

PICTORIAL ESSAY

Magnetic Resonance Imaging of Neurosarcoidosis

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ABSTRACT

Neurosarcoidosis is an uncommon condition with protean manifestations. Magnetic resonance imaging (MRI) is often used in the diagnostic evaluation and follow-up of patients with neurosarcoidosis. Therefore, familiarity with the variety of MRI appearances is important. In this pictorial essay, the range of possible patterns of involvement in neurosarcoidosis are depicted and discussed. These include intracranial and spine leptomeningeal involvement, cortical and cerebral white matter lesions, corpus callosum involvement, sellar and suprasellar involvement, periventricular involvement, cranial nerve involvement, cavernous sinus involvement, hydrocephalus, dural involvement, ischemic lesions, perivascular involvement, orbit lesions, osseous involvement, nerve root involvement, and spinal cord intramedullary involvement. Differential diagnoses for each pattern of involvement of neurosarcoidosis are also provided.

Key words: Brain, MRI, neurosarcoidosis, orbit, skull, spine

INTRODUCTION

Neurosarcoidosis is apparent clinically in only about 5% of patients with sarcoidosis.^[1] However, less than 1% of patients have isolated central nervous system involvement.^[2] Cranial neuropathy, particularly facial nerve palsy, is the most common presentation. Other presentations of neurosarcoidosis include encephalopathy, peripheral neuropathy, meningitis, seizure, spinal cord dysfunction, and myopathy. Post treatment, up to 87% of neurosarcoidosis cases show resolution on imaging, which also parallels clinical improvement.^[3] The goal of this pictorial essay is to present the spectrum of MRI features in biopsy confirmed neurosarcoidosis patients in a pattern-based approach. The differential diagnosis for each pattern of involvement of neurosarcoidosis will also be reviewed.

Leptomeningeal involvement

Leptomeningeal involvement occurs in 40% of patients with neurosarcoidosis.^[2] The basilar meninges are most frequently involved. Gadolinium enhancement can be diffuse or nodular on post-contrast T1-weighted magnetic resonance imaging (MRI) [Figure 1].^[4] Perivascular spread can be encountered, producing enhancing foci that are remote from the brain surface [Figure 2]. The MRI differential diagnosis includes the conditions listed in Table 1.

Intraparenchymal mass lesions

Parenchymal mass lesions or granulomas are a fairly common manifestation of neurosarcoidosis, with 35% of cases presenting as multiple supratentorial and/or infratentorial masses and 15% as solitary masses.^[4] These lesions are often intimately associated with leptomeningeal involvement and may represent centripetal spread of

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the disease. Intraparenchymal masses typically show enhancement [Figure 3]. Initially, the lesions can be hypointense on T2,^[5] but are otherwise hyperintense. Central necrosis is rare.^[2] The MRI differential diagnosis includes the conditions listed in Table 2.

Pituitary and hypophyseal involvement

The pituitary gland, infundibulum, or hypothalamus are affected in 18% of patients with neurosarcoidosis.^[6] Cystic masses, enhancing masses, or thickening and enhancement of the infundibulum can be encountered on imaging [Figure 4]. These findings may occur in isolation or in combination with basilar leptomeningeal involvement. The MRI differential

Table 1: Leptomeningeal involvement - MRI differential diagnosis

Lymphomatous meningitis
 Carcinomatous meningitis (i.e., - breast carcinoma)
 Infectious meningitis (i.e., - tuberculosis)
 Meningoangiomas

Table 2: Intraparenchymal mass lesions - MRI differential diagnosis

Metastatic disease
 Gliomas
 Demyelinating disease
 Hemorrhage
 Infarct

Table 3: Pituitary and hypophyseal involvement - MRI differential diagnosis

Lymphoma
 Tuberculosis
 Langerhans cell histiocytosis
 Erdheim-Chester disease
 Metastases

Table 4: Cavernous sinus involvement - MRI differential diagnosis

Meningioma
 Tolosa-Hunt syndrome
 Infection
 Cavernous hemangioma
 Perineural tumor spread
 Thrombophlebitis

diagnosis includes the conditions listed in Table 3.

