Imaging of Neurosarcoidosis

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Introduction

Sarcoidosis is an idiopathic systemic disease characterized histologically by the formation of non-caseating granuloma. The disease affects all parts of the body, especially the lungs and lymph nodes. In the head and spine, the most typical imaging appearance is thickening and enhancement of the leptomeninges, especially around the base of the brain, but sarcoidosis may involve the bone, dura, nerve roots, leptomeninges, and parenchyma, individually or in combinations. In this article we will review the clinical and imaging findings of central nervous system involvement with sarcoidosis.

Epidemiology

Sarcoidosis can affect patients of all ages and races, but is most common in the third and fourth decade. Incidence is estimated to be around 20 per 100,000 among Caucasians. African-Americans and North European whites have the highest disease incidence, and women are more frequently affected than men. The exact cause of sarcoidosis is unknown. It is known that there are genetic factors that confer increased susceptibility to the disease. Also, the granuloma formation is initiated by T-lymphocytes responding to a specific, but unknown antigen.

Central nervous system involvement is quite common in autopsy series, with about one fourth of patients with systemic disease showing histologic evidence of central nervous system involvement. Symptomatic pre-mortem central nervous system involvement is less common, in only about 5% of cases. Imaging evidence of central nervous system disease, however, is seen in about 10% of patients with systemic disease. It is estimates that less than 1% of patients have isolated central nervous system involvement, without systemic evidence of disease. In cases with symptomatic central nervous system involvement, however, the central nervous system symptoms are frequently the presenting symptoms. For this reason, it is important for the radiologist to recognize the imaging manifestations of neurosarcoidosis.

Clinical Presentation

Clinical symptoms of neurosarcoidosis depend on the site of granuloma involvement and are nonspecific. Facial nerve paralysis (central or peripheral type) and vision loss are common symptoms, as are signs of meningeal irritation, headache, and
seizure. Less common are symptoms of diabetes insipidus such as intense thirst and polyuria, stemming from involvement of the hypothalamus or pituitary. Hydrocephalus is another uncommon clinical feature. Spinal cord involvement may present clinically with lower extremity weakness and other nonspecific signs of myelopathy.

**Diagnostic Tests**

The diagnosis of definite neurosarcoidosis is confirmed by biopsy showing non-caseating granuloma, with an absence of organisms or other etiologic agents. In many cases biopsy is not possible or not desirable, due to the site of involvement. In the absence of histologic proof of systemic disease, the diagnosis can be supported by two or more findings such as typical chest radiograph or Gallium scan findings or elevated serum angiotensin converting enzyme levels.

Patients with neurosarcoidosis have been reported to have elevated serum angiotensin converting enzyme in 5-50% of cases.

**Imaging Findings**

Sarcoidosis can involve any part of the nervous system and its coverings. This review will concentrate on the types of involvement that might be seen on imaging exams of the brain and spine. In both areas sarcoidosis may involve the parenchyma of the brain and spine, nerve roots, the leptomeninges, the dura, and the surrounding bony structures. In most cases, the appearance of lesions is nonspecific, so that sarcoidosis is included in a broad differential diagnosis.

**Brain, Intraparenchymal**

The most common parenchymal abnormality described in some series is multiple non-enhancing periventricular white matter lesions seen as high signal intensity on T2-weighted images. These lesions may be indistinguishable from those that may be seen with vascular disease or multiple sclerosis. Since this type of lesion is quite common in patients without sarcoidosis as well, it is not clear that they are always related to the sarcoidosis. Enhancing parenchymal mass lesions are also commonly reported. Enhancing mass lesions are frequently associated with nearby leptomeningeal involvement, and are thought to represent spread of leptomeningeal disease along the perivascular spaces in many cases. Mass lesions secondary to sarcoidosis may be dark on T2-weighted images, but very cellular metastasis and lymphoma may also have this appearance. Central necrosis is uncommon in sarcoidosis lesions.

