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Case Report



Pulmonary Fat Embolism Syndrome: A Case Report and Literature Review

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Abstract

Background: Fat embolism syndrome (FES) is caused by a systemic inflammatory response arising from embolized fat particles that block blood vessels and disrupt blood supply, particularly in the respiratory microcirculation. Despite its high morbidity and mortality, FES is still challenging to diagnose due to its versatile symptoms.

Case Presentation: In this article, we describe case reports of two patients with pulmonary FES from Zhongnan Hospital of Wuhan University, Wuhan, China. The two patients were diagnosed based on their detailed medical histories, such as a history of liposuction surgery, low oxygen saturation, dyspnea, and chest computed tomography (CT). Both of them received continuous oxygen inhalation therapy and antibiotic treatment. The first patient received additional anti-inflammation and anticoagulation treatment. The symptoms and CT improved after treatments. They were discharged and completely cured.

Literature Review: We obtained and analyzed the clinical manifestations, treatments, and prognosis data of 206 patients diagnosed with pulmonary FES between January 1900 and July 2021 from the China National Knowledge Infrastructure database.

Conclusion: The analysis of our two cases and the literature review suggest that patients with symptoms (such as respiratory system symptoms, nervous system symptoms, cardiovascular system symptoms, and mucocutaneous bleeding) combined with a history of fracture and other risk factors should be considered pulmonary FES cases. Furthermore, respiratory support and glucocorticoid treatment may be effective in preventing the death of pulmonary FES patients.

Keywords: Fat embolism syndrome, Liposuction, Pulmonary fat embolism syndrome

1. Background

Fat embolism syndrome (FES) often occurs after a long bone fracture, surgery, or the contusion of adipose tissue, in which the fat in the tissue forms large fat droplets in the blood and embolizes in the blood vessels of the lung, brain, skin, and other organs (1, 2). Additionally, FES can be induced by many different conditions, including certain metabolic diseases (such as diabetes), alcoholism, collagen diseases, chemotherapy, osteomyelitis, sickle cell disease, and severe infections (3, 4). When fat embolism occurs in the pulmonary vascular system, it is called pulmonary FES. In this article, we present the clinical data of two cases diagnosed with pulmonary FES in our hospital. We also analyzed the clinical features and outcomes of 206 patients reported in the China National Knowledge Infrastructure (CNKI) database from Jan 1900 to July 2021 to improve the understanding of FES and facilitate its medical diagnosis.

2. Case Presentation

Case 1, a 21-year-old female, was admitted to Zhongnan Hospital of Wuhan University after showing low blood oxygen saturation on pulse oximetry for one day. She had received liposuction in both of her thighs in a plastic surgery hospital on April 2, 2018, and her oxygen saturation level decreased to 89% at about 10 p.m. the same day. She had no symptoms like chest tightness, cough, expectoration, or fever. She was administered antibiotics and oxygen inhalation therapy, but her oxygen saturation level did not improve. She was then transferred to our hospital and admitted to the respiratory department on April 3, 2018. The clinical characteristics of the patients are presented in Table 1. Her chest CT showed diffuse exudative lung lesions (Figure 1, top panel). After admission, she was given continuous oxygen inhalation therapy, antibiotic treatment (cefminox sodium 2 g, intravenous drip, anti-inflammation twice а dav), treatment (methylprednisolone 40 mg, intravenous drip, once a day), and anticoagulation therapy (low molecular weight heparin sodium injection, 4000AxaIU, subcutaneous injection, once a day). On April 4, 2018, her chest CT showed significant absorption of the lung lesions (Figure 1, bottom panel), and her blood oxygen saturation increased to 98% (without oxygen inhalation). She was discharged on April 5, 2018.

Case 2, a 30-year-old female, was admitted to our hospital with progressive dyspnea for 10 h. She had received liposuction during the day on March 30, 2021, in a plastic surgery hospital. Around 8:00 p.m. on the same day, she felt short of breath and coughed up pink sputum. She was transferred to the emergency department of our hospital at 2:00 a.m. on

