

Magnetic Resonance Diffusion Weighted Imaging in Cerebral Fat Embolism

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ABSTRACT: The use of diffusion weighted imaging with apparent diffusion coefficient mapping in the diagnosis of cerebral fat embolism is shown here to demonstrate infarcts secondary to fat emboli more intensely than T2 weighted sequences 24 hours after the onset of symptoms. Embolic foci are hypointense on apparent diffusion coefficient mapping consistent with cytotoxic edema associated with cell death and restricted water diffusion. This technique increases the sensitivity for detecting cerebral fat embolism and offers a potentially important tool in its diagnosis.

RÉSUMÉ: Imagerie de diffusion par résonance magnétique dans l'embolie graisseuse cérébrale. L'utilisation de l'imagerie de diffusion par résonance magnétique avec cartographie du coefficient apparent de diffusion pour diagnostiquer l'infarctus secondaire à l'embolie graisseuse visualise mieux ces infarctus que les séquences pondérées T2, 24 heures après le début des symptômes. Les foyers emboliques sont hypointenses à la cartographie par mesure du coefficient apparent de diffusion, ce qui est compatible avec un oedème cytotoxique associé à la mort cellulaire et une diffusion aqueuse réduite. Cette technique est plus sensible pour détecter l'embolie graisseuse cérébrale et pourrait s'avérer un outil précieux pour poser ce diagnostic.

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Fat embolism syndrome (FES) is a collection of signs and symptoms typically occurring 12 to 36 hours after trauma or surgery and consisting of the classical triad of respiratory insufficiency, skin petechiae, and cerebral decompensation.^{1,2} It is often the sequelae of displaced long bone fractures of the lower extremities, and is a potentially lethal complication.³ Neurologic involvement in FES has been termed cerebral fat embolism (CFE) and has traditionally presented a diagnostic challenge. Computed tomography (CT) has demonstrated only limited sensitivity in the diagnosis of CFE.^{4,5} Traditional T1, T2, and proton density magnetic resonance imaging (MRI) sequences have proven effective in the diagnosis of CFE.⁶⁻⁹ Relatively new diffusion weighted imaging (DWI) techniques used in the setting of acute cerebral stroke are more sensitive than T2 weighted imaging.¹⁰ Diffusion weighted imaging may offer improved diagnostic potential in the setting of CFE. The application of DWI in two cases of CFE is discussed.

PATIENT 1

A 25-year-old male presented to a major trauma center following a motorcycle accident. The patient had sustained a closed, transverse, proximal left femur fracture. There was momentary loss of consciousness at the scene with a normal admission head CT scan. The injury was treated by open reduction with intramedullary rod and screw fixation on the same day.

Within 24 hours postoperatively, the patient developed dyspnea, hypoxemia, diffuse pulmonary edema, encephalopathy, subconjunctival and axillary petechiae consistent with a clinical diagnosis of FES. The patient was confused but demonstrated no focal neurological symptoms.

An MRI scan was performed two days after admission. Multiple, bilateral, tiny, punctuate hyperintense foci were identified in the periventricular and deep white matter on T2 weighted images (T2WI) (Figure 1A) and fluid-attenuated inversion recovery (FLAIR) images (Figure 1B). These foci appeared more intense and were more numerous on DWI (Figure 1C). An ADC map demonstrated these areas to be hypointense, consistent with restricted diffusion of water (Figure 1d). Magnetic resonance angiography of the intracranial circulation was normal.

The patient's clinical course was complicated by a retroperitoneal hemorrhage believed to be secondary to heparinization. The patient made a full neurological recovery and was discharged from hospital 12 days following admission.

