electrocardiogram and no patient had significant ST-T wave changes on the exercise electrocardiogram. It is interesting to note that the two patients from these series who underwent coronary angiography were both shown to have disease of the right coronary artery.1,4

Myocardial ischemia should be considered a possible contributing factor to exercise-related heart block, particularly when coronary artery disease is suspected because of a history of chest pain or signs of ischemia during the exercise test. Failure to evaluate the presence and effect of myocardial ischemia may result in unnecessary pacemaker implementation in patients with exercise-related AV block.

REFERENCES

Recurrent Noncardiac Pulmonary Edema Accompanying Pregnancy-induced Hypertension

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Severe pulmonary edema occurred in a patient during the third trimester of two consecutive pregnancies, 17 months apart. Noncardiac origin of the pulmonary edema was demonstrated by normal pulmonary capillary wedge pressures, normal roentgenographic cardiac dimensions with absence of effusions, normal echocardiographic ejection fraction, and elevated thermol dilution cardiac outputs; moderate reduction in serum albumin levels may have contributed. In the setting of pregnancy-induced hypertension, the development of ARDS on each occasion suggests a pathophysiologic link.

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PIH = pregnancy-induced hypertension

Isolated cases of adult respiratory distress syndrome have been reported in pregnant patients with phe nlephri tis.5,6 Pulmonary edema accompanying pregnancy-induced hypertension (PIH) and tocolytic therapy has been reported, although the role of elevated left heart filling pressures is controversial.5,6 We report a young woman who developed noncardiac pulmonary edema requiring mechanical ventilation with PEEP during two pregnancies, each characterized by PIH.

CASE REPORT

First Admission

A 31-year-old woman (gravida 4, para 3-0-0-0) without prenatal care complained of dyspnea and a mild, nonproductive cough. Her last menstrual period was 22 weeks before. She denied myalgias, fevers, sore throat, uterine contractions, dysuria, or vaginal bleeding. Past history was significant for intermittently elevated blood glucose values. She had developed PIH during all previous pregnancies with proteinuria and hypertension but without other abnormalities. There was no history of hypertension apart from during pregnancy, and no history of cardiac, pulmonary, or renal disease. A creatinine clearance measured within the year was 125 ml/min.

On physical examination, she was 83 kg with a temperature of 37°C; blood pressure was 150/100 mm Hg; respiratory rate was 24/min. The lungs were clear, heart sounds were normal, and the abdomen was soft with a 24-week uterus by palpation. There was 1+ pitting edema bilaterally. Reflexes were normal. Admission laboratory data included normal values for electrolytes and blood urea nitrogen (9 mg/dl). The creatinine level was mildly elevated at 1.2 mg/dl. The uric acid value was elevated at 6.8 mg/dl. The

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glucose level was 158 mg/dl. The hemoglobin value was 8.8 g/dl and the white blood cell count was 11,100/cu mm with 80 percent segmented cells, 14 percent lymphocytes, 1 percent atypical lymphocytes, and 4 percent monocytes. The platelet count, prothrombin time, and the partial thromboplastin time were normal. The total protein value was normal at 6.2 g/dl, and the albumin was mildly reduced at 2.6 g/dl (normal, >3.3 g/dl). Fibrinogen was 850 mg/dl (normal for a twin pregnancy), and fibrin degradation products were less than 10 mg/dl. Urinalysis showed 4+ protein and 5 to 10 WBC per high power field.

The patient was treated for hyperglycemia and for a presumed urinary tract infection, with ampicillin. By the evening of the first hospital day, she developed shortness of breath, fever to 38.9°C, tachycardia, and tachypnea. A chest roentgenogram showed diffuse bilateral pulmonary infiltrates and a normal cardiac silhouette. Arterial blood gas values while breathing room air showed a pH of 7.42. Po2 of 61, and Paco2 of 30 mm Hg. Maternal cardiac ultrasound showed normal aortic and mitral valves, normal estimated left ventricular ejection fraction, and no evidence of pericardial effusion. She was treated with a single 20 mg dose of furosemide with a net fluid loss of 800 ml.

Flow-directed balloon catheterization of the pulmonary artery showed the pulmonary artery (PA) systolic pressure was 42 mm Hg, the wedge pressure 13 mm Hg, and the cardiac output 12.5 L/min. A pulmonary arteriogram showed no evidence of emboli. Despite treatment with diuretics, cefoxitin, trimethoprim-sulfamethoxazole, and erythromycin, her oxygenation worsened; after intubation and mechanical ventilation with an inspired oxygen fraction of 0.8 and 10 cm H2O positive end-expiratory pressure, her arterial Po2 was 157 mm Hg (Fig 1). Following delivery of stillborn twins on the third hospital day, she rapidly improved and was extubated five days after intubation. The time course of her improvement in oxygenation is shown in Figure 2. Chest x-ray film and arterial blood gas values returned to normal over the next three weeks (Fig 3). On discharge, her blood pressure was 130/80, and a creatinine clearance value several days before discharge was 88 ml/min. Pathologic examination of the placenta was nonrevealing. Microbiologic cultures of blood, urine, and sputum were sterile. Mycoplasma antibody was minimally elevated at 0.24 ELISA units, and cold agglutinins were positive at 1:256.