**Brain, Leptomeningeal**

Leptomeningeal involvement is perhaps the most typical manifestation of central nervous system sarcoidosis, seen in about 40% of cases. This is usually seen as thickening and enhancement of the leptomeninges on contrast-enhanced T1-weighted images. The enhancement may be diffuse or nodular. There may be spread along the perivascular spaces causing the appearance of intraparenchymal involvement. There is a predilection for the basilar meninges. Leptomeningeal disease can be distinguished from dural disease by involvement of the cortical sulci and perivascular spaces, or the cisterns around the base of the brain. This pattern of involvement is generally indistinguishable from that seen with tuberculosis or lymphoma involving the leptomeninges.
Brain, Hypothalamus and pituitary
Leptomeningeal involvement around the hypothalamus and pituitary infundibulum may be seen with basilar leptomeningeal involvement or as an isolated finding. Again, this is seen as thickening and enhancement on contrast-enhanced T1-weighted images. This isolated involvement of the infundibulum mimics the appearance of histiocytosis.

Brain, Cranial Nerve Involvement
Cranial nerve involvement may occur along with leptomeningeal involvement, or as an isolated finding. There is poor correlation between the imaging evidence of cranial nerve involvement and clinical neuropathy. Clinically, any cranial nerve can be effected, but the most common cranial nerve deficit involves the facial nerve (VII), while radiographically the optic (II) nerves are most commonly abnormal. The optic nerve involvement may occur at the chiasm or intra-orbital portions of the optic nerves, and may be bilateral or unilateral. The differential diagnosis of isolated optic nerve involvement includes optic neuritis and optic nerve glioma. The dural sheath of the optic nerve can also be involved, mimicking an optic nerve meningioma. Sarcoidosis may involve the orbital fat, muscles, lacrimal glands or globe with a diffuse, infiltrative, mass radiographically indistinguishable from orbital pseudotumor.

Brain, Hydrocephalus
Hydrocephalus occurs in 5-12% of patients with central nervous system involvement of sarcoidosis. This may be a communicating type, presumably due to altered cerebrospinal fluid resorption secondary to dural or leptomeningeal involvement, or an obstructive type, due to adhesions or loculations of the ventricular system secondary to leptomeningeal or pial involvement.

Brain, Dural involvement
Dural involvement by sarcoidosis can present as focal dural masses or diffuse dural thickening. Lesions typically enhance homogenously on contrast-enhanced T1-weighted images. They are commonly very dark on T2-weighted images, which can serve as a clue to the diagnosis, but still may be indistinguishable from calcified meningiomas or very cellular dural metastases. Other differential considerations include lymphoma and idiopathic hypertrophic cranial pachymeningitis. The later can also be confused pathologically with sarcoidosis, since it is also a granulomatous process.

Dural and leptomeningeal involvement are rarely present together in the same region. This is thought to be because of the arachnoid barrier cells, a portion of the arachnoid mater that forms a barrier to the spread of disease through the arachnoid membrane.

Brain, Vasculitis
Histologically, a vasculitis-like pattern of involvement of the intracranial vasculature has been reported, with perivascular granulomatous infiltrate. This may be related to autoantibodies to vascular endothelial cells. Non-enhancing white matter lesions seen as areas of high T2 signal intensity on MRI have been attributed to possible
vascular involvement. Despite the clear reports of histologic evidence of vascular involvement in central nervous system sarcoidosis, it is quite rare that brain infarct is a presenting symptom of neurosarcoidosis.

**Skull**

Sarcoidosis lesions in the skull are uncommon. They may be seen in association with other bone disease, or as an isolated abnormality. The lesions show well-circumscribed, non-sclerotic margins (“punched out” appearance), and may show increased tracer uptake on nuclear medicine bone scan. MRI may reveal some enhancing soft tissue within the lesion.

