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CASE REPORT

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Neurosarcoidosis in a young male presenting with intractable migraines, blurry vision, and other nonspecific neurological symptoms case report

Jack Jnani[1*]

Abstract

Background Neurosarcoidosis can have various neurological outcomes and presentations. It is an uncommon diagnosis, especially in young Caucasian males presenting with predominantly migraine headaches.

Case presentation A Caucasian male in his 20s with no medical history presented with 1 month of intractable migraine headaches associated with left sided blurry vision, nausea and vomiting. He has also been having intermittent paresthesia's in the left upper extremity. He reports lightheadedness when moving from sitting to standing and occasionally feels unsteady on his feet. He also endorses night sweats, generalized malaise, and fatigue. On admission, CT chest, abdomen, and pelvis showed diffuse lymphadenopathy above and below the diaphragm, as well as widespread pulmonary nodules. MR head and spine showed multiple and diffuse nodular leptomeningeal enhancements and enhancement foci along the cervical, thoracic, and lumbar spine. Lumbar puncture showed elevated total nucleated cells and protein. Surgical pathology from a right inguinal lymph node showed many scattered multinucleated giant cells and epithelioid histiocytes consistent with non-necrotizing granulomas seen in sarcoidosis. He was treated with high dose steroids with significant improvement in symptoms.

Conclusions The diagnosis of neurosarcoidosis may be challenging, and the differential may include other infectious, neoplastic, and inflammatory conditions. Neurosarcoidosis may present in a young Caucasian male with a constellation of nonspecific neurological symptoms such as cranial nerve palsies, gait imbalance, paresthesia's, and headaches, among other presentations. Neurosarcoidosis may present similarly to lymphoma with constitutional symptoms of night sweats, fatigue, as well as widespread lymphadenopathy. Histopathology may be useful in diagnosis. Neurosarcoidosis may initially respond well to steroid treatment.

Keywords Sarcoidosis, Neurosarcoidosis, Cranial nerve palsy, Steroids

Background

Neurosarcoidosis may present similarly to lymphoma, multiple sclerosis, tuberculosis, and other pathology. Definitive diagnosis may be challenging and require a multidisciplinary approach.

*Correspondence:
Jack Jnani
jjnani@northwell.edu
[1] North Shore University Hospital, 300 Community Drive, Manhasset, NY 11030, USA

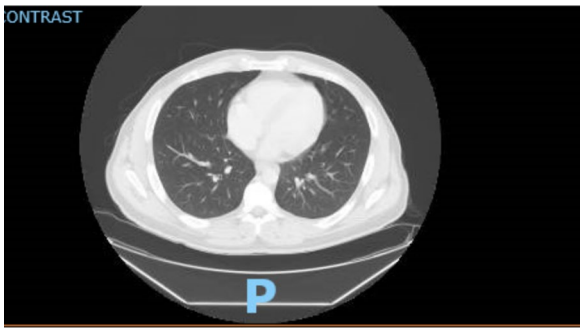

Fig. 1 CT scan showing pulmonary nodules

Case presentation

A Caucasian male in his 20s with no medical history presented with 1 month of intractable migraine headaches, left sided blurry vision, and occasional nausea and vomiting. He states that he usually wakes up with a headache localized to the left temporal and parietal region. He has also been having intermittent paresthesia's in the left upper extremity. He also reports episodes of lightheadedness when moving from sitting to standing and occasionally feels unsteady on his feet. He endorses blurry and double vision worse on left gaze with occasional episodes of partial blindness. In addition, he endorses night sweats, generalized malaise, and fatigue. He has never experienced any of these symptoms before. His mother had multiple sclerosis and his maternal aunt had lupus. On admission, vitals were stable. Body weight was 92 kg, height was 183 cm, and body mass index was 27 kg/m^2. On physical exam, he was alert and oriented to time, person, and place. His speech was fluent, and he had 5/5 muscle strength in all 4 extremities with intact sensation. His affect was appropriate. Cranial nerves 2–12 were intact except for a Cranial nerve VI palsy due to horizontal binocular diplopia with left gaze. Deep tendon reflexes including the biceps, triceps, brachioradialis, and patellar reflexes were 3+, except the Achilles reflex which was 4+ (with non-sustained clonus).

