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Golden Tracheal Secretions and Bronchoalveolar Fluid During Acute Chest Syndrome in Sickle Cell Disease

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Acute chest syndrome (ACS) is the leading cause of ICU admission in patients with sickle cell disease and is characterized by golden sputum, which is commonly attributed to the presence of bilirubin. Three young consecutive patients with homozygous sickle cell disease were admitted for severe acute respiratory syndrome due to ACS. In all 3 patients, tracheal secretions and bronchoalveolar lavage fluid (BALF) showed a yellowish plasma-like stain. After normalization for the plasma-to-BAL urea ratio, BALF protein and lactate dehydrogenase levels were consistent with an exudative process. BALF bilirubin concentrations were very low, implying that the yellowish stain was not related to bilirubin content. The yellowish coloration of tracheal secretions and BALF observed during ACS appears to be related to an intense exudative process rather than to the presence of bilirubin. *Key words: sickle cell disease; acute chest syndrome; yellow sputum; acute respiratory distress syndrome; pulmonary fat embolism; intensive care.* [Respir Care 2015;60(3):1–•. © 2015 Daedalus Enterprises]

Introduction

Acute chest syndrome (ACS) is the leading cause of ICU admission in patients with sickle cell disease.[1] The main complication of ACS is severe acute respiratory syndrome, which can lead to refractory hypoxemia and death. Golden sputum is a hallmark of ACS and is commonly attributed to the presence of bilirubin, also termed biliptysis,[2] even though this term initially referred to the existence of a bronchobiliary fistula.

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Supplementary material related to this paper is available at http://www.rcjournal.com.

Case Reports

Three young female patients with known homozygous sickle cell disease were admitted to our ICU over a 1-week period for acute respiratory failure due to ACS following painful vaso-occlusive crises. The baseline characteristics of sickle cell disease, clinical and laboratory features upon ICU admission, and outcomes of these 3 patients are reported in Table 1. All 3 developed severe acute respiratory syndrome, leading to tracheal intubation, prone positioning, and nitric oxide inhalation treatment. Intravenous antibiotic treatment, combining a third-generation cephalosporin and a macrolide, was administered to all 3 patients, but bacterial blood cultures and respiratory samples re-

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Table 1. Presentation and Outcomes of Patients With Severe Acute Chest Syndrome

	Patient 1	Patient 2	Patient 3
Age, y	21	21	34
Baseline characteristics of sickle cell disease			
Type of hemoglobinopathy	SS	SS	SS
Baseline hemoglobin, g/L	76	80	50
History of ACS in the preceding year	No	Yes	No
Blood transfusion program	No	No	Yes
Hydroxycarbamide treatment	Yes	Yes	Yes
Features upon ICU admission			
Hemoglobin, g/L	75	87	35
Lactate dehydrogenase, U/L	733	364	1920
Total bilirubin, μmol/L	65	88	200
Platelets, 6×10^3 cells/μL	283	257	238
Prothrombin time, %	65	58	48
Serum creatinine, μmol/L	27	45	352
Chest CT scan	Bilateral lung base consolidations without pulmonary thrombosis	Not performed	Bilateral lung base consolidations without pulmonary thrombosis
Echocardiography			
Acute cor pulmonale	Yes	Yes	Yes
Pulmonary artery systolic pressure, mm Hg	60	80	80
Outcomes in ICU			
Orotracheal intubation	Yes (day 2)	Yes (day 1)	Yes (day 1)
Minimal P_{aO_2}/F_{IO_2} before prone positioning, mm Hg	74	73	115
Prone positioning	Yes (day 2)	Yes (day 1)	Yes (day 2)
Nitric oxide inhalation	Yes (day 2)	Yes (day 1)	Yes (day 1)
Venovenous ECMO	No	Yes (day 1)	No
Total number of transfused RBC units	5	10	7
Vasoactive drugs	No	Yes	Yes
Renal replacement therapy	No	Yes	Yes
ICU stay, d	9	5	10
Death	No	Yes	No
SAPS II score	29	61	75

ACS = acute chest syndrome
CT = computed tomography
ECMO = extracorporeal membrane oxygenation
RBC = red blood cell
SAPS II = Simplified Acute Physiology Score II.

mained sterile. The condition improved in 2 patients, who were eventually discharged from the ICU 2 weeks later (patients 1 and 3), whereas one patient (patient 2) required venovenous extracorporeal membrane oxygenation and died on day 5.

