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CT Demonstration of Sarcoidosis of the Optic Nerve, Frontal Lobes, and Falx Cerebri: Case Report and Literature Review

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Sarcoidosis of the optic nerve is reported in 1%–5% of sarcoid patients [1]. Even though it is the second most frequently affected cranial nerve in this disease [1, 2], its involvement has not been demonstrated previously by computed tomography (CT) [3–12]. In addition, despite pathologic descriptions of granulomatous infiltration of the falx [13, 14], transfalcine spread of sarcoidosis has not been described in the CT literature [3–12]. We report a patient with surgically and pathologically proven neurosarcoidosis whose CT scans showed involvement of the optic nerve, falx, and frontal lobes. We also review the CT literature of neurosarcoidosis.

Case Report

A 39-year-old black woman admitted for corrective knee surgery was found incidentally to have pulmonary nodules and right paratracheal adenopathy on an admission chest film. Sinus series because of complaints of frontal headaches and a history of sinusitis revealed diffuse paranasal sinus opacification and a demineralized dorsum. A 1005 EMI CT scan showed a homogeneously enhancing mass in the right frontal lobe with a smaller area of enhancement in the left frontal lobe associated with edema and thick, irregular enhancement of a shifted anterior falx (fig. 1). An angiogram demonstrated an avascular right frontal lobe mass and no arteritis. Laboratory investigation revealed sputum and bronchial washings negative for acid-fast bacilli, yeast, and fungi; negative cytology; a nondiagnostic bronchial biopsy; and normal serum calcium. A right frontal craniotomy was planned but the patient refused surgery.

When the patient was admitted 6 months later with focal seizures, severe right frontal headaches, left-sided weakness, left hemianesthesia, and anosmia, CT showed that the solidly enhancing right frontal lobe mass had increased in size and the falx now demonstrated nodular and irregular enhancement. A right frontal craniotomy uncovered a well encapsulated right frontal lobe mass. The mass was completely removed and permanent microscopic sections showed findings compatible with sarcoidosis (fig. 2). The sections revealed extensive noncaseating granulomatous inflammation involving the leptomeninges, cerebral cortex, and subcortical white matter. The granulomas were comprised of central plump epithelioid cells with eosinophilic cytoplasm and multinucleated giant cells of both Langhans and foreign body types with rare cytoplasmic formation suggestive of asteroid body. There was no evidence of casseous necrosis. Stains for bacteria, mycobacteria, and fungi were negative.

Over the next 22 months, the patient was admitted to the hospital three times for evaluation of recurrent generalized seizures, headaches, blurred vision, nausea, vomiting, and a painless loss of vision in the right eye. Ophthalmologic examination revealed right optic nerve atrophy. The nerve was pale and was associated with a marked color perception defect. Visual acuity was 20/200 right eye and 20/20 + 2 left eye. On each of these three admissions, CT showed more edema, more mass effect, and more enhancement of the left frontal lobe hyperdense nodules and falx (fig. 3). However, these 1005 EMI and 8800 GE CT scans of 10-mm-thick sections of the brain did not reveal the etiology of the patient's visual loss. Nevertheless, on her most recent admission, a GE 8800 CT scan of the sella and orbits of 5 mm sections demonstrated a mildly hyperdense lesion of the intracranial portion of the right optic nerve and chiasm that enhanced with administration of contrast material (fig. 4).

Other pertinent hospital workup included the following: elevated prolactin (64 ng/ml); a nonspecific increase in beta and gamma globulins; positive antinuclear antibodies; normal angiotensin-converting enzyme (17 U/ml); positive gallium scan showing increased activity in the mediastinum posteriorly; and positive skin biopsy of a plaque and nodule on the left cheek and left chin showing granulomatous inflammation of the skin consistent with sarcoidosis. Steroid therapy was begun, which resulted in resolution of the patient's weakness. There was no improvement, however, in the patient's visual acuity.

