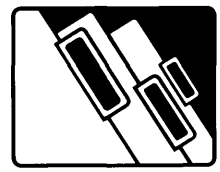
Case Report



Mixed Acid-Base Abnormalities in Diabetes

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This study is a description of a patient who exhibited diabetic ketosis associated with an alkalosis rather than acidosis and a review of eight previously reported cases. Precipitating factors for this syndrome are severe vomiting with loss of hydrogen, potassium, and chloride ions, and dehydration. The ingestion of alkali may also result in this mixed acid-base disturbance. Treatment consists primarily of replacement of potassium and chloride. All reported patients had received large doses of insulin for initial therapy; however, limited insulin (20 U) therapy in this patient almost completely reversed the metabolic abnormality within 12 hours. DIABETES CARE *1*: 362–364, NOVEMBER–DECEMBER 1978.

The accumulation of acetoacetic and β-hydroxybutyric acid is the most common disturbance of hydrogen ion homeostasis in uncontrolled diabetes mellitus; however, on rare occasions a mixed acid-base disorder may occur in diabetic ketosis which results in metabolic alkalosis rather than acidosis.

CASE REPORT

A 57-yr old black female was admitted to the medical intensive care unit of the University of Texas Medical Branch on 19 October 1977 for acute management of hyperglycemia, hypokalemia, and ketosis. She had been confined to a wheelchair as a result of a previous cerebrovascular accident causing left-sided hemiparesis. Her past medical history was further highlighted by a total abdominal hysterectomy, hypertension treated with aldactazide, and diabetes mellitus diagnosed in 1968 and managed by diet plus 40 U NPH insulin daily. No information was available concerning her previous state of diabetic control.

Two weeks before admission she developed nausea and vomiting associated with diarrhea that persisted for 6 days. One week before admission, obstipation was noted followed by increasing abdominal distention, lethargy, and refusal to eat. On day of admission, she vomited large amounts of feculent material after having an enema.

Physical examination revealed this black, female patient to be thin, poorly responsive, and very weak. Blood pressure was 110/90; pulse, 96/min; respirations, 24/min; temperature, 36.6°C; and body weight, 55 kg. Poor skin turgor, soft eyes, and dry mucous membranes were present. Her lungs were clear. The point of maximal impulse (PMI) was in the fifth intercostal space at the anterior axillary line. A grade 2 systolic ejection murmur at the apex was noted. The abdomen was distended, nontender, and tympanitic with only occasional bowel sounds. No organomegaly or masses were found. Rectal exam revealed liquid green stool, guaiac negative. Neurologic exam showed a left central seventh nerve palsy, hyper-reflexia, paresis of the upper and lower left extremities, and a Babinski's reflex on the left.

Roentgenogram of the chest showed cardiomegaly with clear lung fields. An electrocardiogram demonstrated atrioventricular dissociation with an atrial rate of 90, ventricular rate 120, right axis deviation, incomplete right bundle branch block, and ST depression plus T-wave flattening, anteriorly, suggesting hypokalemia (Figure 1).

Initial laboratory studies included: hemoglobin, 10 g/100 ml; hematocrit 30.6%; white blood cell count, 6500; sodium, 140, potassium, 0.8; chloride, 69, and carbon dioxide, 42 meq/liter; urea nitrogen 9 and glucose 648 mg/dl; serum "acetone," tested by the Acetest tablet method, was positive diluted at 1:8 but was negative at 1:16; lactic acid was 2.2 meq/liter; and arterial blood gases were P_{CO_2}, 56 mm Hg, and P_{O_2}, 55 mm Hg, pH 7.55.

