Title: Significance of the T2*-weighted gradient echo brain imaging in patients with infective endocarditis

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Abstract

Background: Although aneurysm formation accompanying parenchymal hemorrhage is one of devastating complications in the central nerves system (CNS), imaging studies of the brain are not routinely warranted in patients with infective endocarditis (IE). To assess the clinical importance for detecting silent lesions in the central nervous system, we investigated hypointense signal spots detected on the brain T2*-weighted MR imaging in patients with IE.

Methods and Results: Eleven patients with IE were retrospectively reviewed. Seven patients (63.6%) showed hypointense signal spots on T2*-weighted MR images. The number of hypointense signal spots increased within only a few weeks in five patients.

Conclusion: The brain T2*-weighted MR imaging in patients with IE may have a potential role to detect CNS lesions with clinical significance of potentially high risk of intracranial hemorrhage. T2*-weighted hypointense signal spots may be specific to brain involvement, and be quite useful in monitoring CNS lesions associated with IE, even if they are asymptomatic.

Key words: Infective endocarditis, intracranial infectious aneurysm, T2*-weighted magnetic resonance imaging

Significance of the T2*-weighted gradient echo brain imaging in patients with infective endocarditis

Infective endocarditis (IE) is a disease accompanying considerable morbidity and mortality[1]. In patients with IE, central nerves system (CNS) involvement has been reported to develop in 20 to 40%[2,3]. Infectious aneurysms (IAs), which are mostly small lesions in the intracranial arteries, manifest a variety of clinical presentations and have a mortality rate as high as 60%[1]. Although some IAs heal with only medical therapy even if they rupture, others may increase in size and number. Although T2*-weighted magnetic resonance (MR) imaging could be sensitive to magnetic susceptibility effect even in small lesions in the CNS, its implications for IE lesions has not yet been fully elucidated [4-8, 22-24]. In this study, we evaluated hypointense signal spots detected on the brain T2*-weighted MR imaging in patients with IE and assessed the clinical importance for detecting silent lesions in the CNS.

Patients and Methods

We retrospectively reviewed consecutive cases of IE treated at the Nagasaki University Hospital from June 2006 to July 2007. All patients were diagnosed as having IE

according to the modified Duke criteria. This study included only patients in whom the brain T2*-weighted MR imaging was performed. The initial and follow-up imaging in all patients were undertaken with the 1.5-T scanner (Signa CV/i; GE Healthcare, Milwaukee, WI) with a standard head coil. T2*-weighted MR imaging used a gradient echo pulse sequence with repetition time: 650 ms; echo time: 23 ms; flip angle: 20°; acquisition matrix: 256 x 224; number of signal averaged: 2; section thickness: 6mm; gap width: 2 mm; field of view: 22 cm^2. Eleven patients with IE met the inclusion criteria, comprising 7 men and 4 women with mean age of 54 years (range, 23-79 yr.). Clinical presentation, MRI findings, and treatments in the patients were reviewed.

Results

Clinical characteristics and MRI findings of all patients are shown in Table 1. The most common initial symptoms were fever in four (35.5%), and lumbago in three patients. Others had shoulder pain, general fatigue, emotional change, and hemiparesis. The most common predisposing conditions for IE included mitral or aortic valvular incompetence in eight, and a dental procedure in two, and prosthetic heart valve in one patient. The intervals between the clinical manifestation and the diagnosis of IE were relatively long (5 days to 5 months).

Intracranial abnormalities were identified on the brain MR images in eight patients (72.7%) including subarachnoid hemorrhage in three, cerebral infarct in three, intracerebral hemorrhage in two and subdural hematoma in one patient. All patients including nine who had undergone cardiac surgeries for IE were neurologically asymptomatic, but one patient (Case 8) showed right hemiparesis at the time of brain MR imaging. Cerebral angiography (CAG) was performed in four patients, two of whom were found to have IAs and underwent the aneurysm resection. Seven patients (63.6%) showed T2*-weighted hypointense signal spots (Table 1). The number of the hypointense spots had increased within only a few weeks (14-28 days) in five patients with multiple lesions.

Nine patients (81.9%) including two who had undergone surgery for intracranial IAs had good recovery. One patient died following the cardiac surgery because of postoperative disseminated intravascular coaglopathy. Another patient presented severe disability because of cerebral infarction.

