Typhoid Fever Associated With Adult Respiratory Distress Syndrome*

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Adult respiratory distress syndrome (ARDS) is rarely reported in association with typhoid fever despite the fact that sepsis is a common manifestation and endotoxemia has been described in this multisystem condition. We describe the course of a patient with ARDS and typhoid fever. With conventional treatment of the lung injury and with specific antimicrobial therapy, the patient survived. Recent consensus definitions of sepsis and ARDS simplified reporting of this case. Clinicians caring for individuals from or recent visitors to developing countries should be aware of the association of typhoid fever, sepsis, and ARDS.

(Chest 1994; 105:1873-74)

ARDS=adult respiratory distress syndrome; CK=creatine kinase; S typhi=Salmonella typhi

There is only one case report of adult respiratory distress syndrome (ARDS) associated with typhoid fever. The rarity of reported cases may be a result of underdiagnosis or underreporting of typhoid-associated ARDS in developing countries. With increasing immigration to North America from areas of prevalence of typhoid fever, it is likely that clinicians will see more of these cases. We present what we believe to be the first reported case of survival after ARDS associated with typhoid fever.

Case Report

A 23-year-old Filipino man was transferred to the ICU because of respiratory distress. Three weeks before admission to the ICU, he had moved to Canada and 1 week later, developed nausea, vomiting, chills, and a fever of 38.5°C and was hospitalized because of diarrhea, jaundice, and splenomegaly. During the subsequent week, he became confused and progressively more short of breath. *Salmonella typhi* grew in blood cultures. Ampicillin, 1 g, was given every 6 h by intravenous (IV) infusion. Through the following week, he developed anemia, leukopenia, and thrombocytopenia. On the day of transfer, he developed excessive bleeding at venipuncture sites and severe respiratory distress requiring muscle paralysis, endotracheal intubation, and mechanical ventilation. Prothrombin time (PT) was 16 s and partial thromboplastin time (PTT) was 74 s. Arterial blood gas analysis showed pH 7.30, PaO₂ 44 mm Hg, and PaO₂ 52 mm Hg with inspired oxygen fraction (FIO₂) 1.0. Creatine kinase (CK) was elevated at 1,830 μ/L.

In the ICU, blood and stool cultures were positive for *S typhi*, and, on the advice of a consultant in infectious diseases, chloramphenicol 1 g IV was given every 6 h for 24 h, then 500 mg were given every 6 h. Diarrhea resolved after 3 days of bowel rest and antibiotic therapy. Bilirubin decreased from 5.3 mg/dl (91 mmol/L) on admission to ICU to 1.9 mg/dl (32 mmol/L) on discharge. Aspartate aminotransferase (AST) (normal values 4-28 μ/L) was 167 μ/L on admission and 29 μ/L 4 days before discharge while alkaline phosphatase was 101 μ/L on admission and rose to 228 μ/L on discharge. Serum amylase (normal values 10 to 70 μ/L) increased from 125 μ/L to 234 μ/L over the first 5 days in ICU but was normal by discharge. Stool cultures became negative after 48 h. Fever of 58°C continued until discharge from the ICU 11 days after admission.

Blood pressure was within normal limits while heart rate (apart from a brief episode of supraventricular tachycardia at 180 beats per minute [BPM]) was 110 to 130 BPM throughout the ICU stay. Chest auscultation revealed crackles in all lung fields and copious watery secretions were suctioned from the endotracheal tube. Diffuse air-space disease was present in all 4 quadrants of the chest roentgenogram and initial arterial blood gas analysis showed pH 7.32, PaO₂ 51 mm Hg, and PaO₂ 89 mm Hg with minute ventilation 12 L, FIO₂ 0.9 and positive end-expiratory pressure (PEEP) 10 cm H₂O. Heart sounds were normal and there were no murmurs. Cardiac index was 3.9 L per min per m². After 24 h of increased minute ventilation, dobutamine 5 μg/kg/min, paralysis with pancuronium, and diuresis with furosemide, arterial blood sampling revealed pH 7.43, PaO₂ 89 mm Hg, and PaO₂ 95 mm Hg with minute ventilation 12 L, FIO₂ 0.5 and PEEP 7 cm H₂O. However, the patient required 9 days to wean from mechanical ventilation. Fiberoptic bronchoscopy showed no mucosal abnormalities, and samples obtained from the tracheobronchial tree were negative on microbiologic examination.

Platelet count increased from 21X10⁹/mm³ (21X10⁹/L) to 255X10⁹/mm³ (255X10⁹/L) and white cell count increased from 3,100/mm³ (3.1X10⁹/L) to 10,500/mm³ (10.5X10⁹/L) (polymorphs 58 percent and lymphs 37 percent) to 5,400/mm³ (5.4X10⁹/L) (differential normal) by discharge from ICU. The PT and PTT were initially elevated at 19 and 73 s respectively. Thrombin time was 7.4 s, fibrinogen level 200 mg/dL (2.0 g/L) and D-dimer test was 2,000 ng/ml (2 mg/L) (compatible with disseminated intravascular coagulopathy). Blood concentrations of factors II, VII, IX, and X were low at 25 to 58 percent (0.25-0.38 μ/ml) while other factors were normal. Clinical coagulopathy resolved within 2 days of replacement therapy, and PT and PTT were normal 5 days before discharge from the ICU.