Discussion

Sarcoidosis is a multisystem disease of unknown etiology that frequently affects the lymph nodes, lungs, liver, spleen, skin, salivery glands, and phalanges of the hands and feet [2, 13]. This granulomatous process also involves the eye and its adnexa, including the conjunctiva, lacrimal gland, uvea, cornea, sclera, retina, lens, and optic nerve [1, 15]. In

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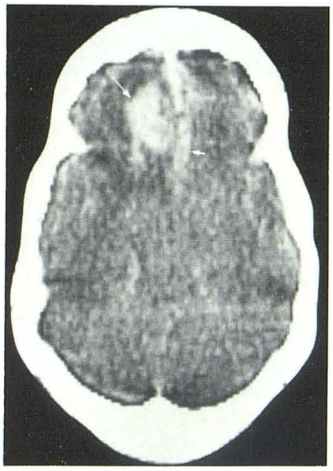


Fig. 1.—Densely enhancing mass (*long arrow*) in right frontal lobe with edema, involvement of falx (*short arrow*), and subtle involvement of left frontal lobe.

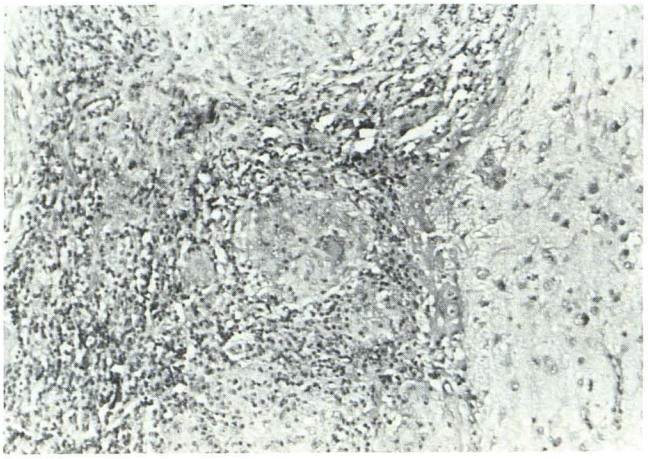
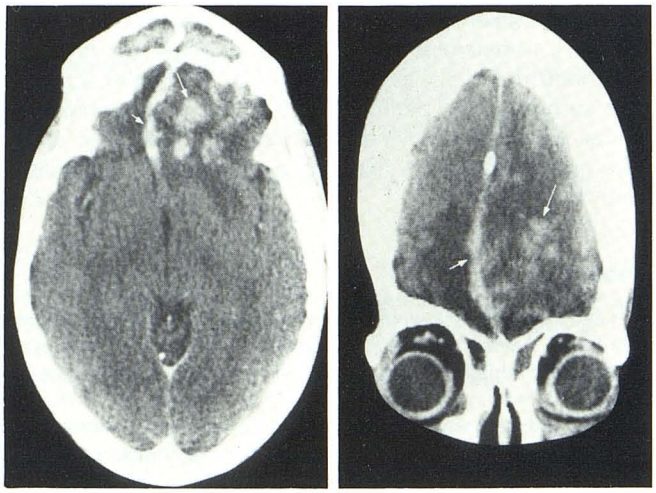


Fig. 2.—Noncaseating sarcoid granuloma with Langhans giant cell on right. Normal cerebral cortex on left.

fact, ophthalmic changes are among the most frequent extrathoracic manifestations of sarcoidosis, occurring in about 21%–28% of cases [1]. Involvement of the nervous system, however, is less common, averaging 4%–8% of sarcoid cases [2, 3]. Neurologic symptoms are usually noted only after other organs have been affected [14]. However, they can be the first or only manifestation of this disease (the latter occurring in about 1.5% of cases) [2, 3].

The CT findings in neurosarcoidosis reflect the pathologic changes in this disease. Intracranial sarcoidosis most often affects the leptomeninges at the base of the skull [2, 10, 14, 16]. Granulomatous infiltration of the basal meninges leads to compression and invasion of the cranial nerves with resultant cranial nerve palsies [4]. The facial nerve is most often affected, followed by the optic nerve. This process causes diffuse enhancement of the basal cisterns on CT scans [4]. However, discrete, solidly enhancing extraaxial nodules can also be seen [6, 8, 12]. Extension of this chronic meningitis to the optic chiasm, hypothalamus, floor of the third ventricle, and pituitary gland accounts for the abnormal contrast uptake that is seen in the suprasellar, parasellar, sellar, and subfrontal regions [2, 3, 10, 12, 13]. It also accounts for the patient's visual difficulties, diabetes insipidus, insomnia, obesity, amenorrhea, and impotence [2, 3, 13]. When the leptomeningitic process spreads over the convexities, enhancement of the sylvian fissures and cortical sulci is evident [6]. Seizures may occur at this stage [3]. Lethargy, headache, nausea, and vomiting may develop when communicating or obstructive hydrocephalus is detected on CT [3, 6]. Ventricular enlargement is a common complication of neurosarcoidosis, caused either by active arachnoiditis or by fibrotic adhesions.

