

Case Reports

Sarcoidosis Presenting With Stroke

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A 25-year-old black man with sarcoidosis presented with transient ischemic attacks followed by sudden, persistent right hemiparesis. He gave a history of recent, recurrent lower motor neuron facial palsy. Computed tomography demonstrated an infarct in the left internal capsule. Chest x-ray film showed bilateral hilar and mediastinal lymphadenopathy and multiple opacities in the lung fields. Serum angiotensin converting enzyme concentration was raised, and a Kveim test was positive for sarcoidosis. Despite clear pathologic reports of cerebral vasculitis in neurosarcoidosis, the occurrence of stroke is extremely rare. (*Stroke* 1989;20:400–405)

Sarcoidosis involves the nervous system in approximately 5% of cases.^{1–3} The most common presentation of neurosarcoidosis is a cranial neuropathy, usually facial, followed in frequency by meningoencephalitis and, less often, intracranial mass lesions. Despite clear evidence of granulomatous involvement of cerebral vessels in sarcoidosis from pathologic studies,⁴ stroke-like events in sarcoidosis are extremely rare. We therefore describe a case of sarcoidosis in a young man who presented with transient ischemic attacks (TIAs) followed by completed stroke resulting from a capsular infarct.

Case Report

A 25-year-old black man was admitted to the hospital for investigation of five episodes of sudden weakness and numbness of his right arm and leg, which had occurred without higher function deficit during the previous 24 hours. The patient recovered from his first four attacks completely within 10 minutes; the symptoms of the fifth attack persisted. Direct questioning was otherwise negative.

At the age of 6 years, the patient had developed right-sided lower motor neuron facial weakness, diagnosed as Bell's palsy, from which he recovered within 4 weeks. At the age of 16 years, the right-sided lower motor neuron facial palsy recurred; again the patient recovered within 4 weeks. Four months before his current admission, the patient developed a third recurrence of right lower motor neuron facial weakness and recovered completely within 2 weeks. Neither he nor his family had other

significant medical history. Both of his parents were born in the West Indies, but the patient was born in the United Kingdom and had never been abroad. He worked as a heavy-goods vehicle driver. He smoked 20 cigarettes a day and drank 2 pints of beer per week. He was not taking any medication or drugs.

General examination was normal. His speech was slurred but not dysphasic. He could not support his own weight because of right-sided weakness. There was upper motor neuron right-sided facial weakness and a severe flaccid right hemiparesis affecting the arm more than the leg, with ipsilateral hyperreflexia and extensor plantar response. Although he complained of right-sided numbness, sensory examination was normal. There were no other abnormalities.

Cranial computed tomography (CT) performed 24 hours after the onset of hemiparesis showed an area of nonenhancing low attenuation in the left internal capsule extending into the corona radiata, consistent with infarction (Figure 1). These CT appearances were unchanged 4 weeks later. Chest x-ray film and thoracic CT scan showed bilateral hilar and mediastinal lymphadenopathy and multiple rounded opacities in both lung fields (Figure 2). The erythrocyte sedimentation rate was 1 mm/hr, and complete blood count was normal. The corrected serum calcium concentration was 2.69 (laboratory normal range 2.10–2.60) mmol/l. Serum IgG concentration was elevated at 1710 (normal range 660–1320) mg/dl. Serum immunoelectrophoresis showed a mild polyclonal increase in γ -globulin. Serum angiotensin converting enzyme concentration was elevated to 100 (normal range 16–53) units/ml. Pulmonary function tests showed a restrictive defect with a vital capacity of 66% of predicted values and a reduced transfer factor (diffusion capacity) of 61% of predicted values. Flexible bronchoscopy revealed erythematous areas in the main bronchi of both lungs, but bronchial and transbronchial biopsies