In all 3 patients, tracheal secretions and bronchoalveolar lavage fluid (BALF) showed a yellowish plasma-like stain (Fig. 1, B–D; see the supplementary video at http://www.rcjournal.com). After normalization for the plasma-to-BAL urea ratio, BALF (vs plasma) protein (patient 1, 54 vs 57 g/L; patient 2, 45 vs 55 g/L) and lactate dehydrogenase (patient 1, 1,890 vs 1,529 U/L; patient 2, 795 vs 512 U/L) levels were similar and consistent with an exudative process. BALF bilirubin concentrations were 7 (patient 1) and 5 (patient 2) μmol/L, implying that the yellowish stain was not related to bilirubin content. Interestingly, tracheal secretions of patient 3 exhibited the same color as her plasma (Fig. 1C). Finally, in patients 1 and 2, 30% of alveolar macrophages were stained with Oil Red O (Fig. 1E), indicative of lung fat embolism.[3-5]

Discussion

Golden sputum is a classic and pathognomonic sign of ACS, which is often associated with pulmonary fat embolism.[3-5] This yellowish coloration appears to be related to an intense exudative process rather than to the presence of bilirubin. Of course, this finding has limited

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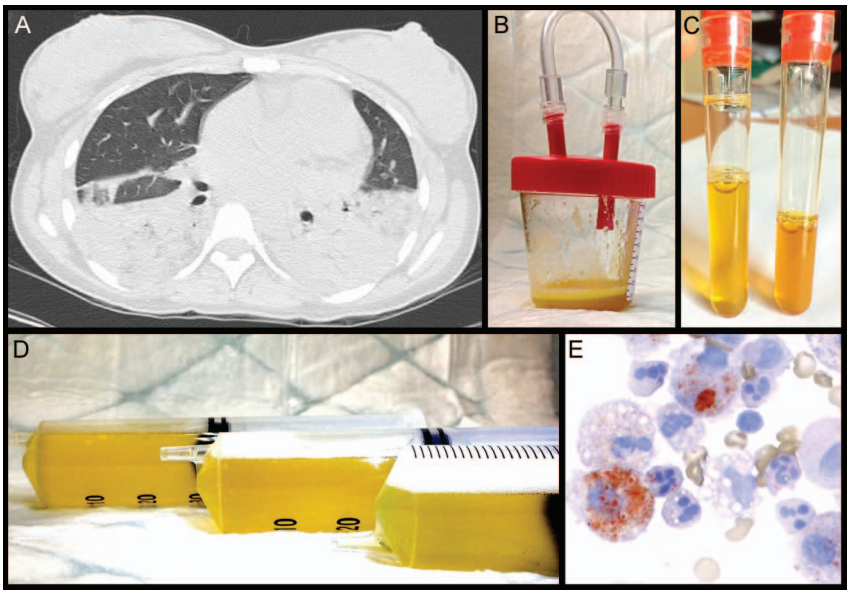

Figure 1. Golden tracheal aspirates and bronchoalveolar lavage fluid (BALF) in patients with severe acute chest syndrome. A: Contrast-enhanced chest computed tomography scan depicting typical bilateral lung base consolidations in patient 1. B: Tracheal secretions from patient 1. C: Tracheal secretions (left tube) and plasma (right tube) from patient 3 showing the same yellowish color. D: Macroscopically golden BALF from patient 1. E: Cytological examination of BALF from patient 1 showing alveolar macrophages stained with Oil Red O.

clinical implications for the current management of patients with ACS. However, understanding the pathophysiologic phenomena underlying this yellowish stain, which is not commonly reported during ARDS in patients without sickle cell disease, could be of paramount importance for the management of ACS. Future studies aiming at determining the components of this peculiar alveolar fluid (eg, using proteomics) could allow for the identification of specific diagnostic or therapeutic markers of ACS.

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REFERENCES

1. Cecchini J, Lionnet F, Djibré M, Parrot A, Stojanovic KS, Girot R, Fartoukh M. Outcomes of adult patients with sickle-cell disease admitted to the ICU: a case series. Crit Care Med 2014;42(7):1629-1639.
2. Brandstetter RD, Kabinoff GS. Bilioptysis: a sign of pulmonary capillary permeability injury. Heart Lung 1998;27(2):121-122.
3. Godeau B, Schaeffer A, Bachir D, Fleury-Feith J, Galacteros F, Verra F, et al. Bronchoalveolar lavage in adult sickle cell patients with acute chest syndrome: value for diagnostic assessment of fat embolism. Am J Respir Crit Care Med 1996;153(5):1691-1696.
4. Lechapt E, Habibi A, Bachir D, Galacteros F, Schaeffer A, Desvaux D, et al. Induced sputum versus bronchoalveolar lavage during acute chest syndrome in sickle cell disease. Am J Respir Crit Care Med 2003;168(11):1373-1377.
5. Maitre B, Habibi A, Roudot-Thoraval F, Bachir D, Belghiti DD, Galacteros F, Godeau B. Acute chest syndrome in adults with sickle cell disease. Chest 2000;117(5):1386-1392.