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Damage to the Contralateral Thalamus after Magnetic Resonance Imaging-guided, Focused Ultrasound Surgery for Essential Tremor: A Case Report

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Abstract

This study involved a 73-year-old man who underwent thalamotomy via magnetic resonance imaging (MRI)-guided, focused ultrasound surgery, in which the left thalamic ventral intermediate nucleus is targeted, as a treatment for action tremor of the right-hand fingers caused by essential tremor. Following treatment, the action tremor of the right-hand fingers mostly disappeared, but new symptoms of paresis and sensory impairment were evident in the left upper and lower limbs. Head MRI exhibited a hyperintense lesion on diffusion-weighted imaging and a decreased apparent diffusion coefficient in a region of the right thalamus following the anterior choroidal artery, medial posterior choroidal artery, and thalamogeniculate artery territory. Through an extensive literature search, only two reports of cavitation were found as a contributory cause of irreversible brain damage during focused ultrasound surgery, and both cases involved damage to the thalamus on the treated side. Along with a review of the literature on the mechanism of onset, a case of irreversible brain damage to the thalamus contralateral to the treated side is reported.

Keywords: focused ultrasound surgery, essential tremor, brain damage, cavitation

Introduction

Since 2019, magnetic resonance imaging (MRI)-guided, focused ultrasound surgery has been covered by Japanese National Health Insurance for the treatment of drug-resistant essential tremor. Focused ultrasound surgery is a widely employed, minimally invasive treatment[1)] that does not necessitate deep electrode implantation or trepanation. Cavitation may take place during high-power sonication, and if this occurs, the power is reduced to avoid adverse events. Therefore, reports of adverse events possibly due to cavitation in focused ultrasound surgery are rare.[2,3)] Through an extensive literature search, two cases were found in which cavitation during focused ultrasound surgery may have caused irreversible brain damage,[2,3)] and in both cases, the thalamus on the treated side was damaged. In the present case, irreversible brain damage to the contralateral thalamus was identified after treatment. This case report involves a discussion of the literature.

The patient and his family provided informed consent for this case report.

Case Report

This report presents a 73-year-old man with a chief complaint of finger tremor. He had a history of hypertension, diabetes mellitus, and polycythemia vera and was taking aspirin and amlodipine. He was a non-smoker and drank two 180-mL bottles of sake per day. He has no family history of essential tremor. He stopped treatment with medication due to non-effectiveness. Administration of aspirin was continued as per his request because he was at

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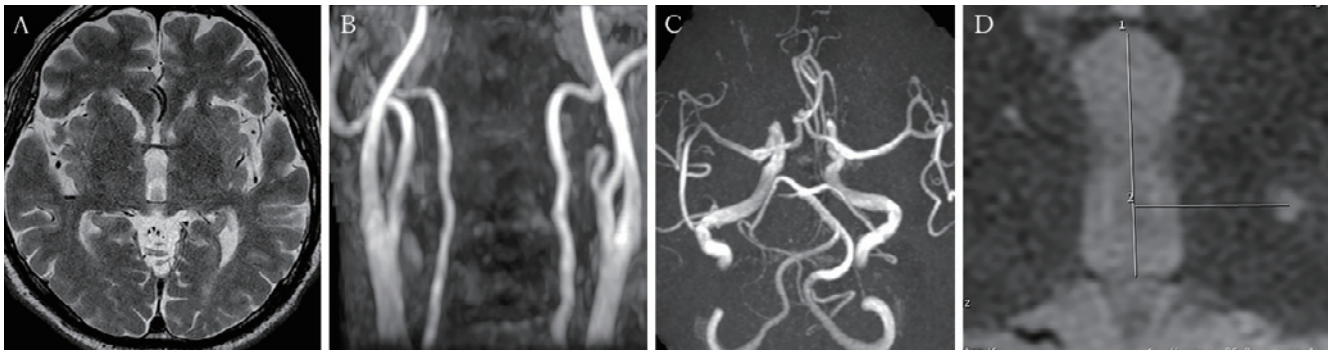

Fig. 1
A: There were almost no white matter lesions on MRI T2-weighted images prior to treatment.
B, C: There was no stenosis or occlusion in the main intracranial and cervical arteries on magnetic resonance angiography prior to treatment.
D: MRI T2-weighted image during sonication targeting the left thalamus. The right thalamus depicts no signal change.

risk for a stroke.