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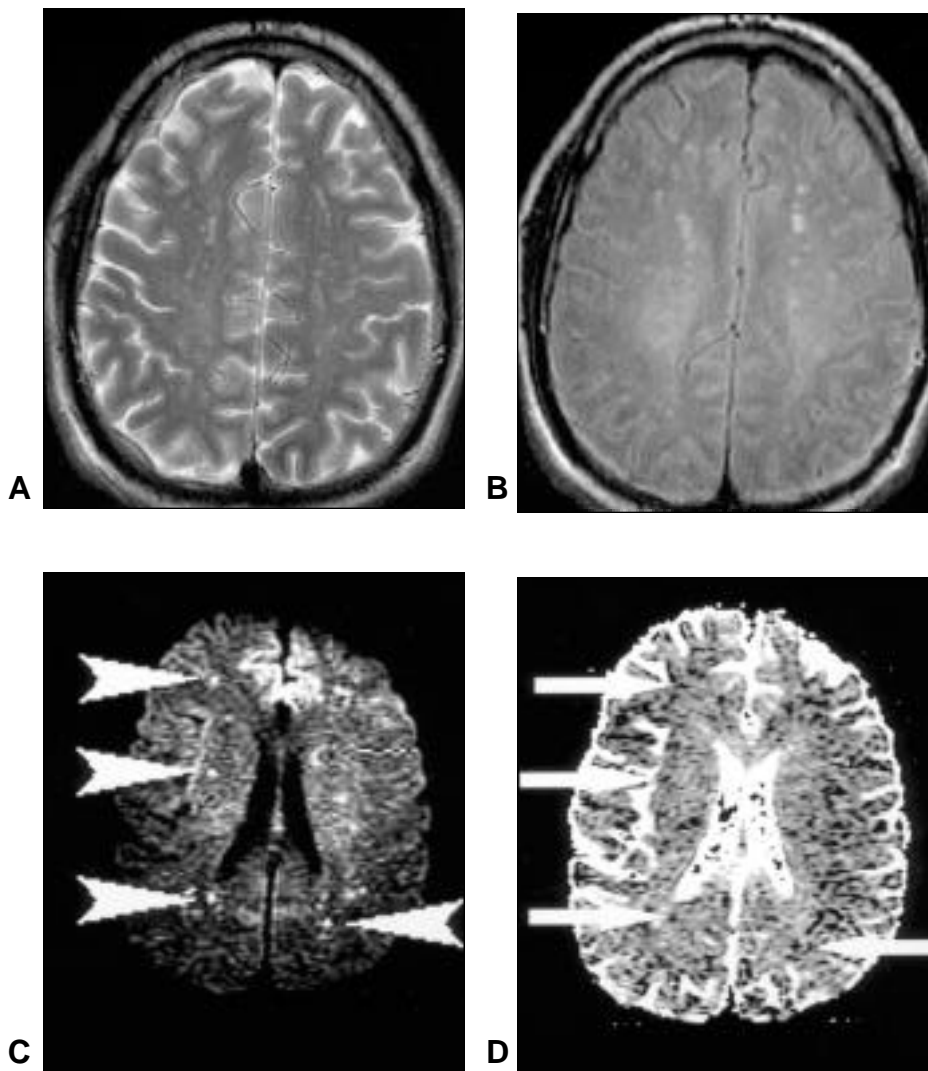


Figure 1: Patient 1 postoperative MRI two days postadmission. (a) Axial T2 weighted and (b) FLAIR images show multiple hyperintense foci throughout the subcortical and periventricular white matter. (c) Diffusion weighted images (DWI) and (d) apparent diffusion coefficient (ADC) map shows hyperintense (arrowheads) and hypointense (arrows) foci respectively, corresponding to regions of restricted water diffusion.

PATIENT 2

A 23-year-old male was involved in a low speed motor vehicle accident. The patient was hemodynamically stable at the scene, showed no evidence of head injury, and there was no alteration in his consciousness en route to hospital. The initial chest radiograph and CT of the head were normal.

The following morning the patient underwent open reduction and internal fixation of open fractures to the right femur and tibia with insertion of intramedullary rods into the femur and tibia. Immediately postoperatively, the patient was obtunded out of proportion to the degree of anesthesia and went into hypoxemic respiratory failure in the recovery room. Neurological examination revealed mixed decorticate and decerebrate posturing, no spontaneous limb movement, and bilateral upgoing plantar responses. Brainstem reflexes were intact. A repeat CT scan of the head was normal.

