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Original Article

Recovery after Cerebral Fat Embolism

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SUMMARY

Background: The recovery of cerebral fat embolism (CFE) is continuous and slowly progressive. No current studies evaluate the stages of the recovery. In this paper, we discussed the clinical course of six patients diagnosed with CFE after traumatic bone fractures using a two-stage evaluation.
Methods: A total of six patients were retrospectively included between 2010 and 2016. All patients were diagnosed using magnetic resonance imaging (MRI). We divided their recovery into two stages: 1) regaining of consciousness and 2) recovery of cognitive status. The Glasgow Coma Scale and Mini-Mental State Examination (MMSE) were used to evaluate consciousness and cognition. Examination of the Babinski sign was recorded at the onset. The functional outcome was assessed by the Modified Rankin Scale (MRS).
Results: All patients initially showed a marked reduction in the level of consciousness, followed by gradual recovery. The mean time to regaining consciousness was 6.8 ± 1.5 days, but the mean time to regaining normal cognition was 21.4 ± 22.0 weeks. Two patients presenting Babinski sign showed longer recovery times compared to others. The mean MMSE score at the first stage was 21.3 ± 1.2, and at the second stage was 28.8 ± 1.9. The MRS scores revealed favorable functional outcomes at the last follow-ups.
Conclusion: CFE is a serious condition that has a favorable outcome. Although it is difficult to conclude whether the MMSE score is correlated with the time of recovery, a positive Babinski sign may be a simple clinical indicator of a longer recovery period.

1. Introduction

Fat embolism syndrome (FES) remains a rare, but potentially life-threatening complication of long-bone fracture. It classically presents with the triad of hypoxia, petechiae, and altered mental status.[1] The neurological involvement of the brain in fat embolism is called cerebral fat embolism (CFE).[2] Observation of clinical symptoms and computed tomography (CT) are not always helpful in diagnosing CFE, and the clinical features do not always meet Gurd's criteria. Only magnetic resonance imaging (MRI) is believed to be useful in detecting CFE.[3,4] The duration of coma or the period during which mechanical ventilation is required in CFE is variable. Prolonged coma or a neurological sequela is also observed in some cases.[5]

Traumatic bone fracture is a common and considerable issue in the aged people because of the higher incidence of falls, the co-existed underlying diseases such as osteoporosis, and the usage of multiple drugs which may potentially include the one that would affect the bone quality. It is important to precisely identify the CFE in the elderly patients and evaluate the prognosis and recovery process. In this paper, we have discussed the clinical course of six patients diagnosed with CFE after traumatic bone fractures and their recovery times. We hypothesized the CFE was self-limited and had a favorable outcome, and the presence of a Babinski sign may be associated to a longer recovery time.

2. Materials and methods

For this study, a retrospective review of CFE was conducted at a tertiary healthcare center from November 2010 to December 2016 and eight patients were enrolled. All of them went through trauma with bone fractures, which was followed by intervention by means of orthopedic operation. Patients were included if they met the listed inclusion criteria: (1) long bone fracture with conscious disturbance; (2) no specific finding in the cranial CT scan at the first moment; (3) specific "starfield" pattern revealed in the following cerebral MRI scan. One patient with previous cerebral infarctions and another with intracranial hemorrhage were excluded. Six patients were included, of whom five were men and one was women with a mean age of 46 years (range: 20–78 years). Clinical manifestations of CFE

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varied widely, from an altered consciousness to seizure and coma. All patients underwent cranial CT examination at initial presentation with altered consciousness. Cerebral MRI was performed on all patients after the event, and an abnormal scattered signal called "starfield" was observed (Figures 1 and 2) on diffusion-weighted imaging (DWI) and T2-weighted and T2 fluid-attenuated inversion recovery (FLAIR)-weighted sequences.[4,6,7]

All patients in the present study showed complete recovery despite their poor initial clinical pictures. Recovery consisted of two stages: 1) regaining of consciousness and 2) recovery in cognitive status. The first stage was defined as regaining a full Glasgow coma scale (GCS) score, and the second stage was defined as return to full cognitive status. Regular neurological examination, including GCS evaluation, was conducted during the daily morning round.

