impede venous return, and syncope ensues from a greater increase in left ventricular obstruction with a resultant decrease in aortic pressure.

In this case, the Valsalva maneuver produced the anticipated response: left ventricular pressure fell and a small gradient resulted from a slightly greater fall in aortic pressure. The gradient disappeared within 2 beats after release of Valsalva and blood pressure promptly returned to control values. However, during a cough paroxysm left ventricular systolic pressure fell only slightly, but a large gradient was produced by a severe decrease in aortic pressure with a very slow return to control levels (Fig 1). Although during the infusion of isoproterenol a marked gradient was also seen, in contrast, this gradient resulted primarily from a rise in left ventricular pressure with only a modest fall in aortic pressure (Table 2).

Following propranolol, a comparable cough paroxysm resulted in a similar fall in aortic pressure. This occurred even though the outflow tract gradient was minimal. Blood pressure, however, returned to control more rapidly than before propranolol.

It appears, therefore, that post-tussive syncope can be explained in this patient by the dramatic drop in blood pressure and its sluggish return. This resembles the condition seen in "hard coughers," and the increased intrathoracic pressure developed during cough places him in that category. Reduction of venous return during a severe cough paroxysm markedly decreases blood pressure. In patients with IHSS, the diminished venous return and consequent reduction in chamber size aggravate the dynamic left ventricular outflow obstruction.

This hypothesis was evaluated during catheterization of two other patients with IHSS who denied a history of cough syncope. During a cough paroxysm induced in these patients, left ventricular outflow gradients increased from 0 to 34, and 0 to 66 mm Hg respectively. Aortic pressure fell from 152/100 mm Hg to 114/80, and 120/65 to 92/50. Neither patient was able, however, to increase intrathoracic pressure above 75 mm Hg.

It is of interest to note that large doses of propranolol were effective in the prevention of the cough-induced syncope in this patient. The observation that propranolol markedly reduced the post-tussive gradient and resulted in a more rapid return of blood pressure, suggests that reflex sympathetic stimulation occurs during a cough paroxysm, increasing contractility and augmenting outflow obstruction. Beta-adrenergic blockade would be expected to decrease dynamic outflow obstruction resulting from increased sympathetic activity, but to have lesser effect on obstruction produced by a decreased venous return and reduced chamber size.

Thus it appears that post-tussive syncope in IHSS may result from an unusually strong paroxysm of cough with increased dynamic left ventricular outflow obstruction. Beta-adrenergic blockade may be effective in preventing syncope by markedly reducing the dynamic obstruction produced by reflex sympathetic stimulation.

**REFERENCES**


**Altered Pulmonary Capillary Permeability Complicating Recovery from Diabetic Ketoacidosis**

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Self-limited noncardiogenic interstitial pulmonary edema probably reflecting altered permeability of the pulmonary capillary membrane is reported in a patient being treated for severe diabetic ketoacidosis. The possible etiology, associated findings, and therapy with continuous positive airway pressure (CPAP) by facemask are discussed.

Altered permeability of the pulmonary capillary membrane resulting in interstitial or alveolar pulmonary edema, or both, has been recognized in conjunction with the many disease processes associated with the adult respiratory distress syndrome (ARDS).1 Similarly, a

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separate capillary leak syndrome characterized by the massive transudation of proteins and other macromolecules from the pulmonary intravascular space has been described in association with endotoxemia. A review of recent literature, however, has failed to reveal prior documentation of such instability of the pulmonary capillaries in association with diabetic ketoacidosis except when complicated by some other pathologic process.

**CASE REPORT**

A 24-year-old black woman with a history of insulin-dependent diabetes since age 11 entered for her 12th admission for treatment of ketoacidosis after a one-day history of malaise, low-grade fever, polyuria, and nausea without emesis. Initial evaluation revealed a rectal temperature of 35°C; blood pressure, 108/52 mm Hg; blood glucose level, 766 mg/100 ml; serum acetone, positive at 1:16 dilution; arterial pH, 7.01; PaCO₂, 10 mm Hg; PaO₂ on room air, 96 mm Hg; and base deficit, more than 30 mEq/liter. Serum sodium level was 128 mEq/liter; potassium, 5.4 mEq/liter; chloride, 97 mEq/liter; and bicarbonate, 4 mEq/liter. Chest x-ray examination revealed bilateral alveolar infiltrates consistent with interstitial edema. Central venous pressure was zero.

After three hours the patient had received 140 units of regular insulin intravenously, 3 liters of normal saline, and 50 mEq of bicarbonate, but she remained acidotic. She also had become hypoxic with arterial pH of 7.04, PaCO₂ of 15 mm Hg, and PaO₂ of 60 mm Hg on FIO₂ of 0.7; therefore, therapy with continuous positive airway pressure (CPAP) was initiated via a tightly fitted facemask during spontaneous breathing with a 4 cm H₂O inspiratory pressure and 14 cm H₂O pressure during exhalation (4/14 cm H₂O). Repeat chest x-ray examination showed worsening of the diffuse infiltrates in both lungs (Fig 1). Serum albumin level was 2.23 gm/100 ml with total protein concentration of 6.0 gm/liter, serum osmolality of 325 mOsm/kg, and blood glucose level of 260 mg/100 ml. Infusion of 25 gm of salt-poor albumin did not alter arterial oxygenation. The results of the electrocardiogram were normal.

