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LETTER TO THE EDITOR

Ischemic stroke due to sarcoidosis: the arterial wall enhancement on magnetic resonance imaging

Makoto Kobayashi[1]

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Dear Editor,

Sarcoidosis is a multisystem granulomatous disorder that primarily affects the lungs and lymph nodes, followed by the skin, liver, eyes, heart, and musculoskeletal system. Symptomatic neurological manifestation occurs only in approximately 5% of sarcoidosis patients, including cranial mononeuropathy, intracranial or spinal cord mass, hydrocephalus, limb peripheral neuropathy, and stroke [1–3]. Although stroke is a rare complication, in the pathological studies, sarcoid granulomas tend to affect the leptomeninges, Virchow–Robin perivascular spaces, and adventitia of cerebral arteries with occasional invasions to the media and intima [4]. The damage to the vasculatures provokes ischemic and hemorrhagic strokes. In particular, ischemic stroke has become increasingly detectable with the advent of diffusion-weighted magnetic resonance imaging (MRI) and the lesion is typically small because sarcoid granulomas preferentially affect small- and medium-sized arteries [4]. Here, we report a unique patient with sarcoid neuropathy who developed a large ischemic stroke due to stenosis in the inferior trunk of the left middle cerebral artery (MCA). Notably, MRI detected the wall enhancement of the trunk and contiguous leptomeningeal lesions.

A 57-year-old woman presented with drooping of the left-sided face for 2 weeks. Her medical history included bronchial asthma, diabetes mellitus, and hypertension. The neurological examination revealed left peripheral facial palsy and reduced tendon reflexes in the four limbs. Initially, she was admitted for suspected Bell's palsy and successfully treated with intravenous steroid therapy. While the patient was in the hospital, MRI detected small infarctions in the left pontomedullary junction (Fig. 1a) and right cerebral peduncle (Fig. 1b), and oral clopidogrel 75 mg/day was started. After the steroid therapy, she was discharged and followed up with the antiplatelet medication.

One month later after the discharge, she was hospitalized again for gradually progressive malaise, diplopia, and tingling sensation in the four limbs. On admission, she presented with right eyelid ptosis, supraduction and adduction palsies of the right eye, left peripheral facial palsy, right dominant lower extremity muscle weakness of grade 4 on the Medical Research Council scale, and absent tendon reflexes and paresthesia in the upper and lower extremities. The routine blood tests, including serum calcium, were unremarkable, except for the blood glucose concentration at 272 mg/dL. The serum level of soluble interleukin-2 receptor was elevated (1170 U/mL; normal range, 145–519 U/mL), and those of angiotensin-converting enzyme and lysozyme were normal. Electrocardiogram and echocardiogram were not remarkable, but chest computed tomography showed swelling of the lymph nodes in the mediastinum and bilateral pulmonary hilum. In these lymph nodes, abnormal tracer accumulations were observed on 18F-fluorodeoxyglucose positron emission tomography (Fig. 2a). Transbronchoscopic needle biopsy of the mediastinum lymph node was performed and the microscopic investigation displayed noncaseating granulomas (Fig. 2b). In the nerve conduction study of the right upper and lower extremities, compound muscle action potential of the median nerve was decreased with increased F wave latencies in the median, tibial, and peroneal nerves. Brain fat-suppressed T1 MRI with gadolinium detected abnormal enhancements in the right oculomotor nerve (Fig. 2c, oblique arrow), bilateral abducens nerves (Fig. 2d, vertical arrows), left vestibulocochlear and facial nerves (Fig. 2d, oblique arrow), caudal part of the fourth ventricle (Fig. 2d, transverse arrows), and leptomeninges of the cerebrum and brainstem. Arterial walls were enhanced in the right MCA (Fig. 2c, vertical arrow), left MCA, and right vertebral artery. On spinal cord gadolinium MRI, abnormalities were also observed in the right C6 nerve root (Fig. 2e, arrow) and cauda equina (Fig. 2f, arrows). Based on these findings, she was diagnosed as having multiple cranial

