Case Report

Primary Neurosarcoidosis Mimicking Gallbladder Pathology

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ABSTRACT: A 40-year-old African American male with long standing headaches and unintentional weight loss presented with nausea, vomiting, and blurry vision. Laboratory findings include hyponatremia and mildly raised liver enzymes. He underwent cholecystectomy six months prior for unexplained nausea and vomiting, which in hindsight was likely neurologic-induced vomiting from neurosarcoidosis. Brain imaging revealed diffuse, leptomeningeal, nodular enhancement involving the brain, brainstem, and upper cervical spinal cord. Further work up showed extensive lymphadenopathy above and below the diaphragm, solitary liver lesion, and multiple lytic lesions involving bones. Iliac spine biopsy revealed ill-defined, non-caseating granulomas with giant cell reaction infiltrating bone fragments. Acid-fast bacilli and fungal stains were negative. Patient was treated with steroids. Diagnosis of neurosarcoidosis is challenging in the absence of physical signs and symptoms. However, radiological and pathological correlation in clinical suspicion of sarcoidosis is helpful in more accurate diagnosis and timely management of the patient.

KEYWORDS: *Granuloma, Sarcoidosis, Hyponatremia, Lymphadenopathy.*

Introduction

Neurosarcoidosis (NS) is a rare but important cause of neurological morbidity.

It occurs in 5%-15% of patients with sarcoidosis of which only 1% of patients displaying neurological symptoms at initial presentation.

NS can involve any part of the nervous system with the cranial nerves and meninges being the most commonly involved [1,5].

Pathogenesis of neurosarcoidosis is unknown [4].

The diagnosis of NS is possible in patients with sarcoidosis and new symptoms of neurological origin and is often a diagnosis of exclusion [3].

Clinically, NS can mimic infective, inflammatory, and neoplastic processes [6].

The diagnosis of NS requires imaging and cerebrospinal fluid analysis for elevated proteins and oligoclonal bands.

Sarcoidosis outside the nervous system requires biopsy and histopathological evaluations for non-caseating granulomatous inflammation [3].

On imaging, NS is present as solitary of multiple nodules, cranial nerve lesions, hydrocephalus, or periventricular lesions.

Parenchymal lesions may be seen in about 20% of cases.

Magnetic resonance imaging (MRI) was the study of choice to evaluate central nervous system (CNS) involvement.

Diagnosing CNS nodular lesions from neoplastic or infective disorders in the absence of leptomeningeal involvement is always challenging.

Advanced neuroimaging techniques such as ^{18}F-FDG-PET is can help identify neural and extra-neural sarcoidosis localization [6].

Symptomatic patients are treated with corticosteroids and immunosuppressants.

Refractory cases are treated with anti-tumor necrosis factor alpha [1,2,3,5,6].

Case Report

A 44-year-old African American male with history of hypertension and sleep apnea presented with several months of nausea/ vomiting, headaches, and blurry vision.

The patient also reported significant unintentional weight loss in the last year.

He denied fever, recent infection, cold or heat intolerance, dysphagia, hematemesis, hemoptysis, hematuria, and hematochezia/ melena.

He underwent cholecystectomy six months prior for unexplained nausea and vomiting.

Physical examination was unremarkable.

Serum electrolytes revealed mild hyponatremia.

Liver enzymes were mildly elevated.

Hepatitis B, C, and HIV profile were negative.

All other pertinent laboratory tests including TSH, FT4, HbA1c, BUN and creatinine were within normal limits.

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MRI of the brain showed diffuse leptomeningeal nodular enhancement involving the brain, brainstem, and upper cervical spine.

Multiple T2/hyperintense signals were seen in supratentorial and infratentorial regions of the brain.

PET/CT showed extensive bilateral cervical, supraclavicular, axillary, hilar, mediastinal, retroperitoneal, and iliac lymphadenopathy, left hilar consolidation with bilateral upper lobe perilymphatic nodules, and solitary liver lesion.

Multiple lytic bone lesions were identifiable (Figures 1, 2).