Seven hours after admission, with the patient on CPAP of 14/20 cm H₂O, a transtracheal aspiration was performed. Two hours later, she became agitated suddenly, complained of midsternal chest pain, removed her facemask, and rapidly became unresponsive and hypotensive with a systolic arterial pressure of 50 mm Hg; but she maintained normal sinus rhythm. Laboratory tests revealed a serum glucose level of 78 mg/100 ml and a potassium level of 4.9 mEq/liter. The patient was intubated, connected to a ventilator, and given 50 ml of 50 percent dextrose solution and 100 mEq of bicarbonate; she had rapid normalization of arterial pressure and return of sensorium. Chest x-ray films showed diffuse interstitial pulmonary edema plus mediastinal and interstitial emphysema, but no pneumothorax (Fig 2).

The patient’s diabetes was stabilized, and over the next 34 hours she was maintained on mechanical ventilation with a positive end-expiratory pressure (PEEP) of 5 to 10 cm H₂O. She remained alert except for one episode of unresponsiveness and hypoxia (PaO₂, 25 mm Hg) associated with a weaning attempt from the ventilator with spontaneous breathing via a T-tube. As the patient’s tidal volume and inspiratory capacity were adequate, she was extubated but provided CPAP via a facemask to prevent additional hypoxemia. A Swan-Ganz catheter was inserted for guidance of further fluid administration and revealed a pulmonary artery mean pressure of 22 and a pulmonary artery wedge pressure of 10 mm Hg. Blood volume and serum lactate level were normal. Blood, sputum, and initial urine aerobic and anaerobic cultures were all sterile, but coagulase-positive staphylococci were present in a chronic skin ulceration on the patient’s buttock.

The patient continued to be alert, but remained dependent on CPAP (5/12 cm H₂O) for the following six days. Dye-dilution cardiac output determinations on and off CPAP were approximately equal at 6.35 liters/min. Her intake and output were balanced hourly, and supplemental albumin was administered in an effort to maintain a serum level of 2.5 gm/100 ml. There was no decrease in PaO₂ following albumin administration at this time, indicating no further capillary leakage.

The patient was subsequently weaned from CPAP and on the tenth hospital day transferred from the intensive care unit to another floor. Follow-up chest x-ray films demonstrated complete resolution of the pulmonary infiltrates.

Figure 1. Chest x-ray film five hours after admission demonstrating advanced pulmonary edema.

Figure 2. Chest x-ray film one hour following transtracheal aspirate for cultures. Note interstitial and mediastinal emphysema as well as pulmonary edema.

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DISCUSSION

In a review of severe and fatal cases of diabetic ketoacidosis, Beigelman and Warner\(^1\) reported the occurrence of myocardial infarction and pulmonary edema but did not describe pulmonary insufficiency in the absence of embolus, sepsis, infection, or left ventricular failure. The patient cited in the present paper had no electrocardiographic evidence of myocardial injury; and consistently normal pulmonary artery wedge pressures, blood volume, and serum lactate levels further support a noncardiac etiology for the clinical and radiographic pulmonary edema observed. However, frequently recognized causes\(^2\) of noncardiogenic pulmonary edema, such as cerebral injury, drug ingestion, shock, endotoxemia, and peripheral soft tissue injury, were not present. The possible etiologic roles of the mild hypothermia, progressive hypoxia, and acidosis that were present in this woman were also reviewed. In a large series of patients with profound accidental hypothermia,\(^3\) no occurrence of noncardiogenic pulmonary edema was noted. Similarly, hypoxemia to an arterial oxygen saturation of 75 percent specifically did not increase capillary loss of albumin experimentally in normal men.\(^4\) Another investigator,\(^5\) however, has observed pulmonary edema with normal pressures in the left side of the heart following severe hypoxia, especially when associated with respiratory acidosis. Pure metabolic acidosis in an experimental model\(^6\) has produced interstitial congestion and alveolar edema with corresponding increases in both right and left ventricular end-diastolic pressure, suggesting both myocardial depression and increased pulmonary vascular resistance.

The presence of thickening and other changes in the capillary basement membranes of muscle, skin, kidney, eye, and intestine in diabetic and prediabetic patients is well known, though some variation in occurrence is recognized in the juvenile diabetic.\(^7\) The significance of these changes with regard to capillary membrane integrity in those tissues studied has been shown to be an increased rate of albumin and globulin movement into the extravascular space via a greater number of the larger capillary endothelial pores and a general increase in membrane permeability.\(^7,8\) To our knowledge, such changes have not been documented in the pulmonary vasculature.