✉ Makoto Kobayashi
ma-ko@pg7.so-net.ne.jp

[1] Department of Neurology, Asahi General Hospital, 1326 I, Asahi, Chiba 289-2511, Japan

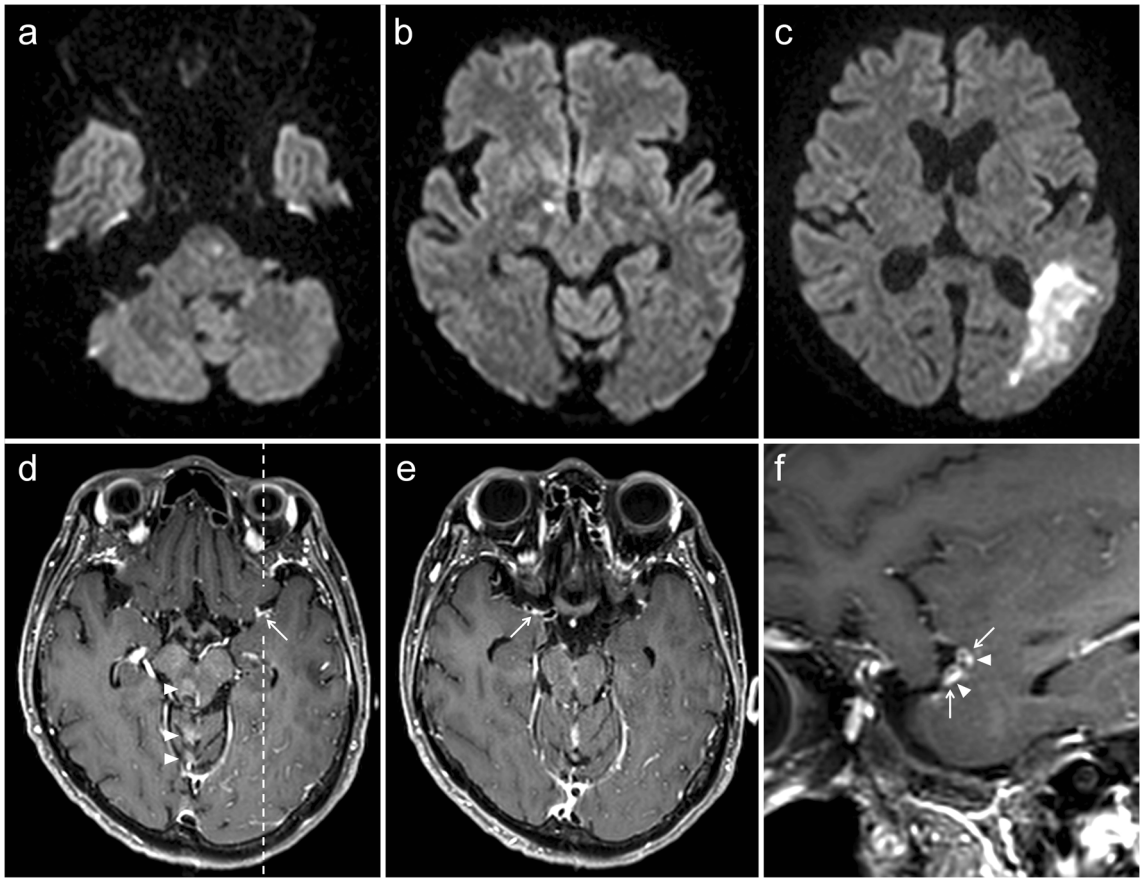

Fig. 1 During the initial hospitalization, diffusion-weighted magnetic resonance imaging (MRI) detected small high-intensity lesions in the left pontomedullary junction (**a**) and right cerebral peduncle (**b**). When the patient developed a major ischemic stroke during the second hospitalization, MRI showed abnormalities (**c**–**f**). On diffusion-weighted MRI, large high-intensity lesions were observed in the distribution of the left middle cerebral artery (MCA) inferior trunk (**c**). Brain fat-suppressed gadolinium T1 MRI revealed wall enhancements in the left superior and inferior trunks (**d**, arrow) and right main trunk (**e**, arrow) of the MCAs. On the sagittal image indicated by the dashed line in panel **d**, the lesions invaded the whole circumferences of the left superior trunk (**f**, oblique arrow) and left inferior trunk (**f**, vertical arrow). Gadolinium enhancements were also observed in the leptomeninges near or contiguous to the trunks (**f**, arrowheads) with artifacts in the midbrain and cerebellum (**d**, arrowheads)

nerve palsies and limb polyradiculopathy due to sarcoidosis. Treatment was started with intravenous methylprednisolone 1000 mg/day for 3 days followed by oral prednisolone 40 mg/day. Her symptoms gradually improved, and the restricted eye movements and facial palsy were almost completely recovered with mild right leg weakness. The prednisolone dosage was maintained for 2 weeks and subsequently reduced to 35 mg/day.