History of current illness

Fifty years earlier, he had stayed at a Buddhist temple for work training that was related to Buddhist altars. During that time, he was using his right hand to hold chopsticks but with difficulty because his hand trembled from tension. After learning about focused ultrasound surgery on television a year earlier, he visited our facility and was admitted for MRI-guided, focused ultrasound surgery.

Neurological findings

The patient was lucid, and his body temperature was 36.2°C; blood pressure, 122/75 mmHg; and heart rate, 58 bpm. There were finger tremors of 5 Hz in the right hand and 2 Hz in the left hand, which worsened during posture holding and action. No tremor of the neck or during speech was observed, and no extrapyramidal signs and no other abnormal findings were found.

Test findings

Blood test results were WBC 10,160/μL, RBC 5,720,000/μL, Hb 14.9 g/dL, hematocrit 49.0%, platelet count 650,000 μL, HbA1c (NGSP) 6.6%, PT-INR 0.92, HDL-C 60 mg/dL, LDL-C 149 mg/dL, neutral lipids 139 mEq/dL, serum glucose 114 mg/dL, and CRP ≤ 0.3 mg/dL. No abnormal findings on head computed tomography or MRI were found (Fig. 1A-C).

Clinical course

The tremor did not occur in a specific position and was voluntary; thus, it was not assumed to be due to dystonia. The tremor was action tremor, improved by drinking alcohol, and had been present for more than 5 years. The patient also had no extrapyramidal signs and was therefore diagnosed with essential tremor on the basis of the diagnostic criteria of Deuschl *et al.*[4] The tremor, which was drug-resistant, was treated via focused ultrasound surgery. After admission, he scored 25 points in a preliminary assessment on Part A of the clinical rating scale for tremor, primarily with finger tremor during writing and action. On day 2 of admission, tremor of the right upper limb due to right essential tremor was treated with MRI-guided, focused ultrasound, which primarily targets the left thalamic ventral intermediate nucleus (Vim). Treatment was carried out by a neurosurgeon, using Exablate 4000 (Insightec, Haifa, Israel) with a 1.5-T MRI device (GE Medical Systems [Tokyo, Japan]). First, local anesthesia was given by injecting 1% mepivacaine hydrochloride in the front, back, left, and right sides of the scalp (four sites), and a stereotactic head frame was fixed to the head. A membrane was then placed on the head, and the frame was fixed to the transducer. The space between the scalp and the transducer was filled with coolant at approximately 15°C-20°C. The skull density ratio was 0.36, the element number was 969, and the skull area was 396 mm^2. Ultrasound was employed at 0.66 MHz. The target was the left Vim, 7.2 mm anterior to the posterior commissure, 17.5 mm left lateral to the midline, and 1.5 mm above the line between the anterior and posterior commissures (Fig. 1). Calcified areas above the line between the anterior and posterior commissure were excluded beforehand as non-pass areas for ultrasound. Strong cavitation occurred during the seventh sonication at 1200 W for 26 s (Fig. 2). At this stage, the patient had no other symptoms of dizziness, and his blood pressure was elevated by approximately 20. After the seventh sonication, the de-aerated water was replaced, and the power was reduced to 1000 W to minimize the risk of recurrent cavitation, calcification was checked again, and the treatment was completed with one additional sonication. Immediately after treatment, the action tremor in the patient's right upper limb had mostly disappeared, and there was no evidence of paresis or sensory impairment in the right upper limb; however, he had a symptom of swaying

