Diffusion-Weighted Magnetic Resonance Imaging in Brain Death

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Background—Traditionally the diagnosis of brain death is established on the basis of a combination of clinical signs and paraclinical methods. Diffusion-weighted MRI is a new method sensitive to cerebral ischemia. Its value in brain death has not been demonstrated until now.

Case Description—A patient was referred to MRI with suspicion of a brain stem stroke. Echo-planar whole-brain, multislice, diffusion-weighted MRI was performed in addition to conventional sequences and MR angiography sequences. In addition to the extensive bilateral hyperintensities observed on T2-weighted images, diffusion-weighted MRI showed diffuse hyperintensities involving both hemispheres as well as a severe drop in the apparent diffusion coefficient in both affected hemispheres. There was also transtentorial herniation with compression of the brain stem as well as absence of flow voids on the T2-weighted images and absence of intracranial vessels on MR angiography. On the basis of the clinical and imaging findings, it was concluded that the patient was in a state of brain death. The patient died the same day.

Conclusions—With the use of new fast techniques such as diffusion-weighted imaging, now MRI can not only display anatomic changes associated with severe brain suffering but can also demonstrate ultrastructural changes secondary to brain death and differentiate them from edematous changes seen on T2-weighted images. (Stroke. 2000;31:539-542.)

Key Words: brain death ■ magnetic resonance imaging ■ magnetic resonance imaging, diffusion-weighted

Brain death is the irreversible cessation of function of the brain, including the brain stem; the diagnosis of brain death is primarily based on clinical criteria, usually supported by confirmatory tests.1 Diffusion-weighted MRI (DWI) of the brain is establishing itself as a sensitive method for the detection of cerebral ischemic changes2–4; the use of DWI to determine brain death has not been reported previously. Traditionally, brain death has been demonstrated with angiography or radiotracer methods. MRI has been shown to demonstrate brain herniation and absent vascular flow.5–8 We report the case of a 78-year-old woman who was found unconscious one morning and who was admitted to our hospital with signs of pyramidal tract lesions. MRI of the brain showed diffuse T2-weighted hyperintensities of both hemispheres as well as transtentorial herniation of the left temporal lobe, leading to compression of the brain stem. On DWI, both hemispheres showed restricted diffusion corresponding to severe ischemia, with a drop in the values of the apparent diffusion coefficient (ADC). There was no flow in the carotid arteries. On the basis of these findings, it was concluded that the patient was in a state of brain death.

Case Report

This 79-year-old woman was hospitalized because of sudden coma with irregular convulsions of her 4 limbs. The subject had a history of ischemic cardiac disease with myocardial infarction. Additionally, there was a history of ischemic cardiac disease with myocardial infarction 5 years previously, chronic atrial fibrillation, and a right hemispheric transient ischemic attack in 1994. Clinical examination at admission revealed deep coma with a Glasgow Coma Scale score of 4 (extension of 4 limbs after painful stimuli); small but reactive pupils of the same size; decreased corneal reflexes on the left more than on the right; absent oculocephalic reflexes; normal coughing and breathing; and tetrahyperreflexia with Babinski's sign bilaterally. The patient was transferred to the medical intensive care unit of our institution and intubated. The next day MRI of the brain was performed.

Examination Technique

DWI was performed on a 1.5-T Magnetom Vision system (Siemens Medical Systems), equipped with a head coil, with an echo-planar sequence. An isotropic sequence was used (repetition time [TR]=4000 ms, echo time [TE]=133 ms, field of view [FOV]=210 mm, matrix=128×128, number of excitations=4) with b values of 0 and 972 s/mm². The diffusion coefficients were calculated on a pixel-by-pixel basis, and ADC maps were generated with online software available from the manufacturer. Normal ADC values obtained previously in 30 volunteers are as follows: white matter,
0.825×10⁻³ mm²/s; gray matter, 0.750×10⁻³ mm²/s. Then axial T2-weighted imaging (TR=3176 ms, TE=98 ms, 5.0-mm-thick slices, FOV=148×148, matrix=150×256) was performed, followed by coronal T2-weighted imaging (TR=3640 ms, TE=96 ms, 4.0-mm-thick slice, FOV=160×160, matrix=280×512, 2 acquisitions). Subsequently MR angiography was performed with a time-of-flight sequence.