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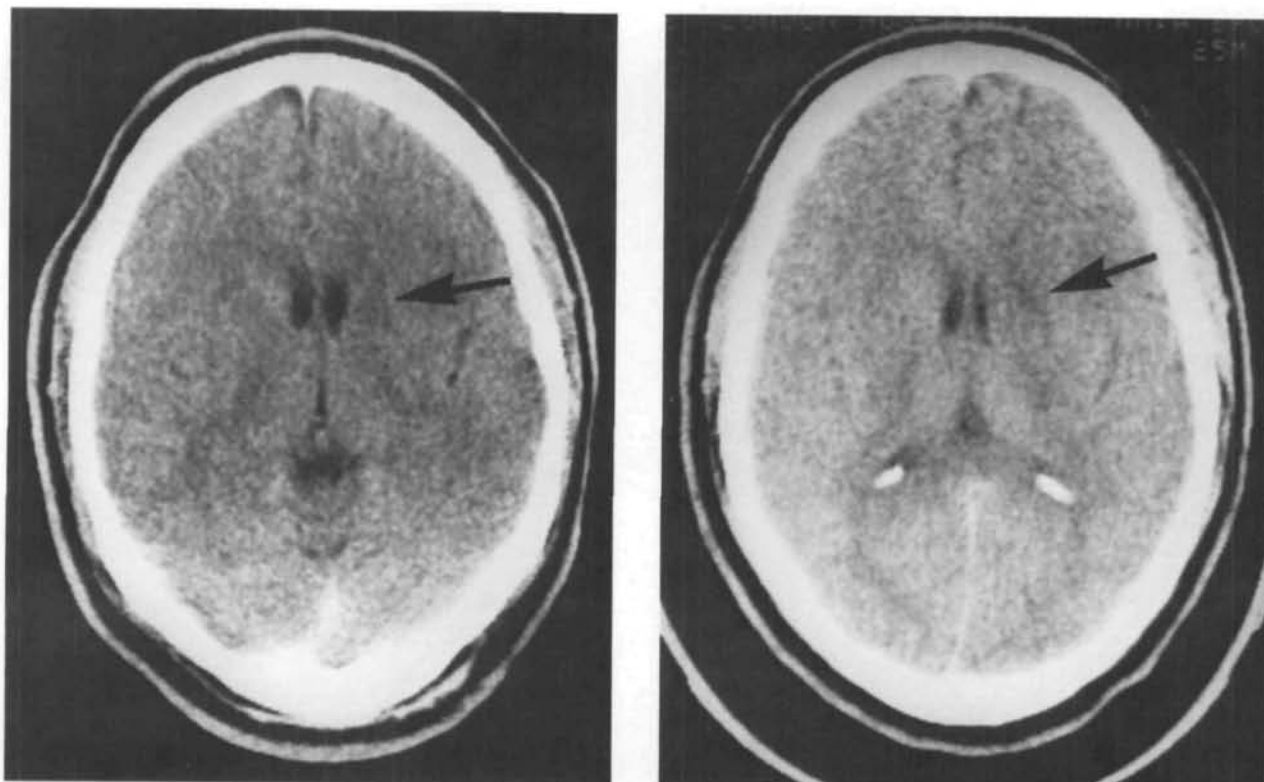


FIGURE 1. Contrast-enhanced cranial computed tomograms showing area of low attenuation in left internal capsule (left) extending into corona radiata (right) consistent with cerebral infarction.

and attempted percutaneous lung biopsy of a peripheral opacity obtained normal lung. A Mantoux test at 1:1000 was negative. A forearm Kveim test biopsied at 6 weeks was positive for sarcoidosis. Findings from the following investigations were normal or negative: autoantibody screen, clotting screen, infectious diseases screen including VDRL, thyroid function, vitamin B₁₂, serum folate, ophthalmologic examination, electrocardiogram, echocardiogram, left carotid angiogram, and cerebrospinal fluid (CSF) examination. The patient was unable to tolerate magnetic resonance imaging (MRI).

His right hemiparesis slowly resolved spontaneously, and 1 month after its onset the patient had fully recovered. He remained well without medication 12 months after the onset of hemiparesis. Follow-up investigations showed spontaneous improvement of the peripheral pulmonary opacities and lung function.

