Pulmonary CT imaging findings in fat embolism syndrome: case series and literature review

Authors: Min Qi, Haixia Zhou, Qun Yi, Maoyun Wang and Yongjiang Tang

Background
Fat embolism syndrome (FES) is a rare life-threatening complication, which commonly affects the lung. Currently, the most widely accepted criteria for the diagnosis of FES are the Gurd and Wilson Criteria established nearly 40 years ago, but without pulmonary images involved. Our study aims to analyse the pulmonary computed tomography (CT) findings seen in FES.

Case presentation
This report enrolled four cases of FES with lung involvement. The main symptoms and signs included dyspnea, disturbance of consciousness, anemia, thrombocytopenia and, most notably, ground-glass opacities, septal thickening, ill-defined centrilobular nodules, and patchy consolidation were demonstrated on bilateral lungs. Combining the clinical manifestations and laboratory tests, the diagnosis of FES was confirmed. With the treatment of steroids, anti-coagulation and supportive treatment, the four patients' symptoms were relieved, abnormalities in chest CT were absorbed significantly and the patients were finally discharged.

Conclusions
There are several common manifestations of FES in pulmonary CT images, and the lung parenchymal features give more information for the diagnosis of FES than the pulmonary vessel findings. Given the absence of a gold standard diagnostic test for FES, further investigation to explore new diagnostic criteria of FES involving pulmonary radiological features is needed in the future.

KEYWORDS: Fat embolism syndrome, pulmonary imaging, chest computed tomography, case report

DOI: 10.7861/clinmed.2022-0428

Methods
Four patients who were diagnosed as FES in our hospital between 2014 and 2020 were enrolled and their clinical information, including clinical manifestations, laboratory findings and pulmonary CT imaging, were collected (Table 1, Table 2). In addition, we performed an extensive literature review of FES.
cases by searching the MEDLINE database (through PubMed) (Search strategy: Mesh Term ‘fat embolism syndrome’, English language, human species) and EMBASE database (Search strategy: Emtree terms ‘fat embolism syndrome’/exp, English language, human species) from 1 January 2000 to 31 July 2022. An analysis of the data contained in the case reports was conducted carefully. Patients who met one of the following criteria were included:

- case and case series met the Gurd and Wilson Criteria of FES with pulmonary involvement.19
- computed tomographic pulmonary angiography (CTPA) or tissue pathology imply PFE and patients had clinical symptoms.

The exclusion criteria were:

- cases and case series did not include patients’ basic information (age, gender etc.)
- case and case series did not include CT descriptions of pulmonary parenchyma or pulmonary images after the occurrence of FES.

The article screening process is shown in Fig 1. For all patients, clinical characteristics, including age, gender, type of injuries and surgeries or presence of susceptible diseases conditions, time from injuries or surgeries to symptom onset, clinical symptoms and signs, laboratory findings and pulmonary CT images of lesions at initial presentation were reviewed. Of those, clinical symptoms, signs and laboratory findings mainly involved the parameters mentioned in the Gurd and Wilson criteria.19 Pulmonary CT images showed lesions including ground-glass opacities (GGOs), septal thickening, nodular opacities, consolidation and pleural effusion on CT or high resolution CT,22 and pulmonary fat embolism seen on CTPA.25 For all the 181 patients, the presence of lesions in the bilateral lungs were analysed on thoracic CT images. GGOs were defined as hazy increased lung opacity with preservation of bronchial and vascular margins. Nodular opacities were defined as rounded or irregular opacities, well or poorly defined, measuring within 1 cm in diameter. Septal thickening referred to the thickening of any septa and so render septa visible. Consolidations were

<table>
<thead>
<tr>
<th>Case</th>
<th>ARDS</th>
<th>Assisted ventilation</th>
<th>PO2 (mmHg)</th>
<th>PFE</th>
<th>GGO</th>
<th>Septal thickening</th>
<th>Nodular opacities</th>
<th>Consolidation</th>
<th>Pleural effusion</th>
<th>Resolution time (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>A</td>
<td>A</td>
<td>120</td>
<td>A</td>
<td>P</td>
<td>P</td>
<td>P</td>
<td>A</td>
<td>A</td>
<td>6</td>
</tr>
<tr>
<td>2</td>
<td>P</td>
<td>P</td>
<td>115.6 (FiO2 0.9)</td>
<td>A</td>
<td>P</td>
<td>P</td>
<td>P</td>
<td>P</td>
<td>A</td>
<td>5</td>
</tr>
<tr>
<td>3</td>
<td>A</td>
<td>A</td>
<td>91</td>
<td>A</td>
<td>P</td>
<td>P</td>
<td>P</td>
<td>A</td>
<td>A</td>
<td>26</td>
</tr>
<tr>
<td>4</td>
<td>A</td>
<td>A</td>
<td>56.1</td>
<td>A</td>
<td>P</td>
<td>P</td>
<td>A</td>
<td>P</td>
<td>P</td>
<td>7</td>
</tr>
</tbody>
</table>