However, 26 days after initiating the steroid treatment, the patient reported that she had progressively become incapable of understanding spoken words. On neurological examination, she had paraphasic errors with difficulties in naming, repetition, and comprehension. Diffusion-weighted MRI revealed high-intensity lesions in the distribution of the inferior trunk of the left MCA (Fig. 1c). Three-dimensional time-of-flight magnetic resonance angiography (MRA) showed signal losses in the left superior and inferior trunks (Fig. 3a, vertical arrows) and right main trunk (Fig. 3a, oblique arrow) of the MCAs, while no abnormality was found in the right vertebral artery. On gadolinium T1-weighted MRI with fat suppression, wall enhancements were detected in the left MCA superior and inferior trunks (Fig. 1d, arrow), right MCA main trunk (Fig. 1e, arrow), and right vertebral artery. These wall enhancements showed circumferential involvements (Fig. 1f, arrows) and were largely unchanged in comparison with those on MRI performed before the steroid treatment. Moreover, leptomeningeal lesions were observable on the surface of the cerebrum and contiguous to the MCA wall lesions (Fig. 1f, arrowheads). Since the MRI and MRA findings with the progressive symptom suggested thrombosis of the inferior trunk of the left MCA, an intravenous antithrombotic drug (argatroban 60 mg/day for the first 2 days and 20 mg/day for the next 5 days) and a free radical scavenger (edaravone 60 mg/day for 2 weeks) were initiated with increased oral antiplatelet medications (aspirin 200 mg/day and clopidogrel 75 mg/day). The patient's language impairment gradually improved but persisted. After the aspirin was discontinued and oral prednisolone was tapered to 30 mg/day, she was discharged. At outpatient follow-up visits, the prednisolone