During the next 24 hours, the patient developed thrombocytopenia and anemia. No petechiae or rash was observed. An MRI of the brain 24 hours after admission revealed numerous small T2 (Figure 2a) and FLAIR (Figure 2b) hyperintense foci throughout the brainstem, cerebellar hemispheres bilaterally, the basal ganglia, the thalami bilaterally, and the cerebral hemispheres bilaterally. T2 hyperintense lesions were also noted throughout the cerebral white matter bilaterally in both subcortical and periventricular locations. All of the lesions, as well as multiple other lesions not detected on T2WI, demonstrated hyperintensity on DWI (Figure 2c) and decreased signal on the ADC map (Figure 2d) in keeping with small infarcts. No lesions were seen on the T1 weighted images (T1WI) (Figure 2e). Gradient echo images showed no evidence of hemosiderin deposition (Figure 2f). Magnetic resonance angiography of the intracranial circulation was normal. The diagnosis of multifocal infarcts secondary to fat embolism was made.

On day 12, the patient's neurological status was unchanged. A repeat

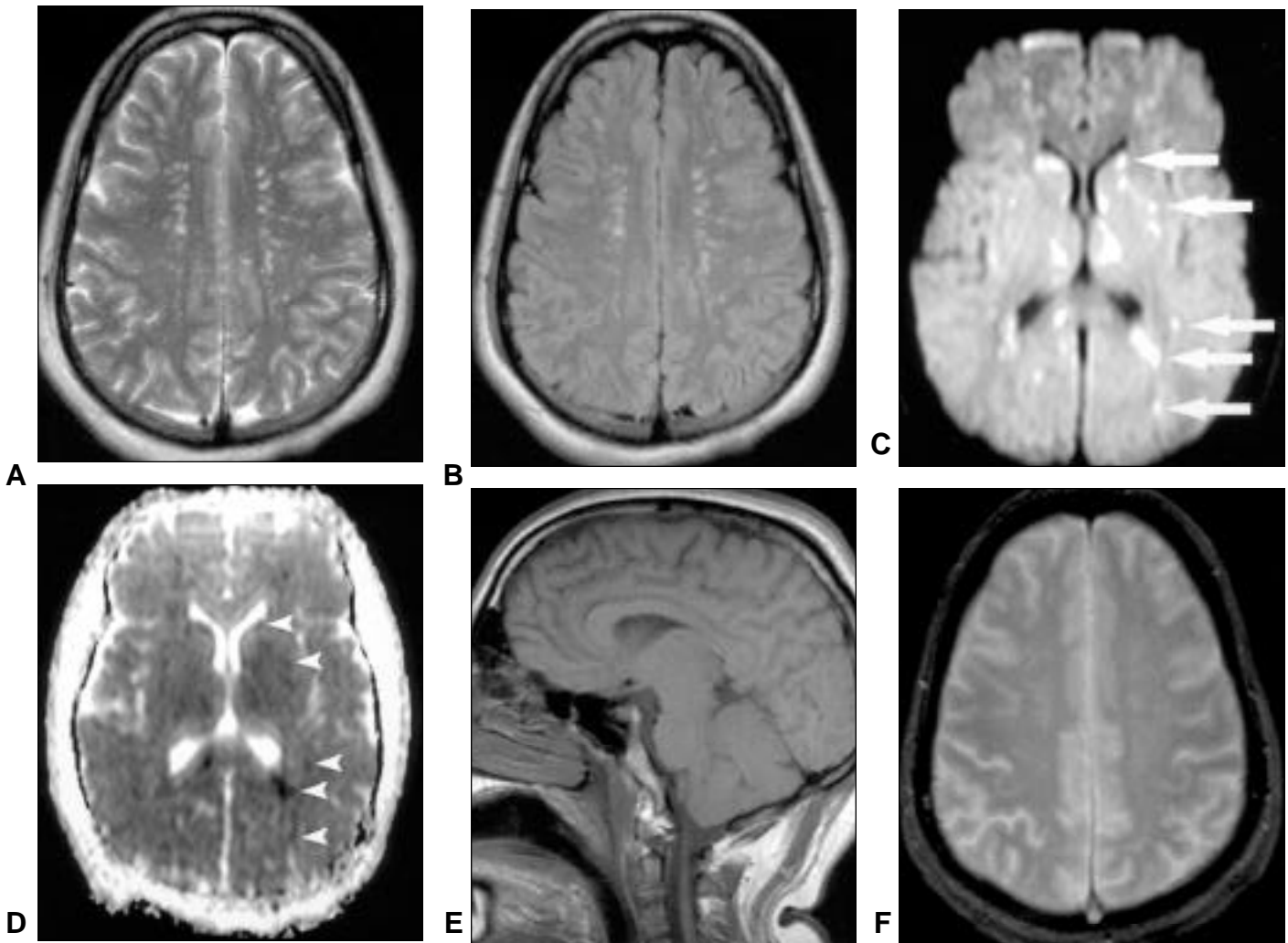