Illustrative cases

Patient 1

A 23-year-old woman, who had a history of cardiac surgery for the ventricular septal

defect, suffered headache and general fatigue after a dental treatment. She was admitted to a local hospital, and diagnosed as IE. She was transferred to our institute, and underwent the aortic valve replacement. After the procedure, computed tomography (CT) of the brain revealed a parenchymal hematoma in the left frontal lobe (Fig. 1A). Both CT Angiography (CTA) and cerebral angiography (CAG) demonstrated an aneurysm at the distal branch of the left middle cerebral artery (Fig. 1B). She underwent left frontotemporal craniotomy, and the aneurysm was resected. Preoperative T2*-weighted MR imaging demonstrated multiple hypointense signal spots, although the relevant lesions were not demonstrated by either CTA or CAG (Fig. 2).

Patient 2

A 75-year-old man was transferred to our institute because of a fever of unknown origin. Transesophageal echocardiography revealed vegetation at the mitral valve and led to the diagnosis of IE. He had no neurological symptoms, but brain T2*-weighted MR imaging demonstrated several hypointense spots with edema formation (Fig. 3, A and B). MR angiography showed no aneurysms. Interestingly, the number of the T2*-weighted hypointense spots increased asymptomatically, whereas the perifocal edema disappeared following three-week antibiotherapy (Fig. 3, C and D). The patient

underwent the mitral-valve plasty, however his general condition deteriorated postoperatively because of pneumonia and the renal failure. He was treated intensively, but he died three months after the cardiac surgery.

Discussion

Intracranial IAs are less common (2-4% of endocarditis cases) but they produce potentially devastating neurological complications such as intracerebral or subarachnoid hemorrhage[9-11]. Since IAs can be clinically silent and some of them could resolve by antibiotic therapy, actual incidence of IAs is considered to be higher than the ones reported in the literatures[12]. IAs may result from septic embolism of vegetations to the arterial vasa vasorum or the intraluminal space, and result in subsequent spread of infection through the intima and outward the vessel wall[12]. Time interval from septic embolism to aneurysmal dilation can be as short as 24 hours[13]. Regardless of its high complication rate, at present, conventional CAG remains as gold standard in diagnosing intracranial IAs [1, 12]. However, intracranial bleeding is not always secondary to rupture of IAs but often to other situations such as necrotic arteritis [14]. In addition, in our case 2 with no aneurysm detected on MR angiography, the number of the T2*-weighted hypointense spots increased as the perifocal edema disappeared following

three-week antibiotherapy. These findings suggest that pathological changes other than IA formation or symptomatic hemorrhage could also play a role in CNS involvement in patients with IE. Therefore, less-invasive and repeatable studies such as MR imaging could be indicated in neurologically asymptomatic patients with IE.

The present study demonstrated that the T2*-weighted MR imaging could detect intracranial abnormalities in 63.6% of the patients with IE, and in 60% of patients without any neurological signs, which was higher than we had expected. Brain T2*-weighted MR imaging has been reported to demonstrate various etiologies of hypointense spots, which result from the deposition of hemosiderin (old hemorrhage), ferritin, calcium, the presence of other metallic materials and air[15]. It could also detect remnants of previous cerebral microbleeds (MBs)[16-18], which are usually defined as small, round, foci distinct from vascular flow voids, leptomeningeal hemosiderosis, and nonhemorrhagic subcortical mineralization[19]. MBs are considered as a general marker of microvascular vulnerability with the incidence of 3.1-6.4%[19, 20] in healthy individuals, and 56%[21] in hypertensive patients. There are only two previous reports that refer to the relationship between T2*-weighted hypointense lesions and the presence of IE, and current study is the first case series discussing the clinical significance of the brain T2*-weighted MR imaging associated with IE[22-24].

Even a young patient (Case 1) had multiple T2*-weighted hypointense signal spots, and the number of such lesions increased within only a few weeks in five cases (Case 1, 2, 3, 7 and 8). Most lesions appeared in cortex, subcortex and around sulci, which were anatomically different from MBs as seen in patients with chronic hypertension, cavernomas, and amyloid angiopathy. In which situation, abnormalities detected on T2*-weighted MR imaging of the brain may indicate potentially high risk of intracranial bleeding. Therefore, we recommend T2*-weighted MR imaging in patients with IE, even if they are neurologically asymptomatic, both for routine screening and follow-up procedures.

Our study has limitations because of small number of the patients and short follow-up period. Further studies with large number of patients and a longer follow-up period are required.

Conclusion

The brain T2*-weighted MR imaging in patients with IE may have a potential role to detect minor abnormalities related to IE, with clinical significance of high risk of intracranial hemorrhage. T2*-weighted hypointense signal spots might be specific to brain involvements of IE, and be helpful in diagnosing and monitoring CNS lesions in

patients with IE.