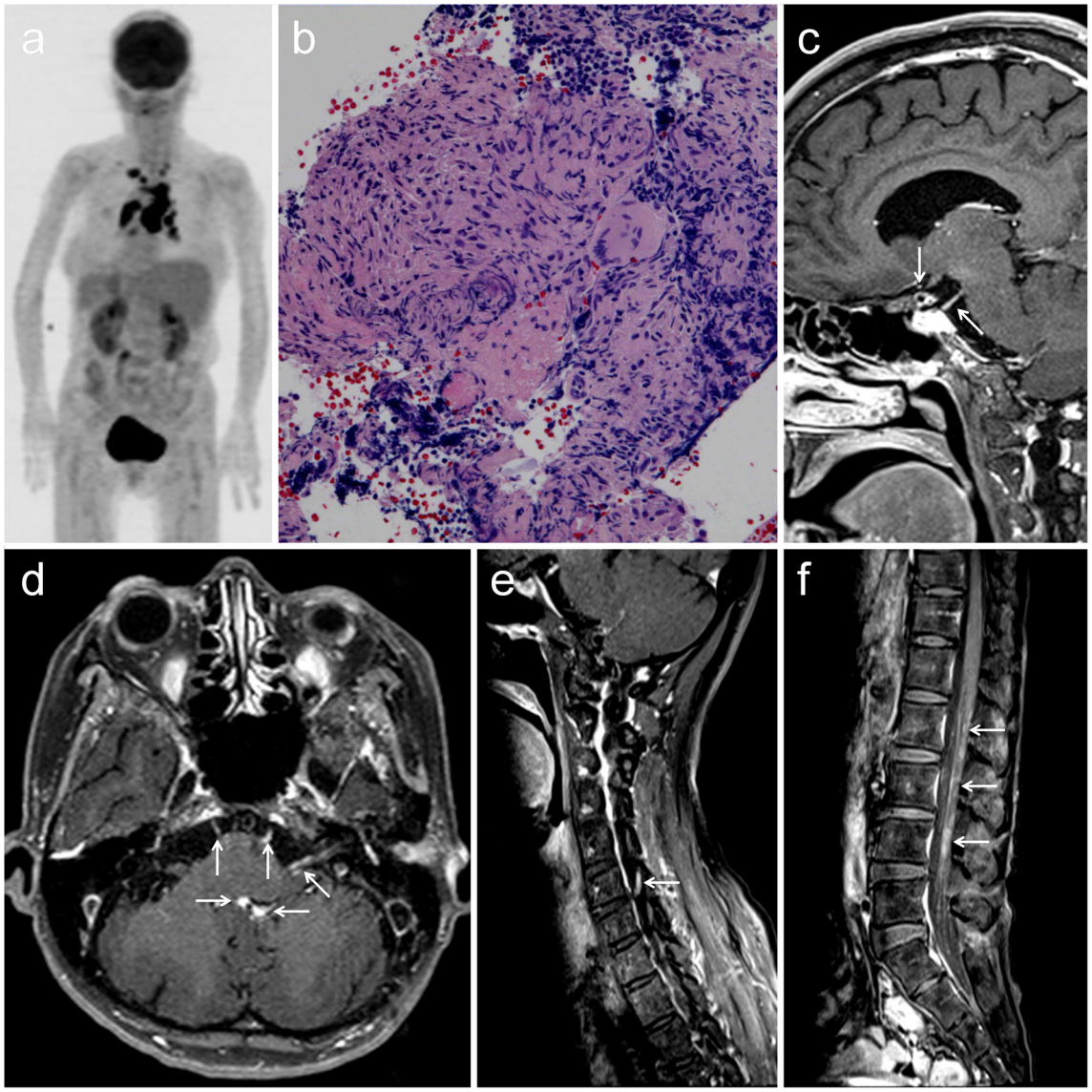

Fig. 2 On 18F-fluorodeoxyglucose positron emission tomography, abnormal tracer accumulations were detected in the mediastinum, bilateral hilum, and left supraclavicular lymph nodes (**a**). Microscopic investigation of the mediastinum lymph node revealed noncaseating granulomas consisting of aggregated epithelioid cells and multinucleated giant cells (**b**, hematoxylin and eosin staining). Brain T1-weighted gadolinium magnetic resonance imaging (MRI) with fat suppression revealed abnormal enhancements in the right oculomotor nerve (**c**, oblique arrow), bilateral abducens nerves (**d**, vertical arrows), left vestibulocochlear and facial nerves (**d**, oblique arrow), caudal part of the fourth ventricle (**d**, transverse arrows), and wall of the right middle cerebral artery (**c**, vertical arrow). Moreover, the right C6 nerve root (**e**, arrow) and cauda equina (**f**, arrows) were enhanced on spinal cord MRI

was gradually reduced to 10 mg/day without recurrence. Moreover, after 15 months of steroid treatment, MRA showed partial improvement of the MCA signal losses (Fig. 3b).

