SHORT REPORTS

Diabetic ketoalkalosis: a readily misdiagnosed entity

An essential part of the treatment of diabetic ketoacidosis is the replacement of fluid and electrolytes. Though routine use of alkali is questionable, it is often used in the early stages of treatment. We describe two patients diagnosed as having diabetic ketoacidosis who were later found to have a metabolic alkalosis. The use of alkali replacement in these patients would have been inappropriate and potentially hazardous.

Case reports

Case 1—A 24-year-old woman who had been treated with insulin for 11 years was admitted to hospital in December 1974 with a history of nausea for three weeks, severe vomiting for 24 hours, and diarrhoea for four hours. She was drowsy, hiccuping, dehydrated, and overbreathing, with acetone on her breath. Urine analysis showed 2% glucose and 3+ ketones. Diabetic ketoacidosis was diagnosed, and after standard investigations had been ordered she was given a normal saline infusion, potassium chloride supplements, and hourly intramuscular insulin. Subsequently the results of the initial investigations showed a metabolic alkalosis (see table). Within six hours all biochemical values were normal. The vomiting ceased within 48 hours, and a barium-meal examination at this stage showed nothing abnormal. Studies of autonomic nerve function showed only marginal abnormalities. During the next six months she was admitted twice in unequivocal diabetic ketoacidosis. In December 1975 she was admitted with a history and clinical features identical with those of December 1974.

Results of initial biochemical investigations

	Case 1		Case 2
	December 1974	December 1975	
Blood sugar (mmol/l)	19·0	13·0	30·5
Serum sodium (mmol/l)	135	140	129
Serum potassium (mmol/l)	3·8	4·5	4·2
Blood urea (mmol/l)	8·0	11·0	11·5
Hydrogen ion concentration (normal) 35-45 nmol/l)	28	26	33
P_{CO_2} (normal 4·7-6·0 kPa)	5·5	5·0	5·4
Standard bicarbonate (normal 22-26 mmol/l)	34	30	30
Serum aspartate aminotransferase blank	High	High	High

Conversion: SI to traditional units—Blood sugar: 1 mmol/l ≈ 18·0 mg/100 ml. Serum sodium: 1 mmol/l = 1 mEq/l. Serum potassium: 1 mmol/l = 1 mEq/l. Blood urea: 1 mmol/l ≈ 6·0 mg/100 ml. P_{CO_2}: 1 kPa ≈ 7·5 mm Hg. Standard bicarbonate: 1 mmol/l = 1 mEq/l.

Urine analysis showed 2% glucose and 3+ ketones. Plasma Ketostix result was positive. Diabetic ketoacidosis was again diagnosed and she was treated as before. Investigations again showed a metabolic alkalosis (see table).

Case 2—A 50-year-old man known to have had diabetes for four years and being treated with dietary restriction complained of fatigue, polyuria, and polydipsia for three weeks. For a week he had had heartburn and been taking alkalis. For three days he had been vomiting repeatedly. On admission he was found to be dehydrated, restless, hiccuping, and tachypnoeic, with acetone on his breath. Urine analysis showed 2% glucose and 3+ ketones. Diabetic ketoacidosis was diagnosed and he was given intravenous normal saline, potassium supplements, and hourly intramuscular insulin. Results of laboratory tests are given in the table. Within six hours he was well. He declined further gastrointestinal investigations.

Discussion

These two patients showed many features of true diabetic ketoacidosis and not surprisingly were diagnosed as ketoacidotic rather than ketoalkalotic. Two similar cases have been reported.[1 2] The entity of diabetic ketoalkalosis is easily misdiagnosed and is probably more common than is generally recognised.

A feature of the disorder is severe vomiting. The resulting loss of hydrogen, potassium, and chloride ions and, in some cases, self-medication with alkalis more than counteract any tendency for a metabolic acidosis to develop at a time when diabetes is uncontrolled and lead to a metabolic alkalosis. Our first patient was admitted twice for unequivocal ketoacidosis in the interval between her episodes of alkalosis, suggesting that the latter does not develop simply because such patients are resistant to ketoacidosis.

Ketonuria (ketostix +++) is not always a reliable guide to the degree of ketonaemia.[3] Nevertheless, the presence of ketonuria together with the high blank reading in the serum aspartate aminotransferase analysis[4] and the acetone on the breath all suggest a raised level of plasma ketone bodies in our patients.

These cases underline the importance of a hydrogen ion measurement in the initial investigation of patients thought to be in diabetic ketoacidosis and further indicate the need for caution in the routine use of alkali replacement.