Cavernous sinus involvement

The cavernous sinus is rarely involved in neurosarcoidosis. These lesions can produce cavernous sinus syndrome, which include painful ophthalmoplegia.^[7] Lesions enhance and may have a dural tail [Figure 5]. The MRI differential diagnosis includes the conditions listed in Table 4.

Hydrocephalus

Hydrocephalus occurs in 5% to 12% of patients with neurosarcoidosis.^[2] The hydrocephalus is usually communicating secondary to leptomeningeal/dural involvement [Figure 6]. However, obstructive hydrocephalus can result secondary to ventricular system adhesions or loculations, which may cause trapped ventricles [Figure 7].^[8] There may be altered signal intensities of the cerebrospinal fluid in the isolated ventricle due to elevated protein concentrations.

Dural involvement

Dural involvement occurs in 34% of patients with

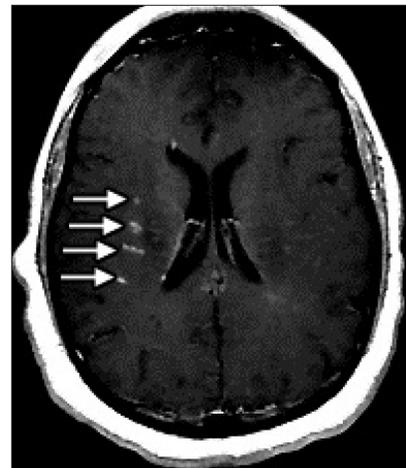


Figure 2: Perivascular involvement. There are several enhancing foci in the right hemisphere along a perivascular distribution (arrows).

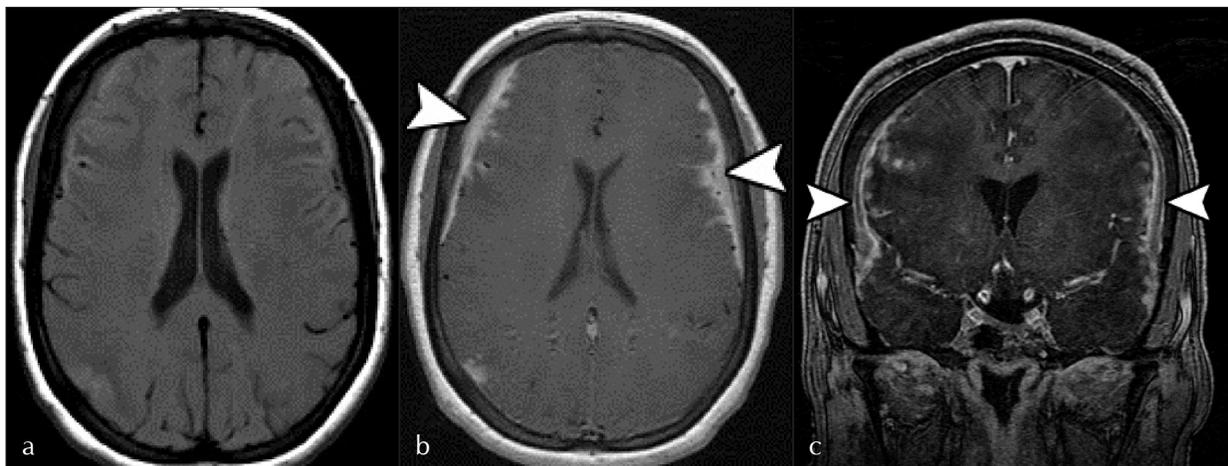


Figure 1: Leptomeningeal Involvement. (a) Pre-contrast T1, and (b) post-contrast axial, and (c) coronal sequences show widespread leptomeningeal thickening and enhancement along the convexities of the brain (arrowheads). Both diffuse and nodular patterns are evident.

