The patient was kept warm in bed and the rash gradually faded during the course of a week. The discoloration lightened through red and brown, and on discharge from hospital only slight residual staining remained. There was no evidence of a falling haemoglobin, and after discharge she suffered no further symptoms. The cold agglutinins, however, were still present after a month. When reviewed three months later the haemoglobin was normal and cold agglutinins were absent.

Comment

Skin eruptions occur in about 5% of patients with infectious mononucleosis and these have been reviewed (McCarthy and Hoagland, 1964). A reticular discoloration of this kind seems not to have been previously reported. It is likely that this rash was related, firstly, to the cold agglutinins present, producing an area of particular stasis on exposure to the cold night, and, secondly to a bleeding tendency which caused the rash to become haemorrhagic.

Although red cell autoantibodies acting in the cold are the rule in infectious mononucleosis they do not normally give rise to symptoms. Capra *et al.*, (1969) found an indirect acting IgG anti-i antibody in 90% of patients with this disorder, and an IgM anti-i cold agglutinin may be present in between 7% (Jenkins *et al.*, 1965) and 26% (Worlledge and Dacie, 1969) depending on the criteria used. These antibodies being directed mainly against fetal rather than adult red cells rarely cause a haemolytic anaemia. Anti-I, which is directed against adult rather than fetal red cells, does occur in infectious mononucleosis occasionally, and Worlledge and Dacie (1969) referred to 12 such cases with haemolytic anaemia reported in the literature. The present patient undoubtedly had a high titre anti-I, but there was no evidence of haemolytic anaemia.

Mild thrombocytopenia is a fairly common manifestation of infectious mononucleosis. Carter (1965) found counts of less than 100,000/mm^3 in 8 out of 57 patients. Haemorrhagic complications are very rare. The cause of the thrombocytopenia is not clear but is likely to be abnormal consumption.

Abnormalities of coagulation are very rare. The prolonged activated partial thromboplastin time was not further investigated, but there are at least three possible causes for it.

It might have been caused by liver damage, as in the case described by Schumacher and Barcay (1962). This is unlikely since this patient's liver damage was very minor, and factor VII levels, which are usually the most sensitive to liver damage, were, on the evidence of the prothrombin time, unaffected.

Intravascular coagulation might account for a fall in platelets and of clotting factors of the intrinsic system while leaving the extrinsic system unaltered. There are two cases in the literature in which this may have occurred. Wintrobe (1967) referred to a patient with afibrinogenaemia, and Dodsworth and Burns (1971) reported on a patient with hypofibrinogenaemia and thrombocytopenia who responded to treatment with heparin. In neither case was an increased level of fibrin degradation products reported. I cannot exclude this as a cause, but the typical red cell changes were not seen on the blood film.

In infectious mononucleosis a wide array of irregular autoantibodies appear, and it is possible to conceive of antibodies to clotting factors causing a prolonged partial thromboplastin time. I cannot exclude this, but no such case has been previously reported.

I am grateful to Dr. I. S. Bailey for permission to report the case of a patient under his care, and to the Long Ashton Agricultural Research Station for meteorological information.

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Severe Hyponatraemia in Hyperlipaemic Diabetic Ketosis

J. A. BELL, P. J. HILTON, G. WALKER

British Medical Journal, 1972, **4**, 709–710

The occurrence of spuriously low measured plasma electrolyte values in the presence of hyperlipaemia has been recognized for some time (Albrink *et al.*, 1955). This is due to displacement of the plasma water by lipid so that the water content of a given volume of plasma is depressed below its normal value of 94·5%. By conventional flame photometry techniques the electrolyte content of a measured volume of plasma is determined irrespective of its water content. Therefore in the presence of high concentrations of a displacing substance there will be important and variable discrepancies between the measurements obtained and the true concentrations of electrolytes in the aqueous phase, which is what determines their biological effects. Measurement of osmolality by depression of freezing point is not influenced by the presence of displacing substances and reflects the concentration of solutes in the plasma water. It is recognized that uncontrolled diabetes, especially when of gradual onset, may be accompanied by severe hypertriglyceridaemia (Bagdade *et al.*, 1967). We report here an extreme example of such a case with consequent complications in the management of fluid and electrolyte balance.

St. Thomas's Hospital, London S.E.1
J. A. BELL, M.R.C.P., Registrar, Intensive Therapy Unit
P. J. HILTON, M.R.C.P., Senior Medical Registrar
G. WALKER, M.R.C.P., M.R.C.PATH., Senior Lecturer, Department of Chemical Pathology

Case Report

In 1969 the patient, a 35-year-old married housewife, presented with tiredness and urinary frequency. She was found to have a urinary infection and glycosuria, with a typical diabetic glucose tolerance curve. At that time she weighed 80 kg and she was started on a 130-g carbohydrate diet; however, she failed to attend for follow-up.

