

OPEN ACCESS

Full open access to this and thousands of other papers at <http://www.la-press.com>.

Fat Embolism Syndrome: An Autopsy-Proven Case Involving a Patient on Dialysis and Systemic Scleroderma

Nahoko Nishimura¹, Shogo Banno¹, Yukihiro Kimura¹, Sayaka Maeda¹, Mizuki Kobayashi², Kumi Kawai², Norihiro Suga¹, Keisuke Suzuki¹, Naoto Miura¹, Toyoharu Yokoi² and Hirokazu Imai¹

¹Division of Nephrology and Rheumatology, Department of Internal Medicine, University School of Medicine, Nagakute, Aichi, 480-1195, Japan. ²Department of Clinical Pathology, Aichi Medical University School of Medicine, Nagakute, Aichi, 480-1195, Japan. Corresponding author email: imaihiro@aichi-med-u.ac.jp

Abstract: A 66-year-old woman receiving continuous ambulatory peritoneal dialysis developed acute respiratory distress 12 hours after a fall. Blood gas analysis revealed hypoxia (PaO₂ 67.7 torr) and metabolic acidosis with an increased anion gap, consistent with lactic acidosis (lactate, 86.5 mg/dL; normal range, 4.0–16.0). Magnetic resonance imaging showed a lumbar vertebral body fracture. On the fourth hospital day, the patient died of multiorgan failure and disseminated intravascular coagulation. Postmortem studies revealed fat emboli in the systemic circulation, ie, fat embolism syndrome. Diagnosing fat embolism syndrome can be difficult in patients on dialysis or in those with collagen vascular or pulmonary diseases.

Keywords: A-aDO₂, acute respiratory distress, diagnostic criteria, fat embolism syndrome, hypoxia, lactic acidosis

Clinical Medicine Insights: Case Reports 2014:7 7–12

doi: [10.4137/CCRep.S12636](https://doi.org/10.4137/CCRep.S12636)

This article is available from <http://www.la-press.com>.

© the author(s), publisher and licensee Libertas Academica Ltd.

This is an open access article published under the Creative Commons CC-BY-NC 3.0 license.



Introduction

Fat embolism syndrome (FES) is defined as the presence of fat emboli not only in pulmonary system but in the systemic circulation as well, with systemic ischemic or inflammatory signs such as neurological, renal, and cutaneous manifestations.¹ This condition may result in a fatal outcome. Pulmonary fat emboli occur in more than 90% of patients with long-bone fractures,² but the frequency of FES is reported to be between 0.9% and 11% following multiple bone fractures or lower long bone or pelvic fractures.²⁻⁴ Other conditions such as orthopedic surgery⁵ and liposuction for obesity⁶ have been reported as causes of FES. However, FES is very rare with vertebral body fractures⁷⁻⁹ despite their relatively high prevalence in the general population.¹⁰

This is the first English-language case report describing FES following traumatic vertebral body fracture in a patient receiving continuous ambulatory peritoneal dialysis (CAPD) for anuric renal failure secondary to scleroderma renal crisis (SRC). We discuss the diagnostic criteria and therapeutic options for FES with a literature review.

Case Report

A 66-year-old woman was transferred to the Aichi Medical University Hospital emergency room because of severe back and abdominal pain after she slipped and fell 12 hours earlier. Prior to this, she had been treated with antihypertensive medication for 11 years. Ten years prior to admission, she was diagnosed with systemic scleroderma and was started on prednisolone (PSL) at 15 mg/day. Seven months prior to admission, CAPD was started for anuric renal failure secondary to SRC due to difficulties in creating a vascular access site as a result of systemic scleroderma. She was maintained on CAPD without any problems. Two months prior to admission, her blood pressure stabilized at 100–120/60–80 mmHg. Although PSL was continued at 9 mg/day, the following medications were discontinued: an angiotensin-converting enzyme inhibitor, an angiotensin receptor blocker, and a calcium channel blocker. One week before admission, blood gas analysis drawn while breathing room air showed pH 7.43, PaO₂ 96 torr, PaO₂ 39.4 torr, and serum bicarbonate 25.3 mmol/L, a normal study.

