Occult Mucous Airway Obstruction in Diabetic Ketoacidosis*

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Four patients with diabetes mellitus and no underlying clinical pulmonary disease were found to have extensive unilateral mucous occlusion of a major central bronchus. None of the patients had significant nasogastric findings suggestive of pulmonary secretions, and chest roentgenographic films were normal. Arterial blood gas evaluation failed to reveal the usual hypercapnia during ketoacidosis, thus prompting bronchoscopic examination or deep airway suctioning. These interventions disclosed and resolved the mucous obstruction of the compromised bronchus. Antibiotic therapy, based upon bronchial secretion Gram stain and culture, was successfully instituted in all patients. Lethargy and autonomic neuropathy are proposed as contributing factors responsible for occult mucous plugging in diabetic patients in ketoacidosis. The absence of hypopneas in this setting may be the only clue to silent mucous plugging of airways.

Clinical involvement of the respiratory tract may be a complication of diabetic ketoacidosis (DKA). Most of the pulmonary consequences of diabetes appear to be noninfectious, while there may also be an association with bacterial and fungal pneumonia. Although mucous plugging has been noted in obtunded and implied in one diabetic patient, it has not previously been cited as a specific complication associated with DKA. We describe four patients without the usual hypopneas during DKA who were found to have clinically occult mucous plugging of major bronchi. Once occlusion was relieved, antibiotic therapy was instituted and their medical course was uncomplicated. A normal arterial carbon dioxide level in DKA should alert the clinician to the possibility of silent mucous obstruction of airways.

Case Reports

Case 1

A 26-year-old man with insulin-dependent diabetes mellitus (IDDM) associated with impotence and a neurogenic bladder was admitted. Regular and NPH insulins were his only medications. He was afebrile with heart rate of 130 bpm, blood pressure 130/70, and respiratory rate 26/min. He was lethargic and confused with absent Kussmaul's respirations. Auscultation of the lungs was normal. The blood glucose level was 923 mg/dl with blood urea nitrogen (BUN) 62 mg/dL, creatinine (Cr) 3.7 mg/dl and computed anion gap 34 meq/L. The white blood count (WBC) was normal. Urinalysis revealed 4+ ketones. Arterial blood gas (ABG) analysis on room air (RA) revealed a pH of 7.16, Pco2 37, P02 96 and HCO3 13. Blood was drawn for culture and the patient was treated with intravenous (IV) regular insulin and vigorous hydration with 45 percent NaCl solution. Potassium chloride and potassium phosphate were given as necessary, although no episode of hypokalemia was noted. As his blood glucose level decreased with treatment and he became more alert, it was noted that repeat ABG on RA continued to show metabolic acidosis and a fall in Pco2; pH was 7.24, Pco2 40, P02 84 and HCO3 was 16. Lung examination results were still unremarkable with no pulmonary symptoms. A lung perfusion scan was performed to rule out pulmonary emboli as the cause for the fall in oxygen tension. The perfusion scan revealed total absence of blood flow to the left lung; a ventilation scan demonstrated no ventilation to the left lung. The large ventilation defect in the left lung prompted flexible fiberoptic bronchoscopic (FFB) examination 12 hrs after admission, which demonstrated thick mucoid secretions occluding the left main stem bronchus. Gram stain of mucous obtained by bronchoscopy demonstrated numerous polymorphonuclear leukocytes (PMNs) and Gram-negative bacilli. Repeat ABG analysis on RA after FFB showed improvement with a pH of 7.36, Pco2 30, and P02 97. The patient was started on therapy with cefazolin sodium. Bronchoscopic aspirate and blood cultures ultimately grew Klebsiella pneumoniae. Review of previous hospitalizations for DKA revealed an ABG level (on RA) demonstrating compensated metabolic acidosis: pH 7.01, Pco2 16, P02 128 and HCO3 4. After a two-week antibiotic course and stabilization of his diabetic state, he was discharged in good condition. Pulmonary function tests prior to discharge revealed no abnormality in air flow.

Case 2

A 31-year-old woman with IDDM associated with urinary retention was admitted for lethargy. Her medicines included regular and NPH insulin and acetaminophen for intermittent headaches. On physical examination, she was afebrile with a BP of 125/64, HR 119/ bpm and RR 26/min. Kussmaul's respirations were absent. Lung examination revealed a slight diminution of breath sounds in the left lung. The blood glucose level was 720 mg/dl, BUN 44 mg/dl and WBC 12,800/cu mm with a normal differential count. ABG analysis on RA revealed a pH of 7.33, Pco2 47, P02 71 and HCO3 20. Urinalysis demonstrated 4+ glucose, 2+ ketones, 3 WBC and no bacteria. The chest x-ray film (CXR) was normal. The patient's DKA was

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treated with intravenous regular insulin and hydration with .45 percent NaCl solution. Potassium phosphate was given as necessary, with no episode of hypokalemia noted. She appeared to have obstruction of airflow in the left lung, possibly due to aspiration of a foreign object when she was lethargic. FFB was performed eight hours after admission and disclosed thick, tenacious secretions in both major bronchi. The left main stem bronchus was almost totally occluded. Five ml of normal saline solution was introduced to aid in liquefaction of secretions. Post-bronchoscopy CXR remained normal, with improvement noted on repeat ABG analysis. Gram stain of mucous secretions from FFB revealed numerous PMNs with Gram-positive diplococci. Penicillin therapy was instituted; FFB culture grew *Streptococcus pneumoniae.* Blood cultures drawn on admission were negative. The patient's previous records included ABG analysis (on RA) during DKA that demonstrated a pH of 7.10, PaCO2 21, PaO2 97, and HCO3 8. A ten-day course of penicillin, along with correction of DKA, resulted in satisfactory condition and discharge from the hospital. Pulmonary function test results were normal.