The Mini-Mental State Examination (MMSE) was used to evaluate the mental status and cognition of patients at the two different stages.[8,9] The resulting score of more than or equal to 25 is regarded as indicating complete recovery of the cognitive status in the second stage. The Babinski sign, which has been incorporated into the standard neurological examination to determine the integrity of the cortical spinal tract, was recorded at the initial instance of altered consciousness and used as a parameter in this study. As the presence of the Babinski sign was generally considered an upper motor neuron sign, we evaluated and followed up every patient's neurological recovery of the motor system using the Modified Rankin Scale (MRS) at the time point when patient reached full recovery in cognitive status. MRS measures the degree of disability or dependence in the daily activities of people who have suffered a stroke or other causes of neurological disability.[10] It is a 7-point disability scale with possible scores ranging from 0 (no residual symptoms) to 6 (dead).

This study was conducted according to the tenets of the Declaration of Helsinki and was approved by the MacKay Memorial Hospital Institutional Review Board, and all patients have provided informed consent, including for publication.

3. Results

We followed up the six patients for a mean follow-up duration of 8.2 months. There were no significant findings in cerebral CT, and all cases of CFE were diagnosed by MRI. All patients experienced altered levels of consciousness before diagnosis of CFE. Some had altered levels of consciousness preoperatively (patients 1–3 and 6), and others had it postoperatively (patients 4 and 5). The time interval between trauma and the onset of neurological symptoms ranged from 4 to 70 h, and the initial GCS score at the onset of CFE ranged from 4 to 12. The Babinski sign was positive in two of six patients at the first instance of altered sensorium (patients 2 and 3). None of the patients had petechiae over the skin. Two of the patients experienced respiratory dysfunction after trauma/surgery and required artificial ventilation during treatment. The clinical findings are summarized in Table 1.

Mean time to regaining of consciousness (first stage) was 6.8 days, but the mean time to normal cognition (second stage) was 21.4 weeks. Mean MMSE score at the first stage was 21.3, and at the second stage was 28.8. MRS score evaluated in six patients at the second stage ranged from 1 to 4. The recovery, though slow, was complete in all patients (Table 2).

We noted that patients with a positive Babinski sign at the beginning needed a longer total recovery time. The mean recovery times in patients with a positive Babinski sign were 8.5 days in stage I

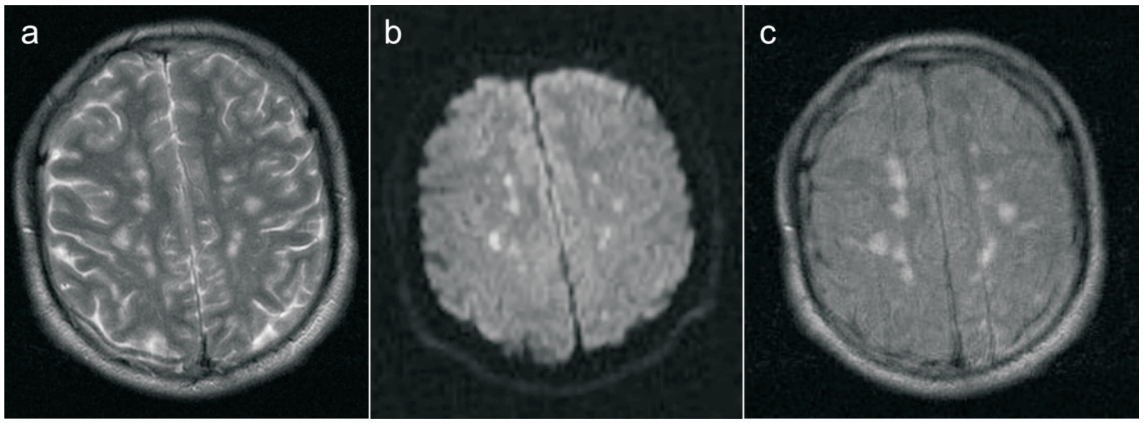

Figure 1. Brain magnetic resonance images of a 21-year-old man (patient 3) with a left femoral shaft fracture showing a "starfield" appearance. a) T2-weighted sequences; b) Diffusion-weighted imaging sequences; and c) T2 fluid-attenuated inversion recovery sequences.