DWI showed diffuse hyperintense areas covering almost both hemispheres entirely, corresponding to diffuse edema (Figure 1). ADC values were as follows: frontal gray matter, 0.45 mm²/s; frontal white matter, 0.397×10⁻³ mm²/s; parietal gray matter, 0.475×10⁻³ mm²/s; parietal white matter, 0.388×10⁻³ mm²/s; occipital gray matter, 0.509×10⁻³ mm²/s; occipital white matter, 0.293×10⁻³ mm²/s; temporal gray matter, 0.509×10⁻³ mm²/s; temporal white matter, 0.480×10⁻³ mm²/s; basal ganglia, 0.547×10⁻³ mm²/s; and cerebellar hemisphere, 0.753×10⁻³ mm²/s. The axial MR images showed diffuse brain swelling with hyperintense areas in both hemispheres, more on the left on T2-weighted imaging (Figures 2 and 3).

Areas of hemorrhage in the right-sided basal ganglia were also noted. The ventricular system was shifted slightly to the right. Additionally, there was a mass in front of the pons on all axial imaging modalities (Figure 2), which corresponded to the herniated medial temporal lobe on the coronal images (Figure 3). On conventional MRI modalities there was no flow void in the carotid arteries; on the MR angiography sequences there was an absence of flow in both carotids as well.

The neurological examination after the MRI showed an intubated comatose patient who had deteriorated neurologically. On the basis of these findings together with the MR results, the patient was considered to be in a state of brain death. The patient died later the same day.

Discussion

With more widespread organ transplantation programs being available, interest in an accurate diagnosis of brain death has increased. The clinical diagnosis of brain death relies on the presence of a deep unresponsive coma, no brain stem function, and no respiratory reflex, usually supported by further tests. Tests previously used to establish the diagnosis of brain death include (1) nuclear medicine studies, which show an absent intracranial perfusion in the presence of normal extracranial circulation; (2) conventional cerebral angiography; and (3) electroencephalography or Doppler ultrasound. Electroencephalography, which was not performed in this case, is known to have induced wrong diagnoses. MRI has already been shown to demonstrate phenomena such as the absence of flow voids in the internal carotid arteries, as well as absence of cerebral perfusion and increased enhancement of facial structures (eg, the “hot nose sign”). Orrison et al found the MR criteria of brain death to include the following: transtentorial herniation and foramen magnum herniation, absent intracranial vascular flow voids, poor differentiation

Figure 1. Diffusion-weighted MR slice at a maximum b value (TR=4000 ms, TE=135 ms, FOV=210 mm, matrix=128×128, number of excitations=4) of 972 s/mm². Both hemispheres are hyperintense, corresponding to a drop in the ADC. In the right basal ganglia there is an area of signal loss corresponding to hemorrhage. Only the right-sided occipital cortex is slightly spared.

Figure 2. Axial T2-weighted slice (TR=3176 ms, TE=98 ms, 5.0-mm-thick slices, FOV=148×148, matrix=150×256) at the same level as Figure 1 showing diffuse hyperintensity in the left-sided cortex as well as in the medial right-sided temporal lobe. A prepontine mass that is also hyperintense is shown as well.
DWI provides an approximation of the molecular motion of water molecules in a tissue sample. In the case of cerebral ischemia, it is believed that after reduction in cerebral blood flow and the beginning of ischemia, there is a dysfunction of the membrane-bound Na,K-ATPase pump, leading to the entrance of extracellular water into the cells and consequent swelling. Studies in animal models of stroke have shown these findings to correlate with the appearance of changes on DWI, in which an increase in signal (hyperintensity) corresponds to a decrease in local water mobility and a decrease in the ADC. However, similar decreases in the ADC may also be seen in other circumstances, such as hypoglycemia, spreading depression, and status epilepticus. The common mechanism in these conditions is an abrupt shift of water from extracellular to intracellular compartments; eventually a simple reduction of intracellular water motion or an increase in intracellular viscosity is a possible explanation for the decrease in ADC. Studies of human stroke have now shown a method to demonstrate early cerebral ischemia. However, not all hyperintensities seen on DWI may correspond to ischemia, and there is still some debate regarding the eventual significance of these changes. In venous infarction, there seems to be an important vasogenic rather than cytotoxic component to the edema; this was demonstrated in an animal model by Röther et al and reported in a human case by Corvol et al.