Discussion

This young man presented with a history of recent lower motor neuron facial palsy followed by TIAs, culminating in a completed stroke due to cerebral infarction. He was found to have mediastinal lymphadenopathy with rounded pulmonary opacities, and erythematous nodules were found on bronchoscopy. The association of these features with increased serum IgG, mildly raised serum calcium, and markedly raised angiotensin converting enzyme concentrations and a positive Kveim test is diagnostic of sarcoidosis.⁵ Facial palsy is one of the most common

manifestations of neurosarcoidosis. The close temporal relation of the patient's stroke and his most recent facial palsy and the maximum extent of pulmonary shadowing suggested that the TIAs and cerebral infarct were also caused by sarcoidosis involving the central nervous system.

Stroke is an extremely rare complication of sarcoidosis, and no cases were encountered in two recent large series.^{1,2} In contrast, neuropathologic studies of sarcoidosis have consistently shown evidence of vascular involvement.^{4,6-12} These studies characteristically show granulomatous meningitis involving predominantly the basal meninges, with frequent parenchymal and occasional ependymal involvement.⁴ The parenchymal granulomas tend to invade the cerebral substrate along the Virchow-Robin spaces and are distributed perivascularly.⁶ In addition, granulomatous invasion of the blood vessel walls is frequent, with vasculitic disruption of the media and internal elastic lamina. Several cases have shown granulomatous vessel stenosis or occlusion sometimes clearly associated with small cerebral infarcts.^{4,6-9,12} Microscopic and lacunar infarction is a common finding.^{4,6,10-12} In a few cases the granulomatous angiitis has been accompanied by acute necrotizing arteritis, resulting in fibrinoid necrosis, obliteration of the arterial lumen, and intense leukocyte infiltration similar to that of polyarteritis nodosa.^{4,6,9} Granulomatous vasculitis preferentially involves vessels the caliber of the perforating arteries,⁴ although in one report larger arteries