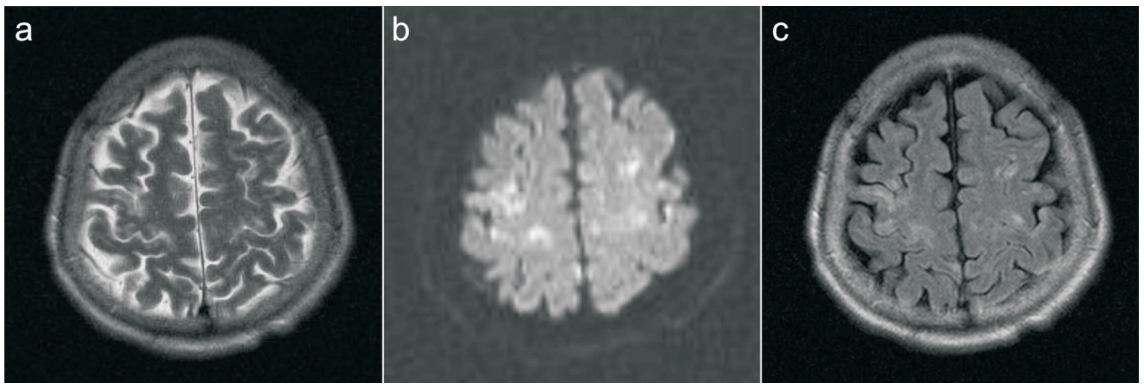

Figure 2. Brain magnetic resonance images of a 73-year-old woman (patient 5) with right bipolar hemiarthroplasty periprosthetic fracture showing a "starfield" appearance. a) T2-weighted sequences; b) Diffusion-weighted imaging sequences; and c) T2 fluid-attenuated inversion recovery sequences.

Table 1
Patient characteristics.

Patient number	Age/Sex	Injury	Ad GCS	Onset GCS	Onset time	Onset time (h)	Babinski sign
1	43/Male	Left femur shaft fracture L4 compression fracture Left tibia shaft fracture	14	12	Pre-op	47	–
2	59/Male	Left femoral shaft fracture Left iliac wing and crescent fracture Left 4th, 5th, 7th ribs fracture Mandible comminuted open fracture	7	4	Pre-op	4	+
3	21/Male	Left femoral shaft fracture	15	8	Pre-op	16	+
4	78/Male	Right femur intertrochanter fracture	15	12	Post-op	70	–
5	73/Female	Right Bipolar hemiarthroplasty periprosthetic fracture Vancouver B2	15	6	Post-op	8	–
6	20/Male	Right tibia shaft open fracture, Gustilo type II Right calcaneus fracture	15	8	Pre-op	40	–

Ad: admission, GCS: Glasgow Coma Scale, Pre-op: pre-operation, Post-op: post-operation.

Table 2
Patient's recovery time and clinical score.

Patient number	1st stage (days)	1st stage (MMSE)	2nd stage (weeks)	2nd stage (MMSE)	2nd stage (MRS)
1	7	20	5.9	29	1
2	9	20	50.4	25	2
3	8	21	48.1	30	1
4	6	22	13.7	29	2
5	6	23	8.9	30	4[a]
6	5	22	1.3	30	1
Mean	6.8 ± 1.5	21.3 ± 1.2	21.4 ± 22.0	28.8 ± 1.9	

MMSE: Mini-Mental State Examination, MRS: Modified Rankin Scale.
[a] The patient had the underlying disease of Parkinson's disease before the onset of cerebral fat embolism.

and 49.3 weeks in stage II, whereas those in the patients with a negative Babinski sign were 6.0 days and 7.5 weeks in stages I and II, respectively. No relation was observed between the presence of a Babinski sign and the MRS score recorded at the second stage. Imaging studies revealed that CFE lesions were not limited to any particular areas, and the distribution in each patient was different. No specific common rule for lesion distribution could be detected in the images of these six patients (Table 3).

Although all patients attained complete neurological recovery with good cognitive function, one patient was reported to have had a change in personality after injury according to his family (patient 1).

4. Discussion

CFE can be present without a pulmonary component, potentially because smaller fat globules may traverse the pulmonary microvasculature and reach the systemic circulation. Alternatively, CFE may be caused by fat globules via a patent foramen ovale.[11] Echocardiograms were performed in four of our patients, but we did not detect a patent foramen ovale or shunt.

Early MRI in patients with neurological symptoms after trauma, even in the absence of pulmonary and dermatological findings, should be the goal.[12] Some studies have suggested that the "star-field pattern" on DWI and T2-weighted MRI can serve as an early and sensitive indicator of CFE in the context of long-bone fracture.[4] Other authors have also emphasized the importance of DWI and T2-weighted MRI as the most favorable tools to detect CFE.[13,14] Some authors have studied the validity of MRI to detect and grade the severity of CFE. Takahashi et al. graded these changes from grade 0 to grade 3, which was correlated with GCS at the onset of CFE and degree of clinical neurological impairment.[15] In our study, we did not adopt Takahashi's grading owing to poor inter-observer reliability.