**Spine, Intramedullary**

Spinal neurosarcoidosis can cause an array of imaging findings, which include intramedullary, intradural extramedullary, extradural, vertebral and disc-space lesions. Intramedullary sarcoidosis is an uncommon manifestation of sarcoidosis that often causes severe neurological sequelae. It occurs in less than 1% of sarcoidosis cases. Usually spinal cord involvement is not isolated or the first manifestation of the disease, helping to presume the diagnosis and avoid spinal cord biopsy. From the imaging point of view, intramedullary sarcoidosis is nonspecific with a broad differential diagnosis including neoplasm, multiple sclerosis, and fungal infections.

Sarcoidosis spinal lesions usually appear as fusiform enlargement of the spinal cord in the cervical or upper thoracic level. On MRI the spinal cord is enlarged with high signal intensity in T2-weighted images, low signal intensity in T1-weighted images, and patchy enhancement after contrast administration. Other findings, such as calcifications, cyst formation, and extradural involvement are rare findings also described. The correct diagnosis and early treatment with steroids can minimize neurological complications and decrease the disease morbidity, but the imaging improvement of intraspinal lesions does not correlate well with clinical improvement.

**Spine, leptomeningeal and dural**

Extradural intradural lesions are usually represented by leptomeningeal infiltration; present in up to 60% of spinal cord lesions. The leptomeningeal involvement may be visualized on contrast-enhanced T1-weighted MRI as thin linear leptomeningeal enhancement or small nodules. Clinical manifestations are not well correlated with MRI findings. Extradural sarcoid granulomatous masses are. The extradural mass-like lesions have a dural base and involve cervical, thoracic and lumbar spine without predilection. The characteristic low T2 signal found in dural intracranial sarcoidosis is not described in spinal lesions. The differential diagnosis for the imaging findings includes meningioma, nerve-sheath tumors, lymphoma, carcinomatous metastasis, chloroma, haemangiopericytoma and other granulomatous depositions.

**Spine, bone**

Osseous involvement in sarcoidosis is reported in 1% to 13% of patients. The actual frequency is probably higher because most of the osseous lesions are asymptomatic and patients are not screened routinely. Small tubular bones of the hands
and feet are most commonly involved. Less common skeletal involvement includes long tubular bones, skull, ribs, spine and pelvis.

Vertebral lesions are rare and usually occur in the lower thoracic and upper lumbar spine. Clinical manifestations include pain, tenderness and neuralgia. The imaging findings are usually multiple well-defined lytic lesions with sclerotic margins in the vertebral body. They may extend into the pedicles and paraspinal region. Sclerotic lesions, mimicking blastic metastasis, mixed lytic/sclerotic and disk involvement is rare. MRI shows multiple lesions with low T1 signal, high T2 signal and enhancement after contrast or low T1 and T2 signal in sclerotic lesions. The imaging findings are not specific enough to make the diagnoses of sarcoidosis. In the absence of confirmed disease elsewhere in the body, biopsy is usually necessary to rule out diseases causing similar appearing lesions such as metastasis, myeloma, lymphoma and tuberculosis.

Treatment

There is not consensus on the best treatment or efficacy of treatment of neurosarcoidosis. Treatment of symptomatic patients is usually begun with high dose corticosteroids. If there is clinical response to treatment, steroid dose may be lowered for a maintenance period or even discontinued. There is poor correlation between symptom resolution and resolution of imaging findings, especially with spinal cord lesions. There is a high rate of progression or recurrent symptoms, and recurrent imaging findings. Patients with enhancing brain lesions showed worsening, no change, or recurrence of symptoms on treatment in 75% of cases. Methotrexate has been used as a second-line treatment, although the effectiveness is not clearly established.

Conclusion

Central nervous system involvement occurs in a significant proportion (5-25%) of patients with systemic sarcoidosis. Patients with systemic disease may initially present with neurological symptoms, and rarely, disease may be isolated to the central nervous system. The typical imaging feature is thickening and enhancement of the leptomeninges, especially around the base of the brain. Other imaging findings, such as enhancing or non-enhancing parenchymal lesions, dural and bone lesions also occur in the head and spine. There is a high rate of progression and recurrence following treatment, so that imaging follow up is recommended.