Second Admission, 17 Months Later

The patient presented to the emergency department with an intrauterine pregnancy at 30 weeks’ gestation, complaining of nonproductive cough, dyspnea, chills and vomiting. For several hours before admission, she experienced uterine contractions. Her temperature was 38.9°C, the pulse was 90, and the blood pressure was 130/90. The respiratory rate was 20. Physical examination of the heart and lungs was normal. There was a 30 week uterus; the cervix was 3 cm dilated and 50 percent effaced, with a breech...
presentation. Arterial blood gas values on room air showed a pH of 7.42, PO₂ of 42 mm Hg, and PCO₂ of 30 mm Hg. The chest x-ray film showed bilateral infiltrates without cardiac enlargement or effusions. She was intubated and ventilated with 100 percent oxygen.

Pulmonary arterial catheterization showed the cardiac output was 12 L/min, PA pressure was 45/12 mm Hg, and the wedge pressure was 10 mm Hg. After delivery of a viable infant, the mother was treated empirically with diuretics, ampicillin, and erythromycin. Despite net fluid loss of more than 2,000 ml in the first 24 hours and treatment with 10 cm H₂O PEPE, her arterial oxygen saturation fell below 90 percent when the inspired O₂ fraction was lowered below 0.6. Urine protein excretion was 25 g/24 h. The BUN value was 9 mg/dl, and the creatinine level was 1.4 mg/dl. The white blood cell count reached a maximum of 17,000/cu mm, without immature neutrophils. The serum protein value was moderately reduced at 5.3 g/dl, and the albumin value was reduced at 2.1 g/dl. All cultures of blood, sputum, and urine were sterile. The HIV antibody levels were negative by ELISA. The patient required mechanical ventilation for seven days. Two weeks after delivery, urinary protein excretion fell to 10 g/24 h; repeat creatinine clearance value was 63 ml/min. She was discharged one week later with normal blood gas values and chest x-ray film.

**Discussion**

Adult respiratory distress syndrome describes the findings of severe hypoxemia and diffuse pulmonary infiltrates in the setting of catastrophic illness and in the absence of cardiogenic pulmonary edema. This patient presents several unusual features of the syndrome. First, she represents, to our knowledge, the only reported instance of recurrent ARDS, where recurrences were separated by apparent full recovery and discharge from the hospital. Additionally, our patient had none of the classic risk factors for ARDS. She had received no blood transfusions, had no trauma, pancreatitis, or pulmonary emboli detectable at arteriography. There was no history of drug allergy, and signs of respiratory distress antedated administration of in hospital medications.

Sepsis was considered as a possible initiating factor, but the white blood cell count was within the normal range of third trimester pregnancy, there was no increase in immature forms, and there were no manifestations of altered perfusion that may accompany sepsis. Of the possible sites of sepsis, three deserve special attention. First, although the initial urine sediment contained white blood cells, the absence of white blood cell casts, positive urine cultures or costovertebral angle tenderness argued against pyelonephritis. Second, neither sputum smears and cultures obtained nor blood cultures showed bacterial pathogens. The elevated cold agglutinin titer might have indicated an atypical pneumonia, but absence of fever, myalgias, and upper respiratory symptoms makes this diagnosis unlikely. By itself, atypical pneumonia causes ARDS only rarely, and two separate episodes of atypical pneumonia each occurring during the third trimester of pregnancy and each causing ARDS seems an unlikely explanation. Finally, systemic sepsis can accompany choioamnionitis, but neither microbiologic nor pathologic studies of the placenta supported this possibility.

Other known causes of respiratory distress in the peripartum period are unlikely. Amniotic fluid or air embolism usually occur during labor or delivery. In addition, there were none of the accompanying features of amniotic fluid embolism, such as disseminated intravascular coagulation. Peripartum cardiomyopathy was highly unlikely, given the normal early echocardiographic function, high cardiac output, and normal left ventricular filling pressures. It is tempting to speculate that the microvascular injury responsible for edema and proteinuria in PH is also predisposed to protein and fluid leak into the pulmonary interstitium. To our knowledge, no studies have been performed to investigate fluid flux in the lung in patients with PH. Because of the mildly decreased serum protein concentrations, this patient's pulmonary edema may have been exacerbated by decreased plasma oncotic pressure. It is not likely, however, that the modest level of hypoproteinemina observed upon the second admission was a major contributing factor, and on the first admission, the serum protein concentration was normal.

A possible association between ARDS and PH was found by Benedetti and colleagues, who reported a series of ten patients with PH and pulmonary edema. Although seven patients had wedge pressures and cardiac indices that suggested hydrostatic edema, three others had wedge pressures 10 mm Hg or less with normal cardiac indices, suggesting increased permeability. This study was a retrospective analysis that did not address mechanisms of ARDS.

We suggest that a combination of influences usually associated with extrapulmonary microvascular injury may have been responsible for this patient's noncardiogenic pulmonary edema. On the basis of this case and other reported cases of ARDS accompanying pregnancy, we believe that further investigation of pulmonary vascular integrity during pregnancy is warranted.

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