ARDS = acute respiratory distress syndrome; PO2 = partial pressure of oxygen; FiO2 = fraction of inspired oxygen; PFE = pulmonary fat embolism; GGO = ground glass opacities; P = present; A = absent.
defined as homogeneous increases of attenuation in pulmonary parenchyma that obscured the margins of vessels and airway walls. Other CT manifestations, like pleural effusion and filling defects of fat attenuation within the pulmonary arteries, were also recorded.

**Results**

From January 2000 to July 2022, 1,388 related articles were searched for screening. Among them, 123 articles involving 177 FES patients with pulmonary involvement were identified (see supplementary material S1). With the other four FES patients admitted to our hospital, there were 181 cases in total for analysis.

**Case presentation**

**Case 1**

A 39-year-old woman presented with dyspnea after liposuction from abdomen and lumbar region and was admitted to our emergency department. She underwent bilateral breast prosthesis implantation 8 years ago. On arrival, she was tachycardic and drowsy, and multiple petechial rashes were seen on the anterior surface of the chest wall. CTPA demonstrated diffuse GGOs. There were no filling defects within pulmonary arteries (Fig 2a and Fig 2b). She was diagnosed with FES and supportive treatments were given. Finally, her symptoms relived and she was discharged.

**Case 2**

A 35-year-old man had undergone liposuction under general anesthesia, with a total aspirate volume of 1.8 liters obtained from the abdomen and lumbar regions. The patient suddenly became unconscious, with dyspnea and cyanosis, and his heart rate and oxygen saturations dropped after he was extubated and transferred to ward for monitoring. Cardiopulmonary resuscitation and vasopressors were administered, and the patient was intubated with invasive ventilation. After the spontaneous rhythm of the heart restored, he was transferred to the intensive care unit of our hospital. The obtained CTPA showed diffuse nodular opacities, bilateral GGOs and consolidation, without filling defects within pulmonary arteries (Fig 2c and Fig 2d). These findings confirmed the diagnosis of FES. After supportive treatment, the patient’s pulmonary imaging improved and he was discharged.

**Case 3**

A young woman aged 17, with her right tibia and fibula fractured in a car accident, received bone casting and traction in a local hospital. 4 days later, she presented with dyspnea and was admitted to our hospital. On examination, her vital signs were stable. The CTPA showed nodular opacities, GGOs and septal thickening, no perfusion defects within pulmonary arteries (Fig 2e and Fig 2f). Blood investigations showed moderate anemia and thrombocytopenia. Due to the combined history and clinical manifestation, the patient was diagnosed with FES. The patient’s symptoms relived after 1 week’s treatment with steroids and anticoagulation.

**Case 4**

A 41-year-old woman had an augmentation mammaplasty and liposuction from the abdomen and lumbar region under general anesthesia; the surgery was uneventful. After 2 hours she became drowsy and then lost consciousness, with dyspnea and cyanosis, and oxygen saturation dropped sharply to 16%. Oxygen therapy, epinephrine and dexamethasone were given, and the patient recovered consciousness, but she still felt dyspnea and had cough with blood-tinged sputum and was transferred to our hospital. On arrival, the patient was conscious with vital signs stable. The arterial blood gas (ABG) showed respiratory failure with PO\textsubscript{2} 56.1 mmHg. Laboratory findings demonstrated anemia and thrombocytopenia. The chest CT showed bilateral pulmonary consolidation, GGOs, and septal thickening, without filling defects within pulmonary arteries in CTPA (Fig 2g and 2h). The diagnosis of FES was made and steroids and anti-coagulation drugs were given. Finally, the patient fully recovered and was discharged.
Demographic characteristic and causes of fat embolism (Table 3)