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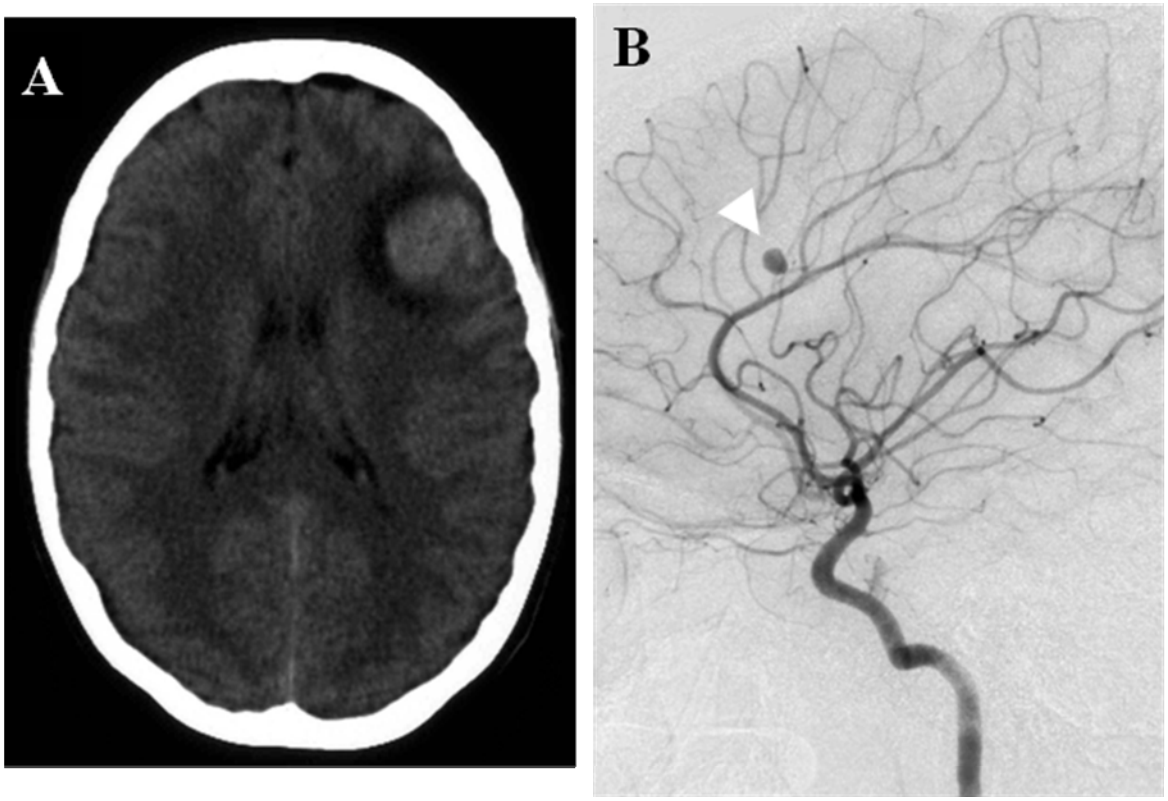

Figure 1. Plain CT (A) showed a hematoma in the left frontal lobe. Cerebral angiography (B) revealed an aneurysm at the distal branch of the left middle cerebral artery.