Figure 2: Patient 2 initial postoperative MRI at 24 hours postadmission. (a) T2 weighted and (b) FLAIR images show multifocal T2 hyperintense lesions involving both cerebral hemispheres, the subcortical white matter, both thalami, and basal ganglia. Regions of restricted diffusion are evident (arrowheads) with increased signal on the (c) DWI (B1000) and decreased signal (arrows) on the (d) ADC map corresponding to the regions of T2 hyperintensity. (e) Sagittal T1WI shows no visible increased signal suggestive of macroscopic fat deposition. (f) Gradient echo images show no evidence of hemosiderin deposition.

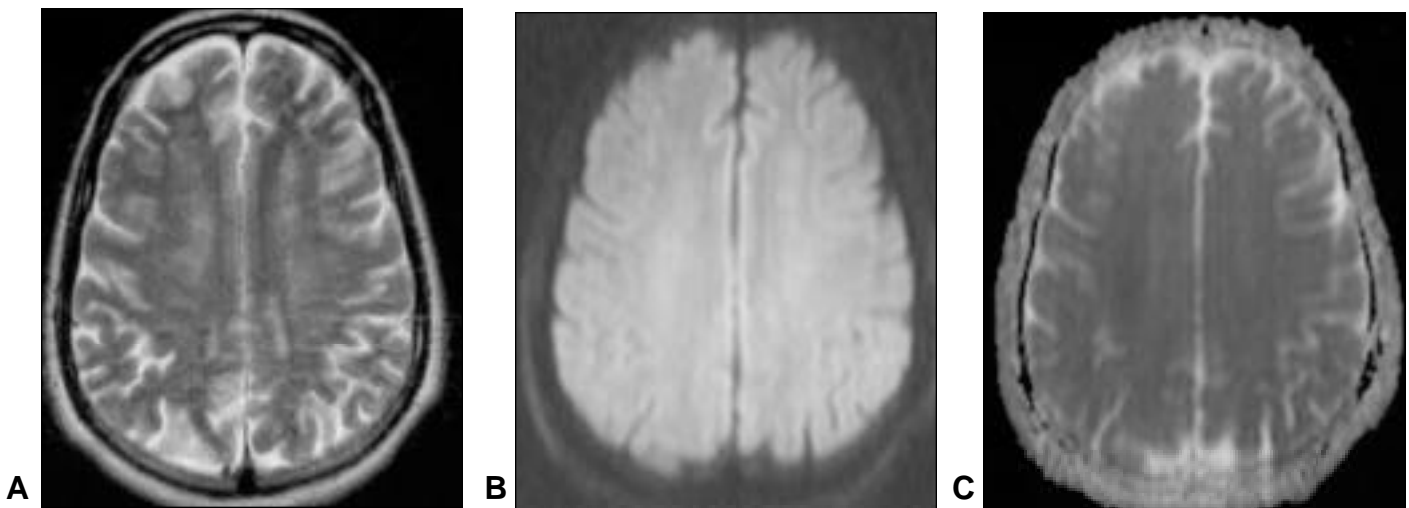


Figure 3: Patient 2 follow-up MRI at 34 days postadmission. (a) Complete resolution of the T2 hyperintense lesions. (b & c) Complete resolution of the lesions on (b) DWI and (c) ADC map.

MRI of the brain demonstrated confluence of the T2 hyperintense lesions and return of normal signal on the DWI and the ADC map. The results of echocardiography were normal. A transcranial Doppler bubble study showed no right-to-left shunting. Two weeks postoperatively, the patient began to open his eyes but would not follow commands or move his limbs. At six weeks, he was moving all limbs and was walking with minimal assistance. He was able to perform all activities of daily living but was unable to write and demonstrated a constructional apraxia.