Among the enrolled patients, there were 117 males and 64 females, ranging from 11 years to 91 years old, with a median age of 29.0 years. The average time from traumatic injury or surgery procedure to the onset of symptoms was 1 (0–2) days. The most common cause of FES was traumatic bone fracture (133/181), especially the femoral fracture (60/181), followed by multiple bone fractures (42/181), tibial and fibula fractures (26/181), liposuction and fat grafting (22/181), vertebral fractures (3/181), humerus fracture (2/181), total hip arthroplasty (1/181), total knee arthroplasty (3/181), bilateral sinus floor augmentation (1/181), lung transplantation from donor-acquired FES (4/181), renal angiomyolipoma/malignant tumor (7/181), bone marrow necrosis (6/181), others (malignant with chemotherapy, hyperinflammation state) (2/181), and unknown (2/181).

Table 3. Demographic characteristic and causes of FES

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Male (117/181)</td>
<td></td>
</tr>
<tr>
<td>Female (64/181)</td>
<td></td>
</tr>
<tr>
<td>Age/years (M, IQR)</td>
<td>29 (22–46)</td>
</tr>
<tr>
<td>Time from injuries/surgeries to symptom onset in days (median, interquartile range)</td>
<td>1 (0–2)</td>
</tr>
<tr>
<td>Type of injuries/surgeries/diseases</td>
<td></td>
</tr>
<tr>
<td>Femoral fracture</td>
<td>60/181</td>
</tr>
<tr>
<td>Tibial and fibula fractures</td>
<td>26/181</td>
</tr>
<tr>
<td>Multiple bone fractures</td>
<td>42/181</td>
</tr>
<tr>
<td>Vertebral fracture</td>
<td>3/181</td>
</tr>
<tr>
<td>Humerus fracture</td>
<td>2/181</td>
</tr>
<tr>
<td>Total hip arthroplasty</td>
<td>1/181</td>
</tr>
<tr>
<td>Total knee arthroplasty</td>
<td>3/181</td>
</tr>
<tr>
<td>Bilateral sinus floor augmentation</td>
<td>1/181</td>
</tr>
<tr>
<td>Lung transplantation from donor-acquired FES</td>
<td>4/181</td>
</tr>
<tr>
<td>Liposuction and fat grafting</td>
<td>22/181</td>
</tr>
<tr>
<td>Renal angiomyolipoma/malignant tumor</td>
<td>7/181</td>
</tr>
<tr>
<td>Bone marrow necrosis</td>
<td>6/181</td>
</tr>
<tr>
<td>Others (malignant with chemotherapy, hyperinflammation state)</td>
<td>2/181</td>
</tr>
<tr>
<td>Unknown</td>
<td>2/181</td>
</tr>
</tbody>
</table>

Fig 2. The radiological manifestations of four patients. (a) Pulmonary CT showed diffuse ground-glass opacities (GGOs). (b) Computed tomographic pulmonary angiography (CTPA) revealed no filling defects within pulmonary arteries. (c) Chest CT showed diffuse nodular opacities, bilateral GGOs and consolidation. (d) No filling defects within pulmonary arteries detected by CTPA. (e) Chest CT showed nodular opacities, GGOs and septal thickening. (f) CTPA showed no perfusion defects within pulmonary arteries. (g) Chest CT showed bilateral pulmonary consolidation, GGOs and septal thickening. (h) No filling defects was found by CTPA.

