

## CASE REPORT

# Diagnostic significance of fat globules in blood in fulminant-type fat embolism syndrome

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**Abstract**

Fat globule detection in the blood in fat embolism syndrome (FES) diagnosis remains controversial. This case illustrates two life-threatening, possibly FES-related, episodes with dramatic increases in blood fat globule level. Future studies should aim at evaluating the significance of the quantitative changes in blood fat levels in diagnosing FES.

**KEYWORDS**

droplet, lipid, pulmonary thromboembolism, trauma

## 1 | INTRODUCTION

Fat embolism syndrome (FES) typically occurs after major trauma, generally involving fractures of the pelvis and/or the femur, and manifests clinical symptoms 12–72 h after insult.<sup>1</sup> It is a clinical diagnosis based on cerebral symptoms, as well as the symptoms of respiratory distress, a petechial rash with or without acute circulatory failure, kidney injury, thrombocytopenia, or anaemia.<sup>2</sup> FES develops after bone fixation surgery.<sup>3</sup> Although fat entering from the fractured bone marrow into the systemic circulation plays a vital role, fat detection in blood has not been widely performed for diagnosing FES, and the significance of fat globules in the blood remains unknown.

In this report, we describe a case of a trauma patient who developed two episodes of severe circulatory and respiratory compromise that finally resulted in cardiac arrest, presumably due to FES. In particular, we retrospectively investigated the serial changes in fat globules in the blood smear samples of this patient in association with clinical deterioration.

## 2 | CASE PRESENTATION

A 63-year-old man was injured by hitting a truck while driving a car. He was hospitalized with a left pelvic, multiple vertebral, and multiple rib fractures. The pelvic fractures were complicated ones, reaching the pubic, ischium, ilium, and sacroiliac joint. On admission, the hemoglobin, hematocrit, and platelet values were 16.8 g/dl, 50.1%, and  $217 \times 10^3/\mu\text{l}$ , respectively. His general status was stable, except for severe delirium that developed on days 2–4 after admission.

On day 6 of admission, he underwent vertebroplasty of the 12th thoracic vertebra and a posterior fixation surgery at the level between the 3rd thoracic and the 3rd lumbar vertebrae. Immediately after the 6-h operation, when his body position was changed from prone to supine in the operating room, his blood pressure declined to 48/25 mm Hg and his oxygen saturation decreased from 99 to 90% with an inspiring 40% fraction of oxygen. Although these symptoms soon improved, the severe delirium relapsed when he was brought to the general

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ward. The blood test performed immediately after the operation revealed an increased serum creatinine from a baseline level of 0.54 mg/dl to a postoperative level of 1.82 mg/dl.

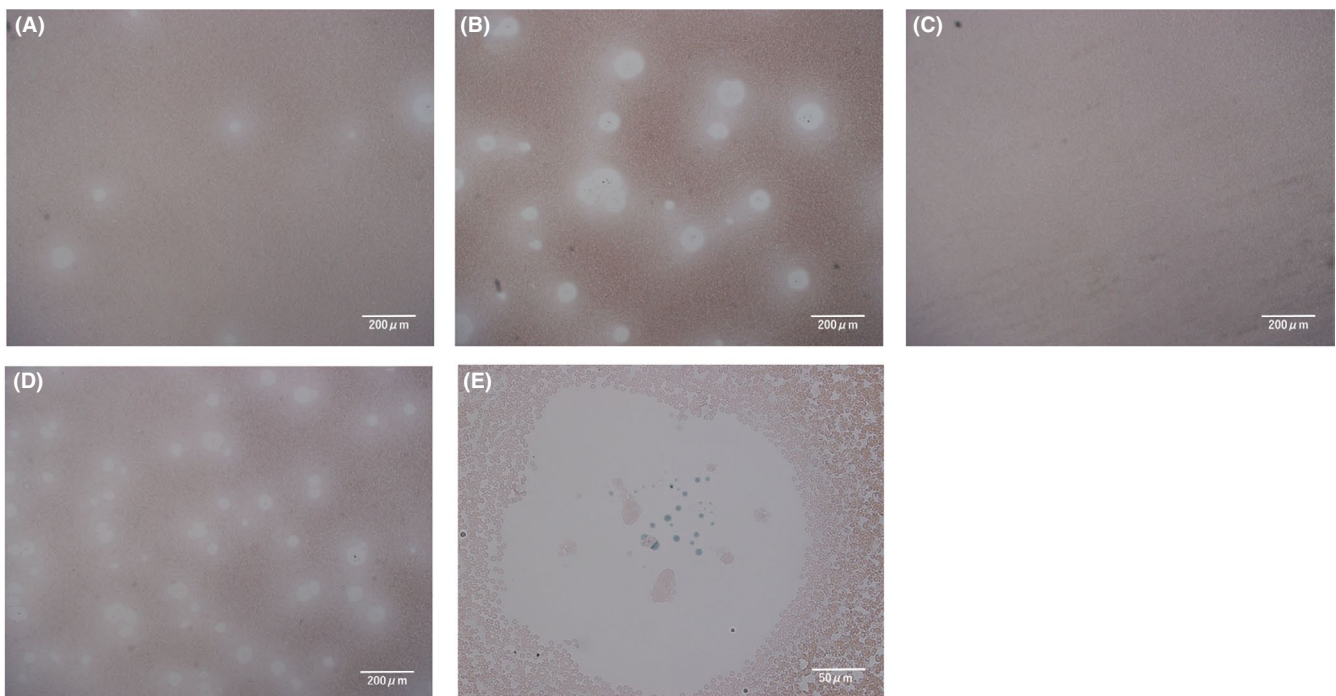
On day 8, immediately after the postural change in the general ward, he suddenly lost consciousness, with the blood pressure and heart rate being 68/26 mm Hg and 116 beats per min, respectively. The medical emergency team was called, and he was promptly intubated. Transthoracic echocardiography showed marked enlargement of the right-sided heart accompanied by McConnell's sign that showed akinesis of the mid-free wall with apical hyperkinesis of the right ventricle. Subsequently, ventricular fibrillation occurred, and cardiopulmonary resuscitation was initiated. We suspected that the patient had massive pulmonary thromboembolism, then initiated venoarterial extracorporeal life support using a heart-lung machine. The spontaneous circulation returned 30 minutes after cardiac arrest. The life-supporting treatment, including extracorporeal membrane oxygenation and mechanical ventilation, along with medical treatment, was continued.

