Hyperosmolar Hyperglycemic Nonketotic Coma in a Patient Undergoing Emergency Cholecystectomy

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In recent years the syndrome of hyperosmolar hyperglycemic nonketotic coma has become widely recognized, and numerous case reports have appeared in the medical literature.[1-6] In none of these reports was the patient subjected to anesthesia and surgical operation. We had a patient in whose case the diagnosis was made soon after her admission to the hospital who underwent emergency cholecystectomy seven hours later. The case illustrates certain features of the syndrome and points out the therapeutic challenges posed by such a surgical patient.

REPORT OF A CASE

A 76-year-old Caucasian woman with known maturity-onset diabetes, hypertension, angina, and congestive heart failure entered the hospital with a history of back pain, followed by nausea and persistent vomiting of 24 hours' duration. Because of her stuporous state and urinary incontinence, she was brought to the emergency ward by her daughter. Prior to the present illness, she had been alert, but had spent much time in bed.

Past medical history included: two previous hospital admissions for chest pain, with no proof of myocardial infarction, diabetes mellitus diagnosed and treatment begun several months earlier with chlorpropamide, 500 mg/day; hypertension of 180/100 mm Hg treated with chlorothiazide, 500 mg/day; congestive heart failure managed with digoxin, 0.25 mg/day. Her other medications included sublingual administration of nitroglycerin as needed and diazepam, 15 mg daily.

Physical examination revealed that the patient was obese and obtunded, with mottled skin, pale dry lips, pulse rate 144/min, temperature 101 F, blood pressure 90/60 mm Hg, and respiratory rate 40/min and labored. The oral membranes were parched, neck veins were flat, and the chest was clear, except for a few basilar rales. On examination, the abdomen was distended and quiet, with tenderness in the right upper quadrant. The femoral pulses were weak. Central venous pressure was 5 cm H_2O.

Initial arterial blood values were: P_{O_2}, 79 torr; P_{CO_2}, 23 torr; *p*H, 7.50; Na^+ 132 mEq/l; K^+ 2.8 mEq/l; osmolarity 329 mOsm/l. Venous blood values were: blood glucose, 726 mg/100 ml; serum acetone, negative; BUN 26 mg/100 ml; LDH 675 U/ml; alkaline phosphatase 11.4 Bodansky U/ml; lactate 4.67 mEq/l; hemoglobin 17.2 g; hematocrit 50 per cent; leukocyte count 24,000 per cu mm (61 polys, 29 bands, 9 myelocytes, 1 metamyelocyte). Urinary values were: pH, 5; trace albumin; 4+ glucose; 0 acetone.

The diagnosis was cholecystitis and cholangitis, septicemia, and hyperosmolar hyperglycemic nonketotic coma. Therapy consisted of administration of fluids, insulin (table 1), penicillin, and chloromycetin.

The patient was brought to the operating room six hours after admission in improved condition. The blood pressure was 160/60 mm Hg, pulse rate, 100/min, and respirations were less labored. She was arousable, but was unable to cooperate or answer questions. Urinary glucose was 4+ and blood glucose 360 mg/100 ml, with no acetone in either fluid. A percutaneous arterial line was placed in a radial artery and the ECG was continuously monitored. After 10 minutes of breathing oxygen by mask, anesthesia was begun with thiopental, 50 mg, and succinylcholine, 80 mg. With application of cricoid pressure, a #34 Rusch endotracheal tube was placed and the cuff inflated. Anesthesia was maintained for four hours with N_2O and O_2, 50 per cent, thiopental, 100 mg, morphine, 8 mg, and *d*-tubocurarine, 37 mg.

At operation a gangrenous gallbladder with pus in the common duct was found, and cholecystectomy with exploration of the common duct was performed. Central venous pressure gradually increased to 21 cm H_2O. Because urinary output was only 10 ml during the first hour of operation, furosemide, 40 mg, was given. Urinary output gradually increased to 90 ml/hour. The patient received 80 mEq of KCl.

Three blood cultures taken in the emergency ward grew Enterobacteriaceae sensitive to chloromycetin. Following operation the patient remained in the intensive care recovery room for approximately 48 hours. Ventilation was controlled during this time. On the second postoperative day mechanical respiratory assistance was discontinued and the trachea extubated. The patient's mental

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status slowly improved, so that the by the third postoperative day she was able to communicate verbally. Over the next few days she gradually regained her usual mental status.

