Neurosarcoidosis: Longitudinal Experience in a Single-Center, Academic Health Care System

Jennifer Lord MD[1,3], Rae Bacharach DO[1], Jonathan Galli MD[1], Jacob Kresser BS[2], Julia M. Klein MSN, FNP-C[1], L. Dana DeWitt MD[1], M. Mateo Paz Soldan MD PhD[1,3], John Rose MD[1], John Greenlee MD[1], Stacey L. Clardy MD PhD[1,3]

[1]Department of Neurology, University of Utah [2]Departments of Internal Medicine and Bioinformatics, University of Utah [3]George E. Wahlen Veterans Affairs Medical Center

Objective

Describe the demographics and clinical characteristics of patients within the University of Utah Healthcare system with neurosarcoidosis.

Background

- Sarcoidosis is a multi-organ inflammatory disorder characterized by formation of non-caseating granulomas.
- Although it most commonly affecting the lungs, skin, and eyes, nervous system involvement is seen in 5-15% of patients[1,2].
- The clinical phenotypes associated with neurosarcoidosis are diverse, although most commonly presents with cranial neuropathy or meningeal involvement[1,3].
- There is a paucity of literature regarding epidemiological data on patients with neurosarcoidosis.
- No FDA-approved therapies currently exist, leaving physicians with limited guidance for optimal treatment regimens, and even less data on patient outcomes.

Methods

Retrospective chart review from 1/1/2013 to 8/24/2018 within the University of Utah electronic medical record system for the following criteria:

1. At least one ICD-9-CM code 135 or ICD-10-CM code D86* (sarcoidosis)

2. At least one visit with a University of Utah clinician in the Neurology Department within the University of Utah electronic health record.

Definite, probable, and possible neurosarcoid was determined based on the diagnostic criteria proposed in Stern et al.'s "Definition and Consensus Diagnostic Criteria for Neurosarcoidosis". [4]

Results

135 Charts Reviewed

Excluded:
- **75 Did Not Meet Criteria**
- **4 Insufficient Data**

56 Patients Met Diagnostic Criteria

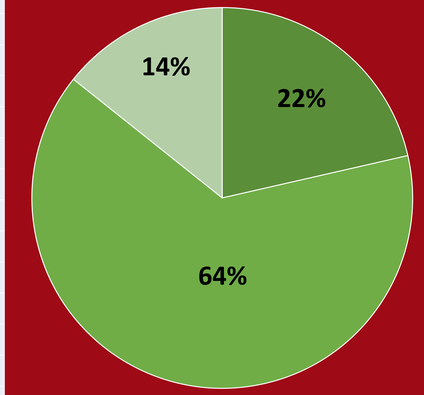
Demographics	N/(%)
Male	21 (37.5%)
Female	35 (62.5%)
Caucasian	47 (89%)
African-American	5 (9%)
Hispanic	3 (5%)
Asian	1 (2%)
Mean Current Age	59
Mean Age of Neuro Symptom Onset	49
Deceased	2
Family History of Autoimmunity	15 (27%)
Family History of Sarcoidosis	6 (11%)
Average Months Followed	63

Presenting Symptom	N/(%)
Limb sensory disturbance	19 (34%)
Cranial neuropathies	17 (30%)
Headache	12 (21%)
Peripheral neuropathy	12 (21%)
Dizziness/imbalance	11 (20%)
Weakness	8 (14%)
Vertigo	4 (7%)
Memory/cognitive deficits	3 (5%)
Tremor	3 (5%)
Seizures	2 (4%)
Aeseptic meningitis	2 (4%)

Disease Characteristics	N/(%)
CNS Involvement	45 (80%)
PNS Involvement	15 (27%)
Systemic Involvement	
Lung	28 (50%)
Ocular	14 (25%)
Cardiac	2 (4%)
Skin	4 (7%)
Liver	2 (4%)
Joint	15 (27%)
Bone	1 (2%)
Presented with Neuro Symptoms First	36 (64%)
Average Relapses	1.6

Diagnostic Evaluation	N/(%)
Evidence on MRI	
Brain	35 (63%)
C Spine	13 (23%)
T Spine	15 (27%)
L Spine	4 (7%)
CSF Studies	
CSF WBC > 5	13/26 (50%)
Lymphocyte Predominance	17/19 (89%)
CSF Protein > 50	16/29 (55%)
Oligoclonal Bands Present	6/21 (29%)
CSF ACE >2.5	4/16 (25%)

Diagnostic Criteria Met



Treatment	Improved (N)	Stable (N)	Failed (N)
Prednisone	19	13	19
Methotrexate	5	9	12
Azathioprine	5	1	7
Infliximab	10	9	3
Rituximab	0	2	2
Mycophenolate Mofetil	0	2	6
Plaquenil	1	0	0
Cyclophosphamide	1	0	1

Discussion and Conclusions

- Patients were followed between 1 month and 19 years (average of 5 years and 3 months).
- Due to demographics of our referral base, our patient population varies from previous studies with 83% Caucasians and 1/3 male.
- Sixty-four percent of patients presented with neurological symptoms consistent with 50-70% of patients in the existing literature[2].
- CNS involvement was significantly more common than PNS (80% vs 27%).
- The most common presenting symptoms were limb sensory changes and cranial neuropathies.
- 51 of 56 patients were started on prednisone as initial treatment, and 62% remained stable or improved. All but 10 patients were switched to additional immunotherapy.
- Infliximab, a chimeric monoclonal antibody biologic drug targeting TNF-α, was the most effective therapy with 86% of patients remaining stable or improving. This robust response is likely due to TNF-α's critical role in granuloma formation[1,5].
- Mycophenolate mofetil and Rituximab were the least effective medications.
- Strengths of this chart review include size, duration of time followed, and well-documented response to treatments. Limitations include incomplete medical charts.

References

1. Ibitoye RT, Wilkins A, Scolding NJ. Neurosarcoidosis: a clinical approach to diagnosis and management. *Journal of Neurology*. 2017;264(5):1023-1028.
2. Leonhard SE, Fritz D, Eftimov F, Kooi AJVD, Beek DVD, Brouwer MC. Neurosarcoidosis in a Tertiary Referral Center. *Medicine*. 2016;95(14)
3. Pawate S, Moses H, Sriram S. Presentations and outcomes of neurosarcoidosis: a study of 54 cases. *QJM: An International Journal of Medicine*. 2009;102(7):449-460.
4. Stern BJ, Royal W, Gelfand JM, et al. Definition and Consensus Diagnostic Criteria for Neurosarcoidosis. *JAMA Neurology*. 2018;75(12).
5. Gelfand JM, Bradshaw MJ, Stern BJ, et al. Infliximab for the treatment of CNS sarcoidosis. *Neurology*. 2017;89(20):2092-2100.