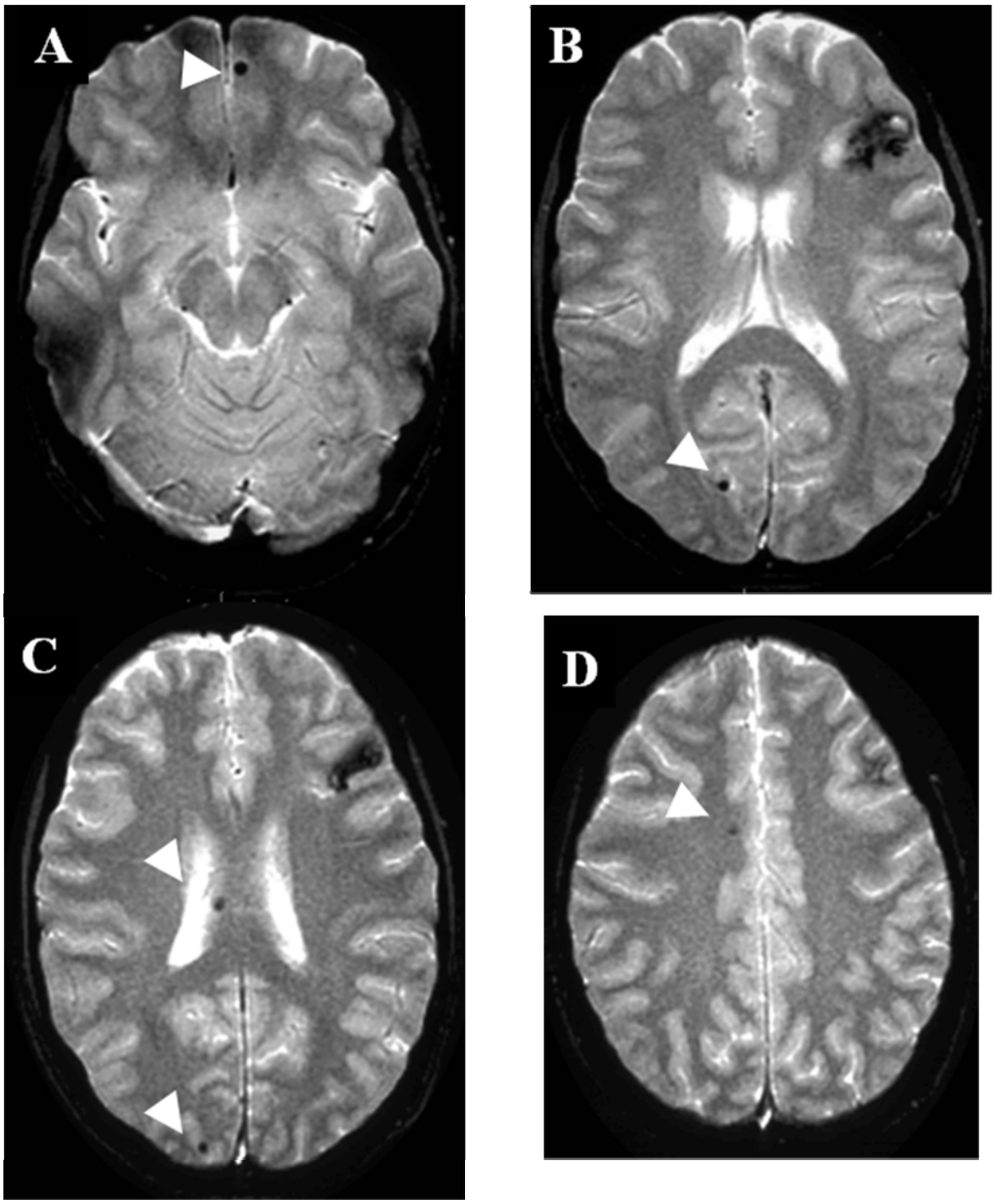

Figure 2. T2*-weighted MR imaging demonstrated multiple hypointense spots (arrowhead) in the cortex, subcortex and around sulci.