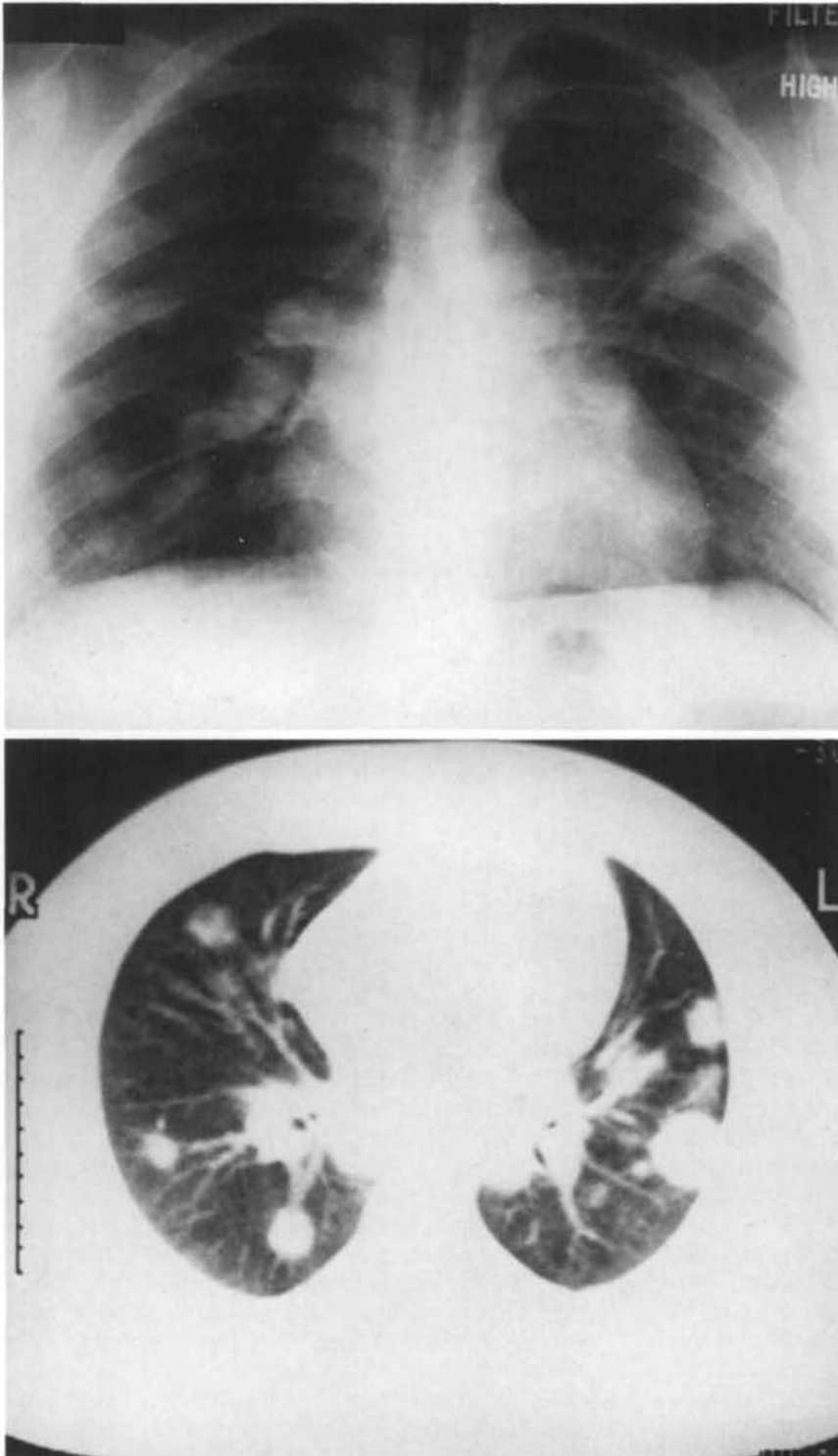


FIGURE 2. *Chest x-ray (top) and thoracic computed tomogram (bottom) showing bilateral hilar and mediastinal lymphadenopathy and multiple rounded opacities in both lung fields.*

(including the middle cerebral artery) were affected.⁸ Veins may be involved, particularly in the periventricular regions.⁹

Table 1 summarizes the published pathology reports of neurosarcoidosis in which information is adequate for comparing the clinical features with the neuropathology. Despite the consistent finding of vasculitis in the brain, most patients with vasculitis at autopsy did not have a history of stroke; instead, they pre-

sented with a slowly progressive encephalopathy characterized by headache, seizures, confusion, dementia, or coma, associated with multifocal neurologic signs. Nevertheless, a few case reports confirm occasional stroke-like events in neurosarcoidosis. Herring and Urich⁴ described the sudden onset of a brainstem stroke in a 29-year-old black man (Case 6, Table 1) with sarcoidosis subsequently found to have a pontine infarct associated with

TABLE 1. Associated Clinical and Pathologic Features in Case Reports of Neurosarcoidosis

Author	Case no.	Clinical features				Neuropathologic features												
		Stroke	Encephalopathy	Seizures	Cranial neuropathy	Mass lesion	Granulomatous meningitis	Parenchymal granulomas	Perivascular round-cell infiltration	Perivascular granulomas	Granulomatous vasculitis	PAN-like vasculitis	Arteries involved	Veins involved	Small-vessel stenosis or occlusion	Microscopic infarction	Hemorrhage	
Meyer et al ⁶	1		+				+											
Camp and Frierson ⁷	1		+	+			+	+										
Reske-Nielsen and Harmsens ⁸	1	+		+	+		+	+										
Robert ⁹	1		+			+	+											
Schonell et al ¹⁰	1		+	+			+	+										
Herring and Urich ⁴	1	+					+	+										
	2		+	+			+	+										
	3		+	+	+		+	+										
	4		+	+	+	+	+	+										
	5		+	+	+		+	+										
	6	+					+	+										
	7			+			+	+										
Caplan et al ¹¹	1					+	+	+										
	2	+					+	+										
Manz ¹²	1		+				+	+										
	2		+				+	+										
	3			+		+	+	+										
	4			+		+	+	+										
	5		+			+	+	+										

TIA, transient ischemic attack; PAN, polyarteritis nodosa.

granulomatous vasculitis. The patient of Reske-Nielsen and Harmsen⁸ presented with the sudden onset of aphasia and right-sided sensory and motor symptoms, followed some months later by progressive encephalopathy. In his recent series of 50 cases of neurosarcoidosis, Oksanen³ mentions hemiparesis as developing acutely in three patients without giving further details.

