NEUROLOGICAL MANIFESTATIONS OF DIABETIC KETOSIS

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Severe diabetic ketosis is usually easy to recognize and seldom presents diagnostic difficulties. However, when ketosis is associated with or accompanied by bizarre neurological features, the latter may so dominate the clinical picture that the ketosis may be unrecognized for some time, with grave consequences to the patient. The following cases are reported in view of the unusual presentation of diabetic ketosis and because some of them were not recognized as such on admission or soon after.

Case 1

An African female aged 70 was admitted with the diagnosis of cerebrovascular accident. She gave a history of fits 4 days before admission and was found to be stuporose, with right hemiparesis and right facial palsy. The blood pressure (BP) was 130/100 mm.Hg. Shortly after admission she became restless and had a convulsion. The possibility of a space-occupying lesion producing the fits and hemiparesis was considered. The cerebrospinal fluid (CSF) contained 340 red cells, 6 lymphocytes and 2 polymorphs, per cu.mm., and chlorides (NaCl) 800 mg., proteins 15 mg. and glucose 285 mg. per 100 ml. In view of the high CSF glucose, the blood glucose was estimated and found to be 370 mg. per 100 ml. and the urine to contain sugar and acetone. The serum content as mEq. per l. was Na 126, K 3·9, Cl 121, and CO_2 11·3. Subsequently, the patient developed Kussmaul breathing and was clinically dehydrated, and acetone was smelt in the breath. At that stage there was no doubt about the diagnosis of diabetic ketosis. The response to soluble insulin and intravenous fluids was good; next day the patient was able to walk and residual hemiparesis disappeared within a few days. She was discharged on 60 units of lente insulin daily.

Case 2

An African female aged 50 was admitted as a possible case of postencephalitic parkinsonism with marked left hemiballismus. Movements of the left side of the body began 2 weeks previously. The pulse rate was 132 per minute and BP 150/90. There was rotatory nystagmus, more marked to the right side, with weakness, hypotonia and increased reflexes on the left side. The patient presented a diagnostic problem with features of extrapyramidal and cerebellar involvement. The CSF glucose was 310 mg. per 100 ml. and the blood glucose 530. The serum Na was 126 mEq. per litre and the chlorides 146. The urine contained 4+ sugar and acetone. Treatment with soluble insulin and intravenous fluids produced good results, the hemiballismus and other neurological features disappearing in a day and the hemiparesis over a few weeks. The patient was discharged on 40 units of lente insulin daily.

Case 3

An African male aged 40 years was referred from an outlying hospital with a history of repeated convulsions and twitchings of the left side of the body of one week's duration. Sedation had proved ineffective in controlling the twitchings. He was progressively losing consciousness. As the urine contained sugar and ketone bodies he was given 80 units of insulin over 6 hours. His urine then became sugar- and acetone-free, his level of consciousness improved, and twitchings became much less marked. The CSF contained 70 mg. of protein per 100 ml. and 565 mg. of glucose.

Admitted as a case of fits for investigation, he had a convulsion in the ward involving the left side of the body. His pulse was 100 per minute and BP 85/60. A day after admission he became deeply comatose, developed Kussmaul breathing, and was severely dehydrated. The development of left 3rd-nerve palsy, dilatation of both pupils, which did not react to light, twitchings of the left side of the body, and convulsions, raised the possibility of a subdural haematoma. The blood glucose at that stage was 580 mg. per 100 ml., and the urine contained 4+ sugar and acetone. Despite vigorous therapy with intravenous fluids and soluble insulin (1,170 units in 15 hours, both intravenous and intramuscular), the patient died 5 days after initial presentation at the outlying hospital. Necropsy revealed no cause of death apart from diabetic ketosis.

Case 4

An African female aged 36 was admitted to hospital with gangrene of the right leg and possible diabetes mellitus. The

patient was conscious, but had persistent twitchings of the right side of the body. There was severe dehydration. The blood glucose was 556 mg. per 100 ml., with 4+ sugar and acetone in the urine. The patient was treated with insulin, intravenous fluids, and antibiotics, despite which she became oligaemic and died 2 days after admission. At necropsy, diabetic gangrene, pulmonary oedema and hepatic necrosis were found.

Case 5

An African female aged 31, admitted on numerous occasions, was suffering from porphyria, diabetes mellitus, and bilateral otitis media and mastoiditis. The diabetes was satisfactorily controlled on 40 units of lente insulin daily. Ketosis developed when the middle-ear disease flared up. During the ketotic phase she had fits and twitchings of the left limbs and face. In view of the middle-ear disease and mastoiditis, spread of infection to the meninges and brain was considered, but on 3 different occasions lumbar puncture was completely normal. Moreover, the twitchings and fits disappeared as soon as ketosis was controlled, although the infection was still present. On one occasion the patient was admitted for investigation as a case of left hemiplegia, and on another as epilepsy. At present she is completely free of infection but twitchings sometimes develop when ketosis is present.