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Table 1. Clinical characteristics of the two cases				
Clinical characteristics		Case 1	Case 2	
Vital signs	Temperature Puke rate Respiratory rate Blood pressure	37.2°C 94 beats per min 20 breaths per min 118/73 mmHg	36.9°C 77 beats per min 20 breaths per min 122/73 mmHg	
	Yellow staining and bleeding points on the skin and mucosa	Negative	Negative	
Physical examination	Pulmonary auscultation	"Wet" crackles in the right lower lung field	"Wet" crackles on both lung bases	
	Cardiac examination Abdominal examination	Normal Normal	Normal Normal	
Blood routine examination	White blood cells	10.89×10 ⁹ /L	22.00×10 ⁹ /L (March 31, 2021) 15.83×10 ⁹ /L (April 4, 2021) 20.53×10 ⁹ /L (March 31, 2021)	
	Neutrophil	9.87×10 ⁹ /L	13.39×10 ⁹ /L (April 4, 2021)	
Blood coagulation picture	Fibrinogen-C D-dimer Prothrombin time Standardized ratio of prothrombin Prothrombin time activity N-terminal brain natriuretic peptide	573 mg/dl Normal Normal Normal Normal Normal	Normal 2310 μg/L 16.1 seconds 1.47 56% 282 pg/ml (March 31, 2021)	
Urine analysis	Urine protein Red blood cell	Positive (+) 67.60/uL	Normal Normal	
Others	Cardiomyo globin C-reactive protein Procakitonin Erythrocyte sedimentation rate	Normal Normal Normal 27 mm/h	530.0 ng/ml 72.6 mg/L 0.35 ng/ml Normal	
Blood gas analysis	Potential of hydrogen Arterial oxygen pressure Arterial carbon dioxide pressure Oxygen saturation	7.40 60 mmHg 33 mmHg 89% (without oxygen therapy)	7.36 88 mmHg 25.1 mmHg 95% (with oxygen inhalation, 2L/min)	



Figure 1. Chest CT scan of Case 1. Top panel: Chest CT scan of patient 1 on April 3, 2018, showing diffuse exudative lesions in both lungs. Bottom panel: Chest CT scan of the same patient on April 4, 2018, showing significant absorption of bilateral lesions

March 31, 2021. Her chest CT showed patchy opacifications in both lungs (Figure 2, top panel). The clinical characteristics of the patients are presented in Table 1. She was administered oxygen inhalation therapy and antibiotic treatment (biapenem 300 mg, intravenous drip, twice daily). On April 4, 2021, her chest CT showed apparent absorption of both lung lesions (Figure 2, bottom panel). Her blood oxygen saturation increased to 96% (without oxygen inhalation therapy). She no longer felt dyspnea and

had no other discomfort. All her vital signs were normal, and she was discharged on April 7, 2021.

3. Literature Review

Fat embolism was used as the search keyword in the CNKI database. This resulted in 163 studies and 206 cases of pulmonary FES as of June 2021 (the data are summarized in Table 2). The age of the pulmonary FES patients ranged from 4-85 years, with



Figure 2. Chest CT scan of Case 2. Top panel: Chest CT scan of patient 2 on March 31, 2021, showing patchy shadows in both lungs. Bottom panel: Chest CT scan of the same patient on April 4, 2021, showing absorption of the bilateral lesions

Table 2. Summary of clinical characteristics among 206 patients with pulmonary fat embolism syndrome reported in published literature

Information category		Total number of cases (n=206)	Cases (Proportion) N (%)
Gender		Male	153 (74.27%)
		Fracture	171 (83.01%)
Pathogenic cause		Liposuction	9 (4.37%)
		Other types of surgery or trauma	26 (12.62%)
Clinical manifestations	Respiratory system	Dyspnea, shortness of breath, cough, expectoration, hemoptysis, lung rales, chest tightness, chest pain, and cyanosis	185 (89.81%)
	Nervous system	Blurred consciousness, drowsiness, delirium, coma, agitation, blurred vision, speech disorder, and headache	161 (78.15%)
	Skin mucosa	Bleeding points on the subconjunctival, neck, anterior chest, and axillary skin	91 (44.17%)
	Cardiovascular system	Tachycardia, hypotension, cold limbs, and cardiac arrest	106 (51.46%)
	Fever	Temperature greater than 38°C	96 (46.60%)
	Chest CT or X-ray	Spot-like consolidation or "blizzard"-like changes in the lungs	93 (45.15%)
	Fat droplet	Fat droplets in blood, sputum, and urine	42 (20.39%)
	Platelet	Platelet progressive decrease; platelet less than 100×10^9 /L	31 (15.05%)
	Arterial partial pressure of oxygen	Arterial oxygen partial pressure of less than 60 mmHg	66 (32.04%)
	Blood oxygen saturation	Blood oxygen saturation of less than 95%	65 (31.55%)
Chest imaging findings		Ground glass and patchy consolidation	90 (45.15%)
Diagnostic- mothod		Autopsy	35 (16.99%)
Diagnostic- includu		Clinical diagnosis	171 (83.01%)
Prognosis		Recovery	150 (72.82%)
		Death	56 (27.18%)

an average age of 36. Of the 206 patients, 150 recovered and 56 died, resulting in a mortality rate of 27.18%. Of the 150 patients in the recovery group, 146 (97.33%) received respiratory support therapy, and 122 (81.33%) received glucocorticoid treatment. Of the 56 patients in the death group, 26 (46.43%) received respiratory support therapy, and 28 (50%) received glucocorticoid treatment. Regarding the onset of the disease, most pulmonary FES cases occurred one to three days after injury among these 206 patients. Regarding the treatment time, the median treatment time of patients in the recovery group was seven days, with the longest being 130 days. The median time from disease onset to patient death in the death group was five days, with the shortest time from onset to death being only half an hour.

