Magnetic Resonance Imaging Findings in Cerebral Fat Embolism: Correlation with Clinical Manifestations

[Article: Presented At The 28Th Annual Meeting Of The Western Trauma Association, February 22-28, 1998, Lake Louise, Alberta, Canada]

Takahashi, Makoto MD; Suzuki, Ryuta MD; Osakabe, Yoshimi MD; Asai, Jun-Ichiro MD; Miyo, Takayasu MD; Nagashima, Goro MD; Fujimoto, Tsukasa MD; Takahashi, Yoshiki MD

From the Department of Neurosurgery (M.T., R.S., J.-I.A., T.M., G.N., T.F.), Showa University, Fujigaoka Hospital, and Department of Emergent Care Medicine (Y.O., Y.T.), Showa University, Fujigaoka Hospital, Yokohama, Japan.
   Address for reprints: Ryuta Suzuki, MD, Department of Neurosurgery, Showa University, Fujigaoka Hospital, 1-30 Fujigaoka, Aoba-ku, Yokohama, 227-8501, Japan. email: ryuta@med.showa-u.ac.jp.

Abstract

   Objectives: Cerebral fat embolism (CFE) is a serious complication after fracture of long bones. The mortality rate of CFE may be high. However, recent progress in treatment may decrease the mortality. We studied the validity of magnetic resonance imaging (MRI) to detect and grade severity of CFE in 11 patients with CFE.

   Methods: Glasgow Coma Scale score, PaO_2, $PaCO_2$ at the onset, and minimal hemoglobin and platelet levels were monitored, and phagocytes in bronchoalveolar lavage fluid were counted. Brain computed tomographic and MRI scans were performed serially. MRI findings were graded into four categories according to the severity of $T_{2-weighted}$ images.

   Results: High-intensity T_2 signals were identified in the various brain regions as early as 4 hours after onset of CFE. The maximum MRI grade significantly correlated with Glasgow Coma Scale score at the onset of CFE ($p < 0.01$). High-intensity T_2 signal lesions fused and enlarged with time. In most cases, they diminished within 2 weeks. Three patients had persistent morbidity.

   Conclusion: MRI-$T_{2-weighted}$ imaging seems to be the most sensitive imaging technique for diagnosing CFE, and correlates well with the clinical severity of brain Injury. With the aid of proper treatment for pulmonary fat embolism, CFE is a potentially reversible disease that can have a good outcome.

Key Words: Fat embolism, Cerebral fat embolism, MRI, Brain edema.

   Cerebral fat embolism (CFE) is a serious complication after fractures of long bones. Although the incidence of CFE may be as low as 0.9 to 2.2% among patients with a long bone fracture, [1] CFE is not uncommon among patients admitted to trauma centers. The mortality associated with fat embolism has been reported to be 13% to 87%; [1-3] however, this rate has decreased with recent progress in respiratory and intensive care. [4] Early diagnosis and intensive respiratory care are mandatory for

achieving good outcome.

Specific diagnostic criteria of fat embolism were proposed by Gurd and Wilson. [2] However, many cases are difficult to diagnose, and the diagnostic criteria for CFE have little prognostic value. We report 11 cases of clinically proven CFE with serial magnetic resonance imaging (MRI) and computed tomography. A close relationship between the clinical manifestations and MRI appearances of the brain in patients with CFE is proposed.

MATERIALS AND METHODS

Between June of 1991 and October of 1994, 14 patients were admitted to the emergency center of Showa University Fujigaoka Hospital with the diagnosis of fat embolism according to the criteria of Gurd and Wilson [2] (Table 1). Among those patients, 11 patients presented with delayed neurologic deterioration and were diagnosed as having CFE. The patients' clinical manifestations are listed in Table 2. All patients experienced respiratory distress due to pulmonary fat embolism (PFE) followed by depressed level of consciousness or confusion with a latent period of 11 to 48 hours (28.0 +/- 12.4 hour, mean +/- SD) after trauma. Of 11 patients, 10 patients were transferred to the emergency center of Showa university Fujigaoka Hospital from local hospitals because of deteriorating neurologic status.