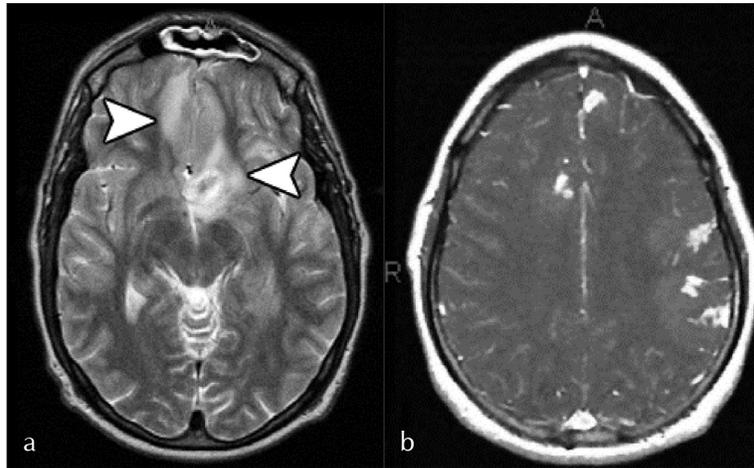


Figure 3: (a) Axial T2 and (b) post-contrast T1 sequences show numerous cortical and subcortical white matter lesions in the bilateral cerebral hemispheres, which are hyperintense on T2 (arrows) and demonstrate enhancement.



Figure 4: (a) Sagittal and (b) coronal images of pituitary and hypothalamus involvement. There is extensive enhancement of the pituitary gland (arrow) and stalk (arrowhead), which is markedly enlarged.

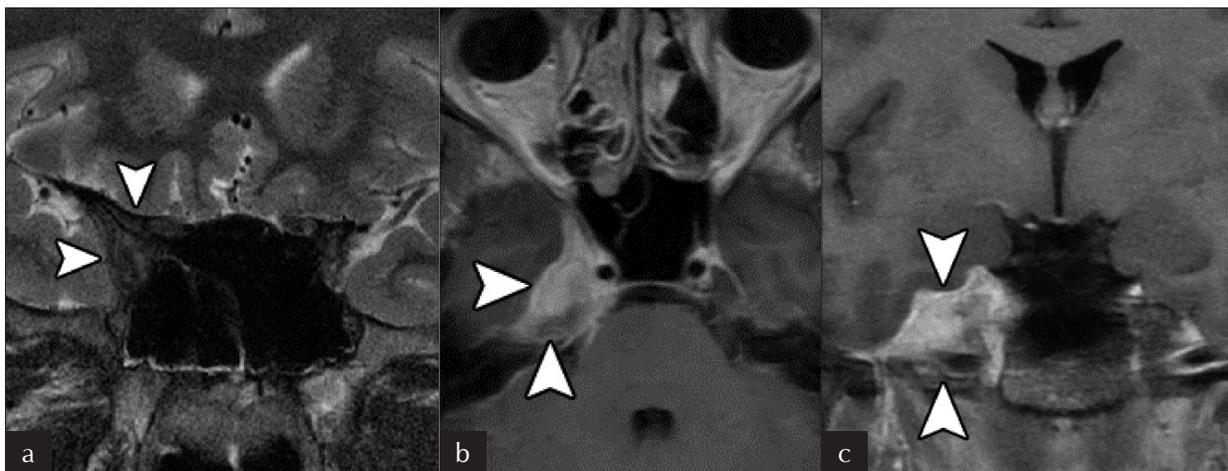


Figure 5: Leptomeningeal Involvement. (a) Pre-contrast T1, and (b) post-contrast axial, and (c) coronal sequences show widespread leptomeningeal thickening and enhancement along the convexities of the brain (arrowheads). Both diffuse and nodular patterns are evident.

neurosarcoidosis.^[6] The posterior fossa is most commonly involved. Lesions are usually hypointense or isointense

on T2 [Figure 8]. There can be strong enhancement of the thickened dura. The MRI differential diagnosis includes the

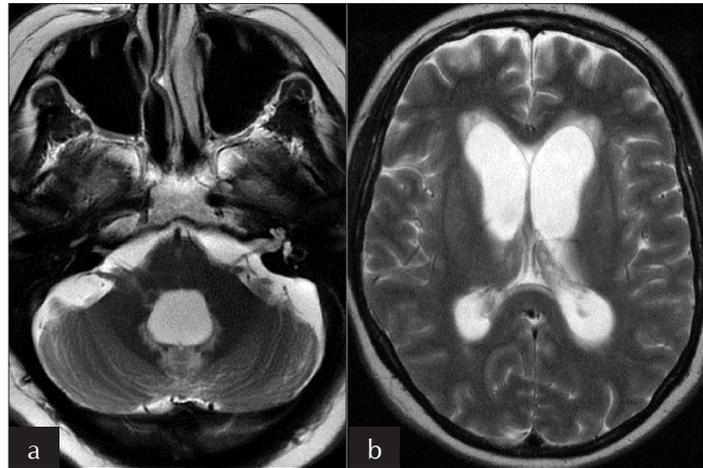


Figure 6: Hydrocephalus. Axial T2-weighted sequences at the level of the (a) fourth ventricle and (b) lateral ventricles show dilatation of these structures.