Patients 2 and 3, who reported positive Babinski signs at onset, had significantly longer recovery times than did the other four patients. The Babinski sign is a common manifestation in acute ischemic stroke patients that is attributed to a pyramidal tract injury and is unrelated to stroke severity.[16] A retrospective review of 351 cases of acute ischemic stroke revealed that a Babinski sign was observed in 32.8% of cases[17] and another investigation of acute hemorrhagic and ischemic stroke patients revealed a 64.8% incidence of Babinski signs.[18] The relationship between a Babinski sign and the lesion pattern or territories involved in stroke have seldomly been explored in MRI studies. Qu et al. found that a higher NIHSS score and basal ganglia infarct predict the presence of a Babinski sign and in contrast, a Babinski sign is unrelated to the functional outcome of acute stroke patients.[17] In our case series, there were three patients (Patient 2, 3, 5) whose brain lesions involved bilateral basal ganglia and a Babinski sign was observed in two of them. Although these two patients were noted to have longer recovery times in cognitive status, they demonstrated good functional outcomes that were equal to those of others at the time point of the second stage. The results met the conclusion of Qu et al.'s review. Given that the Babinski sign has little clinical relevance for the management of acute ischemic stroke, the results in this series aim to propose that a Babinski sign may provide prognostic information related to longer

Table 3
Sites of cerebral fat embolic (CFE) lesions on magnetic resonance imaging (MRI).

Patient number	Lesion position
1	Right posterior frontal lobe, right corona radiata, right thalamus, right callosal splenium, and left hippocampus
2	Bilateral fronto-temporo-parieto-occipital lobes, bilateral basal ganglia, bilateral thalami, brainstem and bilateral cerebellum
3	Bilateral fronto-temporo-parietal lobes, bilateral basal ganglia, bilateral thalami, and bilateral splenium of the corpus callosum
4	Bilateral corona radiata, left frontal lobe, left temporal lobe, left external capsule, left thalamus, and left cerebral peduncle
5	Bilateral fronto-temporo-parieto-occipital lobes, bilateral thalamus, bilateral basal ganglion, and bilateral cerebellar hemisphere
6	Right thalamus, bilateral internal capsules, bilateral corona radiata, and bilateral centrum semiovale

recovery time in CFE. However, further bigger studies was needed to obtain statistically significant data.

Proper care of orthopedic patients who potentially have CFE involves prompt diagnosis, immediate symptomatic care, and early coordination with a neurologist as well as medical investigations to rule out other causes of symptoms. Complete neurological recovery or recovery with minor neurological deficits has been reported in many case reports.[19–21] However, there were also some opposite outcomes reported in other studies. We assume that despite the favorable outcomes in the end, the recovery time of each individual case differs depending on their unique situation. Metting et al. reported persistent cognitive dysfunction in a patient with CFE associated with head injury.[22] Srikanth et al. reported two patients whose recovery was complete after approximately 5.5 months, which is considered delayed.[5] Fortunately, all six patients in our study recovered without developing any neurological sequelae. Although the Patient 5 scored 4 in her MRS assessment at stage two, it was not worse than her original status before traumatic injury due to her underlying Parkinson disease. For the one patient with a reported personality change, the probable explanation would be that the ischemic lesions secondary to the emboli were mainly scattered in the right posterior frontal lobe, right corona radiata, right thalamus, and left hippocampus, thereby influencing the emotional and cognitive behavior of the person.

Our study has several limitations including the small number of cases, relatively short follow-up period, and heterogeneity of the series. Although the small sample size contributed to the difficulty in obtaining statistically significant data, we aimed to demonstrate the clinical course and recovery of our small group of patients along with the impressive MRI findings. Owing to the retrospective nature of the study and the rare incidence of CFE, the heterogeneity of the series could not be avoided. However, this does not influence the aim of this study. Another limitation is the appropriateness of using the MMSE in this scenario. Owing to the short time required to administer it and its ease of use, it is valuable for cognitive assessment in the clinician's office or at the bedside. However, the MMSE is more often used to estimate dementia and progression of cognitive impairment. There is no recorded evidence regarding the validity of the MMSE in patients with CFE.

In conclusion, CFE is a rare complication of both long-bone fracture and long-bone instrumentation. Early advanced imaging, including exigent MRI, should be obtained for any unexplained coma after an orthopedic traumatic injury or after undergoing an orthopedic surgery. CFE is a serious condition that has a favorable outcome. Although it is difficult to conclude whether the MMSE score is correlated with the time of recovery, a positive Babinski sign may be a simple clinical marker related to a longer recovery period based on the stage of recovery.

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Declarations of any potential financial and non-financial conflicts of interest

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