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Cerebrovascular symptomatic involvement in sarcoidosis

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Abstract

Clinical reports of cerebrovascular system involvement in sarcoidosis are extremely rare though pathological studies frequently describe granulomatous cerebral arterial and venous lesions. We report the case of a 47-year-old man with a history of pulmonary sarcoidosis at age 32 and abducens palsy at age 40, who presented cerebral pseudotumoral histologically proven sarcoidosis. He was admitted for acute left hemiplegia. Brain CT scan and MRI demonstrated a right posterior parietal haematoma associated with a superior sagittal sinus occlusion. He received intravenous corticosteroids and anticoagulant therapy. Six months later, he presented a right motor status epilepticus. MRI revealed new parenchymal haematomas. Cerebral angiography demonstrated cerebral vasculitis.

Key words: Sarcoidosis; angiitis; thrombophlebitis.

Introduction

Sarcoidosis is a multisystem granulomatous disease of unknown aetiology that affects the nervous system in 5-10% of patients (8, 12). When present, neurological impairment is the first clinical manifestation in half of patients and is isolated in 12.5% of cases (9). In neurosarcoidosis, the basal meninges are affected by the characteristic noncaseating granuloma composed of multinucleated giant cells surrounded by lymphocytes (12). Vascular manifestations are extremely rare. We report a case of sarcoid angiitis associated with a dural sinus thrombosis.

Case report

A 47-year-old man was admitted to the neurological department of Lille hospital with left acute hemiplegia. He had a history of pulmonary sarcoidosis, diagnosed at the age of 32 and treated effectively with steroids. At the age of 40 he presented with a left abducens palsy; cerebral magnetic resonance imaging (MRI) and cerebrospinal fluid (CSF) examination were normal and he improved without treatment. One year later, he complained of progressive headache; the MRI scan showed two large gadolinium-enhanced frontal lesions with perilesional oedema. Stereotaxic biopsy demonstrated a typical sarcoid granuloma (Fig. 1). The patient

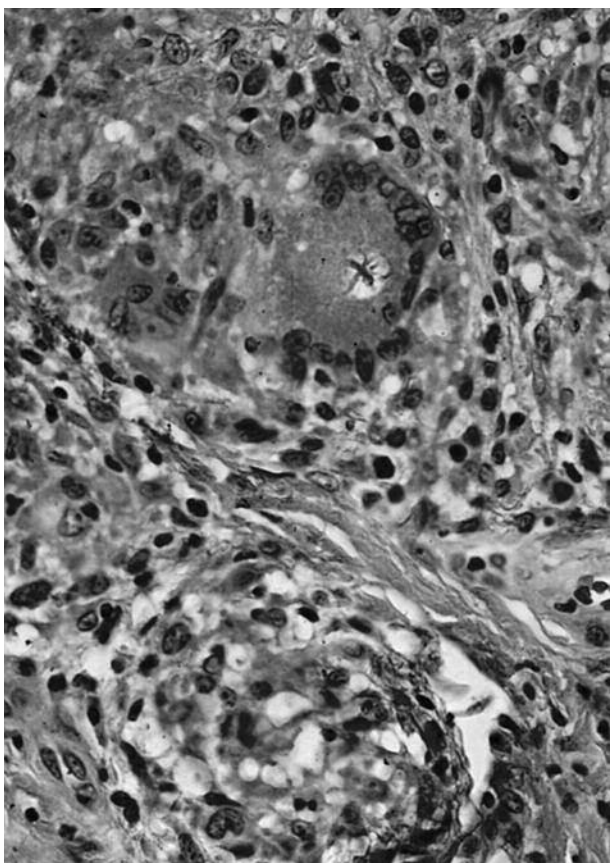

Fig. 1. — Photomicrograph of the frontal stereotaxic biopsy specimen showing a non caseous granulomatous inflammatory lesion including an asteroid body within a multinucleate giant cell characteristic of neurosarcoidosis.