Discussion

This patient had many features of typhoid fever including enteritis with diarrhea, hepatic involvement, pancreatic involvement, splenomegaly, increased CK, anemia, leukopenia, and clotting disturbances. Pulmonary manifestations have rarely been reported and consist of bronchitis, pneumonia, lung abscess, empyema, and the above-mentioned case of ARDS. According to the American College of Chest Physicians and the Society of Critical Care Consensus Conference guidelines, this patient had sepsis. Body temperature was greater than 38°C, heart rate was greater than 90 BPM, respiratory rate was high and WBC count was less than 4,000/mm³ in the presence of infection. According to Murray et al., the patient had a lung injury severity score of 3.3 (severe) on day 1 and 2.3 (moderate) on day 2 because of air-space disease in all 4 quadrants of the chest roentgenogram on both days, a hypoxemia score of 4 on day 1 and 2 and on day 2, and a PEEP score of 2 and 1 on days 1 and 2 respectively. Time course of resolution of lung involvement was compatible with acute lung injury developing into a chronic phase. No other cause for ARDS was identified. The association of ARDS with typhoid fever is not surprising because ARDS and the systemic inflammatory response syndrome occur with Gram-negative infections. Endotoxin has been detected in the blood of patients with typhoid fever. Sputum cultures are usually negative for *S typhi* in cases of...
pulmonary involvement. Specimens obtained by bronchoalveolar lavage failed to show bacterial infection in this case. Chloramphenicol, ampicillin, and cotrimoxazole are commonly used to treat typhoid fever and have a high cure rate, but a significant relapse rate. Cefoperazone, in a study of 32 patients, had a cure rate in excess of 90 percent and no relapse. Systemic steroids have been reported to decrease mortality in severe typhoid fever. To our knowledge, this is the first patient to survive ARDS associated with typhoid fever. Specific antibiotic therapy was followed by negative cultures and clinical improvement. Therapy of the ARDS was supportive and was directed at keeping fluid balance negative, which is a strategy associated with improved survival. Typhoid fever should be included in the differential diagnosis of ARDS with sepsis if the patient originates from or has recently visited a developing country.

ACKNOWLEDGMENTS: The authors thank Dr. R. J. Byrick for reviewing the manuscript and the members of the Department of Anaesthesia at St. Michael's Hospital for their support.

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Transcatheter Intravascular Urokinase for Loculated Pleural Effusion*

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Two patients who had undergone coronary artery bypass graft surgery in the mid-1980s and who had repeat coronary artery bypass graft procedures in 1992 developed loculated, bloody pleural effusions. Percutaneous catheter drainage and installation of intrapleural urokinase led to resolution of these loculated effusions without morbidity. This procedure should reduce the length of hospitalization and treatment for patients with loculated pleural effusions. (Chest 1994; 105:1874-76)

Intracavitary urokinase has been successfully utilized in percutaneous abscess drainage and in promoting drainage of both hemorrhagic and fibrinous loculated pleural effusions. We present two cases of hemorrhagic loculated effusions occurring after coronary artery bypass grafting procedures. Both were successfully evacuated by transcatheter drainage in conjunction with urokinase infusion.

CASE REPORTS

Case 1

A 74-year-old white man, who had undergone coronary artery bypass graft surgery in 1985, was readmitted to the hospital on December 14, 1992, with accelerating angina and again underwent coronary bypass surgery on December 16, 1992. His postoperative course was complicated by low-grade fever. A chest x-ray film showed patchy basilar atelectasis and increased density in the left pleural space. His WBC count was less than 10,000/mm³. His admission hemoglobin value was 15.2 g/dl but dropped to 8 g/dl by December 23, 1992.

On January 1, 1993, he was seen for a pulmonary consultation. He was complaining of shortness of breath and had a low-grade temperature, a heart rate of 90 beats per minute, and a respiratory rate of 20 breaths per minute. A chest x-ray film, including bilateral decubitus films, showed a subpulmonic right pleural effusion and a large left pleural effusion. Thoracentesis yielded 1,200 ml of port wine-colored bloody fluid from the right and 1,800 ml of similar fluid from the left hemithorax. The patient responded to thoracentesis with decreased shortness of breath. A repeat chest x-ray film showed a persistent density in the left hemithorax. Five days later, a computed tomography (CT) scan of the chest with supine and prone imaging was performed. It showed a moderate free-flowing right effusion and a large left effusion that appeared...

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