Initial impression was diabetic ketosis associated with severe hypokalemic alkalosis and volume depletion, and possible small bowel obstruction. Nasogastric suction was begun; a central venous catheter was placed; and fluid replacement was started with 0.154 M saline supplemented with

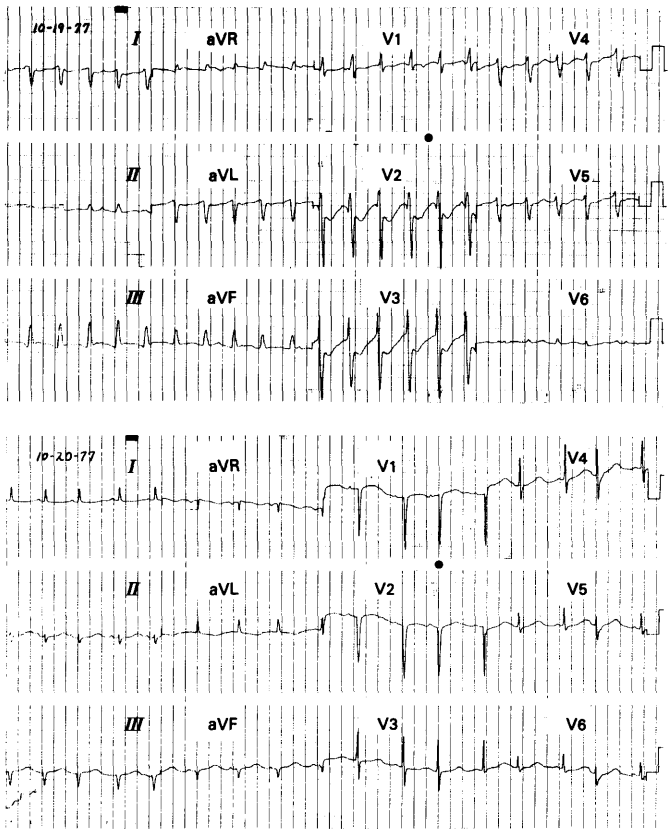

FIG. 1. Electrocardiogram on admission (above) and 12 hours later (below).

potassium chloride and potassium phosphate at a rate of 45 meq potassium per hour. Fluids were given i.v. at an initial rate of 500 ml/hour. 10 U of regular insulin was given i.m. on admission and repeated 8 hours later. She was begun on gentamicin and chloramphenicol.

The patient improved dramatically by 12 hours after admission and was asking to sit up. She had return of spontaneous bowel sounds, decreasing abdominal distention, and began having copious amounts of green-gray, guaiac-negative stool. Therapy over the 12-hour period had included a total of 6850 ml fluid and 640-meq potassium replacement. Laboratory data at this time included potassium, 3.0, sodium, 155, chloride, 92, and carbon dioxide 41 meq/liter. Plasma glucose was 127 mg/dl. Serum acetone was now negative undiluted. The electrocardiogram had improved significantly (Figure 1) as had her abdominal radiogram. Fluid therapy was tapered and oral feedings were started on the third hospital day. Antibiotics were discontinued.

The patient continued to have frequent liquid stools and required approximately 80 meq KCl daily to maintain a serum potassium above 3.0 meq/liter. No etiology for her diarrhea was found by proctoscopy, barium enema, stool culture, examination of stool for ova and parasites, or immunoelectrophoresis for amebiasis.

A small sacral decubitus ulcer was noted on the fifth hospital day, and a temperature of 39.4°C developed on the ninth hospital day. Blood, urine, sputum, and ulcer cultures were obtained, and she was again started on chloramphenicol and gentamicin. The ulcer continued to worsen and progressed to massive subcutaneous necrosis of both buttocks. She remained febrile and appeared septic, but blood cultures were negative. She died on the 20th hospital day despite extensive debridement, whirlpool cleansing, and continuation of antibiotics. Glucose was 201 mg/dl; potassium was 4.7 and carbon dioxide 29 meq/liter before death.

Autopsy revealed an abscess cavity extending from the sacrum into the pelvic cavity, dissecting along fascial planes into the anterior abdominal wall. Cultures from the abscess grew *Escherichia coli*, enterococcus, and micrococcus. Postmortem blood cultures grew *E. coli*. Other findings included generalized atherosclerosis, left ventricular hypertrophy, infiltrating ductal carcinoma of the left breast, ischemic enterocolitis, and an old cerebral infarction in the distribution of the right middle cerebral artery. The pancreas was free of tumor. Microscopic examination showed focal hyalinization of the islets of Langerhans.