In addition, on the basis of the initial clinical findings that had prompted the MRI, the suspected preliminary diagnosis was a brain stem stroke; however, only MRI could show the presence of diffuse supratentorial bilateral infarcts, contradicting the clinical findings. MRI in this case could demonstrate the presence of typical findings of brain death: transtentorial herniation, the absence of intracranial vascular flow voids, and poor gray matter/white matter differentiation. Reich et al found a good correlation between imaging and clinical findings with at least a mild degree of vertical displacement on imaging. The addition of DWI allows demonstration of the presence of diffuse ischemia in addition to the hyperintense changes seen on conventional T2-weighted imaging. Indeed, while T2-weighted imaging demonstrates brain swelling and edema, it cannot differentiate between cytotoxic and vasogenic edema, and it is the combined additional use of DWI and ADC mapping that shows that the edema is of a cytotoxic nature and therefore corresponds not only to edema but also to ischemic tissue. While the DWI images themselves are helpful, calculating the ADC helps to establish the nature of the disease since it rules out the presence of T2-weighted changes in the generation of the high signal seen on DWI (the so-called T2 shine-through effect). Therefore, in addition to demonstrating previously known features of brain death, MRI can now, with the addition of diffusion-weighted sequences, demonstrate on the molecular level the deeply ischemic nature of the changes, which are so extensive both anatomically and functionally that they are not compatible with survival. Indeed, the combined findings of absent flow on angiographic MR/ conventional MR images, the presence of decreases in ADC in both hemispheres, and signs of brain stem displacement, as observed in this case, may be helpful in establishing the

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Figure 3. Coronal T2-weighted MR image (TR=3640 ms, TE=96 ms, 4.0-mm-thick slice, FOV=160×160, matrix=280×512, 2 acquisitions) displaying bilateral hemispheric infarcts with consecutive transtentorial herniation of the medial temporal lobe on the left, leading to brain stem compression.

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between gray and white matter, absent intracranial enhancement, carotid artery enhancement, and the hot nose sign. MR angiography does not display the supraclinoid carotid arteries, as in this case. This may be due to the increased intracranial pressure associated with this condition.

On the basis of the imaging findings, it was concluded that the patient had entered a state of brain death. Although she had presented with other slightly different clinical findings initially, she had progressively deteriorated; this shows that the passage into a state of brain death is a continuum and not a sudden event.

To our knowledge this represents the first reported case of the use of DWI in the determination of brain death. This case involved a massive bilateral hemispheric brain infarction with a massive drop in ADC values compared with those of a normal population. In other studies this decrease in ADC values has been to <50% of normal values. For ischemic stroke, Schlaug et al found an approximate drop in the ADC of 41.7%, corresponding to previous animal results of 30% to 60% decreases. Our ADC values were between 35% and 72% (mean value, 57%) of normal expected values and were also associated with T2-weighted hyperintensities beyond those expected in ischemic stroke. While the ADC changes demonstrate the presence of deep ischemia subsequent to absent cerebral blood flow, the T2-weighted hyperintensities simply confirm the presence of these profound changes. Indeed, “conventional” MRI cannot differentiate between cytotoxic and vasogenic edema. Preliminary human data have demonstrated DWI to be a powerful and sensitive tool for the differentiation between cytotoxic and vasogenic edema, as in the case of eclampsia.
diagnosis of brain death in the future in a noninvasive manner, in addition to established clinical findings. The use of DWI for such purposes requires further study.

References
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