Major
  Petechial rash
  Respiratory symptoms plus bilateral signs with positive
    radiographic changes
  Cerebral signs unrelated to head injury or any other condition
Minor
  Tachycardia
  Pyrexia
  Retinal changes (fat or petechiae)
  Urinary changes (anuria, oliguria, fat globules)
  Sudden drop in hemoglobin level
  Sudden thrombocytopenia
  High erythrocyte sedimentation rate
  Fat globules in the sputum

[a] The clinical diagnosis was made when at least one major feature plus four minor features of fat embolism were present. Diagnostic criteria as revised by Gurd and Wilson.[2]

Table 1. Clinical diagnostic criteria of fat embolism[a]

Case	Age (yr)	Sex	Latent Period (hr)	GCS	Minimum Hemoglobin (g/dl)	PaO_2 (mm Hg)	PaCO_2 (mm Hg)	Minimum Platelets	Maximum MRI Grade	GOS
1	19	M	11	3	5.5	42.7	30.1	36,000	3	VS
2	19	M	17	8	7.1	49.4	28.3	43,000	3	SD
3	52	M	48	14	10.2	25.7	44.5	81,000	1	MD
4	19	M	24	6	9.2	35.2	45.5	65,000	3	GR
5	21	M	20	8	9.5	58.8	40.4	129,000	2	GR
6	21	M	45	14	10.8	62.9	32.5	134,000	1	GR
7	20	M	18	13	10.0	62.4	37.6	71,000	1	GR
8	27	M	35	10	8.8	264.4	38.5	111,000	1	GR
9	20	M	23	8	8.7	42.8	27.7	97,000	3	GR
10	24	M	45	14	10.2	282.6	33.7	159,000	2	GR
11	33	M	22	8	6.5	173.1	33.1	49,000	2	GR

[a] GCS, Glasgow Coma Scale Score; GOS, Glasgow Outcome Scale; M, male; VS, persistent vegetative state; SD, severely disabled; MD, moderately disabled; and GR, good recovery.

Table 2. Patients' clinical manifestations[a]

All patients were men, between the ages of 19 and 52 years (mean, 26.7 years). Only two patients were older than 30 years. All were involved in motor vehicle crashes including seven motorcycle crashes, two automobile crashes, and two pedestrians struck by vehicles. The patients presented with one to three long bone fractures in their legs, but they did not demonstrated any neurologic symptoms caused by primary brain damage during the initial period after trauma. Immediately after admission, bronchoalveolar irrigation was performed and fat droplets and alveolar phagocytes in the bronchoalveolar lavage fluid (BALF) were identified.

