

[CASE REPORT]

Cardioembolic Stroke Due to Cardiac Sarcoidosis Diagnosed by Pathological Evaluation of the Retrieved Thrombus

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Abstract:

A 70-year-old woman undergoing glucocorticoid therapy for cardiac sarcoidosis was brought to our hospital with the sudden onset of right hemiplegia and aphasia. Brain magnetic resonance imaging showed a high diffusion-weighted imaging signal in the left frontotemporal lobe and disruption of blood flow in the M1 segment of the left middle cerebral artery. Hence, she underwent thrombolysis and mechanical thrombectomy, resulting in marked improvement in her neurological symptoms. A pathologic evaluation of the thrombus suggested its cardiogenicity, and the absence of any obvious abnormality other than a left ventricular aneurysm indicated stroke due to a cardioembolic etiology secondary to cardiac sarcoidosis.

Key words: stroke, cardiac sarcoidosis, thrombolysis, thrombectomy, ventricular aneurysm

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Introduction

Sarcoidosis is a systemic, granulomatous disease involving various organs, the pathophysiology of which remains unclear. It affects the lungs in as many as 90% of patients, but cardiac involvement is clinically demonstrated in only 2-5% of cases (1). However, autopsy studies and recent advances in cardiac imaging have shown that subclinical cardiac sarcoidosis is more common than believed (1). Due to the rarity of this phenotype, the reported number of cases of cardiogenic cerebral embolism associated with cardiac sarcoidosis is extremely limited.

We herein report a case of ischemic stroke associated with cardiac sarcoidosis, in which cardiogenic embolization was confirmed by thrombectomy.

Case Report

A 70-year-old woman who had been hospitalized at another hospital for heart failure 3 months earlier was referred to the Department of Cardiology of our hospital 2 months earlier for the further investigation and treatment of sus-

pected cardiac sarcoidosis. She had diabetes mellitus but no other medical condition of note. Blood samples showed elevated angiotensin-converting enzyme (ACE: 33.9 IU/L), lysozyme (21.0 µg/mL) and soluble interleukin-2 receptor (sIL-2R: 698 U/mL) levels, and electrocardiography (ECG) showed first-degree atrioventricular block and complete right bundle branch block. Transthoracic echocardiography (TTE) revealed focal anterolateral wall dyskinesia and ventricular aneurysm, and left ventriculography showed an anterior wall aneurysm and turbulent blood flow within the lesion, although there was no obvious thrombus formation (Fig. 1A, B). Contrast-enhanced magnetic resonance imaging (MRI) showed late gadolinium enhancement in the same lesion (Fig. 1C). Coronary angiography ruled out ischemic heart disease. Positron emission tomography showed the abnormal accumulation of fluorodeoxyglucose in the mediastinal and hilar lymph nodes and the left ventricular wall (Fig. 1D, E). Based on these findings, she was diagnosed with cardiac sarcoidosis and started on glucocorticoid therapy.

Fifteen days after the diagnosis of cardiac sarcoidosis was made, she was brought to our hospital with the sudden onset of right hemiplegia and aphasia. Her National Institute of

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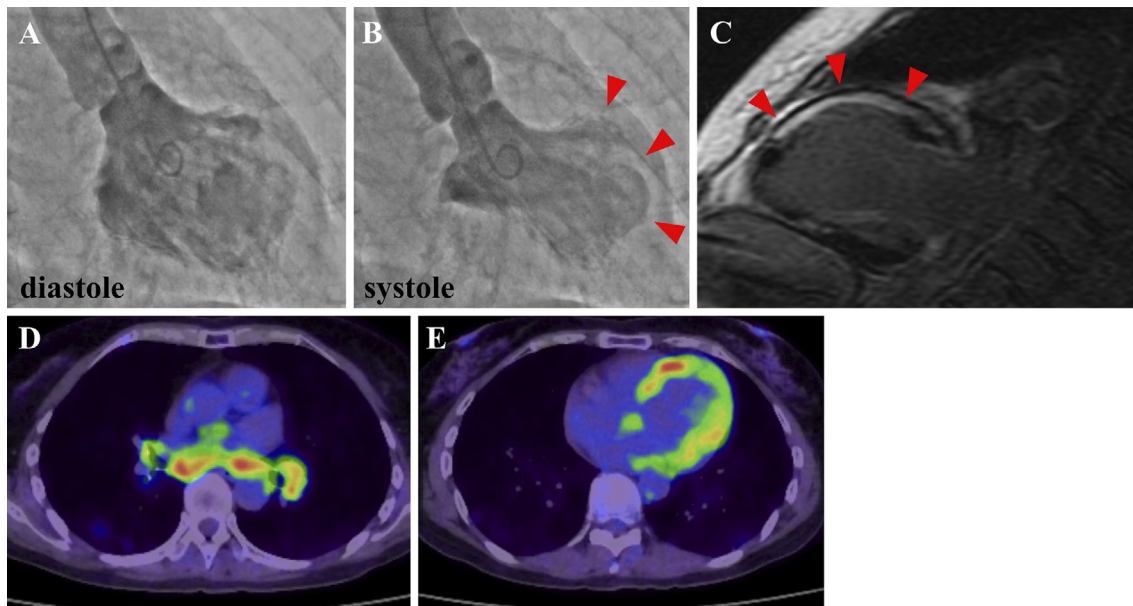