Twelve hours prior to admission, the patient slipped and fell in a passageway in her home and immediately

experienced severe left-sided back pain and abdominal pain. She was transferred to our hospital's emergency room. She had normal mental status and a clear state of consciousness. Her height was 162 cm and her weight was 48.4 kg. Her body temperature was 36.0 °C, pulse was 129 beats/min and regular, respiratory rate was 24 breaths/min, and blood pressure was 154/98 mmHg. A physical examination revealed fine crackles audible in both lower lung fields, severe scleroderma on the upper and lower extremities, and an aggravated blue color and ulcerations on the fingers and feet. Blood oxygen saturation was 92%. Blood gas analysis of a sample drawn while the patient was breathing room air revealed pH 7.32, PaO₂ 67.7 torr, PaCO₂ 17.3 torr, and serum bicarbonate 8.9 mmol/L. The patient had severe metabolic acidosis with an elevated lactate level of 86.5 mg/dL (normal range: 4.0–16.0). The alveolar-arterial oxygen tension difference (A-aDO₂) was 60 (normal range: below 20). Serum sodium was 131 mmol/L, potassium was 4.1 mmol/L, and chloride was 103 mmol/L. The patient's white blood cell count was 13,500/μL, red blood cell count was 259 × 10⁴/μL, hemoglobin was 8.8 g/dL, hematocrit was 26.2%, platelet count was 20.7 × 10⁴/μL, albumin was 2.9 g/dL, blood urea nitrogen was 64.9 mg/dL, and creatinine was 5.12 mg/dL. Aspartate aminotransferase (AST) was 78 IU/L, alanine aminotransferase (ALT) was 56 IU/L, and lactate dehydrogenase (LDH) was 521 IU/L. Her C-reactive protein level was 4.91 mg/dL and anti-nuclear antibody titer was elevated at 1:320 in a speckled pattern. The anti-Scl-70 antibody level was 3600 U/mL (normal range: below 10 U/mL). Blood tests were negative for anti-centromere, anti-RNP, anti-SS-A and SS-B, and myeloperoxidase-anti-neutrophil cytoplasmic antibodies, hepatitis B antigen, hepatitis C virus antibody, and cryoglobulins.

X-rays of the chest, abdomen, and pelvis revealed a large homogenous shadow in the right upper and middle lung fields and a reticular shadow in the left middle lung field (Fig. 1A) and no evidence of pelvic fractures. Computed tomography (CT) of the chest revealed massive infiltration of the right middle lung field (Fig. 1B).

Sagittal T1 weighted and fat-suppressed T2 weighted magnetic resonance imaging (MRI) of the lumbar spine showed a vertebral body fracture at the level of L1 (Fig. 1C).