to the left side. The patient's swaying to the left suggested left-sided paralysis, although the patient was unable to be examined owing to dizziness. Due to unsteadiness when walking, he was returned to his room in a wheelchair. After his dizziness had improved, no paralysis or sensory impairment in the right upper limb was observed via examination 2 hours after treatment, and the tremor had mostly disappeared; however, a manual muscle test revealed grade 4 paresis and grade 7/10 deep sensory impairment of the left upper limb. Head MRI presented a hyperintense area in the right thalamus on diffusion-weighted imaging (Fig. 3 A). In the same area, the apparent diffusion coefficient (ADC) map demonstrated a decreased ADC (Fig. 3B), and the T2-weighted image presented a hyperintensity, which suggests acute cerebral infarction (Fig. 3C). Magnetic resonance angiography exhibited no evidence of stenosis or occlusion of the major arteries (Fig. 3D). A complication of treatment was suspected, and to reduce edema in brain-damaged area, the patient was treated with dexamethasone sodium phosphate. Given that the patient had a history of hypertension, diabetes mellitus, and polycythemia vera, cerebral infarction caused by cerebrovascular disease could not be ruled out. Thus, he was also given aspirin 100 mg/day, which he had been taking prior to surgery, and clopidogrel 300 mg on the first day, which was followed by a maintenance dose of 75 mg/day. Through MRI on the 23rd day after treatment, the brain damage to the right thalamus is now more evident (Fig. 4). The patient showed improvement with subsequent rehabilitation. No worsening of left upper and lower limb paresis or sensory impairment was observed, and he was able to walk almost unaided. He was discharged from the hospital with a modified Rankin Scale score of 2. Following surgery, although there was paresis of the left upper and lower limbs, the right upper and lower limb tremors due to essential tremor improved to 14 points on Part A of the clinical rating scale for tremor.

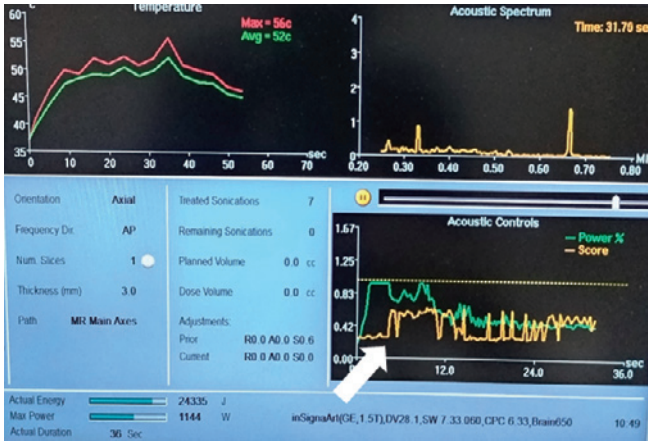

Fig. 2
Cavitation that occurred during sonication (white arrow).

Discussion

In this case, during focused ultrasound surgery of the left thalamus to treat right upper limb tremor due to essential tremor, the patient suffered contralateral brain damage. In both previous reports of brain damage as a complication of focused ultrasound surgery,[2,3] the treated side was affected (Table 1). Through an extensive search of the literature, no reports of focused ultrasound surgery accompanied by contralateral brain damage of the type observed in the present patient were found.

In focused ultrasound surgery, ultrasonic waves are emitted from the transducer for 10-20 s and destroy the tissue both via thermal coagulation and ultrasonic vibrations. Cavitation is essentially one of the main elements in numerous ultrasound treatments.[5-8] Moreover, in focused