Initial MRI of the brain or computed tomographic (CT) scans were performed in 10 cases within 2 days after the onset of neurologic deterioration. The remaining case (case 9) was scanned 8 days after injury. Serial MRI scans of the brain were performed in 10 cases during the follow-up period. Case 6 only received one MRI examination. MRI findings were graded into four categories according to the severity of the brain lesions observed on $T_{2-weighted}$ MRI images (T2WI): grade 0, no abnormalities; grade 1, several small spotty high-intensity lesions seen in the deep white matter or deep brain structures; grade 2, either many small spotty high-intensity lesions or macular lesions which represented confluent spotty lesions in the deep white matter or deep brain structures; grade 3, large macular high-intensity lesions in the deep white matter (Figure 1).
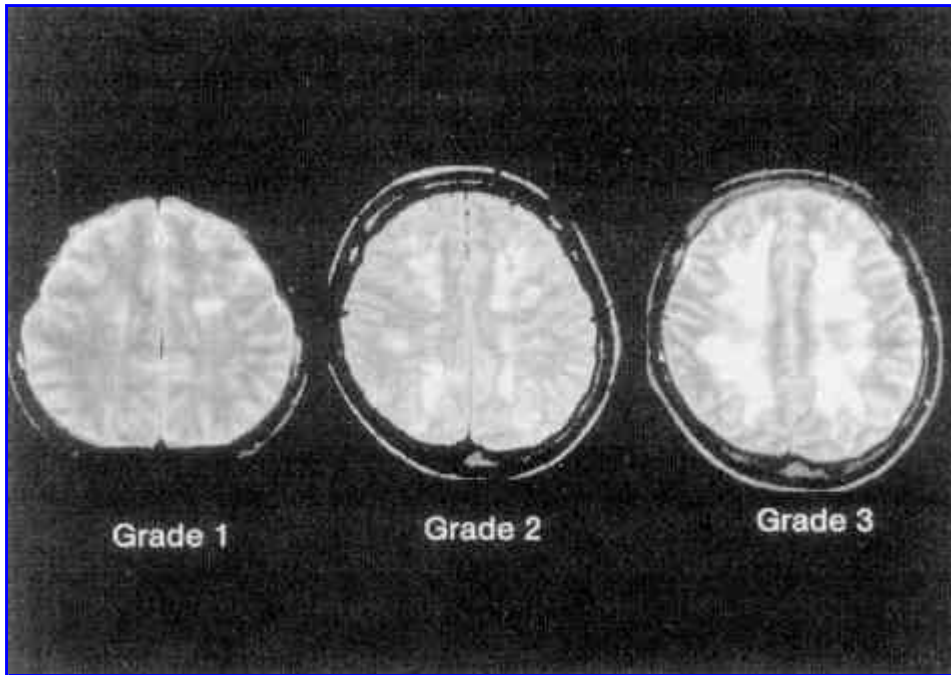
Figure 1. MRI grade for cerebral fat embolism. MRI findings were graded into four categories according to the severity of the brain lesions observed on MRI-T2WI images. Grade 0, no abnormalities; grade 1, several small spotty high-intensity lesions seen in the deep white matter or deep brain structures; grade 2, either many small high-intensity lesions or macular lesions, which represented confluence of the spotty lesions in the deep white matter or deep brain structures; grade 3, large macular high-intensity lesions in the deep white matter.

Appropriate respiratory management for PFE was performed, and drug therapy such as urinary trypsin inhibitor, gabexate mesilate, urokinase, corticosteroid hormone, glycerol, and hyperbaric oxygen therapy were used when indicated. The outcome was determined by the Glasgow outcome scale. [5] A favorable outcome includes those patients with mild or no disability, and a poor outcome includes those patients who were moderately and severely disabled or in a persistent vegetative state. A single regression test was used for statistical analysis, and a p value less than 0.05 was chosen for significance.

RESULTS
Clinical Parameters

The latent periods from presentation to onset of neurologic symptoms ranged from 11 to 48 hours (28.0 +/- 12.4 hours). All patients experienced depressed level of consciousness without focal neurologic symptoms. Glasgow Coma Scale score at the onset of neurologic symptoms ranged from 3 to 14 (9.6 +/- 3.5). During oxygen administration by mask, PaO_2 varied from 25.7 to 282.6 mm Hg (100.0 +/- 90.0 mm Hg); eight patients demonstrated hypoxia (PaO_2 <70 mm Hg). $PaCO_2$ ranged from 27.7 to 45.4 mm Hg (35.6 +/- 5.9 mm Hg), consistent with a state of hyperventilation. The blood gas data improved after tracheal intubation and controlled ventilation, but the level of consciousness remained unchanged.

During the observation period, the minimal HB level was between 5.5 and 10.8 g/dL (8.8 +/- 1.6 g/dL). Seven patients were diagnosed with anemia (HB < 10.0 g/dL). Six patients developed petechiae, and eight patients had minimal platelet levels less than 120,000/[micro sign]L. Fibrin degradation products were increased more than 10 mg/dL in nine cases, but fibrinogen was decreased in only the one documented case of disseminated intravascular coagulopathy (DIC) (case 1).

