Clinical Features and Neuroimaging Findings in Patients with Cerebral Fat Embolism

Yang-Tong Han¹, Jing Tang², Zhi-Qiang Gao³, Hong-Tao Hu¹
¹Department of Neurology, Beijing Jishuitan Hospital, Beijing 100035, China
²Department of Orthopedic Osteology, Beijing Jishuitan Hospital, Beijing 100035, China
³Department of Trauma Osteology, Beijing Jishuitan Hospital, Beijing 100035, China

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INTRODUCTION

Cerebral fat embolism (CFE) is a rare but potentially lethal disease that is usually complicated by long bone fracture, which can develop over 12–72 h. Since the main form of treatment for CFE is supportive, early diagnosis, prevention, and appropriate treatment can reduce mortality and the development of complications. However, due to symptom heterogeneity and imprecise diagnostic methods, CFE may be masked by other clinical conditions that make early detection challenging. Given its low incidence, most clinical studies of CFE are single cases or small case series. To characterize the features of CFE, clinical manifestations, laboratory examinations, and neuroimaging data were evaluated in a large sample of patients with CFE.

METHODS

The current study was a retrospective review of CFE at the Department of Neurology, Jishuitan Hospital (Beijing, China) from 2003 to 2014. The study was approved by the Ethics Committee of Jishuitan Hospital and conducted according to the principles of the Declaration of Helsinki. A diagnosis of CFE was made based on Gurd’s criteria in conjunction with neuroimaging results and initial presentation of neurological symptoms.¹⁰ Patients whose initial neurological symptoms were subsequent to respiratory manifestations, as well as those who were diagnosed with fat embolism syndrome but showed no neurological symptoms, were excluded from the study. On the other hand, patients whose initial symptoms were neurological manifestations with or without subsequent respiratory manifestations were included. Patients with infections, tumors, subdural hematomata, acute cerebrovascular diseases, visceral injuries, or inflammatory diseases were also excluded from the study. Demographic data, clinical manifestations, treatment, prognosis, laboratory examinations, and neuroimaging results were all evaluated.

RESULTS

The study included 10 male and 11 female patients ranging in age from 24 to 71 years (mean age: 34.9 ± 10.6 years). Detailed demographic data, clinical manifestations, and results from laboratory examinations are presented in Table 1. Patent foramen ovale was detected in three of 15 patients who underwent echocardiographic examination. Pulmonary arteriovenous malformations (AVMs) were absent in all nine patients who received chest computed tomography (CT) examination. Altogether, 18 patients recovered without developing neurological sequelae within 1 month of injury and three remained in a coma at the 3-month follow-up.

All patients underwent cerebral CT examination and nine were examined by magnetic resonance imaging (MRI). Five of the nine patients had abnormal multiple scattered long T1 and T2 signals in the bilateral corona radiata and centrum semiovale and four had abnormal multiple stippled long T1 and T2 signals in the bilateral basal ganglia and centrum...
Table 1: Demographic data, clinical manifestations, and laboratory results for study subjects

| Patient number | Gender | Age (years) | Injury | Neurological symptoms | Time (h) | Petechial rash |
|----------------|--------|-------------|--------|-----------------------|---------|---------------|
| 1              | Male   | 34          | Tibia, fibula, femur | Drowsiness, somnolence | 48      | −             |
| 2              | Female | 25          | Femur, pelvic | Coma | 36 | − |
| 3              | Female | 48          | Hip replacement arthroplasty | Delirium, restlessness | 24 | − |
| 4              | Male   | 30          | Tibia, fibula, femur | Drowsiness, somnolence | 34 | + |
| 5              | Male   | 34          | Femur, pelvic | Illusion | 48 | − |
| 6              | Female | 32          | Humerus, ribs | Seizure | 72 | − |
| 7              | Male   | 29          | Tibia, fibula, femur | Drowsiness, somnolence | 40 | − |
| 8              | Female | 48          | Hip replacement arthroplasty | Delirium and restlessness | 48 | + |
| 9              | Male   | 27          | Femur, pelvic | Somnolence | 60 | − |
| 10             | Female | 37          | Bilateral tibia, fibula | Delirium, restlessness | 8 | + |
| 11             | Female | 36          | Tibia, fibula, femur | Drowsiness, somnolence | 48 | − |
| 12             | Male   | 33          | Humerus, ribs | Coma | 24 | − |
| 13             | Female | 32          | Tibia, fibula, femur | Drowsiness, somnolence | 48 | − |
| 14             | Female | 30          | Bilateral tibia, fibula | Delirium, restlessness | 18 | + |
| 15             | Male   | 24          | Tibia, fibula, femur shaft | Drowsiness, somnolence | 48 | − |
| 16             | Female | 17          | Hip replacement arthroplasty | Delirium, restlessness | 6 | − |
| 17             | Male   | 28          | Femur and pelvic | Somnolence | 60 | + |
| 18             | Female | 42          | Tibia, fibula, femur shaft | Drowsiness, somnolence | 36 | − |
| 19             | Male   | 31          | Tibia, malleolus, femur | Delirium, restlessness | 16 | − |
| 20             | Female | 26          | Femur and pelvic | Seizure | 72 | − |
| 21             | Male   | 35          | Tibia, fibula, femur | Drowsiness, somnolence | 36 | − |