Objective

On admission, complete blood count and basic metabolic panel were within normal limits. 25-hydroxy Vitamin D was low at 22.7 ng/mL. Interferon gamma assay was negative, making tuberculosis less likely. CT chest, abdomen, and pelvis showed diffuse lymphadenopathy above and below the diaphragm involving the mediastinal, hilar, and retroperitoneal lymph nodes, as well as widespread pulmonary nodules (Fig. 1). MR head (Figs. 2, 3 and 4) and spine (Fig. 5) showed multiple nodular leptomeningeal enhancements involving suprasellar cistern,

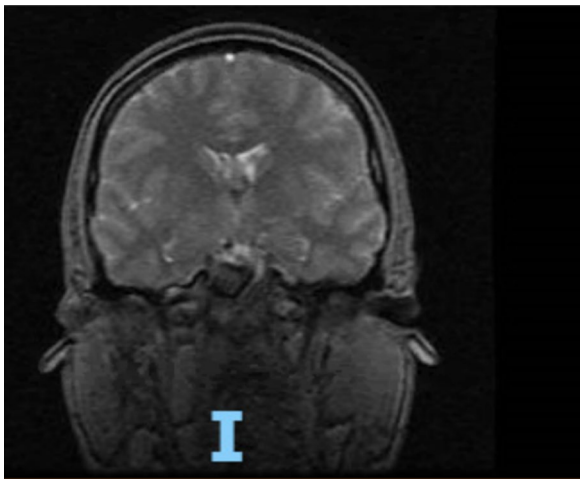

Fig. 2 MRI head showing nodular leptomeningeal enhancement

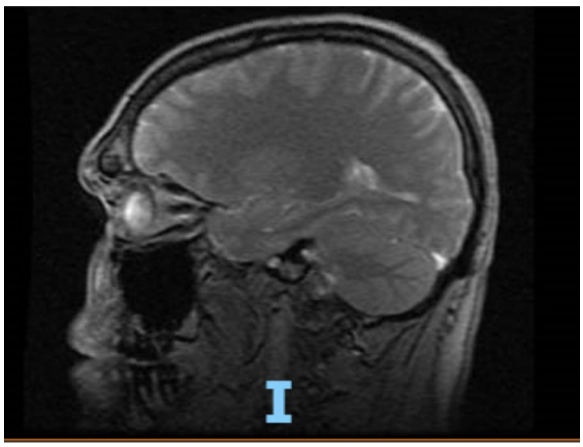

Fig. 3 MRI showing nodular leptomeningeal enhancement

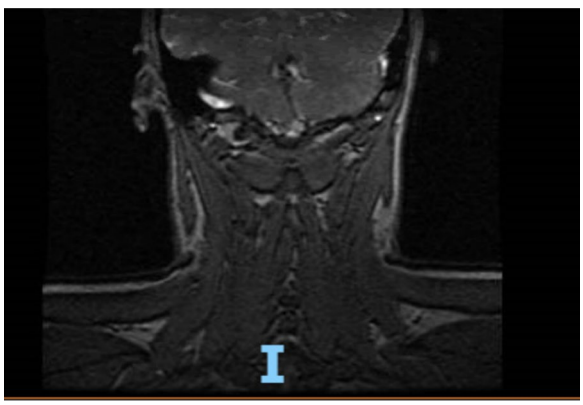

Fig. 4 MRI showing foci of nodular enhancement

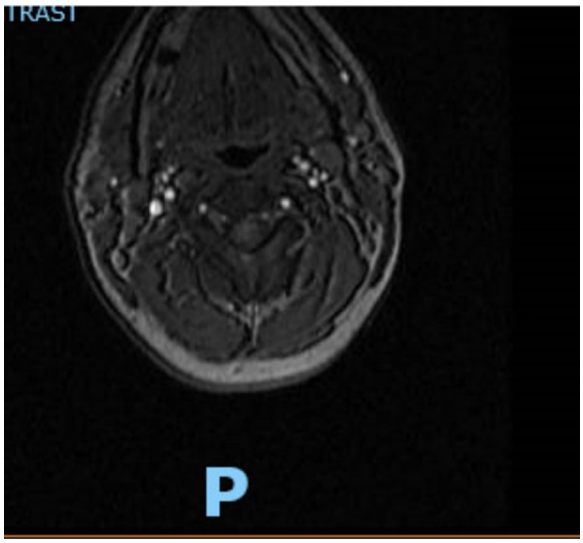

Fig. 5 Cervical spine with nodular enhancement

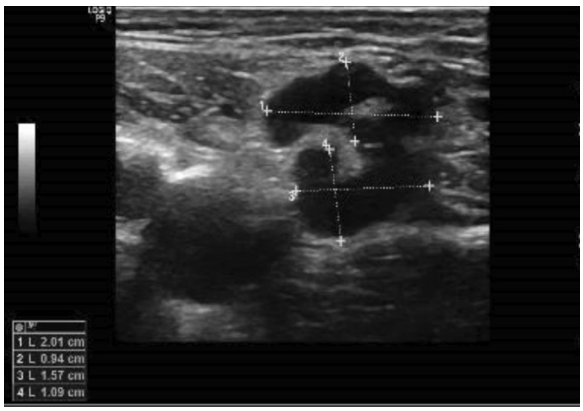

Fig. 6 Biopsy of 2×.94 cm right inguinal lymph node

basilar cistern, posterior fossa, upper cervical canal, optic chiasm, and left cerebellopontine angle. Imaging also showed foci of enhancement along the cervical, thoracic, and lumbar spine with associated cord edema. Lumbar puncture was performed showing total nucleated cells 43/uL, neutrophils 5%, lymphocytes 80%, glucose 43 mg/dL, protein of 205 mg/dL, and angiotensin-converting enzyme 5 U/L (elevated). Lumbar puncture cytology was negative for malignant cells. Surgical pathology from a right inguinal lymph node (Fig. 6) showed many scattered multinucleated giant cells (Fig. 7a–c) and epithelioid histiocytes with rare tiny foci of necrosis in a background of lymphocytic cells consistent with non-necrotizing granulomas.

Treatment