Despite our best efforts, he died of severe brain edema due to ischemic encephalopathy on day 9 of admission.

### 3 | INVESTIGATIONS

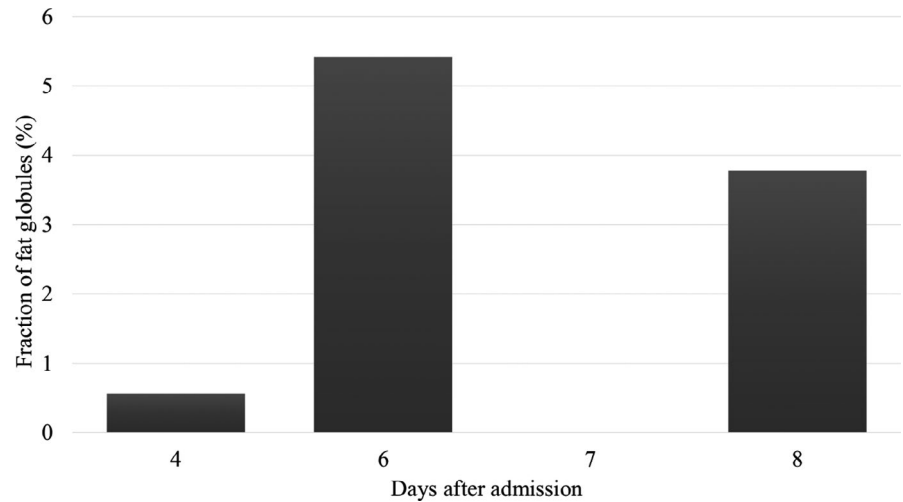
Brain computed tomography (CT) revealed diffuse swelling. A contrast-enhanced CT showed marked enlargement of the right-sided heart, patchy ground-glass appearance in the bilateral lung field, and consolidation in the S6 region of the right lung. However, no thrombus was found in the pulmonary artery. Petechiae were prominent on his skin of the anterior thorax, and his blood test revealed thrombocytopenia with a platelet count of  $75 \times 10^3/\mu\text{l}$ , anemia with a hemoglobin level of 7.5 g/dl, and coagulopathy with an activated partial thromboplastin time of 79.6 (reference range: 25–35) s, prothrombin time-international normalized ratio of 2.31, and D-dimer level of 73.7  $\mu\text{g/ml}$ .