**Case 3**

A 49-year-old woman with IDDM associated with urinary retention was admitted for upper gastrointestinal bleeding following heavy ethanol ingestion the previous night. Prior evaluation of the gastrointestinal tract disclosed gastritis by endoscopy and upper gastrointestinal series. One year prior to admission, she had a permanent tracheostomy inserted for tracheal stenosis related to traumatic intubation during an episode of coma associated with DKA. Her medications included regular and NPH insulin and Mylanta. Physical examination found her to be afebrile, HR 114 bpm, BP 130/70, RR 24/min. There was no Kussmaul's respiration nor any orthostatic change in blood pressure. The tracheostomy tube had a small amount of mucous in its orifice. Auscultatory examination revealed minimal right-sided rhonchi. The stool was dark and guaiac-positive. Hemoglobin level was 9.2 g/dl, with a blood glucose level of 522 mg/dl. Her WBC count and coagulation parameters were normal. Urinalysis disclosed 4+ ketones. CXR demonstrated the tracheostomy tube and clear lung fields. ABG analysis on RA revealed a pH of 7.27, PaCO2 39, PaO2 80 and HCO3 17. A nasogastric tube was inserted and coffee grounds-appearing gastric contents were aspirated which were Hematostat positive. As the hyperglycemia was treated with regular insulin and .45 percent NaCl solution, a fall in hemoglobin level was anticipated. When two units of packed red blood cells were transfused. Repeat ABG analysis on RA demonstrated a pH of 7.25, PaCO2 43, and PaO2 72. Examining her medical records disclosed previous ABG analysis (on RA) when she had DKA with a pH of 7.20, PaCO2 20, PaO2 102, and HCO3 7. Airway compromise was suspected on the basis of minimal unilateral rhonchi. Deep tracheal suction was performed six hours after admission and 20 ml of thick yellow mucoid secretions were obtained. Gram stain revealed PMNs and pleomorphic Gram-negative rods. A repeat ABG on room air after deep suctioning and pulmonary toilet disclosed a pH of 7.38, PaCO2 of 31, and PaO2 of 96. Ampicillin was instituted in addition to aerosolized bronchodilators. *Hemophilus influenzae* grew out of the sputum culture. Recurrent gastritis was treated with antacid therapy while the hyperglycemia was corrected. She was discharged with a stable hemoglobin, diabetic diet, and regular and NPH insulin.

**Case 4**

A 22-year-old man with IDDM associated with impotence was admitted for unresponsiveness to therapy. The only medications were regular and NPH insulin. On physical examination he was lethargic with a HR of 120 bpm, BP 130/80, and RR 36/min. There were no Kussmaul's respirations. Auscultation of the lungs was normal, as was the admission CXR. Blood glucose level was 842 mg/dl, BUN 57 mg/dl, and Cr 2.7 mg/dl. WBC count was normal. Urinalysis demonstrated 2+ ketones. ABG analysis on RA revealed a pH of 7.30, PaCO2 42, PaO2 72 and HCO3 18. Hydration with .45 percent NaCl solution and regular insulin were administered, but repeat ABG analysis six hours after admission still revealed metabolic acidosis with an elevated alveolar-arterial gradient, pH 7.34, PaCO2 37, PaO2 75 and HCO3 20. Review of ABG analysis from prior admission with uncomplicated DKA disclosed a pH of 7.00, PaCO2 14, PaO2 121 and HCO3 4. Repeat auscultatory examination suggested unilateral right lung rhonchi. Chest percussion was instituted; however, the inability of the patient to fully cooperate made this therapeutic means unsuccessful. FFB was performed five hours after admission and demonstrated thick mucous secretions occluding an erythematous right mainstem bronchus. Forty-five ml of mucoid yellow secretions were aspirated. Gram stain revealed PMNs and Gram-positive diplococci. Repeat ABG analysis after bronchoscopic examination demonstrated a pH of 7.37, PaCO2 27, PaO2 94, and HCO3 23. The patient was given penicillin therapy for tracheobronchitis because the culture grew *Streptococcus pneumoniae.* He was successfully treated thereafter with chest physical therapy and aerosolized Alupent for mucokinesis. He was discharged after eight days of hospitalization with a normal ABG analysis (pH 7.41, PaCO2 34, PaO2 91, HCO3 25). Pulmonary function test results were normal.