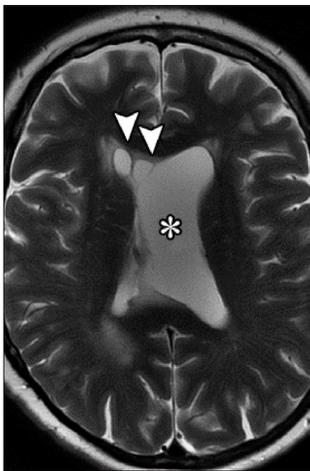


Figure 7: Perivascular involvement. There are several enhancing foci in the right hemisphere along a perivascular distribution (arrows).

conditions listed in Table 5.

Cranial nerve involvement

Cranial nerves are affected in up to 50% of patients with neurosarcoidosis.^[4] There is poor correlation between imaging findings and clinical symptoms. While facial nerve deficits are most commonly found clinically, the optic nerve is the most common cranial nerve to appear abnormal on MRI.^[9] Affected cranial nerves show enhancement and thickening with or without associated leptomenigeal involvement [Figure 9]. The MRI differential diagnosis includes the conditions listed in Table 6.

Lacrimal gland involvement

The lacrimal gland is rarely involved in sarcoidosis. Imaging features on computed tomography (CT) scan include bilateral, asymmetric enlargement with intense enhancement of the lacrimal gland [Figure 10].^[10] The gland maintains its anatomic configuration. A portion of the gland may extend medially along anterior border of the globe. MR

Table 5: Dural involvement - MRI differential diagnosis

Meningioma
Metastasis
Infectious meningitis
Intracranial hypotension
Subdural hemorrhage

Table 6: Cranial nerve involvement - MRI differential diagnosis

Schwannoma
Neuritis
Glioma
Perineural tumor spread

Table 7: Lacrimal gland involvement - MRI differential diagnosis

Inflammatory pseudotumor
Sjogren's syndrome
Wegener's granulomatosis
Lymphoma
Mikulicz syndrome
Adenoid cystic carcinoma

demonstrates hypointense T1 and T2 signal within enlarged glands that also show intense enhancement. The MRI differential diagnosis includes the conditions listed in Table 7.

Osseous involvement

Although osseous involvement occurs in up to 13% of patients, skull and vertebral involvement in neurosarcoidosis is very rare.^[2] The intervertebral body disc spaces can also be affected. Lesions are usually lytic with a punched-out appearance, but can also be sclerotic.^[11] The osseous lesions can also show increased activity on bone scans. On MRI, bone lesions are typically hyperintense on T2 and post-contrast T1 [Figure 11]. However, sclerotic lesions appear hypointense and may not enhance [Figure 12]. The MRI differential diagnosis includes the conditions listed in Table 8.

Spine intramedullary involvement

Intramedullary involvement occurs in up to 25% patients with of neurosarcoidosis.^[6] Lesions cause fusiform cord