| Patient number | Temperature (>38°C) | Tachycardia | Hypoxemia | Hemoglobin drop | Platelet drop | High ESR | Urinary fat drops |
|----------------|---------------------|-------------|-----------|-----------------|---------------|---------|-------------------|
| 1              | +                   | +           | +         | −               | +             | −       | +                 |
| 2              | −                   | +           | −         | +               | −             | +       | −                 |
| 3              | −                   | +           | −         | −               | +             | +       | −                 |
| 4              | −                   | −           | +         | −               | +             | −       | +                 |
| 5              | +                   | +           | −         | −               | +             | +       | +                 |
| 6              | −                   | +           | +         | −               | −             | +       | −                 |
| 7              | −                   | +           | −         | +               | +             | −       | +                 |
| 8              | +                   | −           | −         | −               | +             | +       | +                 |
| 9              | −                   | +           | −         | +               | −             | +       | −                 |
| 10             | −                   | +           | −         | −               | +             | −       | +                 |
| 11             | +                   | −           | +         | −               | +             | +       | −                 |
| 12             | −                   | +           | −         | −               | −             | +       | −                 |
| 13             | +                   | −           | +         | −               | −             | +       | +                 |
| 14             | +                   | −           | −         | +               | +             | −       | +                 |
| 15             | −                   | +           | −         | −               | +             | −       | +                 |
| 16             | +                   | −           | +         | −               | +             | −       | +                 |
| 17             | −                   | +           | −         | −               | +             | −       | +                 |
| 18             | +                   | −           | −         | +               | −             | +       | −                 |
| 19             | −                   | +           | −         | +               | +             | −       | +                 |
| 20             | −                   | +           | −         | +               | −             | +       | +                 |
| 21             | +                   | −           | −         | +               | −             | +       | +                 |

ESR: Erythrocyte sedimentation rate.

The fluid-attenuated inversion recovery sequence MRI showed hyperintense lesions in nine patients. The diffusion-weighted image (DWI) showed multiple scattered bright spots on a dark background (i.e., a starfield pattern) in four patients [Figure 1].

Discussion
The pathogenesis of CFE is still controversial and involves a variety of factors, with no single theory explaining all of the pathophysiological features of CFE. For instance, the infloating theory suggests that fat globules are physically forced into the venous system, resulting in multisystem dysfunction due to the physical obstruction of vessels. On the other hand, the free fatty acid theory proposes that excessive mobilization of free fatty acids leads to severe vasculitis that is secondary to its histotoxic effects.[2] CFE
factors. The deficits were generally brief and mild, and may compared to previous studies might be due to several of focal neurological deficits observed in this study as respectively) that lasted for <1 week. The higher frequency deficits (33% and 23% with ataxia and hemiparesis, some patients in the present study showed focal neurological distinguishing it from cerebrovascular diseases. However, CFE typically presents with drowsiness, somnolence, and delirium, but seldom with focal neurological deficits, suggesting that more severe CFE and a worse prognosis. A short onset time after injury may lead directly to CFE from fat globules via the patent foramen ovale or pulmonary AVM. In contrast, a long onset time could support the free fatty acid theory of CFE.

Of the 21 patients, 11 had multiple (≥3) long bone fractures, suggesting that multiple (≥3) long bone fractures may constitute a risk factor for CFE. These patients may benefit from early fixation and operation. We also found that three patients had concurrent bilateral hip replacement arthroplasty, suggesting that simultaneous bilateral replacement arthroplasty might be a risk factor for CFE. Therefore, a longer time interval between the two operations of bilateral replacement arthroplasty might decrease the occurrence of CFE.

CT lacks sensitivity and is usually unable to detect CFE. However, it may be a valuable method for excluding alternative clinical conditions. In contrast, MRI can reveal characteristic cerebral lesions in the centrum semiovale, subcortical white matter, and ganglionic regions in acute CFE. Some studies have suggested that the starfield pattern on DWIs can serve as an early and more sensitive indicator of CFE in the context of long bone fractures. The rationale for this is based on the fact that abnormalities in signal intensity on T2-weighted image reflect vasogenic edema, which develops at a later stage, whereas the DWI reveals cytotoxic edema, which develops immediately. Recent reports also indicate that T2* sequences can serve as a pathognomonic feature of CFE, due to their sensitivity to blood products, changes in iron content, and the unique distribution in white matter.[3,4]

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Conflicts of interest
There are no conflicts of interest.

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