SHORT COMMUNICATIONS

Fibrinolysis and Peritoneal Dialysis in the Treatment of Diabetic Coma, Complicated by Severe Shock. A Case Report

H. NOBIS, M. FISCHER, F.S. FUCHS, and W. KÖRP

III. Medizinische Abteilung für Stoffwechselerkrankungen, Urologische Abteilung und Zentrallaboratorium des Krankenhauses der Stadt Wien — Lainz, Vienna — Austria

Received: November 2, 1971, accepted: December 6, 1971

Summary. The case of a 19 year old patient with gestational diabetes is reported who has developed diabetes 5 months after delivery in severe insulin resistant keto-acidosis complicated by persistent shock. Since routine coma- and heparin therapy failed, fibrinolysis was applied and peritoneal dialysis was performed because of

renal failure. Therapy resulted in a complete recovery of the patient.

Key words: Juvenile diabetes, ovulation inhibitor, ketoacidotic coma, insulin resistance, shock, blood coagulation, fibrinolysis, acute renal failure, peritoneal dialysis.

Introduction

Advances in the pathology of microcirculation [8, 11] have led to a remarkable improvement in the therapy of severe shock. The importance of a heparin prophylaxis and of fibrinolysis in the treatment of persistent shock complicating diabetic coma has already been stressed by Lasch *et al.* [9] and by Siebenmann and Reutter [19]. To our knowledge both heparin prophylaxis and fibrinolysis have not yet become part of the usual standard therapy [14] of diabetic keto-acidosis. In this paper successful treatment of persistent shock in severe keto-acidosis in a juvenile diabetic by fibrinolysis and peritoneal dialysis will be reported.

Case Report

The 19-year-old female had suffered from anorexia nervosa during puberty, otherwise she had been in good health until 1969 when she became pregnant. During the latter part of pregnancy a glucose tolerance test revealed a slight disturbance of carbohydrate metabolism and she was treated with a diet restricted in carbohydrates. In May 1970 she was delivered of a baby of normal weight at term. In August 1970 treatment with an ovulation inhibitor (oestrogen-gestagen-combination) was started. In October 1970 acute polydipsia, polyuria and marked weight loss occurred. Because of striking loss of appetite and with respect to the previous history of anorexia the tentative diagnosis of anorexia nervosa was made and the patient was admitted to a Psychiatric Clinic. There neuroleptic drug (chlor-prothixene) treatment was initiated. Since the condition of the patient worsened in the following hours and the patient became unconscious, emergency laboratory tests were performed which revealed

positive urine sugar and blood sugar values above 1000 mg/100 ml.

On admission to the metabolic ward of our department the blood sugar amounted to 1400 mg/100 ml, and ketone bodies in serum were strongly positive. The patient showed Kussmaul's respiration. She was in severe shock, anuric and exhibited multiple cutaneous necroses. After initiation of the standard coma therapy (Fig. 1) with insulin (the patient required more than 5500 units in the first 24 h) fluid and electrolytes, blood glucose dropped to about 300 mg/100 ml. The patient became conscious only for a very short time. Since coagulation analysis indicated a consumption coagulopathy due to disseminated intravascular coagulation-syndrome, heparin therapy was started. As shock persisted in spite of continuous heparin therapy, fibrinolysis was initiated with streptokinase. The latter treatment resulted in a marked improvement of the peripheral circulation and an increase of blood pressure within hours. For the first time since admission the patient became fully responsive.

Although the general condition of the patient improved under heparin and fibrinolytic therapy, anuria persisted. Since mannose and furosemide, the latter given in the dose of 2×800 mg per day, showed no effect on diuresis, peritoneal dialysis was started four days after the onset of anuria. At this time blood urea nitrogen increased to 190 mg/100 ml, creatinine up to 7.9 mg/100 ml and uric acid to 18.3 mg/100 ml. Seventy-six hours after initiation of peritoneal dialysis, (performed by a repeated puncture technique, with standardized solutions) urine production started and in the following weeks renal function returned to normal. The patient was dismissed 11 weeks after initiation of therapy. Follow-up studies including

excretory urogram and isotope nephrogram (isotope hippuran clearance) did not show any impairment of renal function.