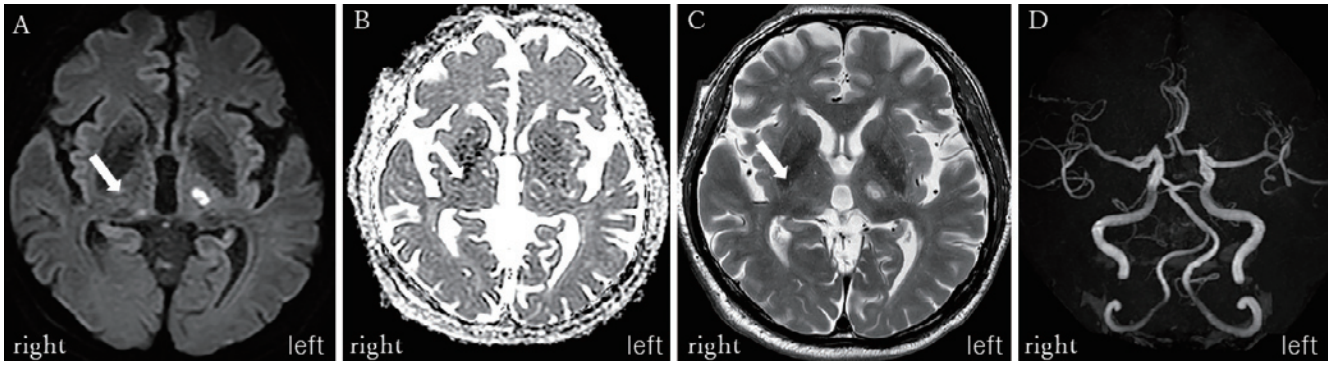

Fig. 3
A, B: Head MRI, 2 hours after sonication. The right thalamus shows hyperintensity on diffusion-weighted images and a decreased ADC on the ADC map (white arrow).
C: Head MRI T2-weighted image, 2 hours after sonication presents a hyperintense region in the right thalamus (white arrow). The lesion in the right thalamus extending outward from the pulvinar toward the internal capsule.
D: There was no obvious occlusion of intracranial arteries observed.

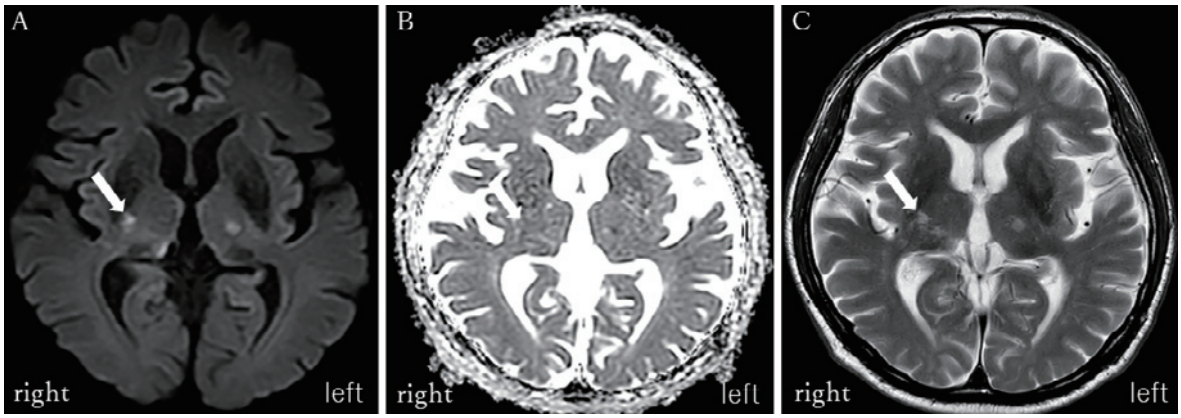

Fig. 4
A, B: Head MRI on the 23rd day after treatment. The right thalamus presents hyperintensity on diffusion-weighted images and a decreased ADC on the ADC map (white arrow).
C: Head MRI T2-weighted image on the 23rd day after treatment shows a hyperintense region in the right thalamus (white arrow). Lesions are now more evident.

Table 1 Patient and procedural details

	Authors	Treatment side	Skull density ratio	Skull vol (mm^3)	Range of energy delivered (J)	Complication side	Complication lesions	When the brain damage was discovered
1	Na Young Jung	Left	0.48	270	3000-18,700	Left	Tadpole-shaped lesions	Under treatment
2	Yamaguchi	Left	0.52	None	None	Left	Tadpole-shaped lesions	Under treatment
3	Yours truly	Left	0.36	396	3000-30,000	Right (contralateral)	Tadpole-shaped lesions	Under treatment