4. Discussion

Both mechanical and biochemical theories have been proposed for the pathophysiology of FES (5, 6). The mechanical th eory hypothesizes that fat enters the bloodstream from the damaged bone marrow or the adipose tissue after trauma or surgery, forming fat embolic particles in the blood vessels that block the blood supply. On the other hand, the biochemical theory hypothesizes that the fat that enters blood circulation after trauma is metabolized and degraded into toxic substances, which induces a wide range of inflammatory reactions. This triggers free fatty acids (FFA) to gather and form fat droplets that enter various tissues and organs through the bloodstream, resulting in a series of symptoms, including pulmonary edema, hemorrhage, and even acute respiratory distress syndrome (ARDS). In our study, both cases had an acute onset, and respiratory failure was not fully explained by cardiac failure or fluid overload, with chest imaging findings of diffuse exudative lesions or patchy shadows in both lungs. The oxygenation index of Case 1 was 285.71 mmHg, and that of Case 2 was 303.45 mmHg. In addition, the symptoms of respiratory distress in the two cases were mild, and nasal tube oxygen inhalation (2 L/min) could improve respiratory distress and hypoxemia. Therefore, according to the Berlin Definition of ARDS (7), neither patient met the diagnosis of ARDS.

Pulmonary FES usually causes multiple system dysfunctions within 24-72 h after disease onset. Typical symptoms of pulmonary FES include respiratory disorders, brain dysfunction, and bleeding points on the skin and mucous membrane (8). Respiratory symptoms, such as dyspnea, hypoxemia, and respiratory failure, are often observed as the initial clinical manifestations of pulmonary FES. Additionally, rhonchus and "wet" crackles or rales are frequently detected in the lungs during auscultation. While severe pulmonary FES patients can have a mortality rate of as high as 50%, the mortality rate varies significantly depending on the severity of the disease. For example, the two pulmonary FES patients from our hospital only exhibited mild symptoms, and both were recovered and discharged within three days post-admission. Additionally, the 206 pulmonary FES patients included both mild and severe cases and thus showed a mortality rate of 27.18%. In the early 1970s, Gurd (9) established the clinical diagnostic criteria of FES, which were modified in 1974 by Wilson and Gurd. Afterward, the Gurd standard became the most commonly used clinical diagnostic standard (Table 3). Despite the significant advancement brought by the Gurd standard in diagnosing FES, the diagnosis can remain challenging due to the lack of specific biomarkers for FES. However, several markers and clinical parameters have been proposed to improve

the diagnosis of FES. For example, it has been shown that FES is likely accompanied by a decrease in hemoglobin and platelets and an increase in inflammation-related indicators, muscle enzymes, troponin I, and D-dimer. Particularly in posttraumatic patients, a progressive increase in the inflammatory factor IL-6 level was shown to help facilitate FES diagnosis (10, 11). Further, detecting fat droplets in blood and urine or lipid inclusion bodies in the lavage fluid in bronchoalveolar lavage was suggested as an auxiliary diagnostic indicator of FES (12).

Additionally, several studies have suggested that a change in the neutral fat concentration in the blood can be used to predict the onset of early FES. Apart from these lab parameters, imaging has been shown to be effective in diagnosing FES. The chest X-ray of early FES patients often indicates no significant changes within the first three days. Afterward, the typical clinical manifestations of FES on chest X-ray are ground-glass and patchy opacities in the middle and upper lung fields, resembling a "snowstorm" appearance (13). Compared to the chest X-ray, highresolution CT is more sensitive and accurate in detecting early lung changes and thus can be used for early and differential diagnoses. CT scans of FES patients usually show ground-glass, nodular, consolidation, or patchy opacification in the lung, along with interlobular septal thickening (14). At present, the diagnosis of FES still mainly depends on excluding other potential diseases according to the medical history (trauma and operation history), clinical manifestations, and auxiliary examination (especially blood oxygen and imaging examination) of the patients (15).

In this study, we presented two cases of pulmonary FES and analyzed clinical manifestations, as well as treatments used in 206 pulmonary FES patients reported in the CNKI database, aiming to provide insights to improve the diagnosis and treatment of pulmonary FES.