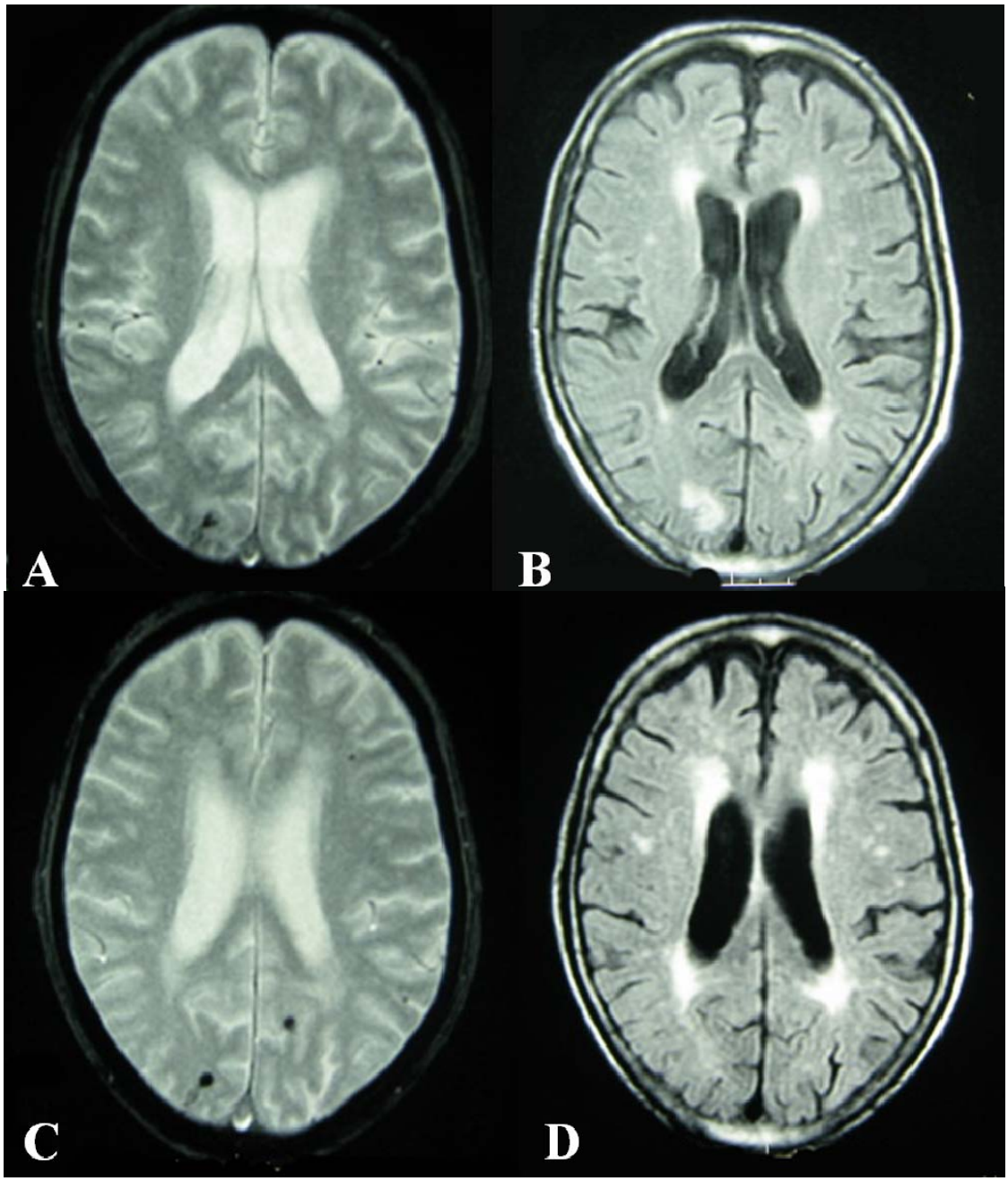

Figure 3. Initial T2*-wighted MR imaging (A) and FLAIR imaging (B) demonstrated several hypointense spots with edema formation. Follow-up T2*-weighted MR imaging (C) and FLAIR imaging (D) revealed that the number of T2*-weighted hypointense spots increased asymptomatically, whereas the perifocal edema disappeared following three-week antibiotherapy.

TABLE. Patient characteristics and MRI findings

Case No.	Age (yr) /sex	Initial symptom	Predisposing condition	Interval between onset and diagnosis	Neurological diagnosis	T2* hypointense signal spot (Number)	Increase at FU	Neurosurgical treatment	Outcome
1	23/F	General fatigue	AR, dental procedure	3m	Cerebral hemorrhage, infectious aneurysm	Multiple (6)	Yes	Resection	GR
2	75/M	Fever	MR	2w	SAH	Multiple (6)	Yes	None	DEAD
3	60/M	Character change	MVP, Hemorrhoidal ligation	3m	SAH, infectious aneurysm	Multiple (5)	Yes	Resection	GR
4	24/M	Fever	MR	2m	None	None	-	None	GR
5	52/M	Fever	MVP, teeth extraction	3m	None	None	-	None	GR
6	47/M	Lumbago	MR	5m	SAH	Single	No	None	GR
7	56/F	Fever	Aortic,mitral valve prosthesis, Cholecystectomy	1w	Subdural hematoma, cerebral infarction	Multiple (7)	Yes	None	SD
8	79/F	Rt. hemiparesis	AR	5d	Cerebral infarction (embolic)	Multiple (7)	Yes	None	GR
9	62/F	Lumbago	MVP	3m	None	None	-	None	GR
10	44/M	Lt. shoulder pain	AR	1m	Cerebral infarction	None	-	None	GR
11	73/M	Lumbago	AR, MR	1w	Cerebral hemorrhage	Single	No	None	GR

AR, aortic regurgutation; MR, mitral regurgitation; MVR, Mitral valve prolapse

m, month; w, week; d, day; SAH, subarachnoid hemorrhage; FU, follow-up; -, no follow-up; GR, good recovery; SD, severe disability