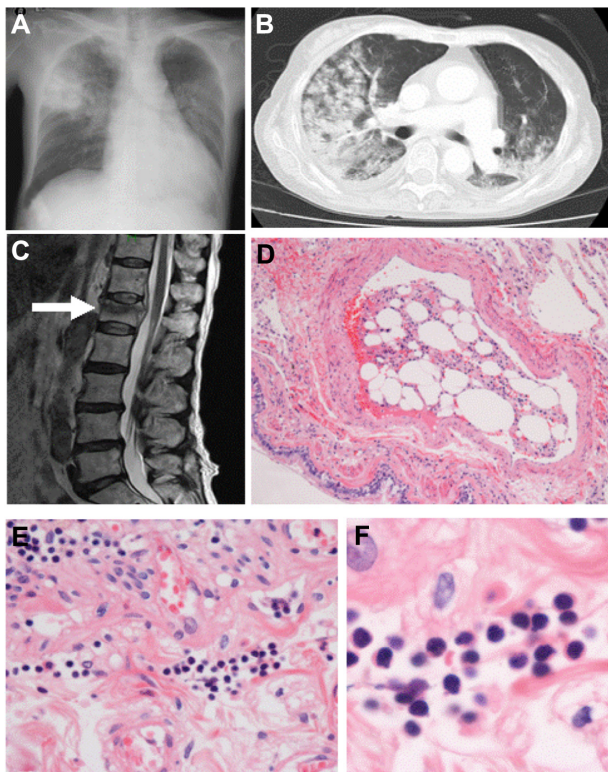


Figure 1. (A) Chest X-rays. A large homogenous shadow in the right upper and middle lung fields and a reticular shadow are present in the left middle lung field. (B) Computed tomography (CT) of the chest. Massive infiltration of the right middle lung field was observed. (C) Sagittal T1 weighted magnetic resonance imaging (MRI) of the lumbar spine. A vertebral body fracture was found at the level of L1 (white arrows). (D) Postmortem pathological studies. Fat emboli including bone marrow cells were observed in the pulmonary artery (HE stain, 100 \times). (E) Postmortem pathological studies. Bone marrow cells were present in an arteriole in the submucosa of the colon (HE stain, 400 \times). (F) Postmortem pathological studies. Higher magnification of the same section showed many myelocytes and erythroblasts (HE stain, 1000 \times).

After admission, we investigated the cause of hypoxia and severe lactic acidosis with oxygen therapy and administration of bicarbonate. On the second hospital day, AST was 2175 IU/L, ALT was 1700 IU/L, and LDH was 4083 IU/L (Table 1). Her level of consciousness rapidly decreased to drowsy. Brain CT demonstrated neither bleeding nor infarction. She was transferred to the intensive care unit on the third hospital day. The mode of dialysis was changed from CAPD to hemodialysis in the ICU. She received 20 units of fresh frozen plasma and 400 mL of red blood cells. Serum levels of creatine kinase rapidly increased to 6320 U/L, along with increases in AST, ALT, and LDH levels. Prolongation of prothrombin time and the international normalized ratio, significantly elevated levels of fibrin and fibrinogen degradation products (FDPs),

and a rapidly decreasing platelet count suggested disseminated intravascular coagulation (DIC), based on the International Society on Thrombosis and Haemostasis (ISTH) criteria. Initially, we made a diagnosis of pneumonia after the vertebral body fracture was identified. The patient's blood pressure dropped to 80 mmHg. On the morning of the fourth hospital day, she died from multiorgan failure and disseminated intravascular coagulation.

Postmortem Pathological Studies

Pathological studies demonstrated fat emboli, including bone marrow cells in the pulmonary artery (Fig. 1D), gastrointestinal artery (Fig. 1E and F), and adrenal glands (data not shown). In both lungs, partial bronchopneumonia and diffuse pulmonary fibrosis were observed. Necrosis was

Table 1. Changes in laboratory data after admission.

	Day after admission			
	1st	2nd	3rd	3rd (night)
Blood gas analysis				
pH	7.32	7.40	7.24	7.32
PaO ₂ (torr)	67.7	52.7	60.9	80.7
PaCO ₂ (torr)	17.3	17.0	15.4	16.3
HCO ₃ ⁻ (mmol/L)	8.9	10.4	6.5	8.4
Lactate (mg/dL)	86.5	69.2	136.2	102.0
Hematology				
WBC (/ μ L)	13,500	16,100	15,900	23,600
Hb (g/dL)	8.8	8.8	10.2	11.0
Plt (10 ⁴ / μ L)	20.7	20.0	11.0	12.7
Chemistry				
Alb (g/dL)	2.9	2.7	3.2	2.9
BUN (mg/dL)	64.9	73.9	30.9	46.4
Cr (mg/dL)	5.12	6.37	2.96	3.88
AST (U/L)	78	2175	3625	7860
ALT (U/L)	56	1700	2958	5374
LDH (U/L)	521	4083	6937	15,224
CK (U/L)		69	6320	
CRP (mg/dL)	4.91	8.62	9.36	
Coagulation				
PT (control) (sec)		19.9	23.6	34.9
		(11.2)	(11.2)	(11.2)
PT-INR		2.42	3.15	5.8
Fibrinogen (mg/dL)		406	371	
FDP (μ g/mL)		41.5	55.5	