Case 6

An African female aged 45 was admitted with the diagnosis of recent cerebral haemorrhage with raised intracranial pressure and coma. The pulse was 120 per minute and BP 150/110. The CSF pressure was 235 mm.H_2O and the fluid contained 28 polymorphs and 6 lymphocytes per cu.mm. and 50 mg. of protein and 172 mg. of glucose per 100 ml. There was 4+ sugar and acetone in the urine. The blood glucose was 265 mg. per 100 ml., and the serum content as mEq. per l. was Na 161, K 4·4, and Cl 88. The patient later volunteered having had a fit before admission. Soluble insulin and intravenous fluids were given with good result. The CSF changes were thought to be the result of epilepsy and no antibiotics were given. She was readmitted later with a history of epilepsy. Acetone and sugar were present in the urine and treatment for diabetes resulted in good response. The CSF on this occasion was normal. On the third admission the patient had a convulsion while on treatment, and the CSF then showed 80 polymorphs and 8 lymphocytes per cu.mm., and protein 73 mg. and glucose 400 mg. per 100 ml. Antibiotics were not withheld this time, because an infective process was not excluded. Treatment for ketosis again produced good result. The patient said that she had fits only during the ketotic phase of diabetes and was symptom-free when the diabetes was well controlled.

Case 7

An African girl aged 13 years was first admitted in 1958 in diabetic ketosis. She responded well to treatment and was discharged on 40 units of lente insulin daily. She was subsequently readmitted on numerous occasions either in diabetic coma or with hypoglycaemia. On her last admission, in 1961, she was comatose but extremely restless, so that intravenous therapy could not be established or secured for any length of time. Restraint by nurses was of no avail. She died on the second day, and at necropsy bronchopneumonia and chronic pancreatitis were found.

DISCUSSION

Laurence[1] found maniacal restlessness and violence in no less than 15 ketotic patients. He also reported a case of diabetic ketosis with deepening unconsciousness during treatment not associated with hypoglycaemia. Gurling[2] reported repeated convulsions in a case of severe diabetic ketosis. The patient, aged 46, had no previous history of fits and there was no organic cause to account for the convulsions. In the present series of cases it is interesting to note that the neurological features disappeared as soon as the ketosis came under control and the fluid and electrolyte imbalance were corrected.

Neurological manifestations may be of vascular origin, the dehydration encouraging thrombosis in the arteries, but the clinical features suggest that this possibility is unlikely. The pathogenesis of coma in diabetic ketosis is not yet fully understood, but prompt and judicious use of insulin and correction of fluid and electrolyte imbalance usually lead to restoration of the conscious state. As insulin alone is unlikely to restore consciousness in diabetic ketosis, and as there may in fact be deepening unconsciousness during treatment associated not with hypoglycaemia but with a reduction in ketonuria and a falling blood sugar,[3] it is tempting to incriminate electrolyte and fluid imbalance[3] as the dominant factor in the pathogenesis of diabetic coma. In support of this theory is the fact that correction of fluid and electrolytes by dialysis without insulin has been shown to restore consciousness in diabetic coma.[4] Moreover, coma may occur in diabetic hyperglycaemia in the absence of ketoacidosis.[5] The coma was thought to be due to dehydration and hyperosmolarity.

It is therefore reasonable to assume that the neurological manifestations may be due to fluid and electrolyte imbalance. All the patients were severely dehydrated though ketosis was not very severe. The gradual onset of neurological manifestations suggested a slowly developing ketosis with gradual but persistent loss of fluids and electrolytes. In ketosis, loss of Na results in a decreased concentration of Na in the extracellular fluids. This produces a suppression of ADH secretion, resulting in increased excretion of water until the concentration of Na is restored. There is thus a sacrifice of volume in the interests of tonicity of body fluids. As the volume deficits assume greater proportions, equivalent losses of water no longer follow and hyponatraemia results. These changes in extracellular fluid produce appropriate changes in the cells. Intracellular overhydration and dehydration may occur. Intracellular overhydration may produce stupor, confusion, coma, and convulsions. Twitching is produced when there is cellular dehydration. As ketosis itself is said to prevent the occurrence of epilepsy, it is unlikely to be the cause of convulsions.

SUMMARY

Seven cases in diabetic ketosis with bizarre neurological manifestations are reported. The importance of recognizing such manifestations as due to diabetic ketosis is emphasized, for prompt treatment produces good results. The pathogenesis of these features is discussed.

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