Among the 206 patients, 93 showed ground glass

Table 3. Gurd standard			
Gurd standard	Index		
Main standards	Respiratory symptoms: shortness of breath, dyspnea, and cyanosis, accompanied by decreased blood oxygen partial pressure, increased blood carbon dioxide partial pressure, and pulmonary imaging findings The neurological symptoms of craniocerebral trauma were excluded: drowsiness, confusion, convulsions, and coma		
Secondary standard	Subcutaneous hemorrhage: bleeding points on the skin and mucosa Arterial oxygen partial pressure of <8.0 kPa (60 mmHg) Hemoglobin decreased (<100 g/L) Pulse rate of >120 beats per min Body temperature of <38°C		
Reference standard	Thrombocytopenia Urine fat drop positive Erythrocyte sedimentation rate of >70 mm/h Increase in serum lipase Blood-free fat drop positive		

The diagnosis can be made when there are more than two main standards, only one main standard, or more than four secondary or reference standards

Table 4. Analysis of two therapies in the recovery group and the death group

Treatment	Recovery group (n=150)	Death group(n=56)	P-value	
Respiratory support therapy	146 (97.33%)	26 (46.43%)	P<0.001	
Glucocorticoid therapy	122 (81.33%)	28 (50%)	P<0.001	
Comparisons were performed between the recovery group and the death group using the Chi-squared test. Data are presented as numbers				

Comparisons were performed between the recovery group and the death group using the Chi-squared test. Data are presented as numbers (percentages)

and patchy opacifications in both lungs' middle and lower lung fields in their lung imaging examination, similar to a classic "snowstorm" appearance. This suggests that the characteristic changes observed in chest imaging can be essential in diagnosing pulmonary FES. In 35 cases where patients received autopsies, lipid droplet vacuoles were found in pulmonary vessels, providing direct evidence for FES diagnosis (16), which can be considered a standard test for FES diagnosis in the future. The main treatments for patients with FES are maintaining saturation, ensuring ventilation, oxygen and maintaining hemodynamic stability. Mechanical ventilation and extracorporeal membrane oxygenation have improved the mortality rate of patients with severe FES (17). Additionally, several other treatment methods have been reported to improve the outcome of FES. For example, Sen et al. (18) found that the inhalation of ciclesonide effectively prevents the onset of FES and hypoxemia in fracture patients. Further, Chen (19) et al. found that the early use of glucocorticoids can reduce the number of blood fat droplets and the toxic reaction of FFA. This, in turn, decreases the production of inflammatory mediators and reduces the adhesion of platelets, alleviating pulmonary edema and increasing the partial pressure of arterial oxygen. In agreement with these findings, we found that (Table 4), of the 150 patients in the recovery group, 146 (97.33%) received respiratory support therapy and 122 (81.33%) received glucocorticoid treatment. On the contrary, of the 56 patients in the death group, only 26 (46.43%) received respiratory support, and 28 (50%) received glucocorticoid therapy. This suggests that respiratory support therapy (P<0.001) and glucocorticoid therapy (P<0.001) can effectively improve the prognosis of pulmonary FES and reduce mortality rates.

5. Conclusion

Pulmonary FES lacks specific symptoms and physical signs in the early stages and can easily cause misdiagnosis or lead to a missed diagnosis. Traditionally, the leading causes of pulmonary FES are bone fractures, orthopedic trauma, or surgery. However, in recent years, the incidence of FES postplastic surgery has increased dramatically due to the rising popularity of plastic surgery procedures, such as liposuction (20). For example, patients in the two cases reported here developed the disease after receiving liposuction. Therefore, pulmonary FES should be considered during diagnosis when patients are referred to the hospital with clinical manifestations, including respiratory, neurologic, or subcutaneous hemorrhage, along with a history of plastic surgery, such as liposuction, and/or a history of fractures or trauma. Effective diagnostic treatment methods, including autopsy, respiratory support, and glucocorticoid therapy, can be administered to potential FES patients to improve their disease outcomes.

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Footnotes

Conflicts of Interest: All authors who have affiliations with Zhongnan Hospital of Wuhan University declare that they do not have any competing interests.

Ethics approval and consent to participate: This study was approved by the Medical Ethics Commission of Zhongnan Hospital of Wuhan University, Wuhan, China, and the patients provided consent to participate.

Consent for publication: Written informed consent for publication of the clinical details and/or clinical images was obtained from the patients.

Informed consent statement: Written informed consent was obtained from the patients to publish this report and any accompanying images.

Data access statement: The generated datasets are available by request to the corresponding author.

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