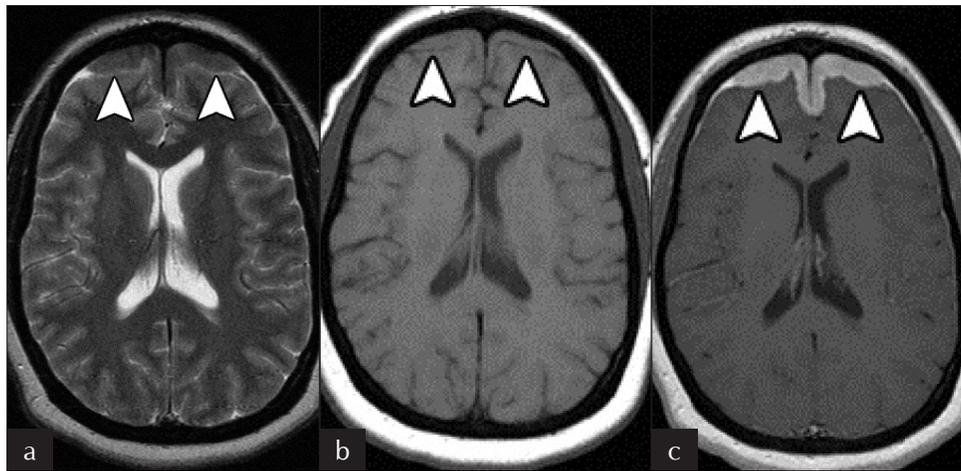


Figure 8: Dural Involvement. There is (a) hypointense T2 and (b) isointense T1 signal in the (c) symmetrically thickened frontal lobe dura, which avidly enhance on post-contrast T1 MRI (arrowheads).

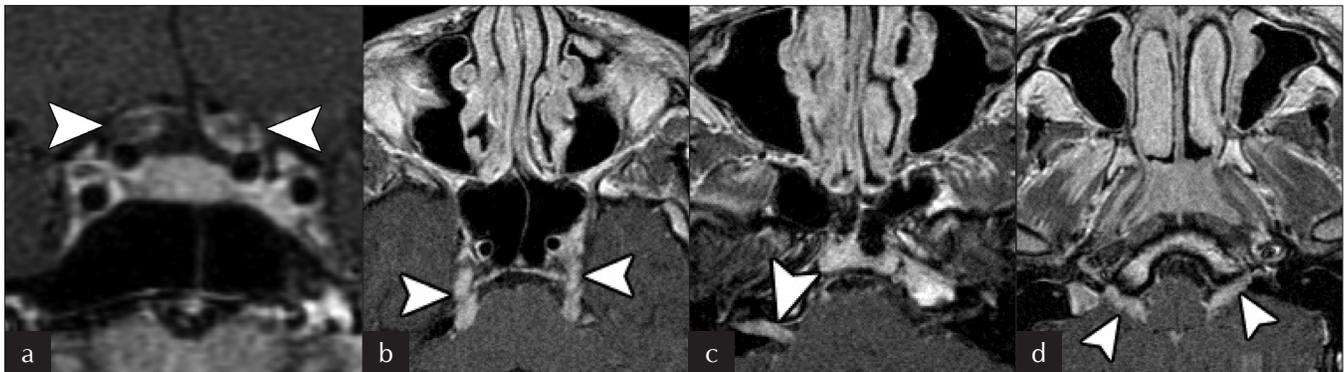


Figure 9: Cranial nerve involvement. (a) Coronal post-contrast T1-weighted MRI shows peripheral enhancement of the bilateral cisternal segments of cranial nerve II. (b) Axial post-contrast T1-weighted sequences at the level of cranial nerve V, (c) cranial nerves VII and VIII, and (d) cranial nerve IX show thickening and enhancement of multiple cranial nerves (arrowheads).

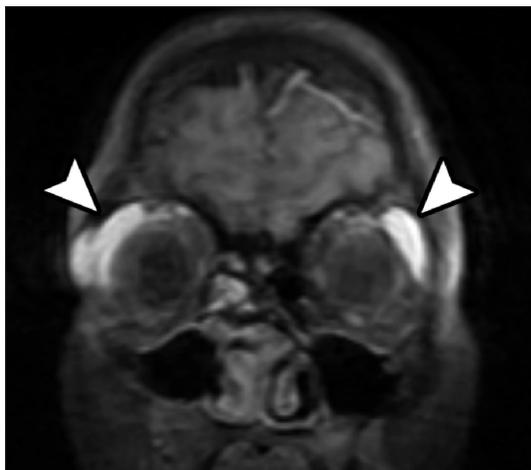


Figure 10: Lacrimal gland involvement. Coronal post-contrast T1-weighted MRI shows bilateral intensely enhancing enlarged lacrimal glands (arrowheads).

enlargement, mainly in the cervical and thoracic regions.^[6] Typically, there is low T1 signal, high T2 signal, and patchy enhancement on MRI [Figure 13]. The MRI differential diagnosis includes the conditions listed in Table 9.