Abbreviations: WBC, white blood cell count; Hb, hemoglobin; Plt, platelet count; Alb, albumin; BUN, blood urea nitrogen; Cr, creatinine; AST, aspartate aminotransferase; ALT, alanine aminotransferase; LDH, lactate dehydrogenase; CK, creatine kinase; CRP, C-reactive protein; PT, prothrombin time; PT-INR, international normalized ratio; FDP, fibrin and fibrinogen degradation products.



observed in the small intestines, descending colon, and liver (data not shown). Fibrointimal sclerosis with adventitial fibrosis in the large- and middle-sized arteries of the kidney and ischemic glomerular collapse with double contouring of the basement membrane (tram-tracking) were compatible with chronic damage or organization resulting from previous SRCs. Incidental papillary adenocarcinoma without metastasis was observed in the left thyroid gland.

Discussion

FES is commonly associated with traumatic fracture of the femur, pelvis, and tibia. It is very difficult to diagnose FES in clinical practice. The diagnostic criteria proposed by Gurd and Wilson¹¹ are typically used, which includes two major criteria or one major criterion with 4 minor criteria compatible with FES (Table 2). Schenfeld et al proposed a quantitative scoring system for diagnosing FES; a score greater than 5 is required to diagnose FES (Table 1).¹² Based on the involvement of the respiratory system alone, Lideque et al added another criterion (Table 1).¹³ There is currently no consensus on how to diagnose FES.¹⁴ In the present

patient, hypoxia with PaO₂ less than 60 torr, the first major item in Gurd and Wilson's criteria, was not met, since her PaO₂ was 67.7 torr. However, severe lactic acidosis suggests tissue anoxia, and a sudden large, 60-torr increase in A-aDO₂ (normal range: less than 10 torr) also suggests pulmonary emboli or infarction compared to the patient's normal blood gas analysis values of pH 7.43, PaO₂ 96 torr, PaO₂ 39.4 torr, HCO₃ 25.3 mmol/L one week before admission. Regarding the decreased level of consciousness, the present patient had normal consciousness upon arrival in the emergency room, but her level of consciousness rapidly decreased the next day. Unfortunately, brain CT could not detect cerebral infarction or bleeding. Normal CT findings led to a decision to not recommend a further MRI study, which is useful tool for diagnosis of FES. Regarding petechiae, the present patient with scleroderma already had thickened skin, telangiectasias, and livedo-like skin lesions. It was very difficult to distinguish whether the rapid progressive blue color on the fingers was due to fat emboli or an aggravation of scleroderma. The present patient fulfilled only one minor criterion, tachycardia, but other criteria such as urinary condition could not be evaluated because she was receiving continuous peritoneal dialysis for anuric renal failure due to SRC. In patients on dialysis and systemic sclerosis, Gurd and Wilson's criteria are unsatisfactory.

The development of FES from pulmonary fat emboli is thought to include two mechanisms: the first is the presence of right-to-left shunting due to an atrial septal defect or patent foramen ovale¹⁵ and the second is that fat tissue, including bone marrow cells, which can pass through pulmonary capillary networks into systemic circulation, which may be associated with fatty acid generation by pneumocytes.¹⁶ In the present case, autopsy did not identify a patent foramen ovale or a right-to-left shunt.

