Neurosarcoidosis Presenting with Non-Pulmonary Symptoms: Hydrocephalus and Vasculitis-Related Stroke as an Uncommon Presentation of a Common Disease

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Background

- Sarcoidosis is a multisystem, granulomatous disease of unknown etiology.
- While pulmonary symptoms (most commonly shortness of breath) are present and predominate in most patients with sarcoidosis, symptoms related to disease in other organ systems can be the primary presenting in some patients.
- Central nervous system involvement by sarcoidosis constitutes a minority of the cases and commonly manifests with cranial nerve (CN) symptoms, often CN III. We report a patient who presented with hydrocephalus-related symptoms along with stroke-like manifestations due to ischemic central nervous system changes in the context of vasculitis.

Methods and Materials

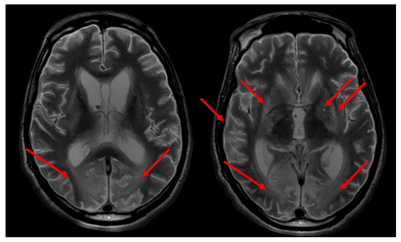
- Clinical features were summarized from the patient's medical record. Key histopathologic features were reviewed.
- A PubMed.gov literature search was undertaken using relevant key words.

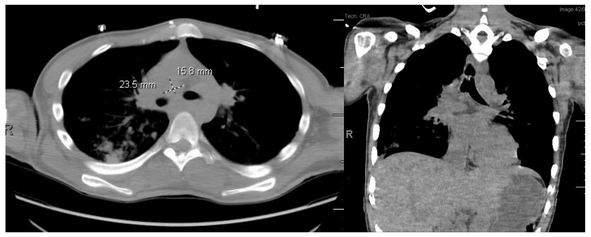
Case Report

- The patient is a 27-year-old man who presented with intermittent headaches with progressive dizziness, ataxia, and blurred vision.
- Communicating hydrocephalus was diagnosed and a ventricular-peritoneal shunt was placed. Imaging of his brain also identified (1) inferior cerebellar cortical infarctions, subacute, bilateral, in the PICA territories, (2) old infarctions involving basal ganglia and occipital lobes, and (3) leukoencephalopathy.
- Toxic-metabolic, global hypoxic-ischemic, infectious, and inflammatory etiologies were considered less likely.
- Thoracic CT scans identified enlarged mediastinal and axillary lymph nodes. Serum calcium was elevated.
- Serum and cerebrospinal fluid angiotensin converting enzyme (ACE) levels were normal. CSF evaluation was negative for (1) meningitis/encephalitis and (2) paraneoplastic encephalopathy by a screening panel.
- A weakly positive elevation in myelin basic protein level was noted but no oligoclonal bands were identified.

Results

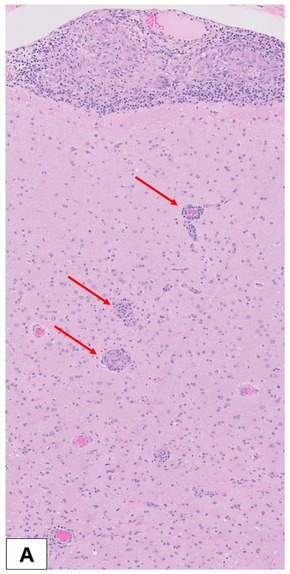
Imaging Findings

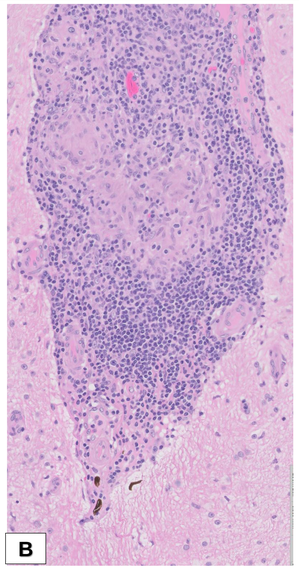


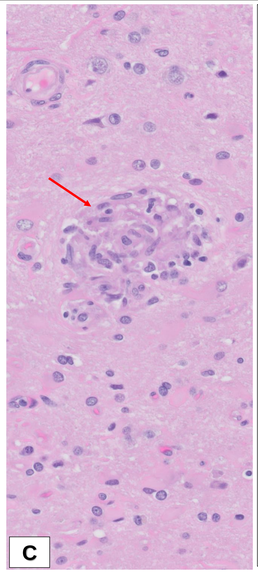


- **Brain MRI**: T2-weighted imaging identified subacute and chronic infarcts including in the bilateral occipital lobes, left temporal lobe, and basal ganglia (Arrows)
- **Chest CT Scan**: Imaging of the chest identified enlarged mediastinal and axillary lymph nodes and patchy nodular opacities with consolidation predominantly in the right lower lobe .