Discussions and conclusions

Currently, the widely accepted diagnostic criteria for FES are the Gurd and Wilson Criteria established nearly 40 years ago, and there is no gold standard test for FES. In 1987, Lindeque et al introduced arterial blood analysis into the diagnosis of FES in tibia or femur fracture patients, corresponding to the respiratory insufficiency in Gurd’s criteria to some extent. In a prospective randomised study, Schonfeld’s criteria were proposed, which gave symptoms and fracture sites corresponding weighted scores (101/137) and acute respiratory failure syndrome (ARDS) (97/149) presented in more than half of the patients. Petechiae was present in 51 out of 105 patients. While in 50 patients retinal signs were mentioned, among them, 20 patients presented with retinal signs and 30 cases without retinal signs. 14 patients presented with renal signs. As with pulmonary imaging, 31 patients had their diagnosis confirmed by CTPA with filling defects in pulmonary arteries. The measurements of the filling defects showed negative mean attenuation values. GGOs were demonstrated in 143 patients, nodular opacities in 125 patients, septal thickening in 122 patients, and consolidation and pleural effusion in 81 and 40 patients, respectively. Among those with follow-up pulmonary CT, the average resolution time was 12.0 (7.0–16.4) days. For those with outcomes recorded, 133 patients survived (133/147).
This, to some extent, could explain the rarity of visualisation of ground-glass opacities presumably mirror the alveolar edema and permeability edema and hemorrhage. Both the mechanical and biochemical theories for what causes the clinical symptoms and pulmonary imaging findings have been widely accepted. The mechanical theory suggests that outside mechanical forces, such as traumatic injury, invasive surgery and liposuction, could disrupt fat globules in the bone marrow and fat tissue into ruptured venules which then enter into pulmonary capillaries or systemic circuit, causing pulmonary and other organs’ dysfunction. Mechanical obstruction of pulmonary microvasculature by fat emboli would also cause ventilation perfusion mismatch with severity proportional to the burden of fat in the circulation. According to the biochemical theory, fat emboli trapped in the pulmonary capillaries release free fatty acids and glycerol, which are toxic to the lung and trigger a cascade of inflammation, resulting in localised endothelial injury, permeability edema and hemorrhage. Both the mechanical and biochemical injuries lead to the clinical manifestations of FES, ranging from hypoxemia, tachypnea and dyspnea to ARDS, consistent with the pulmonary imaging findings. As ground-glass opacities presumably mirror the alveolar edema and hemorrhage, septal thickening may reflect congestion and edema in the interstitium, and centrilobular nodules are believed to reflect the initial vasculogenic insult of fat emboli. However, the mechanical obstruction seems to play a less important role in the pulmonary injury than the inflammatory cascade trigger. This, to some extent, could explain the rarity of visualisation of macroscopic fat emboli within pulmonary vessels in the CTPA. As in our study, there were only 31 patients out of 122 patients with computed tomographic angiograms available that presented with fat emboli in the pulmonary vessels. In practice, FES needs to be differentially diagnosed with pulmonary thromboembolism (PTE) in patients presenting with dyspnea and traumatic history. Compared with PTE, FES has no predictable risk factors like deep venous thrombosis, and usually occurs in settings related to disruption of the fatty tissue. There may be an interval of 12–48 hours between the initiation of trauma or surgeries and the onset of clinical and radiologic findings. The relatively specific symptom of petechiae, which presents within 24–36 h of injury or insult, only occurred in 20–50% of patients and resolved quickly. Furthermore, the differential diagnosis mainly relies on the attenuation of intraluminal filling defects within pulmonary arteries in CTPA; PTE presents with soft tissue attenuation while FES presents with fat attenuation; the emboli thrombus is extremely uncommon. During the global pandemic of COVID-19, it is also important and necessary to consider the differential diagnosis of FES and COVID-19, as they have similar symptoms and radiological findings; however, the SARS-CoV-2 RNA test, recent long bone fractures and traumatic history may provide vital clues.

Our study has several limitations. First, the major limitation is the small sample size, with only four patients included, which limits the further exploring of the new diagnostic criteria that including image findings and the comparison of radiological findings of different etiologies. Second, the pulmonary lobes and lung fields involved were not recorded, which may affect the entire disease evaluation and limit the accurate description of pulmonary images. This study was a retrospective case series and literature review, and full detailed descriptions or CT images could not be acquired in all cases. Last but not least, patients in our study did not receive the same treatment, though there was no standard therapy that would have influenced the resolution time of the radiological lesions.

In conclusion, the occurrence of FES is mostly related to traumatic fracture, arthroplasty, fracture fixation, liposuction and fat transplantation. The common manifestations of FES in pulmonary CT images were GGOs, nodular opacities and septal thickening, and the lung parenchymal features would give more information for the diagnosis of FES than the pulmonary vessel findings. Given the absence of a gold standard diagnostic test for FES, investigation to explore new diagnostic criteria for FES involving pulmonary radiological features is needed in the future.

Ethics approval and consent to participate
The study was approved by the Institutional Ethics Committee at our institution (Ethical review approval number: 2020-713).

Funding
This study was supported by Sichuan Provincial Health Committee(18PJ398) in data collection and manuscript writing.

Supplementary material
Additional supplementary material may be found in the online version of this article at www.rcpjournals.org:
S1 – Articles included in analysis.

References
Pulmonary CT Images in Fat Embolism Syndrome