He was treated with high dose oral steroids (prednisone 125 milligrams (mg) orally daily for 4 weeks), naproxen 500 mg orally twice daily as needed for headache, pantoprazole 40 mg orally daily and Atovaquone 750 mg/5 mL oral solution prophylaxis daily with significant improvement in symptoms. He was discharged home with neurology and ophthalmology follow-up.

Discussion

Sarcoidosis is an immune-mediated disorder characterized by non-necrotizing granulomatous inflammation. Sarcoidosis is an inflammatory condition characterized be heightened immune response to yet-to-be identified antigens. Organs typically involved include the lung (90%), liver (20–30%), lymph nodes (10–20%), eye (10–30%), and nervous system (5–10%) (Bradshaw et al. 2021; Pirau and Lui 2022).

In the USA, sarcoidosis incidence ranges from 35 to 80 cases per 100,000 African American adults and 3–10 cases per 100,000 Caucasian adults. Neurosarcoidosis (NS) is thought to occur in 5–10% of patients with systemic sarcoidosis (Ungprasert et al. 2016).

Neurosarcoidosis can have a variety of presentation including cranial neuropathy (most common is optic and facial nerve involvement), leptomeningitis,

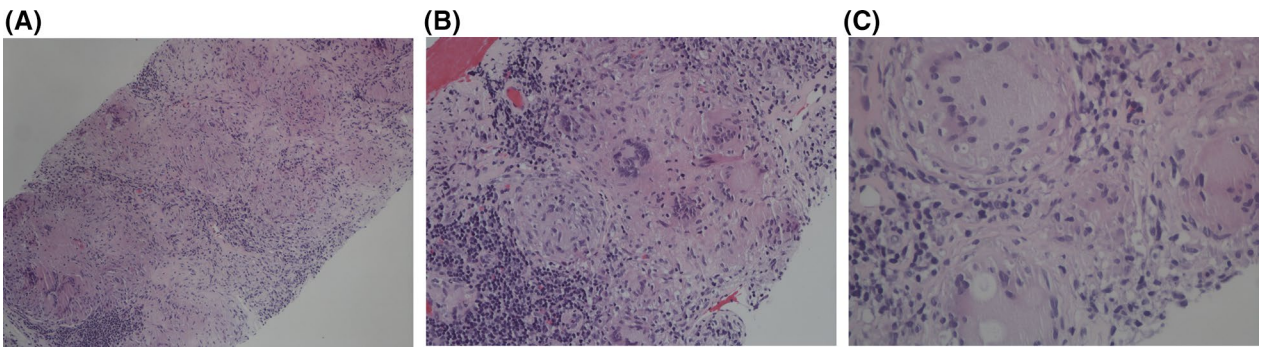

Fig. 7 Histopathology from the lymph node biopsy showing many scattered multinucleated giant cells and epithelioid histiocytes in a background of lymphocytic cells with rare tiny foci of necrosis

parenchymal disease (including seizure, mass lesions, and encephalopathy), vascular disease, hypothalamic and pituitary axis involvement, peripheral neuropathy, and myelopathy (Bradshaw et al. 2021).

The differential diagnosis for widespread lymphadenopathy is broad but includes neoplastic causes such as non-Hodgkin's lymphoma, infectious causes such as tuberculosis or histoplasmosis, and multisystemic disorders such as sarcoidosis. Neurosarcoidosis can have a variety of clinical manifestations overlapping infectious, inflammatory, and neoplastic causes making its diagnosis challenging.