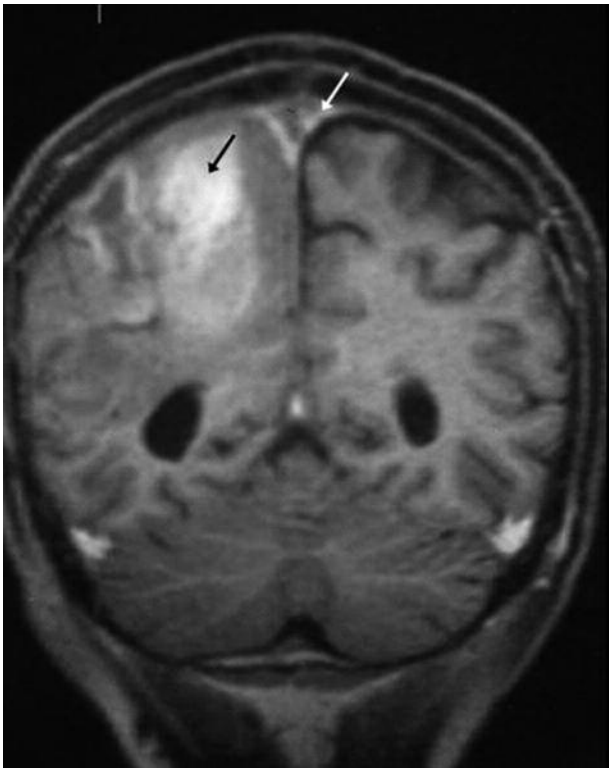

FIG. 2. — Coronal MRI with venous 2D time-of-flight sequence showing superior sagittal sinus thrombosis (white arrow) and an intracerebral haematoma secondary to venous infarction (black arrow).

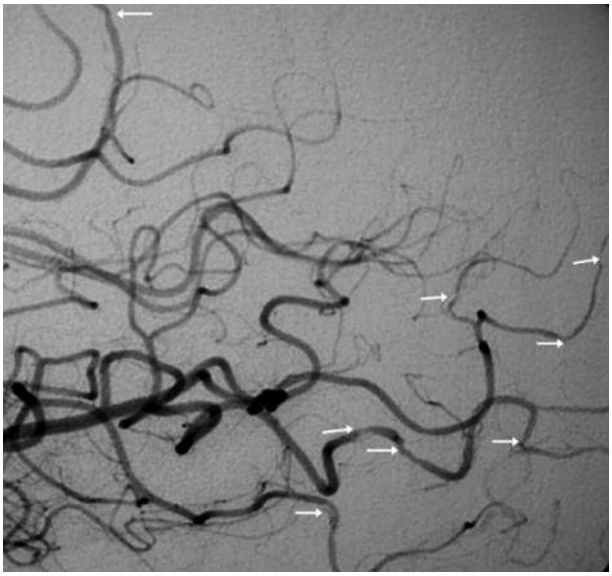

FIG. 3. — Cerebral angiography. Note multiple segmental stenoses of the middle cerebral artery (arrows).

fulfilled Zajicek's diagnostic criteria for neurosarcoidosis (14). After steroid treatment, his condition dramatically improved and the control MRI was normal. At the age of 47, he presented a first generalised tonic-clonic seizure. Brain CT scan was normal and he received sodium valproate. One month later, he presented a left acute hemiplegia. CT scan showed a recent right posterior parietal haematoma associated with older intraparenchymal haematomas. MRI showed similar images and venous 2D time-of-flight magnetic resonance angiography (MRA) sequences demonstrated superior sagittal sinus thrombosis (Fig. 2). The intracerebral haematoma was considered to be secondary to a venous infarction because of the sagittal sinus thrombosis. Biological examination revealed an inflammatory syndrome without anti-phospholipid antibodies. The hemiplegia improved after anti-coagulant therapy and 20 mg prednisone per day. Six months later, despite good therapeutic compliance, he presented a left focal motor status epilepticus resistant to clonazepam and requiring administration of fosphenytoin in the intensive care department. MRI demonstrated new frontal internal and external haematomas and persistent sagittal superior sinus thrombosis. Ophthalmoscopic examination was normal. Cerebral arteriography demonstrated a persistent sagittal superior sinus thrombosis with an effective venous collateral network and multiple segmentary middle cerebral artery stenoses in the branches M2 and M3 (Fig. 3). He thus presented many intraparenchymal haemorrhages due to cerebral angiitis supported by anti-coagulant therapy. Prednisone was increased up to 70 mg daily; methotrexate 15 mg weekly was prescribed and the anti-coagulant therapy was stopped. Six months later, his neurological impairment is currently slowly improving.