All cases were positive for phagocytized lipid in BALF obtained immediately after neurologic deterioration. The percentage of phagocytes containing fat compared with the total number of phagocytes observed in a microscopic field varied from 22 to 75%. This percentage demonstrated a significant negative correlation with the PaO_2 obtained at the onset of neurologic deterioration ($p < 0.01$, $r = 0.974$). The rate of phagocytes containing lipid reflects the severity of pulmonary damage due to fat embolism.

Magnetic Resonance Imaging Findings

Among the 10 initial MRIs performed within 2 days of onset of neurologic deterioration, one was MRI grade 0, five were MRI grade 1, and four were MRI grade 2. One patient showed a normal MRI that was performed within 2 hours after onset of neurologic deterioration; however, the follow-up MRI in that case performed on day 4 revealed MRI grade 1. Four hours was the shortest duration from onset of neurologic deterioration to detection of MRI abnormalities. MRI lesions appeared in the deep white matter, basal ganglia, brain stem, and cerebellum. These regions represent watershed areas or areas perfused by perforating arteries. The lesions appeared as high intensity on T2WI and proton density MRI images, low intensity on T1WI, and low density on CT scans. With the exception of one case, MRI grade 1 or 2 lesions on T2WI, could not be detected by T1WI or CT scan (Figure 2).
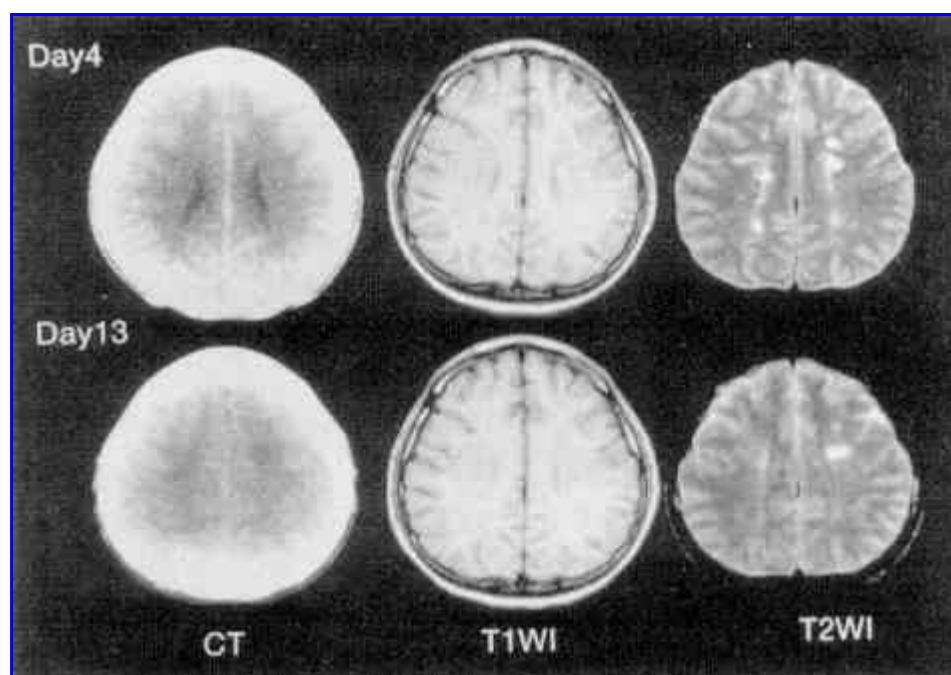

Figure 2. Neuroimagings in case 5. CT scan images, MRI-T1WI, and MRI-T2WI. T2WI performed on day 4 after onset of neurologic symptoms (upper right) shows high-intensity lesions in the cerebral deep white matter (MRI grade 2). T2WI obtained at day 13 when the patient became alert (lower right) demonstrates resolution of the high-intensity areas to MRI grade 1. However, the CT scan and T1WI reveal no detectable abnormalities during the entire follow-up period.

