Hyperosmolar nonketotic diabetic coma

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HYPEROSMOLAR NONKETOTIC diabetic coma is an unusual and uncommon complication of diabetes mellitus. It was first described by Dreschfeld in 1881; he reported two patients whose diabetic coma was not associated with dyspnoea and in whom acetone was not detected in the urine. Between 1915 and 1924, 7 similar cases were reported but with incomplete data (Sheldon and Pyke, 1968).

The condition gained recognition as a distinct clinical entity following the publication of Sament and Schwartz in 1957. Since then Sheldon and Pyke (1968) have collected 53 cases from the literature and reported two cases of their own. As it is a rare complication of diabetes and early recognition is essential for its successful therapy, we report our experience with 2 cases of the syndrome.

CLINICAL RECORD

Case One

P.S.J. a 55-year-old unemployed Southern Indian, presented with drowsiness, slurred speech and weakness of 48 hours' duration. Two weeks before the onset of his illness, he had polyuria and polydipsia.

Physical examination showed that his temperature was 99.8°F and his blood pressure was 130/80. The respiratory and cardiovascular systems were normal. He was drowsy and confused; the tendon reflexes were present and the plantar response was normal. The fundi were normal. At this stage, the diagnosis of a cerebrovascular accident was made.

His diabetic state was not recognised until 32 hours later. At this stage, he was comatose (responding only to noxious stimuli), dehydrated, sweaty and his breathing was stertorous. His temperature was 100°F and his blood pressure was 80/60. The tendon reflexes were sluggish and the plantar response was normal.

Repeated tests of the urine only showed massive glycosuria (brick red with Benedict's test) but no acetonuria (Rothera's test). The blood sugar was 980

mg% and the blood urea was 166 mg%. The serum sodium, chloride and potassium were 145, 108 and 4.5 mEq./L. respectively. The calculated effectively plasma osmolality* was 334 mOsm./L. (normal: 285 to 295 mOsm./L.) His alkaline reserve was 51 vol.% (normal: 50-70 vol.%).

Patient died 14 hours after his hyperglycaemic hyperosmolar nonketotic diabetic coma was recognised. During this period, he was given soluble insulin 300 units intravenously and 525 units subcutaneously; the blood sugar remained high (610 to 1000 mg%). He also received intravenous infusion of 1880 ml. of hypotonic (half normal) saline, 540 ml. of normal saline and 540 ml. of Darrow's solution; his calculated plasma osmolality remained elevated (328 to 344 mOsm./L). Terminally, he became acidotic (alkaline reserve 38 vol%; arterial blood pH 7.120) and was given 370 ml. of 8.4% sodium bicarbonate intravenously. Antibiotics and vasopressors were administered. His coma and hypotension deteriorated and he perished. A postmortem examination was not done.

Case Two

L.C.M., a 50-year-old fruit seller, presented with fever, anorexia and weight loss of two weeks' duration. He had no symptoms of diabetes before the onset of his illness.

Physical examination showed that his height was 63 inches and his weight was 122 lbs. He was moribund and was in shock (blood pressure 70/0 mm. of Hg.) He was dehydrated and was areflexic.

Investigations showed presence of sugar in the urine (red with Benedict's test) but no acetone (Rothera's test) on repeated examinations. The blood sugar was 960 mg.% and the blood urea was 127 mg.%. The alkali reserve was 49 vol%. The serum sodium, chloride and potassium were 159, 118 and 3.0 mEq./L. respectively. The calculated plasma osmolality was 361 mOsm./L.

After being given 258 units of soluble insulin intravenously and subcutaneously during a 24-hour period, his blood sugar fell to 228 mg%. He also received 12 pints of hypotonic (half-normal) saline and 1 pint of Darrow's solution intravenously during this period; as a result of which, his plasma osmolality fell to 305 mOsm./L. He received antibiotics cover with pencillin and streptomycin injections. For his hypertension, noradrenaline infusion was administered.

After 24 hours of infusion therapy, his hyperglycaemia, hyperosmolarity and dehydration were corrected but his coma and hypotension persisted. Over the next 3 days, he was maintained on intravenous infusion of noradrenaline, aramine, hydrocortisone and soluble insulin (average 72 units per day by subcutaneous injections). On the fifth day, his general condition improved and mentally he was more alert. His blood pressure returned to normal. Intravenous fluid therapy was discontinued and oral feeding started. He continued to receive subcutaneous injections of soluble insulin. On the 13th day, his soluble insulin was replaced by 48 units of lente insulin daily. On 48 units of lente insulin, his 2-hour post-prandial blood sugar was 161 mg%. He was discharged on the 15th day.