Correspondence should be addressed to CHW.

[1] Bleicher, S, *Diabetes Outlook*, 1967, **2**, 1.
[2] Roggin, G M, *et al, Journal of the American Medical Association*, 1970, **211**, 296.
[3] Watkins, P J, and FitzGerald, M G, *Diabetes*, 1968, **17**, 398.
[4] Chen, J C, Marsters, R, and Wieland, R G, *Diabetes*, 1970, **19**, 730.

General Hospital, Birmingham B4 6NH
K C LIM, MB, senior house officer
C H WALSH, MD, MRCP, senior medical registrar

Delayed hepatitis after treatment with hepatitis B immune serum globulin

The value of hepatitis B immune serum globulin (HBIG) administration after exposure to hepatitis B surface antigen (HBsAg) has been questioned recently.[1 2] The studies of Seeff *et al*[3] and Grady and Lee[4] seemed to show that HBIG affords complete protection for a few months; the late onset of hepatitis observed in some cases was related to an inapparent second exposure—with a normal delay—in a population continuously at risk at a time when passively acquired antibody against HBsAg had fallen below a protective level. Krugman and Giles[5] claimed that they had not observed a late case of hepatitis when HBIG had been administered less than four hours after exposure. We report here two cases that give some additional information.

Case reports

In our usually HBsAg-negative transplantation unit two nurses pricked themselves accidentally in March 1975 with a needle used on an Italian patient who had been reported as HBsAg-positive a few days earlier when he had arrived in Geneva for renal transplantation. Seven hours after exposure both nurses, who were negative for antibodies against HBsAg, received 4 ml of 16% solution of HBIG (Swiss Red Cross; antibody titre by passive haemagglutination 1/4000). They were negative for HBsAg on radioimmunoassay, and they remained at work.

Twenty-five and 30 weeks later they both had clinical episodes of hepatitis with asthenia, jaundice, arthralgias, and high blood levels of aminotransferases. At the same time they became positive for HBsAg. Clinical recovery occurred within a few weeks. Twelve and 20 weeks after the initial clinical symptoms HBsAg became undetectable in the blood of both patients.

Comment

These cases showed that HBIG only delayed and did not prevent the appearance of an overt clinical hepatitis. This confirms and extends the findings of Seeff *et al*[3] and Grady and Lee.[4] As there was no evidence of a second exposure in our HBsAg-negative unit (the Italian patient left three days after the nurses had pricked themselves and the two clinical histories were completely linked) the hypothesis of a second exposure with a normal delay can definitely be ruled out.

The explanation for late onset cases seems to be that the virus is already established at the time of HBIG administration but that the clinical expression of the disease appears only when antibody concentrations fall to a level at which viral antigens can develop. If no late cases occur when HBIG is given four hours after exposure[5] delay in administration of HBIG seems critical; in our two cases HBIG was given seven hours after exposure and clinical hepatitis developed in both.

The clinical evolution of those two cases was the same as in those of Seeff *et al*[3] and Grady and Lee,[4] although the HBIG we used, delivered by the Swiss Red Cross, had a titre of 1/4000 rather than one of 1/500 000, and treatment was not repeated one month later.

Although Seeff *et al*[3] reported that HBIG depresses active antibody production, HBsAg had cleared from the blood of our two patients a few weeks after the clinical episode.

[1] *British Medical Journal*, 1976, **1**, 241.
[2] *Lancet*, 1975, **2**, 1132.
[3] Seeff, L B, *et al*, *Lancet*, 1975, **2**, 939.
[4] Grady, G F, and Lee, V A, *New England Journal of Medicine*, 1975, **293**, 1067.
[5] Krugman, S, and Giles, J P, *New England Journal of Medicine*, 1973, **288**, 755.

Division de Néphrologie, Hôpital Cantonal Universitaire, Geneva, Switzerland

J P WAUTERS, MD, chef de travaux
M LESKI, MD, professeur de néphrologie

Upper gastrointestinal endoscopy with and without sedation: patients' opinions

Patients tolerate endoscopy of the upper alimentary tract well when diazepam is given intravenously and prefer this to morphine.[1] Diazepam is now accepted as the best method of sedation (though the addition of premedication may be beneficial[2]) but it does have disadvantages. Some patients become violent and may damage the instrument; facilities for caring for semiconscious patients are needed; and talking to patients afterwards is impossible because of their amnesia. Moreover, someone has to drive outpatients home. Possible complications are respiratory depression, inhalation of gastric contents,[3] thrombophlebitis,[4] and even pulmonary embolus.[5] Endoscopy elsewhere in Europe and in Japan is usually done without sedation. We report a study on patients' reactions to endoscopy with and without diazepam.