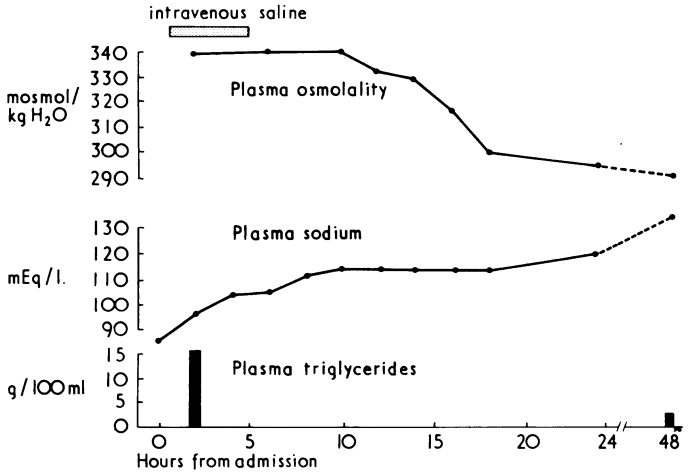
In 1971 she was admitted to hospital with a three-day history of malaise and an eight-hour history of vomiting, confusion, and breathlessness. She was stuporose and clinically dehydrated. The heart rate was 140/min with sinus rhythm, the blood pressure 140/100 mm Hg, and the extremities cold, with vasoconstriction. The respiratory system was normal apart from a respiratory rate of 40/min. The abdomen was generally tender and the liver edge was palpable. There were no localizing neurological signs, but her optic fundi showed intense lipaemia retinalis. There were no eruptive xanthomata.

Laboratory investigations on admission gave the following results: blood glucose 600 mg/100 ml; plasma sodium 86 mEq/l., potassium 2·2 mEq/l., bicarbonate 5 mEq/l., urea 40 mg/100 ml,

calcium 8·1 mg/100 ml, phosphate 1·0 mg/100 ml, creatinine 1·3 mg/100 ml, triglycerides 16,000 mg/100 ml (normal 60-160 mg/100 ml), cholesterol 1,200 mg/100 ml, acetone 4·7 mmol/l. (normal <0·5 mmol/l.); serum aspartate aminotransferase 130 IU/l. (normal 25-65 IUI/l.); blood lactate 2·2 mmol/l. (normal 1-1·8 mmol/l.); W.B.C. 20,600/mm^3, platelet count normal; PaO_2 102 mm Hg, $PaCO_2$ 16 mm Hg, blood pH 7·33. A haemoglobin estimation could not be performed because of the hyperlipaemia. Chest radiograph and electrocardiogram were both normal and microscopical examination of the urine showed scanty cellular casts. Two hours after admission plasma osmolality was 340 mosmol/kg H_2O (normal 285-295 mosmol/kg H_2O). At the same time evaporation to dryness of a known weight of plasma gave a value for plasma water of 71% by weight (normal 94·5%).

The patient was treated with intravenous fluids, potassium supplements, and repeated intravenous and intramuscular injections of insulin. In the first 24 hours a total of 16·5 l. of fluids was infused, of which 7·5 l. was normal saline, 6·0 l. was 5·0% dextrose, and 3·0 l. was 2·5% dextrose. A total of 450 mEq of potassium chloride was infused in the first 24 hours and the urine output was 6·0 l. Osmolality of a random specimen of urine after 20 hours was 355 mosmol/kg H_2O.

Although serial estimations of plasma triglycerides were not made in the acute phase, it would appear that as the triglyceride level fell so the values for plasma sodium and osmolality tended to return to normal. At a time (two hours after admission) when the



Changes in plasma osmolality, measured plasma sodium, and plasma triglycerides.

plasma osmolality was 340 mosmol/kg H_2O the plasma sodium was only 96 mEq/l.; 13 hours later the plasma osmolality had fallen to 316 mosmol/kg H_2O, while the plasma sodium had risen to 114 mEq/l.

The patient recovered quickly from this acute ketotic episode. Within 24 hours she was fully conscious and the peripheral circulation appeared normal. The blood glucose had fallen to 350 mg/100 ml and the plasma acetone to less than 0·1 mmol/l., while the plasma bicarbonate had risen to 18 mEq/l. One day later the plasma triglycerides had fallen to 3,500 mg/100 ml. Details of the saline infusion and changes in the plasma sodium, osmolality, and triglycerides over the first two days are shown in the chart.

The patient's diabetes was controlled subsequently with biphasic insulin (Rapitard) twice daily, and at her most recent outpatient attendance, three months after the acute episode, she remained well.

Comment

The patient is of interest from several viewpoints. She was severely acidotic, with a base deficit of 16 mEq bicarbonate/l., and moderately ketonaemic, with a plasma acetone level of 4·7 mmol/l. It has previously been reported that severe hyperlipaemia with hyperglycaemia is infrequently accompanied by ketoacidosis (Bagdade *et al.*, 1967). It is suggested that there is usually sufficient circulating insulin to inhibit uncontrolled lipolysis, thus preventing ketoacidosis.

The initial rise in plasma sodium in our patient occurred concurrently with the period of saline infusion. At an early stage calculations based on the plasma water content indicated that the patient was in danger of becoming hypernatraemic. When the measured plasma sodium was 96 mEq/l. and the plasma water 71% calculation gave a value for sodium of 136 mEq/l. plasma water. The saline infusion was therefore discontinued when the measured plasma sodium had reached 104 mEq/l. After the saline infusion was stopped and dextrose infusion substituted, the plasma sodium continued to rise and the plasma osmolality fell. Over 22 hours the plasma osmolality fell from 340 mosmol/kg H_2O to 300 mosmol/kg H_2O, while during the same period the blood glucose had fallen only from 400 mg/100 ml to 350 mg/100 ml. Thus the fall in osmolality cannot be explained in terms of a falling blood glucose level.

The repeated estimation of plasma water content is time-consuming, and our experience with this patient indicates the value of plasma osmolality in assessing acute electrolyte disturbances in the presence of severe hyperlipaemia.

We are grateful to Dr. N. F. Jones for permission to report this case.

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