ultrasound surgery, cavitation is caused by the expansion of small air bubbles that are hit during sonication.[3] As power increases, the temperature increases at the sonicated site more rapidly, generating bubbles more easily and making cavitation occur more readily.[9] When cavitation happens in focused ultrasound surgery, the power is reduced until cavitation ceases. Thus, few reports were found,[2,3] in which cavitation was a suspected cause of brain damage as a treatment complication. Previous reports[3,10] have classified cavitation into two types, namely, stable and unstable. Yamaguchi et al[3] reported that stable cavitation causes reversible edematous changes in the tissue, whereas unstable cavitation involves heat and high pressure that may cause irreversible tissue changes, including hemorrhage, and extend to areas beyond the treated site. In the present patient, intense cavitation took place during therapeutic-level sonication above 50°C (Fig. 2), with no noticeable cavitation up to that point. Additionally, MRI during treatment exhibited no lesions in the right thalamus (Fig. 1). On the 23rd day after treatment, MRI revealed lesions in the right thalamus, which extended outward from the pulvinar toward the internal capsule (Fig. 4 A-C). Although it was not certain that the patient's brain damage was caused by cavitation, reports of tadpole-shaped lesions from cavitation injuries are found,[11] and considering the similarities with the present case, it appears that damage due to cavitation cannot be ruled out. The temperature of the right thalamus increased only to approximately 40°C during all sonication, which suggests that the damage was caused by cavitation. Our case also appears to be due to unstable cavitation, as reported by Yamaguchi et al. It seemed that there was almost no effect of sonication on the right thalamus.

The TRUMBI trial reported by Daffertshofer et al evaluated the usefulness of transcranial low-frequency ultrasound at 300 kHz for the treatment of acute stroke.[12] Of the bleeding complications seen in the TRUMBI trial, hemorrhage was also observed in sites other than those exposed to ultrasound. Regarding hemorrhage in areas not exposed to ultrasound, Azuma et al reported that bleeding complications were related to cavitation that resulted from ultrasound waves being reflected multiple times within the cranium.[13] Additionally, Furuhata reported that ultrasound waves are repeatedly reflected within the cranium and

sometimes overlap on the side opposite the treated side.[14] This suggests that although the previous reports[2,3] only described complications on the treated side, complications on the contralateral side are possible, as observed in the present patient.

Head magnetic resonance angiography revealed no occlusion or stenosis of the main artery of the posterior circulation. The lesion in the right thalamus was a high signal area on the diffusion-weighted image of the head MRI, and the ADCmap was decreased, which was the same finding as cerebral infarction. Since the patient's blood pressure was elevated during sonication and this case had a risk of cerebral infarction, the fact that the stress caused by sonication may have caused an accidental cerebral infarction on the contralateral side could not be ruled out. The brain damage in the present case was located in the reflux area of the medial posterior choroidal artery, thalamogeniculate artery, and anterior choroidal artery (Fig. 4), encompassing several vascular territories. The lesions were different from those of normal cerebral infarction and spread radially outward. However, he was treated with antiplatelet agents because cerebral infarction could not be ruled out and the patient had a history of hypertension, diabetes mellitus, and polycythemia vera.

In the case reported by Yamaguchi et al, suspected cavitation occurred during low-power sonication, whereas in the present patient, it occurred during high-power sonication at more than 50°C in the treatment stage. This difference may be the reason why the present patient's lesion developed in the contralateral thalamus.

The present patient's symptoms did not become apparent until after the treatment was completed because both the clinicians and the patient were focused on the symptoms on the treated side. Paresis and sensory impairment of the left upper and lower limbs may have already developed during treatment. This reveals the importance of observing and assessing symptoms both on the treated side and the contralateral side when cavitation takes place. The most important factors in cavitation prevention are control of the circulating water temperature and the oxygen concentration and prevention of ultrasonic waves from passing through calcified areas. Additionally, in cases where there is a high risk of cerebral infarction, such as this case, the possibility of cerebral infarction occurring on the contralateral side during treatment should be considered.

In conclusion, cavitation in focused ultrasound surgery normally has no irreversible effects, but it may cause brain damage in rare cases, as was observed in the present patient. Attention should be paid to contralateral symptoms, considering that brain damage may occur not only on the treated side but also on the contralateral side. For cavitation prevention, control of the circulating water temperature and oxygen concentration and prevention of ultrasonic waves from passing through calcified areas are crucial.

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Conflicts of Interest Disclosure

The authors declare no conflicts of interest that are directly relevant to the content of this article.

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