Vertebral body fractures are rare causes of FES, although the prevalence of vertebral body fractures is approximately 20% in postmenopausal women over the age of 50 years in Europe.¹⁰ There are no detailed data on the prevalence of mild FES in patients with acute vertebral body fractures. One possibility is that a mild degree of fat embolism is associated with vertebral body fractures, but less frequently with FES. Day et al described a case of FES in a patient receiving 25 mg/day of prednisolone following lung transplantation

Table 2. Various diagnostic criteria for fat embolism syndrome.

Gurd and Wilson ¹¹	Schonfeld et al ¹²	Lindeque et al ¹³
Major criteria	Petechiae 5	1. Sustained
1. Petechial rash	X-ray chest	pO ₂ < 8 kpa
2. Respiratory insufficiency	diffuse infiltrates 4	(60 torr)
3. Cerebral involvement	Hypoxemia 3	2. Sustained
	Fever 1	pCO ₂ > 7.3 kpa
Minor criteria	Tachycardia 1	(55 torr)
1. Tachycardia	Tachypnea 1	3. Sustained
2. Fever	Confusion 1	respiratory
3. Retinal changes		rate > 35/min,
4. Jaundice		in spite of
5. Renal signs		sedation
6. Thrombocytopenia		4. Increased work
7. Anemia		of breathing,
8. High ESR		dyspnea,
9. Fat macroglobinemia		tachycardia,
		anxiety
Diagnosis:	Diagnosis:	Diagnosis:
1. Two major criteria,	More than 5	At least one
or		
2. One major		
criterion plus		
four minor criteria		



with numerous non-traumatic vertebral body compression fractures.⁷ They pointed out the role of long-term steroid use in the development of vertebral fractures. Lewis et al reported FES in a patient with a lumbar wedge fractures following a fall.⁸ In the present case, long-term use of steroids may have contributed to the development of fatal FES.

Regarding therapy for FES, supportive therapy and the fixation of fractured bones are essential following bone fracture; however, steroid therapy has also been proposed for treating acute endothelial injury and minimizing the inflammation caused by the release of fatty acids from bone marrow cells.¹² The question of whether steroid administration can prevent FES after bone fracture remains controversial.¹⁶ A meta-analysis showed that steroid therapy decreased the incidence of FES to 78%;¹⁷ however, there was no significant difference in survival rates between patients undergoing steroid therapy and those receiving no treatment. In addition, there is no consensus on whether large or small doses of steroids result in better outcomes.¹⁸ In addition to balanced electrolyte solutions, albumin has been recommended for volume resuscitation because it not only restores blood volume but also binds to fatty acids and may thus decrease the extent of lung injury. Steroids, heparin, alcohol, and dextran have been found to be ineffective.¹⁹

Conclusions

The present patient had autopsy-proven FES following a traumatic vertebral body fracture. Clinical and laboratory findings such as acute respiratory distress, increased A-aDO₂ with lactic acidosis, and acute onset of ischemic skin lesions can help the clinician diagnose FES.

Author Contributions

Wrote the first draft of the manuscript: NN, YK. Contributed to the writing of the manuscript: HI. Agree with manuscript results and conclusions: SM, MK, KK, NS, KS, NM. Jointly developed the structure and arguments for the paper: TY. Made critical revisions and approved final version: TY, SB. All authors reviewed and approved of the final manuscript.

Funding

Author(s) disclose no funding sources.

Competing Interests

Author(s) disclose no potential conflicts of interest.

Disclosures and Ethics

As a requirement of publication the authors have provided signed confirmation of their compliance with ethical and legal obligations including but not limited to compliance with ICMJE authorship and competing interests guidelines, that the article is neither under consideration for publication nor published elsewhere, of their compliance with legal and ethical guidelines concerning human and animal research participants (if applicable), and that permission has been obtained for reproduction of any copyrighted material. This article was subject to blind, independent, expert peer review. The reviewers reported no competing interests.