TIAs have also been occasionally reported in sarcoidosis. Case 1 of Herring and Urich⁴ developed attacks of "giddiness" associated with numbness of the face and right limbs; these attacks were probably TIAs, but migraine is another possibility as the attacks were followed by headache and vomiting. In their early postwar series of 300 cases of sarcoidosis, Ricker and Clark¹³ described one patient who suffered multiple attacks lasting 30–60 minutes and characterized by "loss of comprehension of events"; these attacks may have been aphasic TIAs. Case 2 of Caplan et al¹¹ (Table 1) suffered recurrent spells lasting up to 20 minutes of right arm and facial numbness, slurred speech, and difficulty in controlling the right arm. Wells¹⁴ mentioned two additional cases of TIA. Recurrent TIAs have also been reported as the presenting manifestation of an ipsilateral subdural sarcoid mass lesion.¹⁵

Stroke may also occasionally occur in sarcoidosis as a result of vasculitic intracranial hemorrhage. Case 1 of Caplan et al¹¹ died of a cerebellar hemorrhage with extensive granulomatous vasculitis involving mainly the veins. In his series of 50 patients, Oksanen³ also reported two intracerebral hematomas. In a few other cases, autopsy has revealed hemorrhages not clearly associated with stroke-like events. In one other reported case, recurrent cerebral infarction resulted from cardiac thromboembolism secondary to sarcoid cardiomyopathy.¹⁶ Thus, several different mechanisms may be responsible for stroke in sarcoidosis. In our patient, the TIAs, stroke, and CT findings are consistent with lacunar ischemia and then infarction secondary to granulomatous vasculitis involving the perforating arteries as described in the pathology reports discussed above. The discrepancy between the frequent neuropathologic finding of vasculopathy and the rarity of clinical stroke in sarcoidosis is surprising but may reflect the chronic nature of the inflammation, the diffuse pathology, or the common feature of involvement of only the very smallest arteries.

Our patient illustrates the difficulty of substantiating the diagnosis of neurosarcoidosis without cerebral or meningeal biopsy. In many cases (including our own), the diagnosis must rest on the association of appropriate neurology with other features diagnostic of sarcoidosis. CSF examination may be helpful but not diagnostic, revealing pleocytosis, low glucose or raised protein concentrations, or evidence of intrathecal synthesis of IgG in some patients; however, the CSF is completely normal in 30% of confirmed cases.^{1,3} Ophthalmologic examination may demonstrate suggestive abnormalities

including vitreous lesions, uveitis, periphlebitis, or conjunctival nodules, but it is normal in a third or more patients.¹¹ Cerebral angiography may occasionally show evidence of vasculitis,^{3,17} but it is usually normal, even in the presence of proven vessel involvement, probably because of the small caliber of the affected vessels.^{1,8,11} CT scan may show basal enhancement, mass lesions, or hydrocephalus, but the appearances are nonspecific and rarely diagnostic.¹⁸ In addition, CT and MRI appearances of diffuse white-matter lesions, small cerebral infarcts, and lacunar infarction similar to the findings in our patient have been clearly demonstrated, supporting the occurrence in neurosarcoidosis of small-vessel disease.^{19,20}

The role of steroids in the treatment of neurosarcoidosis has not been clearly established. Because he had recovered substantially by the time the diagnosis was established, our patient was not treated. He has remained well for 12 months after presentation, demonstrating spontaneous remission of neurologic involvement paralleling the course of the systemic disease. Such spontaneous remission is well described.^{1,3} Benefit of steroid treatment has not been proven. In one recent series the course of the disease in steroid-treated patients did not differ significantly from that in untreated patients.³ Nevertheless, some patients appear to respond dramatically to steroids and, although not supported by control studies, an empirical trial of steroid therapy may be justified in patients with severe or progressive neurologic disease.

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