Discussion

The treatment of severe keto-acidosis in diabetes mellitus with insulin, fluid- and electrolyte replacement [6, 14, 18] has become a standard therapy in the last decade. Failure of this therapy has been related to irreparable shock due to prolonged diabetic coma. Cases of non-acidotic hyperosmolar coma have been reported recently by Halmos *et al.* [7], Scharf *et al.*

coagulation syndrome. Since heparin therapy did not seem to have a favourable effect we decided to start a fibrinolytic therapy. To our knowledge, the case of Lasch *et al.* [9] and ours were the only ones in which fibrinolysis has been performed over a prolonged period. It is remarkable that fibrinolysis did not show an effect on renal function in our patient. While the symptoms of shock and of disturbances of peripheral microcirculation disappeared, anuria persisted. Thus it is most probable that both haemodynamic factors as well as changes in blood coagulation seemed to be responsible for the development of renal failure in our patient.

Fig. 1. Course of insulin-, heparin-(1000 u/h and 100 u/h/resp.) and fibrinolytic (streptokinase 100 000 u/h) therapy. Peritoneal dialysis was started on 4th day of anuria (See text)

[17] and Whelton *et al.* [21] in which thrombosis of the abdominal mesenteric vessels and/or pulmonary embolism occurred, leading to eventual death.

While in the aforementioned cases thrombosis occurred primarily in the abdominal vessels and in the vessels of the lower extremities, in the case of Siebenmann and Reutter [19] the patient died in renal failure after severe keto-acidosis; disseminated intravascular clotting and severe glomerular thrombosis was revealed by autopsy. The latter case is reminiscent of a diabetic patient mentioned by Lasch *et al.* [9], that had been treated with fibrinolysis in the course of a severe shock due to diabetic coma.

Our laboratory findings indicated a consumption coagulopathy due to the disseminated intravascular

Since the etiology and the pathogenesis of the disseminated intravascular coagulation syndrome in diabetic keto-acidotic coma have not yet been settled, further investigations should clarify to what extent this is related to shock and peripheral circulatory break-down [10, 13] or other factors like keto-acidosis [2, 12], hyperviscosity due to dehydration and hyperosmolarity [16, 20] or an increased platelet adhesiveness [1]. In our case the administration of neuroleptic drug therapy could have been an additional factor for the development of the severe shock.

Another striking feature in our case has been the development of pseudo-resistance to insulin treatment [15] which could be observed during the first 24 h after initiation of coma treatment. Since neutralizing insulin

antibodies (IgG insulin antibodies determined according to the method of Christiansen [4]) could not be detected and since hypopotassemia and ovulation inhibitor therapy seemed to be of minor importance, it can be assumed that the extraordinary high insulin requirement in this patient might be related to humoral insulin antagonists, previously described by Field and Stetten [5].

Although the etiology and pathogenesis of keto-acidosis and shock in our patient are still open to discussion, this case clearly illustrates that intensive treatment of prolonged shock may lead to complete recovery in diabetic keto-acidosis. We therefore would like to stress that in the treatment of severe shock, complicating diabetic acidosis, fibrinolytic therapy is indicated when heparin therapy alone seems to fail. In cases of prolonged shock the performance of a peritoneal dialysis and/or hemodialysis, as recommended by Chazan *et al.* [3] seems to be indicated.