References

1. Palmovic V, McCarroll JR. Fat embolism in trauma. *Arch Pathol*. 1965;80(6):630–5.
2. Levy D. The fat embolism syndrome. A review. *Clin Orthop Relat Res*. 1990;261:281–6.
3. Fabian TC, Hoots AV, Stanford DS, Patterson CR, Mangiante EC. Fat embolism syndrome: prospective evaluation in 92 fracture patients. *Crit Care Med*. 1990;18(1):42–6.
4. Bulger EM, Smith DG, Maier RV, Jurkovich GJ. Fat embolism syndrome. A 10-year review. *Arch Surg*. 1997;132(4):435–9.
5. Sulek CA, Davies LK, Enneking FK, Gearen PA, Lobato EB. Cerebral microembolism diagnosed by transcranial Doppler during total knee arthroplasty: correlation with transesophageal echocardiography. *Anesthesiology*. 1999;91(3):672–6.
6. Costa AN, Mendes DM, Toufen C, Arrunátegui G, Caruso P, de Carvalho CR. Adult respiratory distress syndrome due to fat embolism in the postoperative period following liposuction and fat grafting. *J Bras Pneumol*. 2008;34(8):622–5.
7. Day JD, Walden SM, Stuart SR, Hutchins GM, Hruban RH. Fatal fat embolism syndrome after numerous vertebral body compression fractures in a lung transplant recipient. *J Heart Lung Transplant*. 1994;13(5):785–90.
8. Lewis D, Jones R, Carpenter C, James S. Fatal fat embolism syndrome following an isolated vertebral fracture. *Acta Orthop Belg*. 2007;73(1):137–9.
9. Lastra RR, Saldanha V, Balasubramanian M, Handal J. Fatal fat embolism in isolated vertebral compression fracture. *Eur Spine J*. 2010;19 Suppl 2: S200–2.
10. Sanfeliix-Gimeno G, Sanfeliix-Genovés J, Hurtado I, Reig-Molla B, Peiró S. Vertebral fracture risk factors in postmenopausal women over 50 in Valencia, Spain. A population-based cross-sectional study. *Bone*. 2013;52(1):393–9.
11. Gurd AR, Wilson RI. The fat embolism syndrome. *J Bone Joint Surg Br*. 1974;56B(3):408–16.
12. Schonfeld SA, Ploysongsang Y, DiLisio R, et al. Fat embolism prophylaxis with corticosteroids. A prospective study in high-risk patients. *Ann Intern Med*. 1983;99(4):438–43.
13. Lindeque BG, Schoeman HS, Dommissie GF, Boeyens MC, Vlok AL. Fat embolism and the fat embolism syndrome. A double-blind therapeutic study. *J Bone Joint Surg Br*. 1987;69(1):128–31.
14. Lee SC, Yoon JY, Nam CH, Kim TK, Jung KA, Lee DW. Cerebral fat embolism syndrome after simultaneous bilateral total knee arthroplasty: a case series. *J Arthroplasty*. 2012;27(3):409–14.



15. Mueller F, Pfeifer C, Kinner B, Englert C, Nerlich M, Neumann C. Post-traumatic fulminant paradoxical fat embolism syndrome in conjunction with asymptomatic atrial septal defect: a case report and review of the literature. *J Med Case Rep*. 2011;5:142.
16. Djelouah I, Lefèvre G, Ozier Y, Rosencher N, Tallet F. Fat embolism in orthopedic surgery: role of bone marrow fatty acid. *Anesth Analg*. 1997;85(2):441–3.
17. Bederman SS, Bhandari M, McKee MD, Schemitsch EH. Do corticosteroids reduce the risk of fat embolism syndrome in patients with long-bone fractures? A meta-analysis. *Can J Surg*. 2009;52(5):386–93.
18. Sen RK, Tripathy SK, Krishnan V. Role of corticosteroid as a prophylactic measure in fat embolism syndrome: a literature review. *Musculoskelet Surg*. 2012;96(1):1–8.
19. Shaikh N. Emergency management of fat embolism syndrome. *J Emerg Trauma Shock*. 2009;2(1):29–33.