.
5. Ibitoye RT, Wilkins A, Scolding NJ. Neurosarcoidosis: a clinical approach to diagnosis and management. J Neurol 2017;264:1023–1028.
6. Hebel R, Dubaniewicz-Wybieralska M, Dubaniewicz A. Overview of neurosarcoidosis: recent advances. J Neurol 2015;262:258–267.
7. Hoitsma E, Drent M, Sharma OP. A pragmatic approach to diagnosing and treating neurosarcoidosis in the 21st century. Curr Opin Pulm Med 2010;16:472–479.
8. Leonhard SE, Fritz D, Eftimov F, van der Kooi AJ, van de Beek D, Brouwer MC. Neurosarcoidosis in a tertiary referral center: a cross-sectional cohort study. Medicine (Baltimore) 2016;95:e3277.
9. Gelfand JM, Bradshaw MJ, Stern BJ, et al. Infliximab for the treatment of CNS sarcoidosis: a multi-institutional series. Neurology 2017;89:2092–2100.

10. Stern BJ, Royal W, Gelfand JM, et al. Definition and consensus diagnostic criteria for neurosarcoidosis: from the neurosarcoidosis consortium consensus group. JAMA Neurol 2018;75:1546–1553.
11. Jolles S. The variable in common variable immunodeficiency: a disease of complex phenotypes. J Allergy Clin Immunol Pract 2013;1:545–556.
12. Jani M, Barton A, Warren RB, Griffiths CEM, Chinoy H. The role of DMARDs in reducing the immunogenicity of TNF inhibitors in chronic inflammatory diseases. Rheumatology 2013;53:213–222.
13. Fritz D, van de Beek D, Brouwer MC. Clinical features, treatment and outcome in neurosarcoidosis: systematic review and meta-analysis. BMC Neurol 2016;16:220.
14. Chapelon C, Ziza JM, Piette JC, et al. Neurosarcoidosis: signs, course and treatment in 35 confirmed cases. Medicine (Baltimore) 1990;69:261–276.
15. Ungprasert P, Carmona EM, Crowson CS, Matteson EL. Diagnostic utility of angiotensin-converting enzyme in sarcoidosis: a population-based study. Lung 2015;194:91–95.
16. Bitoun S, Bouvry D, Borie R, et al. Treatment of neurosarcoidosis: a comparative study of methotrexate and mycophenolate mofetil. Neurology 2016;87:2517–2521.