COMMENT

There have been eight previously reported cases of diabetic patients presenting in apparent diabetic ketoacidosis who were found to be alkalotic rather than acidotic, despite the presence of significant ketonemia (see Table 1). The syndrome was whimsically termed diabetic "ketoalkalosis" by Bleicher, who reported the first case. Several recent letters to the *British Medical Journal*[4–7] have used the term. The suggestion has been made that it is easily misdiagnosed and probably more common than generally recognized.

A common feature of the disorder is severe, prolonged vomiting and dehydration. Ingestion of alkali was also an important contributing factor in two patients (cases 1 and 6, Table 1). The vomiting leads to loss of hydrogen, potassium, and chloride ions, and thus a hypokalemic, hypochloremic metabolic alkalosis ensues. Only one reported case (case 8) had no apparent precipitating cause for alkalosis. One patient (cases 3 and 4) reported by Walsh was admitted twice with "ketoalkalosis," but in the interval between these admissions had unequivocal diabetic ketoacidosis, supporting the view that the alkalosis represents an abnormality in hydrogen ion homeostasis distinct from the diabetic insulin-deprived condition but occurring coincidentally with it.

Therapy should consist of the usual treatment for diabetic ketoacidosis with emphasis on replacing both potassium and chloride. All reported cases before ours received potassium chloride. It is wise, in addition, to use potassium phosphate to replace potassium deficits in order to avoid the hypophos-

TABLE 1
Data from reported cases of diabetic ketoalkalosis

Case	Reference	Age	Sex	Antecedent factors	Plasma glucose (mg/dl)	Na (meq/liter)	K (meq/liter)	Cl (meq/liter)	HCO_3 (meq/liter)	Arterial pH
1	Bleicher[1]	38	M	Vomiting, dehydration Alkali ingestion Pyloric obstruction	900	134	5.1	80	34	7.44
2	Roggin[2]	37	M	Vomiting, dehydration	984	119	4.3*	40	34	7.59
3	Jimenez[3]	58	F	Vomiting, dehydration Pyelonephritis Hydronephrosis	294	147	2.5	74	49	7.57
4	Walsh[4]	24	F†	Vomiting, dehydration	342	135	3.8	—	34	—
5	Walsh[4]	24	F†	Vomiting, dehydration	234	140	4.5	—	30	—
6	Walsh[4]	50	M	Vomiting, dehydration Alkali ingestion	549	129	4.2	—	30	—
7	Melrose[5]	68	M	Vomiting, dehydration	636	139	3.9	—	29	7.53
8	Shirley[6]	70	F	None	476	—	3.6	—	32	7.51
9	Sanders	57	F	Vomiting, dehydration Diarrhea	648	140	0.8	69	42	7.55
Mean values					563	135	3.6	66	35	7.53

* Potassium fell to 2.5 meq/liter shortly after institution of therapy, and the alkalosis worsened; arterial pH increased to 7.94.
† Same patient.

phatemia that is frequently seen in the management of diabetic ketoacidosis.[8]

All of the reported patients with diabetic ketosis associated with alkalosis received insulin. At least one patient (case 2) received a total of 210 U. Our patient received only 20 U of regular insulin i.m. during the first 24 hours with a decrease in plasma glucose from 648 to 56 mg/dl. This suggests that diabetic "ketoalkalosis" might be managed more appropriately by potassium replacement and little or no insulin. There are two reasons for this suggestion. First, insulin makes it more difficult to raise the serum potassium from dangerously low levels in a patient as severely depleted as ours. Second, the blood sugar may decrease with potassium replacement alone in an adult-onset diabetic patient who has some endogenous insulin reserve, since potassium deficiency alone severely attenuates the pancreatic beta cell secretory response.[9] In 1965, Conn showed that the impaired glucose tolerance associated with primary aldosteronism and other states with potassium depletion was due to an inability of the beta cells to respond to glucose. This acquired, beta cell secretory defect was reversed by potassium repletion.

These cases underline the importance of carefully determining the acid-base status of patients who present with hyperglycemia and ketonemia. In particular, when a history of severe vomiting or alkali ingestion is present and dehydration is marked, the physician should be aware that a paradoxical metabolic alkalosis rather than acidosis may exist, requiring judiciously large quantities of potassium and chloride and limited insulin therapy.

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