Two cases associated with a poor outcome demonstrated MRI grade 1 or 2 lesions on the initial MRI; however, the severity of the lesions deteriorated to MRI grade 3. The most severe MRI findings were observed during the first and second week in each case. The brain lesions remained MRI grade 2 for more than 2 months and were associated with multiple infarctions and whole brain atrophy. Serial MRI-T2WI images in case 1 is shown in Figure 3. Cases associated with a good outcome also showed progression of

brain lesions during the first week; however, the MRI grade was less severe than in cases associated with a poor outcome. The maximum MRI grade in patients with a good outcome were two cases as MRI grade 3, three as grade 2, and three as grade 1. These lesions diminished rapidly during the second week and paralleled neurologic recovery. Only one case associated with a good recovery demonstrated brain atrophy on an MRI performed 2 months after onset. The maximum MRI grade during the observation periods significantly correlated with the Glasgow Coma Scale at the onset of CFE ($p < 0.01$, $r = 0.787$).
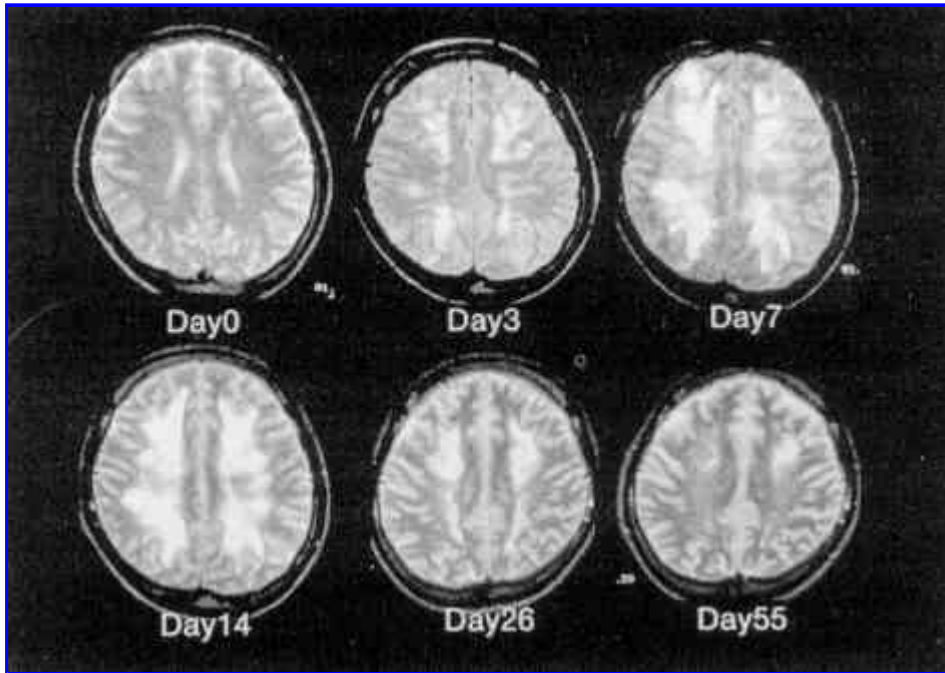

Figure 3. Serial MRI-T2WI in case 1. MRI-T2WI performed 4 hours after onset of neurologic symptoms (day 0) show small, high-intensity lesions in the deep white matter (MRI grade 1). The number of high-intensity spots increased and fused on T2WI obtained at day 3 (MRI grade 2). The lesions progressed until they peaked at day 14 (day 14) (MRI grade 3). By day 26, the lesions diminished (MRI grade 2) (day 26), but still remained as focal infarctions in MRI performed on day 55 (day 55).

Outcome

Six patients among 11 became alert within 10 days of onset of neurologic deterioration. The outcome at discharge included eight patients with good recovery, one moderately disabled patient, one severely disabled patient, and one persistent vegetative state.

DISCUSSION
Systemic Management

As shown in the present study, PFE precede CFE. The presence of fat globules and phagocytized lipid in BALF helped establish an early diagnosis of PFE. [6,7] In addition, the proportion of phagocytes containing lipid directory reflects the severity of the pulmonary condition. Although there is no special treatment for PFE, intensive respiratory management, including oxygen administration, positive expiratory pressure ventilation, corticosteroids, and others have been reported to be effective. [1,8,9]

Fat embolism syndrome also can be complicated by anemia, and coagulopathy or DIC due to enhanced coagulation of platelets. [10] Petechiae were observed in six of our cases. Evaluation of fibrinolysis revealed a decreased platelet count in eight cases and an increased fibrin degradation

products in nine cases, including one case of frank DIC. Although, it has not yet been proposed, a consensus management protocol for fat embolism must focus on prophylactics of DIC as well as on treatment for pulmonary injury.