The presented case had a major ischemic stroke with the arterial wall and leptomeningeal enhancements on MRI. Ischemic stroke has been reported as a rare manifestation of sarcoidosis [1] and is primarily classified as follows: small vessel disease with in situ thrombosis from perivascular granulomatous inflammation, cardiogenic emboli due to sarcoidosis-related heart disease, large artery compression from adjacent mass lesions, or large artery inflammation with in situ thrombosis [4]. A majority of the reported cases are the small vessel disease, but our case may be categorized as the large artery inflammation. While signals were lost in the left superior and inferior trunks and right main trunk of the MCAs on MRA, the arterial wall enhancements were observed nearly in the same locations. Since leptomeningeal lesions are characteristic of sarcoidosis and consist of inflammatory granulomas, the contiguous leptomeningeal lesions may have induced inflammatory change and stenotic fibrosis in the walls of these MCA trunks, resulting in the MRI enhancements and MRA signal losses. In the inferior trunk of the left MCA, the change was probably severe to cause thrombosis.

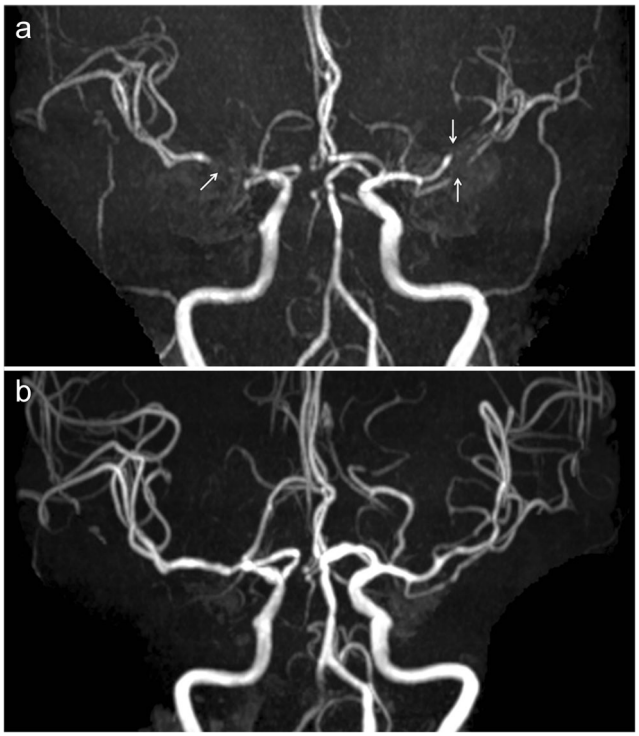

Fig. 3 Magnetic resonance angiography revealed signal losses in the right main trunk (**a**, oblique arrow), left superior trunk (**a**, upper vertical arrow), and left inferior trunk (**a**, lower vertical arrow) of the middle cerebral arteries. These signal losses partially improved after 15 months of steroid treatment (**b**)

In previous articles, arterial wall enhancements on gadolinium T1 MRI indicated intracranial active atherosclerotic plaques and cerebral vasculitis, but they were also reported to be common findings in elderly patients and possibly associated with proliferation of the vasa vasorum with age, especially in the vertebral arteries [5]. The wall enhancement of the patient's right vertebral artery was probably also age-related change, considering this artery was normal on MRA. In contrast, the MCA wall enhancements were regarded as pathological since they involved MRA signal losses, which partially improved after steroid treatment. Although the patient had a medical history of diabetes mellitus and hypertension, the contiguous leptomeningeal lesions and MRA improvement suggested that the MCA wall enhancements were caused by sarcoidosis rather than atherosclerosis.

This case demonstrates that sarcoid granulomas infrequently affect large cerebral arteries with the wall and leptomeningeal enhancements on MRI. In sarcoidosis patients with such large cerebral artery lesions, ischemic stroke can cause severe neurological impairments and should be remembered during diagnosis and treatment.

Compliance with ethical standards

Conflict of interest The author declares that he has no conflict of interest.

Informed consent Obtained.

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