In patients with advanced capillary leakage, endothelial necrosis may be so pronounced that intravenous administration of albumin rapidly results in its deposition in the interstitial tissues, particularly in the lungs. Worsening of the patient's pulmonary edema with reduced arterial oxygenation may then occur secondarily to the osmotic influence of this extravascular albumin. For the past couple of years, we have utilized a technique with 100 percent oxygen test before and after administration of a unit of albumin intravenously. Increase of the alveolar-arterial oxygen tension difference, \(P(A-a)O_2\), or just decreasing \(P_aO_2\) on the same inspired oxygen concentration, after infusion of albumin has been used as a contraindication to intravenous treatment with albumin. On the other hand, if albumin administration results in a decrease in \(P(A-a)O_2\) or an increase in \(P_aO_2\), additional albumin may be infused with minimal hazard. No change in \(P_aO_2\), therefore, as observed in this patient, implies that additional albumin may be given with caution.

Similarly, the transcapillary diffusion of smaller hydrophilic ions, particularly sodium, is increased as measured in the skeletal muscle of diabetics.\(^9\) Thus, the peripheral edema reported in some ketoacidotic patients during treatment may result from these changes in membrane permeability as enhanced by the general sodium retention associated with insulin therapy.\(^10\) Whether similar anatomic and physiologic changes precipitated by acidosis and hypoxia superimposed upon a diabetic angiopathy may have occurred in this patient's pulmonary vasculature is, however, admittedly speculative.

The abrupt occurrence of mediastinal and interstitial air in this case probably resulted from the use of high levels of CPAP during the procedure of transtracheal aspiration, although the presence of pneumomediastinum in diabetic ketoacidosis with and without hyperemesis is well documented.\(^11,12\)

Continuous positive airway pressure breathing is now a well-recognized ventilatory technique in the management of pulmonary edema complicated by hypoxemia.\(^13-19\) It may be utilized in the nonintubated spontaneously breathing patient through use of a tightly fitted facemask, supplemented inspiratory gas flow through a reservoir bag, and a standard PEEP exhalation device. Such a system was used continuously for six days in this patient's therapy and provided up to 14 cm H\(_2\)O inspiratory pressure and 22 cm H\(_2\)O pressure during exhalation. This permitted reversal of marked hypoxemia without reintubation. The patient was able to eat, talk, and ambulate, and experienced only mild facial discomfort from the pressure of the mask.

REFERENCES


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Asymptomatic Pulmonary Granular Cell Tumor Presenting as a Coin Lesion*

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Granular cell tumor is a rare, usually benign neoplasm of neurogenic origin first described in 1926. Only 46 lesions, including the present case, of the 500 reported cases of this tumor, originated within the tracheobronchial tree. The case reported here is distinctly unusual because of its asymptomatic presentation as a coin lesion on chest roentgenogram. Electron microscopic examination of the tumor is presented.

Granular cell tumor is a rare neoplasm, almost always benign. The cell of origin remains in question. When first described by Abrikossoff in 1926, the tumor was believed to be of myogenic origin. At present the concept of a neurogenic origin is most widely accepted. There are about 500 cases in the world literature describing this entity, 45 of which originated in the tracheobronchial tree. The most common sites of origin are the skin, tongue, and breast. Cases of multiple organ involvement have been reported. In only one previous report has a granular cell tumor of the bronchus presented without pulmonary symptomatologic findings, and only two have been described as an isolated coin lesion on chest roentgenogram. This report describes a young hypertensive woman who presented with neurologic symptoms and an asymptomatic coin lesion in the right upper lobe on initial chest roentgenogram.

CASE REPORT

A 39-year-old obese black woman was admitted to Queens Hospital Center complaining of severe headache and sudden onset of weakness of her left upper and lower extremities beginning the night of admission. The patient admitted to smoking ½ pack of cigarettes daily for 15 years. Physical examination revealed an obese black woman in no acute distress with blood pressure of 240/160 mm Hg, pulse of 90 beats per minute, and respirations of 18 per minute. There were no lesions on the tongue, skin, or breasts.

Chest was clear to auscultation and percussion. Extremities showed weakness, brisk reflexes, and decreased sensation of the left upper and lower extremities.

Chest roentgenographic examination revealed the presence of a well-defined round density in the right infraclavicular region measuring 1.5 cm in diameter (Fig 1). The patient had a positive reaction to intermediate-strength purified protein derivative; all subsequent smears and cultures for acid-fast organisms were negative. Perfusion lung scan showed decreased perfusion in the right apical region and right midlung field. No endobronchial lesions were seen on bronchoscopic examination. Multiple biopsies of the right upper lobe bronchus and carina were taken; all were normal. A thoracotomy with right upper lobe resection was done, and the patient recovered uneventfully.

On the basis of the gross and microscopic pathologic findings, a final diagnosis of granular cell tumor was made. The patient has remained asymptomatic and was last seen five months after the surgical resection, having made a complete recovery from the hemiplegia.

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Figure 1. Admission chest roentgenogram showing well-defined round lesion in right upper lobe.