His diabetes was well controlled on 48 units of lente insulin daily. An oral glucose tolerance test (50 grams of glucose load) was performed 3 months later: the fasting, ½ hour, 1 hour, 1½ hours and 2 hours blood sugar were 324, 380, 448, 474, 445 mg%. respectively. He continued to receive daily injection of 48 units of lente insulin. He has been followed up for 5 months and has remained well.

DISCUSSION

The syndrome of hyperosmolar nonketotic diabetic coma consists of (1) absence of ketosis; (2) extreme hyperglycaemia; (3) extreme dehydration; and (4) depression of sensorium (Johnson et al., 1969).

The absence of ketoacidosis indicates that endogenous insulin exists, though relatively small in amount for the level of blood glucose. Thus in patient No. 2 reported by Johnson et al. (1969) the plasma immunoreactive insulin level was 29 μU./ml. at a blood sugar level of 720 mg%. and in Case 2 described by Sheldon and Pyke (1968) the insulin was 40 uU./ml. (blood sugar was 2500 mg%).

This syndrome occurs mainly in the adult onset diabetics in whom endogenous insulin is present. The ages of our two patients are 55 and 50 years; the mean age of the 55 cases collected by Sheldon and Pyke (1968) was 62 years and the age range was 10 to 84 years. A striking exception regarding age of onset was reported by Enrlich and Bain (1967) who described the condition in a 1½-year-old child. The paradox of this syndrome is that once they recover from the coma, they are easily controlled with diet alone though some may require insulin as is seen in our second patient. Absence of ketosis in the hyperosmolar syndrome allows for a degree of protraction of the illness not seen in diabetics with ketoacidosis.

* Plasma Osmolality (mOsm./L.) = 2 x Serum Na (mEq./L.) + $\frac{\text{Blood Glucose in mg\%}}{18}$

This protraction accounts for the more profound osmotic diuresis and dehydration (Johnson et al., 1969).

Hyperglycaemia is extreme in hyperosomolar nonketotic diabetic coma due to a slow, prolonged and progressive deterioration of islet cell function but with persistence of sufficient insulin production to prevent ketosis and to allow time for the syndrome to develop (Johnson et al. 1969). The initial blood sugar in our two patients were 980 and 960 mg%; in the 55 cases collected by Sheldon and Pyke (1968) the mean initial blood sugar was 1120 mg% and the range was 360 to 2760 mg%.

The extreme dehydration and hyperglycaemia account for the hyperosmolarity of the plasma. The calculated plasma osmolarity in our patients were 344 and 361 mOsm./L.; in the series of Sheldon and Pyke (1968), the mean was 371 mOsm./L. and the range was 295 to 462 mOsm./L.

Central nervous system manifestations are seen in most cases; these include coma and fits. Coma was present in our patients. Johnson et al (1969) believe that the degree and duration of hyperosmolarity are important factors in the causation of coma.

Both our patients were not known diabetics before the onset of their illnesses; this is a common feature in hyperosmolar nonketotic diabetic coma.

The mortality of the condition is about 50% (Schwartz and Apfelbaum, 1965 – 1966); one of our two patients perished.

Hyperosmolar nonketotic diabetic coma has been reported as a complication of haemodialysis (Potter, 1966), acute pancreatitis (Halmos, 1966), extensive body burns (Sevitt, 1955), steroid and immunosuppressive therapy (Spenney, Eure and Kreisberg, 1969) and Dilantin (diphenylhydantoin) administration (Goldberg and Sanbar, 1969).

The therapy of hypersomolar nonketotic state of the diabetic embodies the following principles (Johnson et al., 1969):

(1) Early recognition and prompt treatment;
(2) frequent and adequate amount of soluble insulin;
(3) rapid infusion of hypotonic saline solutions initially, followed later by 5% dextrose, and
(4) potassium supplement.

SUMMARY

The syndrome of hyperosmolar nonketotic state in the diabetic consists of

(1) depression of sensorium,
(2) absence of ketosis,
(3) extreme hyperglycaemia, and
(4) profound dehydration.

Two cases of the syndrome in a 55-year-old Indian and a 50-year-old Chinese are described. Both are not known diabetics before the onset of their illnesses. The disease was fatal in one.

The principles of therapy are described.

ACKNOWLEDGEMENTS

We are grateful to Dato Professor G.A. Ransome, C.B.E., P.J.G., D.M.J.K., M.D., M.R.C.S., F.R.C.P., A.M. for permission and encouragement to report the cases.

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