Figure 1. Morphological and functional images that contributed to the diagnosis of cardiac sarcoidosis and a ventricular aneurysm. A comparison of diastole (A) and systole (B) on left ventriculography revealed an anterior wall aneurysm and congestion of blood flow in the lesion (arrows). Cardiac MRI showed an anterolateral left ventricular aneurysm and a positive late gadolinium enhancement lesion surrounding it in contrast-enhanced T1-weighted imaging (C, arrows). Positron emission tomography showed an abnormal accumulation in mediastinal and hilar lymph nodes (D) and the left ventricular wall (E).

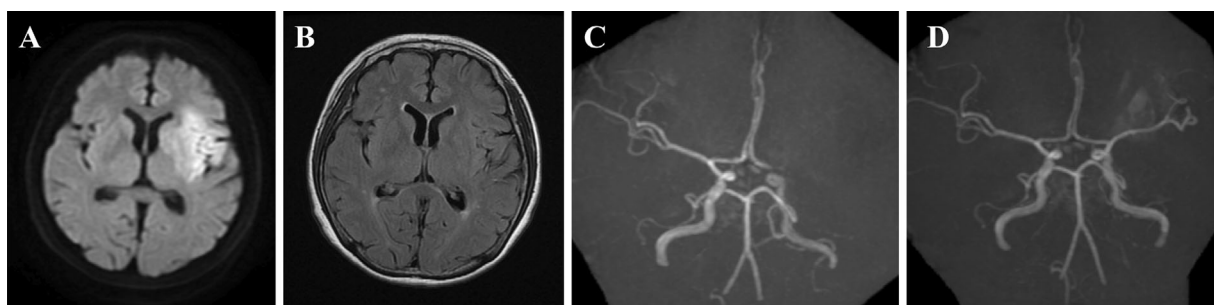


Figure 2. Magnetic resonance imaging (MRI) at the onset and six months after the ischemic stroke. MRI diffusion-weighted imaging (A), fluid attenuation inversion recovery images (B) and angiography (C) at presentation suggested acute infarction in the frontotemporal lobe and blood flow occlusion in the M1 segment of the left middle cerebral artery. MR angiography performed six months after the onset (D) showed no evidence of occlusion or stenosis even after recanalization of the left middle cerebral artery.

Health Stroke Scale (NIHSS) score at the time of admission was 20 points, and brain MRI showed a high diffusion-weighted signal in the left frontotemporal lobe and disruption of blood flow in the M1 segment of the middle cerebral artery (Fig. 2A-C). Thus, we diagnosed her with ischemic stroke due to thromboembolism. Due to the hyperacute stage of the disease, we performed thrombolysis with recombinant tissue plasminogen activator and mechanical thrombectomy, resulting in recanalization of Thrombolysis In Cerebral Infarction (TICI) grade 2c (2). She showed dramatic improvement to a NIHSS score of 0 points by hospital day 4, without any bleeding complications or sequelae. The intracranial

blood vessels lacked atherosclerotic changes, and a pathologic evaluation of the thrombus indicated a fresh thrombus without atheromatous or organized components, consistent with a cardiogenic origin. Blood samples taken on admission showed that the D-dimer level was within normal limits. A repeated Holter ECG showed no atrial arrhythmias, and TTE performed during hospitalization showed a decreased ejection fraction (EF) of 40%. Transesophageal echocardiography (TEE) showed no obvious intracardiac thrombus or patent foramen ovale. Based on these results, we concluded that an embolus associated with the left ventricular anterolateral aneurysm caused the ischemic stroke

and started anticoagulation with warfarin to prevent recurrence of ischemic stroke. At the time of this reporting, it has been six months since her discharge from the hospital without any recurrence of stroke (Fig. 2D) or worsening of sarcoidosis.

Discussion

Recent imaging and autopsy reports suggest that cardiac sarcoidosis is potentially more common than previously reported (1, 3). There are, however, only a few reports of stroke caused by cardioembolism in association with cardiac sarcoidosis (4-7), which suggests a lack of a consensus concerning the general pathogenesis of this condition. Therefore, it is sometimes considered as embolic stroke of undetermined source (ESUS) and there are no guidelines on anticoagulation for stroke associated with cardiac sarcoidosis. In a previous report, a large left ventricular thrombus was found in a patient with cardiac sarcoidosis with reduced EF, and surgical resection showed that the thrombus was pathologically fresh (8). In addition, it has been known for a long time that ventricular aneurysms formed after myocardial infarction are prone to blood flow congestion associated with wall motion abnormalities and secondary thrombus formation and carry a high risk of embolic events (9). In our case, a pathology evaluation showed that the thrombus was fresh and did not contain atheromatous or organized components, which is not specific but is consistent with the previous report of the fresh ventricular thrombus (8). In addition, although there was no evidence of intracardiac thrombus before the onset of stroke, turbulent findings in the ventricular aneurysm on left ventriculography suggested blood flow congestion, which is known to increase the risk of secondary thrombus formation (9). Thus, we considered that the stroke in our case was caused by a freshly developed thrombus originating from the ventricular aneurysm in the presence of low EF.

