Medical Memoranda

Unexpected Death during Treatment of Uncomplicated Diabetic Ketoacidosis

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Ketotic coma accounts for only 1% of deaths in diabetics (Entmacher and Marks, 1965), but the mortality of diabetic coma remains around 10% (Nabarro, 1965). The majority of those who die in diabetic coma do so of vascular or renal complications, but a small number die of uncomplicated ketosis which fails to respond to routine therapy.

Recently there have been reports of young patients in diabetic ketosis who died after an initial improvement, both clinical and biochemical. FitzGerald *et al.* (1961) reported two cases and Young and Bradley (1967) a further two in which this course of events occurred and in which cerebral oedema was found at necropsy. We report a case in which cerebral oedema developed during diabetic coma and which failed to respond to treatment.

Case Report

A 28-year-old housewife was admitted to hospital as an emergency with a history of vomiting and dyspnoea for 24 hours. Diabetes mellitus had been diagnosed two years previously and she had been controlled with insulin zinc suspension and soluble insulin.

On examination she was conscious but drowsy and dehydrated. Acetone was detectable in the breath and she was overbreathing. There were no other abnormal physical signs and no signs of infection. Her blood pressure was 120/80 and her temperature 96° F. (35.6° C.).

Laboratory data on admission included: blood sugar 490 mg./100 ml., alkali reserve 11 mEq/l., serum sodium 130 mEq/l., serum potassium 6.2 mEq/l., serum chloride 87 mEq/l., and blood urea 75 mg./100 ml. Her plasma gave a strongly positive reaction for ketones and her urine contained 2% glucose and was strongly positive to Acetest tablets.

Treatment was started with intravenous normal saline and sodium bicarbonate. She was given 100 units of soluble insulin intravenously and during the first two hours had 1 litre of saline and 100 mEq of sodium bicarbonate. By this time her blood sugar had fallen to 340 mg./100 ml., her serum sodium had risen to 154 mEq/l., and her serum potassium had fallen to 4.7 mEq/l. Her alkali reserve had not risen. Intravenous saline with a further 30 units of soluble insulin was given and two hours later her blood sugar was 250 mg./100 ml. and her serum potassium 3.9 mEq/l. Her alkali reserve had risen to 13.5 mEq/l. and her serum sodium was 154 mEq/l. Intravenous therapy was then changed to alternating 5% dextrose and normal saline with 1 g. of potassium chloride added to each litre. She received 3 litres of fluid and 120 units of soluble insulin over the next eight hours. Her blood sugar was 270 mg./100 ml., serum sodium 140 mEq/l., serum potassium 40 mEq/l., and alkali reserve 15.5 mEq/l. She had passed 2.2 litres of urine since admission, and this now contained only a trace of ketones.

Her level of consciousness had improved during the first 12 hours and at no time did she become hypotensive. After this she became drowsy and two hours later suddenly lost consciousness. She had a sinus bradycardia of 50/min. and her blood pressure was 90/50. Her breathing was stertorous, and her pupils were widely dilated and did not respond to light. There was no papilloedema, but both plantar responses were extensor. Though her respirations were laboured she was not cyanosed. Her blood sugar at this time was 182 mg./100 ml., serum potassium 3.9 mEq/l., serum sodium 141 mEq/l., and blood urea 38 mg./100 ml.

It was thought that a cerebrovascular accident had occurred, so a lumbar puncture was performed. The C.S.F. was clear under a pressure of 240 mm. Its protein content was 31 mg./100 ml., glucose 241 mg./100 ml., and chloride 675 mg./100 ml.; no cells were present.

She was given intramuscular prednisone and intravenous mannitol in an attempt to reduce cerebral oedema. A diuresis occurred, but her condition deteriorated and she died 27 hours after admission. At no time during her final illness did her temperature rise above 97° F. (36.1° C.).

Necropsy revealed gross and microscopical evidence of cerebral oedema. Extensive cellular degeneration was present throughout the cerebrum and was particularly evident in Ammon's horn. Neuronal damage was also extensive in the pons and cerebellum. The only significant change outside the brain was pulmonary congestion.

Discussion

The four cases described by FitzGerald *et al.* (1961) and by Young and Bradley (1967) were those of patients aged 9 to 15 years who appeared to be making satisfactory progress before they lapsed into coma and died. At the time when their condition deteriorated their blood glucose and electrolyte levels were returning towards normal. Our patient was older, but her illness followed a similar clinical pattern. FitzGerald *et al.* (1961) and Taubin and Matz (1968) described cases in which diabetes insipidus developed after treatment for diabetic coma had produced satisfactory biochemical improvement. At necropsy there was widespread necrosis of the hypothalamus and mid-brain.

A post-mortem study by Dillon *et al.* (1936) of the brains of eight patients who died from diabetic coma uncomplicated by vascular or renal catastrophes showed gross and microscopical changes similar to those seen in cerebral anoxia. The changes were similar in all specimens and included a dilated capillary bed, degeneration of nerve cells, and cerebral oedema. Most of the reports of patients dying with hyperosmolar non-ketotic coma do not include cerebral oedema in the necropsy findings (Davidson, 1964; Di Benedetto *et al.*, 1965; Maccario *et al.*, 1965), though it was present in cases reported by Bergoz and Hausser (1964) and by Larcan *et al.* (1963). Cerebral oedema is well recognized in hypoglycaemic coma (Marks and Rose, 1965).