Our patient met the 2018 consortium consensus clinical criteria for neurosarcoidosis evidenced by clinical neurological symptoms, supporting studies with MRI and cerebrospinal fluid analysis, and pathology (gold standard) showing non-caseating granulomas (Bradshaw et al. 2021).

Supportive but nonspecific serum testing include evidence of hypervitaminosis D, elevated serum or cerebrospinal fluid angiotensin-converting enzyme, and elevated soluble interleukin 2 (Bradshaw et al. 2021). A 2019 study showed IL-2 receptor levels to be 88% sensitive and 85% specific for a diagnosis of sarcoidosis (Eurelings et al. 2019).

Cerebrospinal fluid analysis may show a mild to moderate pleocytosis with lymphocyte predominance and elevated protein. Brain and spinal MRI may show areas of leptomeningeal enhancement.

First line initial therapy usually involves high dose steroids (Bradshaw et al. 2021; Voortman et al. 2019). This can be accomplished initially with intravenous therapy followed by an oral steroid taper. Failure of steroid monotherapy is common, and long-term additional therapy may be needed. In addition, steroid tapering may result in recurrence of symptoms and necessitate additional therapy. Methotrexate has been widely studied in the treatment for neurosarcoidosis, with a significant response rate and ability to wean down steroids in certain cases (Voortman et al. 2019). Mycophenolate mofetil is another agent that may lead to reduction in symptoms but has been shown to be inferior to Methotrexate in certain studies (Bradshaw et al. 2021). In severe cases when there is incomplete response to steroids or concern for steroid toxicity, early introduction of tumor necrosis alpha (TNF-a) inhibitor therapy has shown to be beneficial. In a cohort study of 22 patients and a literature review of 1793 patients with neurosarcoidosis, Infliximab, a TNF-alpha inhibitor, demonstrated favorable outcomes and should be considered for patients with aggressive or refractory symptoms (Sambon et al. 2022).

Conclusions

- The diagnosis of neurosarcoidosis may be challenging, and the differential may include other infectious, neoplastic, and inflammatory conditions.
- Neurosarcoidosis may present in a young healthy Caucasian male with a constellation of nonspecific neurological symptoms such as cranial nerve palsies, gait imbalance, paresthesia's, and headaches, among other presentations.
- Neurosarcoidosis may present similarly to lymphoma with constitutional symptoms of night sweats and fatigue, as well as widespread lymphadenopathy.
- Confirmatory diagnosis of neurosarcoidosis may be supported by lymph node biopsy demonstrating non-necrotizing granulomas.
- Neurosarcoidosis may initially respond well to steroid treatment, but other steroid-sparing therapy and TNF-alpha inhibitors may be useful in management as well.

Abbreviations

CT	Computed tomography
MRI	Magnetic resonance imaging
NS	Neurosarcoidosis

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Not applicable.

Author contributions
JJ was responsible for the writing of the report, data acquisition, and analyzation of data included in this report. All authors read and approved the manuscript prior to submission.

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Availability of data and materials
All data generated or analyzed during this study are included in this published article [and its supplementary information files].

Declarations

Ethics approval and consent to participate
The following case report did not require ethics approval. Consent to participate was obtained from the patient.

Consent for publication
Written Informed consent was obtained from the patient included in this report, including permission for publication of data and clinical images.

Competing interests
The authors declare that they have no competing interests.

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References

Bradshaw MJ, Pawate S, Koth LL, Cho TA, Gelfand JM (2021) Neurosarcoidosis: pathophysiology, diagnosis, and treatment. Neurol Neuroimmunol Neuroinflamm 8(6):e1084. https://doi.org/10.1212/NXI.0000000000001084

Eurelings LEM, Miedema JR, Dalm VASH et al (2019) Sensitivity and specificity of serum soluble interleukin-2 receptor for diagnosing sarcoidosis in a population of patients suspected of sarcoidosis. PLoS ONE 14(10):e0223897

Pirau L, Lui F (2022) Neurosarcoidosis. StatPearls Publishing, Treasure Island

Sambon P, Sellimi A, Kozyreff A et al (2022) Epidemiology, clinical presentation, treatment, and outcome of neurosarcoidosis: a mono-centric retrospective study and literature review. Front Neurol 13:970168. https://doi.org/10.3389/fneur.2022.970168

Ungprasert P, Carmona EM, Utz JP, Ryu JH, Crowson CS, Matteson EL (2016) Epidemiology of sarcoidosis 1946–2013: a population-based study. Mayo Clin Proc 91(2):183–188

Voortman M, Drent M, Baughman RP (2019) Management of neurosarcoidosis: a clinical challenge. Curr Opin Neurol 32(3):475–483. https://doi.org/10.1097/WCO.0000000000000684

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