It is not uncommon for tumorlike masses to develop in the dura [13]. This explains why enhancement of the tentorium and the subfrontal space is frequently seen on CT [6, 12]. It also explains why the falx can be invaded [13, 14] and can appear dense, irregular, thick, and nodular on contrast CT, as our case illustrates, and why the frontal lobes can be at risk.



A B

Fig. 3.—Several homogeneously enhancing sarcoid nodules (*long arrows*) on axial (**A**) and coronal (**B**) views in left frontal lobe associated with peripheral edema and infiltration of shifted falx (*short arrows*). Frontal sinus opacification possibly related to sarcoid and postoperative changes in right frontal lobe.

Although less common, invasion of the brain parenchyma does take place in sarcoidosis. The granulomatous process spreads from the leptomeninges into the brain via the perivascular spaces of Virchow-Robin [3, 14, 16]. A granulomatous angiitis results from invasion of the vessel walls by sarcoid tubercles with disruption of the media and internal elastica [16]. The small perforating arteries and veins of the brain are affected most often. Stenosis, thrombosis, infarctions, and parenchymal involvement occur secondarily [3, 16]. Any part of the brain can be affected [2, 13, 14, 16]. Therefore, the clinical manifestations of this disease can be quite variable.

When intraparenchymal extension occurs, slightly hyperdense or isodense nodules of variable size and number that homogeneously enhance with contrast administration are visualized on CT [3, 4, 6, 8, 12]. They frequently are small

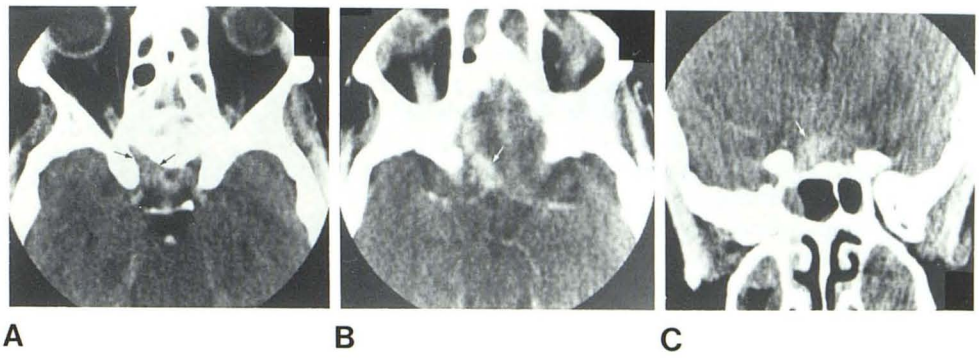


Fig. 4.—Axial (**A** and **B**) and coronal (**C**) sections. Enhancement and thickening of intracranial optic nerve and chiasm (*arrows*) due to sarcoidosis.

and single, such as those reported in the hypothalamus and pituitary gland [10, 11] and often are peripheral in location [4]. However, they can be multiple and can be scattered diffusely throughout the cerebral hemispheres, cerebellum, and/or brain stem [6, 16]. Occasionally, they coalesce and form a large single space-occupying lesion that simulates a neoplasm [3, 8, 14]. They are smoothly marginated and often lack peripheral edema [3, 8, 12]. Mass effects secondary to edema and sizable granulomas, however, have been described [6, 8]. When widespread perivascular invasion of the brain occurs, diffuse contrast enhancement can be seen [9]. This abnormal contrast uptake is probably related to a breakdown in the blood-brain barrier from small vessel arteritis [7, 9]. Other CT abnormalities include low densities in the perivascular white matter and obstructive hydrocephalus [9]. The latter can be secondary to granulomatous ependymitis or to compression of the aqueduct by adjacent nodules [5, 9]. At appropriate bone window settings, lucent defects in the bony calvarium from osseous sarcoidosis can also be seen, but are rare [17]. Rarely the CT scan is normal despite documented central nervous system involvement [8].