Histopathological Evaluation

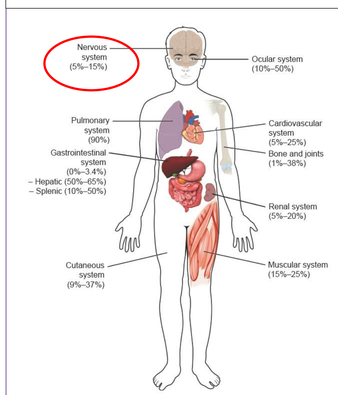






- **Histology**: **A-B.** Multifocal granulomatous inflammation was noted within the leptomeninges and along Virchow-Robin perivascular spaces (Arrows), non-necrotizing. **C.** Blood vessel compromise was noted multifocally, consistent with vasculitis. Neuropil was markedly gliotic consistent with reaction to ischemic injury.
- **Special Stains for Microorganisms**: Bacterial (Gram) Acid fast bacilli (AFB), and fungi (PAS and GMS) stains were negative (Not Shown).

Literature Review



(Al-Kofahi et al. Management of extrapulmonary sarcoidosis: challenges and solutions. 2016)

Box. Proposed Diagnostic Criteria for Central Nervous System and Peripheral Nervous System Neurosarcoidosis

Possible

1. The clinical presentation and diagnostic evaluation suggest neurosarcoidosis, as defined by the clinical manifestations and MRI, CSF, and/or EMG/NCS findings typical of granulomatous inflammation of the nervous system and after rigorous exclusion of other causes.
2. There is no pathologic confirmation of granulomatous disease.

Probable

1. The clinical presentation and diagnostic evaluation suggest neurosarcoidosis, as defined by the clinical manifestations and MRI, CSF, and/or EMG/NCS findings typical of granulomatous inflammation of the nervous system after rigorous exclusion of other causes.
2. There is pathologic confirmation of systemic granulomatous disease consistent with sarcoidosis.

Definite

1. The clinical presentation and diagnostic evaluation suggest neurosarcoidosis, as defined by the clinical manifestations and MRI, CSF, and/or EMG/NCS findings typical of granulomatous inflammation of the nervous system after rigorous exclusion of other causes.
2. The nervous system pathology is consistent with neurosarcoidosis.

   Type a. Extraneural sarcoidosis is evident.

   Type b. No extraneural sarcoidosis is evident (isolated CNS sarcoidosis).

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(12):1546–1553

Diagnosis Using Zajicek Criteria:

(Fritz D, Voortman M, van de Beek D, Drent M, Brouwer MC. Many faces of neurosarcoidosis: from chronic meningitis to myelopathy. Curr Opin Pulm Med. 2017 Sep;23(5):439-446.)

Definite neurosarcoidosis	Positive nervous system histology
Probable neurosarcoidosis	Signs of inflammation in the central nervous system on MRI or CSF (elevated protein, cells, immunoglobulin G indices, or presence of oligoclonal bands) compatible with neurosarcoidosis; and
	Positive histology for a systemic lesion or positive results for at least two of the following tests: ^{18}F-FDG-PET, gallium scan, chest HRCT, serum ACE
Possible neurosarcoidosis	Above criteria not met

ACE, angiotensin-converting enzyme; CSF, cerebrospinal fluid; FDG-PET, fluorodeoxyglucose positron emission tomography; HRCT, high-resolution computed tomography.
Data from [17,24].

- Sarcoidosis is a multisystem, non-caseating granulomatous disease of unknown etiology.
- Respiratory deficits are the most common presenting symptom in most patients (>90%) due to pulmonary interstitial injury and hilar and mediastinal lymph node involvement.
- As sarcoidosis can affect nearly every organ system, presentation with non-pulmonary symptoms is commonly seen.
- Approximately 5-10% of patients with systematic sarcoidosis have CNS involvement.
- Neuro sarcoidosis most often affects the base of the skull and cranial nerves, typically you have involvement of the facial nerve and optic nerve (at the optic chiasm).
- Also can see uveoparotid syndrome, cranial oligoneuropathy (bilateral facial neuropathy), lesions of the cervical of thoracic spine, cauda equina syndrome, pituitary and/or hypothalamus involvement with possible obstructive hydrocephalus are characteristic.
- Vasculitis as an initial symptom of neurosarcoidosis is an uncommon / rare finding.
  - Risk of strokes are increased and seem to happen in many cases of neurosarcoidosis
  - Vasculitis of the cranial arteries tend to cause ischemic strokes
  - Improves with tapering corticoids
- Hydrocephalus is a rare complication, observed in 6-9% of neurosarcoidosis cases.
- Definite Diagnosis:
  - Need pathological confirmation via biopsy showing giant cell epithelioid granuloma without caseous necrosis.

Conclusions

- While pulmonary symptoms predominant in sarcoidosis, sarcoidosis can affect nearly every organ system and presentation with non-pulmonary symptoms is occasionally seen.
- Diagnosis is made in the context of a thorough workup including CT scan of the chest, abdomen, and pelvis.
- Symptoms related to parenchymal vasculitis is an uncommon presentation and brain biopsy is often necessary given the low sensitivity of tests including ACE levels.

References

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