Biopsy of the iliac spine revealed ill-defined non-caseating granulomatous inflammation with giant cell reaction infiltrating the bone fragments (Figure 3).

Acid-fast bacilli and fungal stains were negative.

Fluorescent treponemal antibody absorption (FTA-ABS) was nonreactive, serum muramidase 9.2 (5-11)μg/mL, and ACE levels was at upper normal limit 64 (9-67)μg/mL, CA19-9 within normal limits and alpha fetoprotein was raised 10.7 (<6.1)ng/mL.

The diagnosis of neurosarcoidosis with systemic involvement was made and patient was started with prednisone 80 mg daily with follow up.

Patient consent was obtained through a legal, written consent form before using patient information to construct a case report.

The patient was compliant with the use of his case for research purposes.

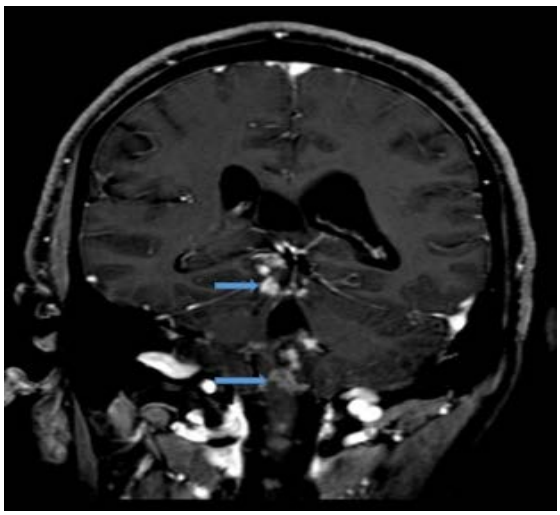

Figure 1. Leptomeningeal enhancement involving brain and cervical spinal cord.

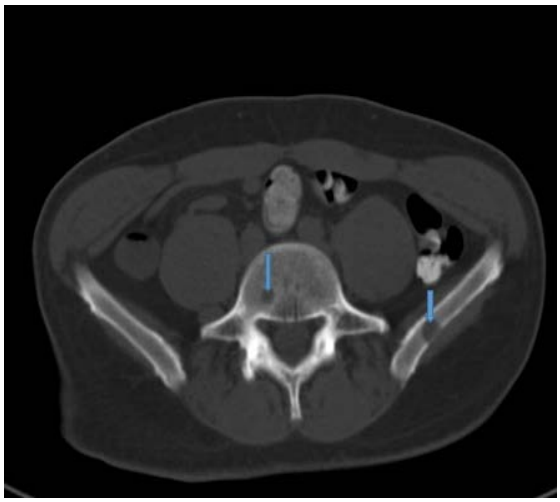

Figure 2. Lytic bone lesion involving vertebral body and iliac spine.