**Discussion**

Although the frequency is not known, our report of airway mucous occlusion in DKA demonstrates a previously unidentified pulmonary complication associated with diabetes. The nature of mucous secretion and mechanism of impaired clearance remain speculative. On the surface, it seems likely that respiratory tract infection may lead to ketosis and in turn result in lethargy, depression of the central respiratory center, and impaired cough and mucous plugging. It is possible, alternatively, that the observation of mucous occlusion is related to altered vagal tone in the airways.

The literature has not clearly defined the role impaired vagal tone may play in contributing to defective mucous clearance. Mucous secretion, however, is regulated by vagal effenter nerves and it has been demonstrated that there is reduced airway vagal tone and diminished cold responsivity in nonsmoking, nonasthmatic diabetic patients with autonomic neuropathy. The presence of mucous in our patients may therefore have been precipitated by infection, with clearance impeded by faulty vagal responsiveness and compounded by a defective cough mechanism in the setting of lethargy. All of our patients had symptoms of autonomic neuropathy as manifested by a neurogenic bladder and impotence, thus suggesting that there was involvement of the respiratory autonomic nerves in these diabetic patients.

Proper mucociliary function is an additional important mechanism ensuring movement of mucous out of the respiratory tract. Although no studies have suggested impaired mucociliary function occurs in diabetic patients specifically, three of our four patients did smoke and smoking has been reported to alter mucokinetic action. Curiously, cigarette smoking appears to be more frequent among insulin-treated diabetic patients.
The state of mucous occlusion in three of our patients was suspected only after the first patient was assessed for pulmonary embolism during treatment for DKA. Case reports have shown that mucous plugging of major bronchi can cause a hypoxic state with an appearance similar to massive pulmonary embolism with normal or near normal chest roentgenograms. A perfusion scan shows a reduced or absent blood flow, while the ventilation scan demonstrates ventilation to be reduced or absent in the lung affected by mucous plugging. This was confirmed in our first patient. The finding, however, of the normal arterial carbon dioxide level during DKA, in retrospect, should have made us consider airways disease first. Indeed, when confronted by the three subsequent patients, our suspicions of occlusive airway disease were confirmed when normocapnia was found.

The "typical" blood gas presentation in DKA is well known to be a metabolic acidosis with low pH, Pco2 and HCO3. Pco2 will then begin to rise with appropriate therapy as HCO3 also begins to rise. On admission, all of our patients had a normal or elevated arterial carbon dioxide level reflecting their airway disease.

Hypoventilation with DKA is a rarely-discussed phenomenon. There have been reports of hypokalemia and subsequent respiratory impairment with DKA. In one case, the possibility of a bronchial mucous plug was considered but discounted due to the fact that "pulmonary secretions were clinically inapparent" and cough was absent. This patient did not undergo nasotracheal suction during the hypoventilatory or recovery periods, or bronchoscopic examination, and conceivably could have had mucous obstruction as a cause of the elevated carbon dioxide level. Furthermore, as in our patients, absence of cough does not preclude the presence of airway secretions.

The arterial oxygen tension in DKA may be surprisingly high due to hyperventilation secondary to acidosis and an increased glucose load. In addition, the production of large amounts of endogenous carbon dioxide from the metabolic acidosis causes a higher respiratory quotient and thus a higher than expected increase in alveolar oxygen tension. We had the benefit of previous arterial blood gas studies from our patients which demonstrated the typically elevated arterial oxygen tension (Table 1). We did not find this hyperoxemia in these patients on readmission. Mucous obstruction most likely resulted in the lower arterial oxygen tension as the carbon dioxide level was normal or elevated in all patients.

Our finding of DKA without hypocapnia supports a speculation by Fulop nearly ten years ago. At that time, he examined the ventilatory response in uncomplicated DKA and reported that most patients with metabolic acidosis and a pH below 7.1 hyperventilated if no lung abnormalities were present. He conjectured that metabolic acidosis associated with a higher Pco2 than expected implicates coexisting respiratory acidosis from acute or chronic pulmonary insufficiency. Mucous airway occlusion in our patients appears to have been responsible for this acid-base disturbance, as described by Fulop.

**CONCLUSION**

We believe we have described a pulmonary condition associated with DKA. It is not clear if tracheobronchial infection initiates the sequence of events in these patients. Possibly less clear are smoking-induced mucociliary dysfunction and the altered defense mechanisms, including cough reflex. Autonomic neuropathy of the tracheobronchial tree may be the common defective denominator, as all of our patients had symptoms of autonomic nerve dysfunction. The patient with diabetes mellitus is known to be at risk for silent myocardial ischemia. Accordingly, it appears that certain patients can have major occlusion of central bronchi of a similarly elusive character. The finding of a normal or elevated arterial carbon dioxide level in DKA may be the only clue to this "silent" disorder. Tracheobronchial suction appears to be therapeutic, with the addition of appropriate antibiotics where indicated.

**REFERENCES**


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**Table 1—Arterial Blood Gases on Room Air**

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DKA = diabetic ketoacidosis