To our knowledge, this is the first report of confirmation of ischemic stroke secondary to cardiac sarcoidosis by a pathological evaluation of the mechanical thrombectomy specimen. Glucocorticoids are known to increase the risk of cerebrovascular disease (10), although we were unable to assess how much the drug affected the pathology in our case. However, since glucocorticoids are the key drug in patients with cardiac sarcoidosis, myocardial morphological abnormalities should be considered an additional risk for ischemic stroke in patients receiving glucocorticoids. Given the above discussion, we suggest considering the administration of prophylactic anticoagulation in patients with cardiac sarcoidosis with an associated ventricular aneurysm and/or low EF in order to minimize the risks of development of a left ventricular thrombus. Even in the absence of obvious thrombus formation, imaging evidence of a ventricular aneurysm and blood congestion within the aneurysm might be an indicator for the initiation of anticoagulation therapy. Future prospective studies are needed to evaluate the advantages of prophylactic

anticoagulation therapy in such at-risk patients.

In conclusion, this is a rare case of ischemic stroke in a patient with cardiac sarcoidosis in whom thrombolysis and mechanical thrombectomy were performed, and in whom the thrombus pathology was consistent with a cardiogenic origin. Cardiac sarcoidosis has a high mortality rate in itself, which can be further complicated by the occurrence of stroke. Notably, cardiac sarcoidosis patients with ventricular aneurysms are at risk for the development of left ventricular thrombi. With the further development of imaging and nuclear medicine technologies, the diagnosis of cardiac sarcoidosis in the general population or in systemic sarcoidosis patients is likely to increase in the future; thus, the indications for prophylactic anticoagulation in high-risk patients, such as those mentioned here, should be developed, as more such cases are likely to occur.

Ethics approval and consent for submitting case reports is usually waived by the ethics review committee of Musashino Red Cross Hospital. We followed the principals of the Declaration of Helsinki and paid cautious attention to protecting the patient's identity.

Written informed consent was obtained from the patients for publication of this case report and any accompanying images.

Raw data were generated at Musashino Red Cross Hospital. Derived data supporting the findings of this study are available from the corresponding author SM on request.

The authors state that they have no Conflict of Interest (COI).

References

1. Kandolin R, Lehtonen J, Airaksinen J, et al. Cardiac sarcoidosis: epidemiology, characteristics, and outcome over 25 years in a nationwide study. *Circulation* **131**: 624-632, 2015.
2. Almekhlafi MA, Mishra S, Desai JA, et al. Not all "successful" angiographic reperfusion patients are an equal validation of a modified TICI scoring system. *Interv Neuroradiol* **20**: 21-27, 2014.
3. Jachiet V, Lhote R, Rufat P, et al. Clinical, imaging, and histological presentation and outcomes of stroke related to sarcoidosis. *J Neurol* **265**: 2333-2341, 2018.
4. Sbramanian M, Yalagudri S, Saggu D, et al. Stroke in cardiac sarcoidosis: need to worry? *Indian Heart J* **72**: 442-444, 2020.
5. Memon M, AlHazza M, Heena H. Stroke presenting as a complication of sarcoidosis in an otherwise asymptomatic patient. *Cereus* **10**: e2362, 2018.
6. Kurukumbi M, Gardiner L, Sahai S, et al. Cardiac sarcoidosis as an uncommon etiology for posterior circulation stroke presenting with alexia without agraphia. *Case Rep Neurol Med* **2018**: 3418465, 2018.
7. Kuwabara M, Ishimura RN, Ishiwata S, et al. Isolated cardiac sarcoidosis presenting with stroke. *Korean Circ J* **48**: 236-239, 2018.
8. Kanemitsu S, Miyake Y, Okabe M. Surgical removal of a left ventricular thrombus associated with cardiac sarcoidosis. *Interact Cardiovasc Thorac Surg* **7**: 333-335, 2008.
9. Keeney EC, Hillis LD. Left ventricular mural thrombus after acute myocardial infarction. *Clin Cardiol* **19**: 83-86, 1996.
10. Sovereign PC, Berard A, Van Staa TP, et al. Use of oral glucocorticoids and risk of cardiovascular and cerebrovascular disease in a

population based case-control study. *Heart* **90**: 859-865, 2004.

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