References

1. Bielawiec, M., Mysliwiec, M., Perzanowski, A.: Platelet adhesiveness in diabetics. *Pol. med. J.* **9**, 1071—1075 (1970).
2. Broersma, R.J., Bullemer, G.D., Mammen, E.F.: Acidosis induced disseminated intravascular microthrombosis and its dissolution by streptokinase. *Thrombos. Diathes. Haemorrh.* **24**, 55—67 (1970).
3. Chazan, B.I., Rees, S.B., Balodimos, M.C.: Dialysis in diabetics. *J. Amer. med. Ass.* **209**, 2026—2030 (1969).
4. Christiansen, Aa.H.: A new method for insulin-binding immunoglobulins in insulin-treated diabetic patients. *Horm. metab. Res.* **2**, 187—188 (1970).
5. Field, J.B., Stetten, D.: Studies on humoral insulin antagonists in diabetic acidosis. *Diabetes* **5**, 391—396 (1956).
6. Froesch, E.R., Rossier, P.H.: Das Coma diabeticum. *Internist* **6**, 400—406 (1965).
7. Halmos, B.P., Nelson, K.J., Lowry, C.R.: Hyperosmolar nonketoacidotic coma in diabetes. *Lancet* **1966 I**, 675—679.
8. Hardaway, R.M.: Shock and disseminated intravascular coagulation. *Thrombos. Diathes. Haemorrh. Suppl.* **20**, 121—146. Stuttgart-New York: Schattauer 1966.
9. Lasch, H.G., Mechelke, K., Nusser, E., Sessner, H.H.: Fibrinolysetherapie im Schock. Experimentelle und klinische Ergebnisse. *Thrombos. Diathes. Haemorrh. Suppl.* **7**, 237—242. Stuttgart-New York: Schattauer 1963.
10. — Huth, K., Heene, D.L., Müller-Berghaus, G., Hörder, M.H., Janzarik, H., Mittermayer, L., Sandritter, W.: Die Klinik der Verbrauchskoagulopathie. *Deutsch. med. Wschr.* **96**, 715—727 (1971).
11. — Riecker, G.: Intensivtherapie beim Schock. *Internist* **10**, 234—239 (1969).
12. Mammen, E.F., Broersma, R.J., Bullemer, G.D.: Blood coagulation parameters in shock and acidosis. *Microcirculation, Hemostasis and Shock*, p. 91—100. Stuttgart-New York: F.K. Schattauer Verlag 1970.
13. McKay, D.G.: Blood coagulation and the generalized Schwartzmann reaction. *Thrombos. Diathes. Haemorrh. Suppl.* **20**, 107—119. Stuttgart-New York: Schattauer 1966.
14. Mehnert, H.: Empfehlungen zur Diagnose und Behandlung des Coma diabeticum. Zusammengefasst nach Referaten und Diskussionsbemerkungen anlässlich eines Round-Table Gespräches am 27. 11. 1970 in München. *Deutsch. med. Wschr.* **96**, 761—763 (1971).
15. Menzel, R., Jutzi, E.: Zum Blutzuckerverhalten bei Rekompensation des Coma diabeticum. *Dtsch. Gesundh.-Wes.* **25**, 727—732 (1970).
16. Riecker, G.: The influence of metabolic factors on microcirculation. *Microcirculation, Hemostasis and Shock*, p. 7—14. Stuttgart-New York: F.K. Schattauer Verlag 1970.
17. Scharf, Y., Nahir, M., Tatarsky, I., Ben Arie, J., Ibaruch, G., Edelman, S.: Fatal venous thrombosis in hyperosmolaric coma. *Diabetes* **20**, 308—309 (1971).
18. Schwab, M.: Coma diabeticum — Pathophysiologie und Therapie. *Internist* **10**, 405—411 (1969).
19. Siebenmann, R., Reutter, F.: Disseminierte intravasale Gerinnung mit Anurie bei Coma diabeticum. *Schweiz. med. Wschr.* **100**, 69—72 (1970).
20. Skovborg, F., Nielsen, Aa.V.: Alteration in blood and plasma viscosities in ketotic diabetics. *Ugeskr. Laeg.* **131**, 1125—1128 (1969).
21. Whelton, M.J., Walde, D., Havard, C.W.H.: Hyperosmolar non-ketotic diabetic coma: with particular reference to vascular complications. *Brit. Med. J.* **1971 I** 85—86.

Dr. W. Korp
III. Medizinische Abteilung für
Stoffwechselerkrankungen
Krankenhaus der Stadt Wien-Lainz
A-1130 Wien/Österreich
Wokersbergenstraße 1