Values for BUN and creatinine continued to increase postoperatively, despite a diuresis of 130 ml/hr. Maximum BUN was 101 mg/100 ml, with creatinine, 3.7 mg/100 ml, on the fourth postoperative day; these values gradually decreased to 25 mg/100 ml and 1.7 mg/100 ml, respectively, by the fourteenth hospital day. A diagnosis of non-oliguric acute tubular necrosis was made. Values for bilirubin and alkaline phosphatase remained above normal during the patient's hospital stay, peaking at 27.2 mg/100 ml and 28.9 U/ml, respectively. A T-tube cholangiogram on the fifth postoperative day revealed no evidence of obstruction. At the time of discharge, tests of liver function were slightly abnormal: bilirubin, 17.0 mg/100 ml total and 14.5 mg/100 ml direct; SGOT 51 U/ml; alkaline phosphatase, 28.9 BU/ml. The patient received antibiotic therapy for two weeks.

Her diabetes was easily controlled postoperatively on a sliding scale of regular insulin, requiring only 0–15 units per day for control of urinary and blood glucose. The hepatic and renal damage were felt to have been the result of sepsis and hypotension that were present on admission. The patient was discharged on the twentieth hospital day.

Discussion

The typical patient in whom hyperosmolar hyperglycemic nonketotic coma occurs is middle-aged to elderly. About half of these patients are known to have mild adult-onset diabetes. Some are insulin-dependent,[7] and, of the survivors, all have abnormal glucose tolerance tests.[1] In most cases there is a precipitating condition, usually a severe concomitant illness: sepsis, as in this patient, pneumonia, pancreatitis, gastrointestinal hemorrhage, uremia, stroke,[1] excessive glucose intake from peritoneal dialysis and intravenous fluids, burns,[8] cardiac surgery,[9] or ingestion of drugs known to aggravate diabetic control, such as diuretics,[10] steroids,[11] or diphenylhydantoin.[12] Most patients (85 per cent) have cardiovascular or renal disease.[2]

Typical findings upon admission to the hospital include blood glucose greater than 900 mg/100 ml; serum osmolality greater than 350 mOsm/l; an altered state of consciousness, including coma; dehydration with associated oliguria; increased hematocrit and BUN. The onset of the syndrome is usually insidious (days to weeks) but may be fulminant, as in this patient. Hyperglycemia leads to marked osmotic diuresis, potassium depletion, and prerenal azotemia. Shock and metabolic acidosis may be caused by the severe dehydration. The mortality from hyperosmolar nonketotic coma has been reported as 40 per cent[13] to 60 per cent.[1]

Most authorities believe that saline solution, 0.45 per cent, is the intravenous fluid of choice for most patients who are not in shock.[1–4] For patients in shock, restoration of an adequate circulating blood volume is the first priority of treatment. This can be done with saline solution, Ringer's lactate solution, plasma, or albumin. The average patient needs 6 to 16 liters of fluid during the early treatment phase (first 12 hours). Potassium depletion is common, and potassium supplements are needed during the initial phases of treatment.[4] Caution must be exercised if serum potassium is above the normal value, *e.g.*, if the patient is acidotic, or if urinary output is inadequate. Precipitous declines in serum potassium were frequently observed early in the course of therapy by Gerich,[2] and in no instance did serum potassium increase.

The average patient requires 300 to 400 units of insulin during the first 24 hours of treatment.[1,4] Arieff recommends that the initial dose of crystalline insulin given be numerically equal to 10 per cent of the blood glucose (*e.g.*, blood glucose = 1,000 mg/100 ml, give 100 units regular insulin), half given intravenously and half subcutaneously. Blood glucose is measured every two hours; insulin is given according to the same formula until blood glucose is less than 250 mg/100 ml. Sugar is then given as either D5W or dextrose in saline solution, depending on serum sodium and osmolarity.

McCurdy points out that this dose of insulin may be too high and that hypotension may be precipitated by decreasing blood volume, as insulin carries glucose and water into cells.[4] Caution should be exercised when regulating the rate of decrease of blood glucose and osmolarity, because cerebral edema is commonly found at autopsy in patients dying in diabetic ketoacidosis. This is rare in nonketotic coma, but it has been reported.[13]

Our patient typifies some of the common

TABLE 1. Results of Laboratory Tests, Insulin

Time	Blood Glucose (mg/100 ml)	Serum Acetone	Urinary Glucose/ Acetone	Serum Osmolarity (mOsm/l)	Na^+ (mEq/l)	K^+ (mEq/l)	pH	P_{CO_2} (mm Hg)	P_{O_2} (mm Hg)
11 AM	762	0	4+/0	329	137	2.8	7.50	23	79
12									
1 PM	574			325	142	3.9	7.37		
2									
3									
4									
5	363	0	4+/0	322	142	3.7	7.32	47	396
6						3.8	7.28	55	149
7	279	0	2+/0						
8					145	4.7	7.28	50	159
9									
10	180		0/0		143	4.9	7.49	29	90
10:30							7.51	30	464
TOTAL									