On day 34, a follow-up MRI of the brain showed complete resolution of the lesions on the T2 weighted sequence (Figure 3a) and the DWI/ADC images (Figures 3b & 3c).

DISCUSSION

Magnetic resonance imaging has proven to be a useful diagnostic tool in CFE.^{6-9,11} Specifically, T2WI is more sensitive than T1WI in the diagnosis of CFE.⁶ This case demonstrates the increased sensitivity of DWI with associated ADC mapping in the detection of CFE.

Diffusion weighted MR imaging is a relatively new technique that is sensitive to the microscopic movement of water. This sequence has demonstrated sensitivity in the diagnosis of acute ischemic stroke.¹⁰ In the cases presented, DWI changes within 24 hours of symptom onset correlate with findings on the T2WI and FLAIR sequences. The conspicuity of the ischemic foci is increased, insofar as their intensity and number on DWI images. These same foci appear hypointense on the ADC map consistent with cytotoxic edema associated with cell death and restricted water diffusion.^{12,13} Recent animal studies of CFE with correlative MR and electron microscopic findings have shown that the enhancement pattern of CFE differs significantly from that of a purely ischemic control group.¹⁴ Cytotoxic edema was confirmed on the diffusion-weighted images in both groups, but the marked enhancement on enhanced T1WI in the CFE group was not present in the ischemic control group. Other reports have suggested that this confirms breakdown of the blood brain barrier associated with the cytotoxic and vasogenic edema characteristic of pathological findings of CFE on electron microscopy.^{14,15} Diffusion weighted imaging and T2WI findings were present as early as 30 minutes post-fat embolization, suggesting these sequences may be a useful diagnostic tool in the hyperacute setting.¹⁴

The embolic foci identified in these cases were centered primarily in the periventricular and deep white matter. White matter is more susceptible to ischemic injury and anoxic cell death. This is by virtue of the paucity of collateral vascularity in white relative to gray matter.² These findings are consistent with neuropathological descriptions of CFE.² At autopsy, multiple petechiae are localized in white matter in patients with CFE.² Microscopically, fat globules from bone marrow block small vessels and capillaries resulting in neuronal cell death and tissue necrosis.² This characteristically affects white matter of the cerebrum and brain stem producing foci of petechial hemorrhage and edema.² As has been suggested by other reports, gradient echo imaging is useful in the search for hemosiderin deposits that determines whether parenchymal hemorrhage, in the setting of diffuse axonal injury, contributes to the findings seen on T2WI and DWI.¹⁵ There were no blood breakdown products seen on the gradient echo images of the second patient, and thus diffuse

axonal injury was not considered to be a prominent contributor to the patient's significant clinical deterioration.

At this time, the pathogenesis is not well-understood, but presumably fat globules travel from the fracture site and enter the systemic circulation by traversing the pulmonary vascular beds or via intracardiac shunts, such as a patent foramen ovale.¹ This may explain why cerebral symptoms are less common than respiratory symptoms in FES.² Alternatively, traumatic injury can cause elevated levels of plasma lipase and catecholamines which mobilize the body's fat stores and result in the release of free fatty acids (FFA) in the blood. The FFAs may cause local inflammatory reactions which result in platelet coagulation and microvascular thrombosis and petechiae.^{16,17} In experimental models, it has been shown that both FFAs and neutral fat can cause vasogenic and cytotoxic edema in the setting of CFE. However, the severity of tissue damage produced by FFAs on electron microscopy is greater than that of neutral fat.¹⁸

The CT findings of CFE are nonspecific, and in the absence of traumatic head injury, often normal.^{4,5} Rarely, low density areas in white matter are seen post long bone fractures.^{5,8} The patients presented here did not demonstrate changes on their admission CTs. This modality may best serve to exclude traumatic brain injury as a cause when CFE is suspected.⁸

These cases illustrate the potential importance of diffusion weighted MRI and ADC mapping in the diagnosis of CFE. It has been suggested by others that DWI should be the first step in a diagnostic algorithm to rule out CFE.¹⁹ A prospective study is currently underway at this institution to further evaluate this role. Specifically, we wish to determine if there is evidence of cerebral edema by DWI techniques in trauma patients who undergo intramedullary femoral nailing following femoral fracture.

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