Patients, methods, and results

One hundred patients (group 1) received pharyngeal anaesthesia with lignocaine and intravenous diazepam given slowly until dysarthria was produced. Another 100 (group 2) had pharyngeal anaesthesia only. A further 100 patients (group 3) were selected for endoscopy without sedation if they were likely to tolerate it well, judging from the results of group 2. Those who might tolerate it badly were given intravenous diazepam. All were sent or given a questionnaire after their endoscopy. The statistical difference between the groups was calculated by χ^2 test. The three groups were similar as regards age (average 54·1 years) and sex (60% men).

The ease of examination and patient response to endoscopy are shown in the table. Significantly more patients in group 2 found the examination unpleasant ($P < 0.001$), were worried about a repeat examination ($P < 0.001$), or preferred a barium meal ($P < 0.001$); the examination failed or was unsatisfactory more often ($P < 0.001$). Differences between groups 1 and 3 were not significant. There was no difference between the groups as regards passage of the instrument or the transient after-effects of sore throat and stomach ache, which were found in 45 and 22% respectively.

Ease of examination and patients' responses to examination. Results are numbers of patients

	Group 1	Group 2	Group 3
Passage of instrument:			
Difficult	10	17	3
Failed	0	4	0
Examination:			
Incomplete or hurried	2	13	0
Remember examination:			
Only just	25	5	43
Not at all	53	3	11
Remember pain:			
On insertion of endoscope	2	37	17
On moving endoscope	4	26	10
Unpleasant retching	8	50	25
Found examination unpleasant:			
Mildly	4	32	10
Severely	2	11	4
Worry about repeat examination:			
No	91	50	85
Yes	8	49	14
Refused it	1	1	1
Prefer barium meal	30	62	25
Prefer endoscopy	62	35	61
No preference	7	2	6
No x-ray examination	1	1	8

Endoscopy was poorly tolerated without sedation by women, patients under 40, and those with vomiting or oesophageal reflux; three-quarters of all these patients would be worried by a repeat examination compared with 9%, 50%, and 15% in groups 1, 2, and 3, respectively. The endoscopist, the patient's smoking habits, and diagnosis did not affect tolerance. Heavy drinkers tolerated endoscopy badly regardless of sedation: half the heavy drinkers in each group would be worried by a repeat examination.

Discussion

Endoscopy without sedation is acceptable to many patients. The advantage is saving time (as patients walk in and out), the easy communication, and reduced risk to the instrument—for example, two young men went beserk under diazepam and damaged the instrument; in both endoscopy was performed easily without sedation later. Nevertheless, an unacceptably large number found it unpleasant without sedation.

The best practice was to select patients for endoscopy without sedation (group 3) according to certain criteria; this led to 61% of patients preferring endoscopy to a barium meal. Men, patients over 40, and those without oesophageal reflux or vomiting are suitable. Young women and those who gag when the pharynx is sprayed usually need diazepam. There is no way of foretelling violent reactions to diazepam; if this happens the instrument should be withdrawn rapidly to avoid damage and then endoscopy may be done later without diazepam.

Careful discussion beforehand is in itself a form of premedication. Some in group 2 had, without us realising it, been told that they would be put to sleep; so anxiety was caused by not giving diazepam. Sight of the endoscope creates fear; bandaging the eyes may cause more worry than it alleviates and was abandoned. Now we dim the light in the endoscopy room and try to produce the instrument with the deftness of a conjurer when we examine the conscious patient.

We thank W S Chao for demonstrating that the technique he learnt in Japan could be used successfully in this country, and Dr K Matthews for the statistical analysis.

[1] Ludlam, R, and Bennett, J R, *Lancet*, 1971, **2**, 1397.
[2] Cook, P J, *et al*, *Gut*, 1974, **15**, 842.
[3] Schiller, K F R, Cotton, P B, and Salmon, P R, *Gut*, 1972, **13**, 1027.
[4] Langdon, D E, Harlan, J R, and Bailey, R L, *Journal of the American Medical Association*, 1973, **223**, 184.
[5] Hoare, A M, *Journal of the American Medical Association*, 1974, **230**, 210.

Queen Elizabeth Hospital, Birmingham 15

A M HOARE, MB, MRCP, senior registrar
C F HAWKINS, MD, FRCP, consultant physician