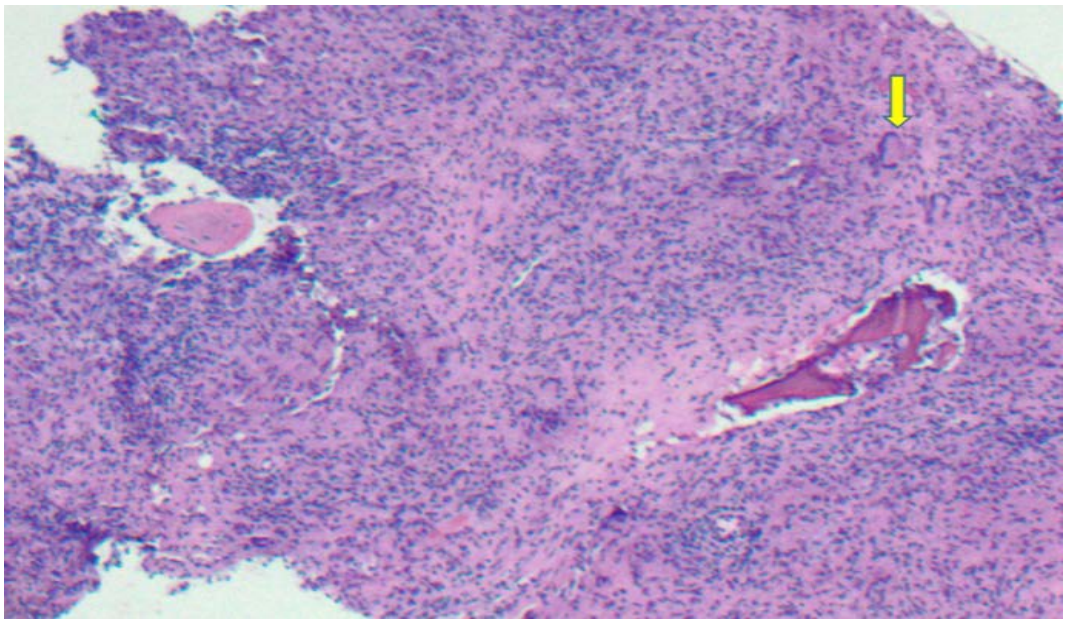

Figure 3. Ill defined granuloma with multinucleated giant cells (arrow) and bone fragments, HE staining, 4x.

Discussion

Unlike systemic sarcoidosis, diagnosis of neurosarcoidosis is complicated due to a lack of unique pathologic and radiologic features. Diagnosis should preliminarily confirm neurological disorder and then assess systemic signs for underlying etiology. Clinical symptoms of neurosarcoidosis are non-specific and may present as seizures, encephalopathy, and hypothalamic/pituitary dysfunction [1].

The most common complications involve the facial nerve among other cranial nerves disorders. Neurosarcoidosis is most often considered when patients with a previous sarcoidosis diagnosis exhibit neurological findings.If neurosarcoidosis is otherwise suspected, patient should be clinically assessed for presence of systemic sarcoid features and exclusion of similarly presenting underlying conditions such as neurological disease, neoplasms, and infections. The presence of neurosarcoidosis preceding systemic sarcoidosis is noted to be very rare, estimated to comprise 1-2% of all sarcoidosis cases [2].

The diagnosis of neurosarcoidosis is supported by strong clinical indicators of underlying sarcoidosis including hilar lymphadenopathy on CT imaging, erythema nodosum upon skin inspection, uveitis, elevated ACE, and positive Kveim test. While the gold-standard diagnosis of sarcoidosis involves presence of non-caseating granulomas on tissue biopsy, neuro-biopsies are avoided due to the high risk of complication [3].

Though nonspecific, CSF and gadolinium-enhanced MRI analysis are the next useful and sensitive diagnostic tests [1]. CSF may display inflammation among other signs such as elevated protein, oligoclonal bands, elevated IgG index, low glucose, and mononuclear pleocytosis. MRI is key in detecting neurosarcoid abnormalities such as intraparenchymal lesions (commonly non-enhancing periventricular white matter lesions), enhanced leptomeninges, diencephalic involvement, and white matter changes.

In contrast to similar multiple sclerosis lesions, neurosarcoid presents with linear enhancement along Virchow-Robin spaces with the meningeal/parenchymal enhancements lasting for a longer period. Hydrocephalus, optic nerve, and cranial nerve lesions have also been noted. MRI of dorsal subpial gadolinium enhancement in more than two vertebral segments and lasting longer than two months despite treatment can be indicative of spinal cord sarcoidosis.

Furthermore, CT may be utilized to detect neurological abnormalities indicative of neurosarcoid, such as hydrocephalus and intercranial calcifications. Imaging of neurological dysfunction in context of an existing sarcoidosis diagnosis provides strong evidence for neurosarcoidosis [4].

Conclusion

Diagnosis of neurosarcoidosis is challenging in the absence of physical signs and symptoms or space occupying lesion of the brain.

However, radiological and pathological correlation in clinical suspicion of sarcoidosis is helpful in more accurate diagnosis and timely management of the patient.

Conflict of interests

None to declare.

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