features of this syndrome. She was elderly, with cardiovascular disease requiring diuretic therapy for congestive heart failure and hypertension. She was known to have adult-onset diabetes and had never had ketoacidosis. She had a very short history of acute illness, somewhat unusual for this syndrome. The typical patient seeks medical care after 12 days of illness.[2] Her precipitating illness was gangrenous cholecystitis with Enterobacteriaceae sepsis. Her survival is unusual, in that, as Arieff points out, all six of his patients who had or developed gram-negative sepsis died; all patients in shock when first seen died, as well as three of five who were hypotensive on admission.[1]

By the time our patient reached the operating room her condition had improved, but she was still quite ill. She was still hyperosmolar, moderately hyperglycemic, and oliguric. She clearly needed further treatment. Induction of anesthesia was rapidly

and Fluids Administered, and Comments

BUN (mg/100 ml)	Hematocrit (Per Cent)	Insulin, Regular (Units)	Fluids	Comments
26	50	50 iv 50 im	Dextrose 2.5 per cent + 0.45 per cent saline solution, 600 ml	Room air Arterial blood
		25 iv 25 im	Ringer's lactate solution, 1,000 ml, +80 mEq KCl	
29		50 iv	0.9 per cent saline solution, 1,000 ml, +40 mEq KCl	
		50 iv	5 per cent albumin in 0.9 per cent saline solution, 750 ml	Blood glucose, >250 mg/ml—Dextrostix
		50 iv	5 per cent albumin in 0.9 per cent saline solution, 750 ml	Blood glucose, >250 mg/ml—Dextrostix
			0.9 per cent saline solution, 1,000 ml, +40 mEq KCl	Operation
	31		0.9 per cent saline solution, 400 ml	100 per cent O_2, spontaneous ventilation
		25 iv	5 per cent albumin in 0.9 per cent saline solution, 250 ml	50 per cent O_2, operating room ventilator
			Whole blood, 1 unit; D5W, 150 ml	80 mEq KCl in operating room
	33		0.9 per cent saline solution, 100 ml	50 per cent O_2, operating room ventilator
			0.9 per cent saline solution, 100 ml	Recovery room
33	32		0.9 per cent saline solution, 100 ml	Room air, Emerson ventilator
			0.9 per cent saline solution, 100 ml; packed cells, 1 unit	100 per cent O_2, Emerson ventilator
		325	Crystalloid, 4,550 ml; albumin, 5 per cent in 0.9 per cent saline solution, 1,750 ml; whole blood, 1 unit; packed cells, 1 unit	

performed with cricoid pressure on the assumption that the stomach might have been full.

The stress which occurs with anesthesia and surgery, especially upper abdominal surgery, has been associated with a hyperglycemic response.[14,15] In this type of case an effort should be made to choose a method of anesthesia with the least effect on the blood sugar.[14]

Like any other critically ill patient, the surgical patient who has this syndrome must be closely monitored, as was done in this case. Postoperatively the patient's lungs were ventilated until the coma lightened and her cardiovascular system had stabilized.

As Arieff points out: ". . . any significant decrease in the mortality of nonketotic coma must come from earlier and more aggressive attacks upon concomitant illness, as well as increased recognition and appropriate therapy of acidosis, shock, renal failure, dehydration,

hyperglycemia, and electrolyte abnormalities."[1]

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Perforation of the Tympanic Membrane, A Complication of Tympanic Thermometry during Anesthesia

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There has been a renewed interest in better and more effective methods of temperature monitoring during anesthesia since the advent of the syndrome known as malignant hyperpyrexia. Tympanic thermometry has been advocated as a practical method of monitoring temperature during anesthesia. Since 1969 there have been numerous articles attesting to the ease of insertion and placement, sensitivity and accuracy, and safety and comfort of the tympanic membrane sensors, without serious complications being reported.[1,2,3] We wish to report a serious complication.

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We have utilized tympanic thermometry in more than 100 cases at the 500-bed Medical University Teaching Hospital since December 1972. Recently we experienced two cases of perforation of the tympanic membrane following the use of a tympanic membrane sensor.

Report of Two Cases

The first patient, a 46-year-old woman, had a vaginal hysterectomy performed under general anesthesia. After induction of anesthesia a commercially available tympanic membrane temperature sensor was placed in the right external auditory canal. Pre-insertion otoscopic examination was not performed, but gross visual examination of the external auditory canal revealed no abnormality. The technique used for insertion was that recommended by the manufacturer and consisted of placing the sensor in the ear canal, pulling down the ear lobe and gently inserting