Table 8: Osseous involvement - MRI differential diagnosis

Intraosseous meningioma
Metastases
Lymphoma
Multiple myeloma
Hemangioma
Langerhans cell histiocytosis
Epidermoid

Spine nerve root enhancement

Infiltration of spinal nerve roots is uncommon in neurosarcoidosis.^[9] These lesions can cause polyneuropathies. On MRI, nodularity or diffuse thickening of the affected nerve roots can be encountered [Figure 14]. Nerve root enhancement is also a common feature. The MRI differential diagnosis includes the conditions listed in Table 10.

Diagnostic considerations

Although the base of the brain is characteristically involved in neurosarcoidosis, this pictorial essay demonstrates that the MRI manifestations of neurosarcoidosis overlap with both benign and malignant entities. Thus, MRI

findings of neurosarcoidosis are not sufficiently specific to render a diagnosis, especially when neurological involvement is the first or only finding with sarcoidosis.^[12,13]

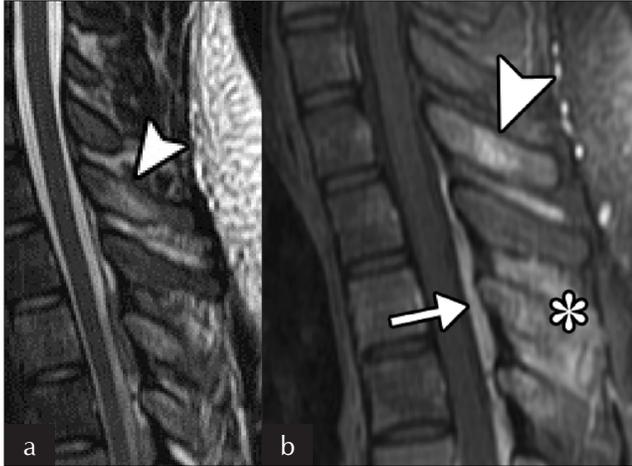


Figure 11: Vertebral involvement. (a) Sagittal T2 and (b) post-contrast T1 sequences show a hyperintense, enhancing focus on the posterior elements of the thoracic spine (arrowhead). There is also enhancement of the interpinous ligaments (*) and posterior extradural enhancement (arrow).

Rather, other parameters must be considered, including clinical presentation, other imaging studies, angiotensin-converting enzyme (ACE) assays, the Kveim test, and biopsy, if necessary. Since the majority of patients with neurosarcoidosis have preexisting lung involvement, the presence of hilar and mediastinal adenopathy

Table 9: Spine intramedullary involvement - MRI differential diagnosis

- Glioma
- Multiple sclerosis
- Acute disseminated encephalomyelitis (ADEM)
- Radiation necrosis
- Fungal infection

Table 10: Spine nerve root enhancement - MRI differential diagnosis

- Acute/chronic inflammatory demyelinating polyneuropathies
- Ependymoma
- Arachnoiditis
- Drop-metastases
- Lymphoma
- Tuberculosis
- Neurofibroma
- Meningioma

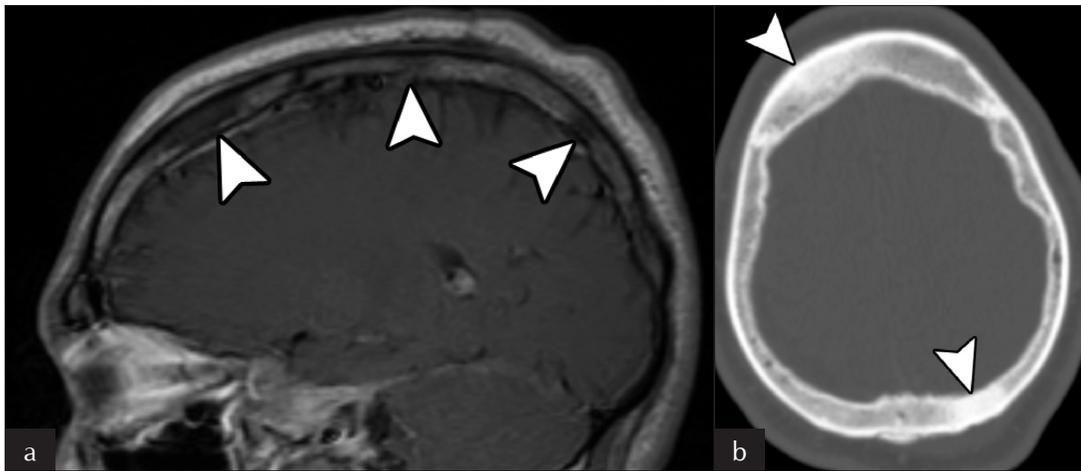


Figure 12: Skull Involvement. (a) Sagittal post-contrast T1-weighted MRI shows multiple non-enhancing hypointense intraosseous skull lesions (arrowheads). (b) The corresponding axial CT image shows that the lesions are sclerotic (arrowheads).