It seems likely that cerebral anoxia preceded the development of cerebral oedema and neuronal damage in our patient, but the cause of the anoxia remains a matter of conjecture. Metabolic acidosis has been shown to lead to an increased cerebrovascular resistance and decreased cerebral blood flow (Schieve and Wilson, 1953). In addition blood viscosity is increased as a result of the dehydration of diabetic ketoacidosis and concentrated blood is unable to take up oxygen as efficiently as normal blood (Ray *et al.*, 1933). Kety *et al.* (1948) found a 40% reduction in cerebral oxygen uptake in diabetic coma.

Posner and Plum (1967) have shown that the level of consciousness in acidotic patients correlates better with the C.S.F. *p*H than with the blood *p*H. They have also shown that giving bicarbonate to these patients lowers the C.S.F. *p*H probably by reducing pulmonary ventilation. Unfortunately we did not measure the C.S.F. *p*H in our patient, and it is not mentioned in the other reports of patients who died in a similar manner.

The place of potassium deficiency in the production of cerebral oedema (Meyer *et al.*, 1965) in these circumstances remains uncertain. A further possible factor is that there may be a delayed clearance of glucose from the C.S.F. and the brain, thereby creating an osmotic gradient apt to produce cerebral oedema (Fulop, 1967). A similar situation may occur after the rapid correction of azotaemia by haemodialysis (Kennedy *et al.*, 1964). In our patient the C.S.F. glucose was 241 mg./100 ml. at the time the blood glucose was 182 mg./100 ml. The administration of fairly large amounts of normal saline intravenously may also have contributed to the development of

cerebral oedema, but if this is so it is surprising that cerebral oedema occurs so rarely in patients treated for diabetic ketosis with intravenous saline.

Until more is known about the aetiology of this form of sudden death in diabetic ketosis it may be advisable to be cautious in the administration of sodium bicarbonate. Furthermore, it may be advisable to reduce the blood glucose in ketotic patients more slowly than is usually advocated, and this could be achieved by the earlier administration of glucose-containing infusions.

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Infected Retro-umbilical Dermoid Presenting as an Acute Emergency

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Primary sepsis in the region of the umbilicus usually presents with umbilical discharge, and the diagnosis of infection in the abdominal wall is self-evident. The main diagnostic problem is to exclude underlying intra-abdominal disease. The case reported here presented as an abdominal emergency, having been referred as possibly a small-bowel obstruction or atypical appendicitis. A foul-smelling umbilical discharge had been present but was ignored by the patient.

CASE REPORT

A 20-year-old house painter was admitted to hospital on 7 December 1967. He complained of having had intermittent central abdominal pain for the previous 10 days. The pain had become constant in the last four days. There was minimal radiation to the sides, more so the right, but no nausea or vomiting. An oblique right inguinal hernial sac had been excised and a Bassini repair carried out 12 weeks previously.

On examination the abdomen was slightly distended and there was marked rigidity of the right half of the abdomen, especially in the lower quarter. The rigidity of the right rectus muscle was particularly noticeable. The umbilicus appeared normal. Bowel sounds were loud and hyperactive. Rectal examination was negative. The clinical findings suggested a spreading peritonitis possibly from a perforated appendix, except for the hyperperistalsis suggesting a mechanical obstruction. The extensive rigidity of the right half of the abdomen was not in keeping with a simple small-bowel obstruction following repair of the inguinal hernia.

Operation.—A lower right paramedian incision was made. The anterior rectus sheath was incised and the rectus muscle retracted. Just below the umbilicus there was an obvious swelling in the posterior rectus sheath measuring about 2 in. (5 cm.) in diameter. The posterior sheath was incised below the swelling and the peritoneum opened. A loop of small bowel was found adherent to the swelling in the posterior sheath but was easily separated from it. There was minimal dilatation of the small bowel above this level. An incision was made into the swelling and about 15 ml. of creamy pus evacuated. The paramedian incision was extended above the umbilicus and the swelling in the posterior rectus sheath was fully explored. This revealed a definite cyst about 2 cm. in diameter within the posterior sheath. Incision into the cyst produced sebaceous-like material. The cyst was connected by a fibrous band to the umbilicus. The umbilicus and the adjoining cyst were removed en bloc and the rectus sheath was repaired. Postoperative recovery was uneventful.

On further questioning the patient admitted to having had a watery foul-smelling discharge from the umbilicus for a week before operation. He had not mentioned this to his own doctor or on admission to hospital. On examination after operative excision the umbilicus appeared superficially normal. A small piece of keratinous debris was removed from the bottom of the umbilical pit to reveal an underlying red patch from where the discharge had probably come. There was no other excoriation of the skin whatsoever.

COMMENT

Cullen (1916), in his monograph on the umbilicus, reported 23 cases of umbilical sepsis five of which were originally described as dermoid cysts. He believed they were all cases of primary umbilical sepsis. Trimingham and McDonald (1945), however, on discussing congenital abnormalities around the umbilicus, emphasized the importance of retro-umbilical dermoids as the basic cause of umbilical sepsis. Greig and Shucksmith (1950) disagreed and considered the most likely cause to be retention of keratinous debris in the umbilical pit associated with maceration of the epithelial lining of the duct wall of the sweat glands predisposing to infection. The present case undoubtedly fits in with Trimingham and McDonald's theory. Histological examination of the cyst buried in the posterior rectus sheath showed stratified squamous epithelium containing dermal papillae, the appearances being identical with normal skin. Pus was found only within the posterior rectus sheath, and the subumbilical connective tissue showed no naked-eye evidence of acute inflammation. The gross thickening of the posterior rectus sheath deep to the cyst indicated a fairly long-standing process and suggested that the primary source of infection lay deep within the abdominal wall.

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