CT is the radiographic study of choice in the investigation and follow-up of central nervous system sarcoidosis [4]. In contrast to conventional radiographic studies, CT directly demonstrates the sarcoid granulomas. Skull films reveal only indirect evidence of intracranial disease, such as a demineralized dorsum from raised intracranial pressure, lytic defects in the bony calvarium, and, rarely, calcifications [3, 4]. Angiograms show nonspecific abnormalities, such as avascular masses or, rarely, vascular blushes or arteritis [3, 4, 11]. While these studies along with chest films and myelograms may provide complementary information, CT remains the mainstay in the diagnosis of neurosarcoidosis [4].

Another advantage to CT is that it allows for the precise localization of sarcoid tubercles and for the direct assessment of ventricular size. This information is invaluable to the ophthalmologist trying to sort out the various etiologies of visual disturbances in this disease. For example, papilledema, optic atrophy, and/or visual field defects can result not only from sarcoid invasion of the meningeal coverings or parenchyma of the optic nerve but also from diffuse granulomatous infiltration of the leptomeninges or from secondary communicating or obstructive hydrocephalus [1, 2]. A determination of which of these mechanisms is responsible for the patient's visual symptoms and signs is often impossible by clinical means alone. CT, however, can make this determination. It can demonstrate abnormal enhancement of the optic nerve and chiasm and can differentiate it from diffuse contrast uptake in the basal cisterns and from hydrocephalus.

CT is also important in clinical management. By localizing sarcoid nodules and by demonstrating ventricular enlargement, CT aids the neurosurgeon planning operative intervention in those few select cases that require excision or in those cases that need shunting [5, 10]. CT also makes it possible to monitor the effectiveness of steroid therapy. In many cases, follow-up CT scans have shown regression or resolution of lesions with steroid administration [6, 7, 9, 18]. In some cases, however, CT has shown persistence of sarcoid granulomas despite steroid therapy. When CT documents resistance to medical therapy, some authors have suggested surgical removal of accessible lesions, such as those in the suprasellar cisterns [10].

The CT findings in neurosarcoidosis are not pathognomonic, however. Diffuse contrast uptake in the basal cisterns can be seen in carcinomatous meningitis as well as in other inflammatory conditions, such as fungal disease, tuberculosis, and bacterial meningitis [4]. Multiple enhancing nodules can be a sign not only of sarcoidosis but also of fungal and mycobacterial infections. Nevertheless, differentiation is still possible. In sarcoidosis, these nodules are solid and do not have a ring configuration, such as may be the case in tuberculosis [18]. Furthermore, sarcoidosis has a peculiar affinity for the visual pathways, which can be documented on high resolution CT if the cuts are 5 mm or less in axial and coronal views. In our patient, 1-cm-thick scans of the brain obtained over a 1½ year interval failed to reveal abnormal enhancement of the optic nerve and chiasm even though the patient had visual loss. Yet another aid to diagnosis is the demonstration on CT of a densely enhancing, irregular, and thickened falx. This finding indicates infiltration of the falx by sarcoid granulomas and also prompts close scrutiny of the frontal lobes for possible extension of disease. The CT diagnosis of neurosarcoidosis, however, should be confirmed by the demonstration of noncaseating tubercles in biopsy specimens, as well as by an appropriate clinical presentation, positive laboratory studies, and abnormalities on complementary radiographic

examinations [2, 3, 15, 19].

In summary, we have reported a 39-year-old woman who developed headaches, recurrent seizures, hemiparesis, hemianesthesia, anosmia, and visual loss over a 2½ year period. Diagnosis of sarcoidosis was established by histologic confirmation of a right frontal lobe granuloma and of two skin lesions. Multisystem disease was documented by abnormal chest films, gallium scan, and elevated serum immunoglobulins and prolactin. Serial CT scans over a 27 month period allowed us to see the evolution of neurosarcoidosis and to discover two new CT features of this disease. To the CT findings already described in the literature as being highly suggestive of sarcoidosis, we would add the following: abnormal contrast uptake in an enlarged optic nerve and/or chiasm and dense nodular enhancement of a thickened, irregular falx. These additional abnormalities, as illustrated by our case, can be of considerable diagnostic aid since the presence of multiple abnormalities on CT adds specificity to the diagnosis of neurosarcoidosis.

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