Magnetic Resonance Imaging Findings

Previously, CT scans have been used for the diagnosis of CFE. Various results have been reported for the CT findings including low density areas, brain swelling, and multiple high-density lesions with peripheral low density regions in the deep white matter. However, many patients do not show any specific abnormalities on CT scans. [11,12] Our results confirm that computed tomography may not be routinely helpful for the diagnosis of CFE. Others have reported that MRI aids the diagnosis of CFE, [13-15] but in each report only a small number of patients was studied. In the present study, we report 11 cases of CFE and perform serial MRI. Our results show that T2WI is the most sensitive imaging sequence for early diagnosis and evaluation of the severity of CFE. Although characteristic changes on T2WI were not detected at the onset, they may be detected as early as 4 hours after the onset of cerebral symptoms. It is important to note that the maximum MRI grade obtained during the hospital course correlated well with Glasgow Coma Scale at the onset of CFE. In other words, the cerebral injuries present at the onset of the neurologic deterioration may not be shown by concomitant imaging, even with MRI-T2WI, which is considered as the most sensitive. However, MRI-T2WI was necessary to detect the very early (approximately 4 hours after symptoms) cerebral injuries of CFE. The characteristics of T2WI in CFE are (1) high-intensity signal abnormalities located in the watershed areas and areas perfused by perforating arteries; (2) diffuse anatomic distribution of the lesions; (3) disappearance of the lesions coincident with the resolution of neurologic symptoms; and (4) later development of brain atrophy and residual multiple small infarctions, especially in cases associated with a poor outcome. The MRI findings in the chronic stages are comparable to postmortem studies that reported multiple infarctions and small hemorrhages in the white matter, basal ganglia, brain stem, and cerebellum. [16] We demonstrated that widespread high-intensity areas on MRI-T2WI in the deep white matter disappeared completely in cases associated with a good outcome. These results suggest that reversible brain edema caused by enhanced permeability of the brain capillaries occurs during the early period after CFE. On the other hand, three cases, including two patients with a poor outcome, demonstrated multiple infarctions on MRI performed more than 2 months after onset. These findings suggest that permanent ischemic lesions caused by fat microemboli in the watershed areas or regions perfused by the perforating arteries may be the primary enduring sequela of CFE.

Mechanisms of Brain Edema Formation

The pathophysiology of the PFE was reported to have similarities with an adult respiratory distress syndrome. [17] Inflammation caused by fat globules in the alveoli activate leukotrienes and other chemical mediators, which enhance capillary permeability. [18] In patients with PFE, many polynuclear leukocytes are observed, and neutrophilic elastase is elevated in BALF. [7] Similar mechanisms may be responsible for the formation of brain edema. It is known that free fatty acids, including arachidonic acid, have important roles in the formation of brain edema. [19,20] The free fatty acids in bloodborne fat globules released from a fractures site may potentiate release and production of prostaglandins, leukotrienes, and thromboxanes. These chemical mediators enhance permeability in cerebral capillaries and may exacerbate brain edema caused by fat microemboli.

CONCLUSIONS

MRI-T2WI is the most sensitive imaging technique for diagnosing CFE at present, and it properly shows the severity of brain damage. T1WI and CT scans are less valuable than T2WI. The diagnostically distinctive findings on T2WI are the high-intensity signal abnormalities located in the deep white matter, basal ganglia, brain stem, and cerebellum. These appear as early as 4 hours after the onset of neurologic symptoms, may become confluent during the first week, and disappear rapidly during the second week. With the aid of proper treatment for PFE, CFE is a potentially reversible disease that can have a good outcome.

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Accession Number: 00005373-199902000-00021