Discussion

Central nervous system impairment in sarcoidosis primarily affects the basal meninges, as reported in almost 100% of cases in pathological studies (8). Granulomas may extend to surrounding regions, including the cranial nerves, hypothalamus, pituitary fossa and the aqueduct of Sylvius (10). Direct cortical infiltration from the meninges can cause cortical irritation as a nidus for seizure activity (8). Granulomas also tend to extend from meningeal surfaces through Virchow-Robin spaces into the brain parenchyma and perivascular area (10). Arterial and venous involvement is frequent in pathological studies and causes granulomatous invasion of the blood vessel walls with disruption of the media and internal elastic lamina. Consequently, stenosis or occlusion may cause small cerebral infarcts. Most frequently,

small arteries, such as perforating arteries, are affected (4). In a few cases an acute necrotizing arteritis with fibrinoid necrosis of the media and intense leukocyte infiltration has been described as an angiitic form of neurosarcoidosis similar to polyarteritis nodosa lesions (6, 15). Most of these vascular lesions are asymptomatic and clinical cases are exceptional (4). Delaney *et al*., demonstrated asymptomatic vascular involvement in 9 of 14 autopsied neurosarcoid cases (8). In the main neurosarcoidosis series in the literature there are no reports of stroke or sinus thrombosis (8, 9, 13). Three cases of acute neurological deficit with vascular cerebral lesions were reported by Oksanen *et al*. in a review of 50 patients with neurosarcoidosis. A few case reports have been published with stroke in neurosarcoidosis (4, 11, 15). In cases of cerebral vascular involvement in sarcoidosis, different infarction mechanisms must first be excluded before diagnosing sarcoidosis angiitis: embolism from cardiac sarcoidosis, infectious angiitis due to immunodepression in systemic sarcoidosis and lacunar infarct due to high blood pressure secondary to sarcoidosic glomerulonephritis (2). Dural sinus thrombosis is extremely rare; only 3 cases have been reported (5, 7, 10). The sagittal superior sinus was always involved and, in the patient of Leeds *et al*., the lateral sinus was also involved (10). Our patient presented the main neurological lesions observed in sarcoidosis: cranial nerve palsy, pseudotumoral cerebral lesions and seizure. He also presented both arterial and venous symptomatic cerebral lesions, which have rarely been reported separately and never in combination. It is debatable whether angiitis or the dural sinus thrombosis was the cause of the first haematoma. The superior sagittal sinus was occluded on the first MRI and also on the MRI 6 months later even though the patient was receiving anticoagulant drugs. The dural sinus thrombosis could thus be older, a hypothesis that is supported by the fact that 6 months' anticoagulant therapy failed to revascularize the dural sinus and that cerebral arteriography showed an efficient collateral venous network near the persistent sinus occlusion. The dural sinus thrombosis could have been asymptomatic and the parenchymatal haemorrhages due to severe granulomatous angiitis. The dural sinus thrombosis could also have been iatrogenic following the lumbar puncture associated with steroid therapy, an occurrence already described in multiple sclerosis (1). Antiphospholipid antibodies associated with the sarcoidosis could explain an increase in thrombosis occurrence but they were absent in our case. Given the steroid-resistant angiitis in this patient, systemic sarcoid-like necrotizing granulomatosis could have been considered if there had been any granulomatous pulmonary involvement (3). Most cases of sarcoid vasculitis improve rapidly with steroid therapy (12). Only one case of systemic sarcoid vasculitis has ever been described associating cerebral haemorrhages with arteriographic angiitis images and systemic signs of vasculitis responsible for extremity gangrene. This particular sarcoid angiitis was resistant to steroids and cyclophosphamide treatment was necessary (14). Another case of cerebral angiitis has also been reported, associated with acute posterior multifocal placoid pigment epitheliopathy and sarcoidosis. Ophthalmoscopic examination is thus essential in angiitis associated with sarcoidosis (2).