Figure 13: Intramedullary spinal cord involvement. (a) Sagittal T2, (b) sagittal T1 and (c) sagittal post-contrast T1 sequences is high T2 signal within the spinal cord (arrowheads). A portion of the lesion demonstrates intense enhancement (arrowhead). The cord is mildly expanded.



Figure 14: Spine nerve root involvement. (a) Sagittal T2 and (b) post-contrast T1 sequences demonstrate high T2 signal within the spinal cord (arrowheads). A portion of the lesion demonstrates intense enhancement (arrowhead). The cord is mildly expanded.

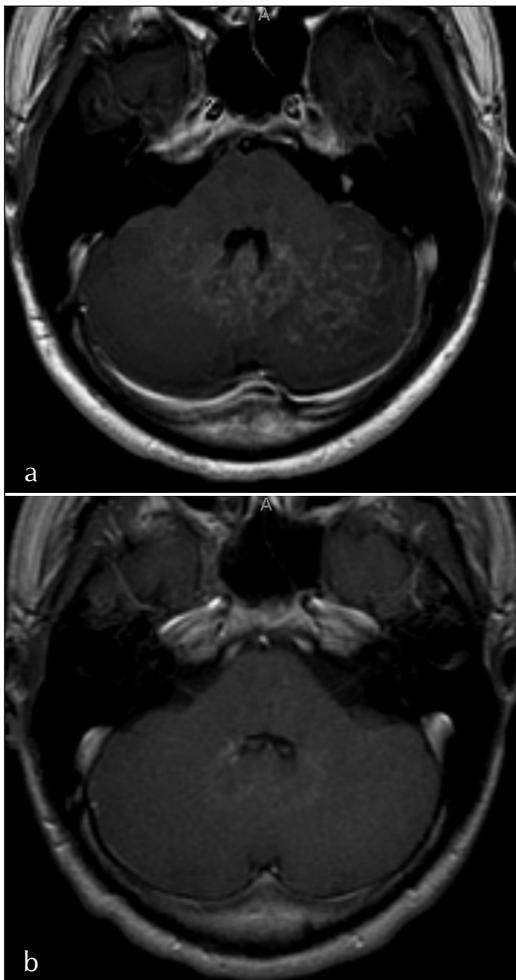


Figure 15: Treatment response. Axial post-contrast T1 sequences (a) before and (b) after initiation of steroids shows near resolution of the serpiginous cerebellar hemisphere lesions within eight months.

and/or parenchymal disease strongly supports the diagnosis. Serum ACE levels are elevated in up to 50% of neurosarcoidosis cases.^[7] Similarly, cerebrospinal fluid ACE

levels tend to be elevated, although this is not specific for neurosarcoidosis since increased ACE levels can also be encountered with meningitis.^[14] The Kveim test is a very sensitive and specific test for sarcoidosis, but is rarely used.^[15] It involves intradermal injection of spleen or liver extract from a patient with known sarcoidosis. The test is considered positive if sarcoid granulomas form several weeks later at the injection site. Histopathology of sarcoid lesions classically reveals non-caseating granulomas. Finally, patients with neurosarcoidosis demonstrate improvement in their clinical symptoms when treated with high-dose steroids. Response to steroid treatment can be monitored with MRI [Figure 15].

Conclusion

Neurosarcoidosis has a wide spectrum of imaging features that mimic both benign and malignant conditions. Virtually any portion of the central nervous system and associated structures can be affected. MRI is highly sensitive for detecting neurosarcoidosis, but is not specific. Therefore, in the differential diagnosis of this entity the imaging patterns included in this pictorial essay should be considered. Finally, the diagnosis is made by exclusion of other entities using a combination of imaging, diagnostic testing, clinical presentation, and sometimes tissue sampling.

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