Based on these findings, we diagnosed the patient with FES according to the Gurd and Wilson criteria.<sup>2</sup> We retrospectively examined fat globules in the peripheral blood by Giemsa staining using whole blood samples preserved in our laboratory. Our findings showed a few white round bodies representing fat globules in the blood sample collected on day 4 (Figure 1A). However, the number of various-sized fat globules increased dramatically after the first collapse on day 6 (Figure 1B). Thereafter, they almost disappeared from the sample collected on



**FIGURE 1** Peripheral blood smears. Arrows indicate fat globules at 40 x magnification. (A–D): Giemsa staining. (E): Sudan black staining. (A) A few white round bodies representing fat globules were observed on the 4th admission day. (B) Immediately after the operation on the 6th admission day, a large amount of fat globules of various sizes was observed. (C) On the 7th admission day, the fat globules almost disappeared. (D) A large amount of fat globules reappeared 1 h before cardiopulmonary arrest on the 8th admission day. (E) The white round bodies were confirmed to be fat globules by Sudan black staining. Drop-like, blue-black materials are recognised in the white round bodies

**FIGURE 2** Serial changes of fraction of the area occupied by fat globules in microscopic field shown as Figure 1A–D. On the 4th day, fat globules occupied 0.56%, but it increased to 5.42% on the 6th day; where the operation of vertebra carried out. Thereafter, the fat globules almost disappeared on the 7th day, but again increased to 3.78% on the 8th day; 1 h before cardiopulmonary arrest



day 7 (Figure 1C) but increased again in the sample collected 1 h before the cardiac arrest on day 8 (Figure 1D). All these findings corresponded to clinical deterioration. Using fat-specific Sudan Black staining, we further confirmed that the white round bodies were definitely fat globules (Figure 1E). Figure 2 shows the serial changes in the fraction of the area occupied by fat globules in the microscopic fields, as shown in Figure 1A–D.

## 4 | DISCUSSION

The clinical course of this patient with major trauma was characterized by two episodes of dramatic circulatory compromise that occurred after changing his body position. Although our snap diagnosis was pulmonary thromboembolism, contrast-enhanced CT showed no signs of thrombus in the pulmonary artery. The patient developed delirium, acute kidney injury, skin petechiae, thrombocytopenia, anemia, and coagulopathy, all of which supported the final diagnosis of FES.<sup>2</sup>

Bajuri et al.<sup>4</sup> proposed two FES variants: an acute fulminant and a classic type. The former type of FES develops in a short period through an obstructive mechanism often accompanied by severe hypotension and hypoxemia, whereas the latter typically exhibits a latency period of 24–36 h through subsequent biochemical reactions presenting with various organ symptoms, including the brain, skin, kidney, and blood cells, as well as coagulation. In our patient, both variants overlapped during the 9-day hospital course.

Importantly, according to our investigation, massive fat globules appeared in the blood samples collected immediately after the two episodes of circulatory collapse. The significance of detecting fat globules in the blood remains controversial: in fact, some diagnostic criteria include it,<sup>2</sup> while others not.<sup>5</sup> One possible explanation for this inconsistency is the lack of specificity. Fat globules in the blood

can be observed in trauma patients without the development of FES and even in non-trauma patients.<sup>6</sup> In patients with traumatic long bone fractures, fat embolism itself in the pathology was observed in >90% of the cases, whereas the incidence of FES, diagnosed based on Gurd's criteria, was 0.9%.<sup>5</sup>

However, in acute fulminant FES occurring through the mechanism of massive embolism of the pulmonary microcirculation,<sup>7</sup> the number of fat globules in the blood might correspond to the clinical symptoms observed in our case. A previous report indicated that fat globules can pass through the pulmonary microcirculation due to their deformability and enter systemic circulation within 3 h after bone surgery.<sup>8</sup> Moreover, fat globules can pass through the patent foramen ovale and other arteriovenous shunts in the subpleural parts of the lungs or anastomoses between the bronchial or pulmonary arteries and capillary net in the peribronchial tissues.<sup>9</sup> Our case indicates that serial changes of the fat globule quantity might have particular significance in some FES cases and should be evaluated in the future.

Our patient developed FES almost a week after the trauma. The fat globules could have possibly entered the systemic circulation intermittently from unstable fractured bones with no surgical fixation. A previous study reported that the period of fat globulaemia lasted longer in patients with long bone fractures treated conservatively than in patients surgically fixed early.<sup>10</sup> If this were the case, stabilizing the fractured bones as early as possible could prevent the risk of FES.<sup>11</sup>

## CONFLICT OF INTEREST

The authors declare no conflicts of interest.

## AUTHOR CONTRIBUTIONS

Author 1: Ayu Asakage: The author contributed to the conception of the work, obtaining patient consent to

request confidential data, analyzing and interpreting data, and submitting the final version of the report for publication. Author 2; Michiko Fujisawa: The author contributed to the critical revision of the report and general advice. Author 3; Tetsuhiro Takei: The author contributed to the critical revision of the report and provided general advice. Author 4; Jiro Kumagai: The author contributed to the pathological supervision for figure creation.

### ETHICAL APPROVAL

The patient provided written informed consent to publish his case, including the publication of images.

### CONSENT

All the mentioned authors consent for publication.

### DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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