Conclusion

Symptomatic cerebrovascular impairment in sarcoidosis is extremely rare and clinical presentation is heterogeneous because a variety of physiopathological mechanisms are responsible for the neurological symptoms. In cases with cerebral haemorrhages, the differential diagnosis between cerebral angiitis and dural sinus thrombosis may be difficult.

REFERENCES

1. Albucher JF, Vuillemin-Azaïs C, Manelfe C, Clanet M, Guiraud-Chaumeil B, Chollet F. Cerebral thrombophlebitis in three patients with probable multiple sclerosis. Role of lumbar puncture or intravenous corticosteroid treatment. Cerebrovasc Dis. 1999;9:298-303.
2. Bodiguel E, Benhamou A, Le Hoang P, Gautier JC. Cerebral infarction, placoid epitheliopathy and sarcoidosis Rev Neurol. 1992;148:746-751.
3. Brevet F, Hachulla E, Courtin P, Gosselin B, Wurtz A, Hatron PY, Devulder B. Systemic form of sarcoid-like necrotizing granulomatosis with ocular, pulmonary and cerebral involvement. Rev Med Interne. 1993;14:243-248.
4. Brown MM, Thompson AJ, Wedzicha JA, Swash M. Sarcoidosis presenting with stroke. Stroke. 1989;20: 400-405.
5. Byrne JV, Lawton CA. Meningeal sarcoidosis causing intracranial hypertension secondary to dural sinus thrombosis. Br J Radiol. 1983;56:755-757.
6. Caplan L, Corbett J, Goodwin J, Thomas C, Shenker D, Schatz N. Neuro-ophthalmologic signs in the angiitic form of neurosarcoidosis. Neurology. 1983;33:1130-1135.
7. Chapelon C, Ziza JM, Piette JC, Levy Y, Raguin G, Wechsler B, Bitker MO, Bletry O, Laplane D, Bousser MG. Neurosarcoidosis: signs, course and treatment in 35 confirmed cases. Medicine (Baltimore). 1990;69:261-276.

8. Delaney P. Neurologic manifestations in sarcoidosis: review of the literature, with a report of 23 cases. Ann Intern Med. 1977;87:336-345.
9. Ferriby D, de Seze J, Stojkovic T, Hachulla E, Wallaert B, Destée A, Hatron PY, Vermersch P. Long-term follow-up of neurosarcoidosis. Neurology. 2001; 57:927-929.
10. Leeds NE, Zimmerman RD, Elkin CM, Nussbaum M, LeVan AM. Neurosarcoidosis of the brain and meninges. Semin Roentgenol. 1985;20: 387-392.
11. Michotte A, Dequenne P, Jacobovitz D, Hildebrand J. Focal neurological deficit with sudden onset as the first manifestation of sarcoidosis: a case report with MRI follow-up. Eur Neurol. 1991;3:376-379.
12. Oksanen V. Neurosarcoidosis: clinical presentations and course in 50 patients. Acta Neurol Scand. 1986; 73:283-290.
13. Pentland B, Mitchell JD, Cull RE, Ford MJ. Central nervous system sarcoidosis. Q J Med. 1985;56:457-465.
14. Spencer TS, Campellone JV, Maldonado I, Huang N, Usmani Q, Reginato AJ. Clinical and magnetic resonance imaging manifestations of neurosarcoidosis. Semin Arthritis Rheum. 2005;34:649-661.
15. Younger DS, Hays AP, Brust JC, Rowland LP. Granulomatous angiitis of the brain. An inflammatory reaction of diverse etiology. Arch Neurol. 1988;45: 514-518.

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