SHORT REPORTS

Prostacyclin deficiency in haemolytic-uraemic syndrome

The haemolytic-uraemic syndrome is characterised by microangiopathic haemolytic anaemia, renal failure, and platelet consumption. Prostacyclin (PGI_2) deficiency may be the primary defect in haemolytic uraemic syndrome and the related condition, thrombotic thrombocytopenic purpura.[1] We report a patient with postpartum haemolytic uraemic syndrome in whom we found evidence of PGI_2 deficiency and who may have responded to intravenous infusion of PGI_2.

Case history

A 31-year-old primigravida with preceding mild hypertension developed severe hypertension (180/120 mm Hg) at 23 weeks' gestation. At this stage creatinine clearance was 140 ml/min. Treatment with increasing doses of methyldopa and other hypotensives failed to control the hypertension and at 31 weeks caesarean section was performed. Four days postpartum her blood pressure remained raised despite large doses of methyldopa and labetalol. Her plasma creatinine concentration was 377 μmol/l (4·26 mg/100 ml), haemoglobin 8·2 g/dl, white blood cell count (WBC) 12 800, and platelet count 45 000. The blood film showed fragmented red cells. The coagulation screen showed a thrombin time of 35 s (normal < 20 s), prothrombin time 11 s (14 s), partial thromboplastin time 27 s (< 36 s), fibrinogen 4·44 g/l (2·00-4·50), and fibrin degradation products 16 μg/ml (<8 μg/ml). The results of a Coombs test and blood cultures were negative and no autoantibodies were found. A high-dose infusion urogram showed symmetrically enlarged, non-obstructed kidneys.

Three units of whole blood and two units of fresh frozen plasma were infused. Her plasma creatinine concentration continued to rise, however, and the platelet count remained below 60 000 with continued evidence of disseminated intravascular coagulation. The plasma concentration of 6-oxo-$PGF_1\alpha$, the chemical hydrolysis product of PGI_2, was 64 pg/ml (normal values in our laboratory using gas chromatography-mass spectrometry[2] were 122±22 pg/ml in 18 normal women, 245±133 pg/ml in 9 women in late pregnancy, and 205±108 pg/ml in 6 women in the early puerperium). Intravenous infusion of synthetic PGI_2 at 6 ng/kg/min produced the characteristic facial flush.[3] The infusion was continued over the next five days. During this time the PGI_2 infusion had a profound hypotensive effect. The patient's blood pressure before infusion rose to 240/130 mm Hg despite methyldopa and labetalol. Over the next three days it was controlled at about 110/70 mm Hg on PGI_2 infusion alone without other therapy. During the PGI_2 infusion her plasma 6-oxo-$PGF_1\alpha$ concentration rose to 1060 pg/ml. On the third day of the PGI_2 infusion her platelet count rose to normal (figure) and the coagulation tests returned to normal. On the fourth day of infusion (ninth day postpartum) she became oliguric, her plasma creatinine concentration had risen to 730 μmol/l (9·25 mg/100 ml), and she developed increasing peripheral and pulmonary oedema. There was no response to intravenous frusemide and peritoneal dialysis was undertaken for 72 hours. During this time she was anuric but thereafter renal function gradually improved and she rapidly recovered.

Eleven weeks after delivery she was in excellent health, although still receiving a combination of methyldopa, propranolol, and frusemide to control her blood pressure. Her haemoglobin was 11·6 g, WBC 5600, platelet count 265×10^9/l (265 000/mm³), plasma creatinine concentration 128 μmol l, and creatinine clearance 48 ml/min.

Comment

The low plasma 6-oxo-$PGF_1\alpha$ concentration in our patient supports the hypothesis that PGI_2 deficiency may be pathogenetic of the haemolytic uraemic syndrome.[1] The prognosis of the syndrome in adults is poor and there is a high risk of irreversible renal failure,[4] although recovery is sometimes spontaneous. In addition to PGI_2 infusion our patient received aspirin and fresh frozen plasma. Antiplatelet drugs are of uncertain value, whereas remission may follow plasma exchange[1] and in thrombotic thrombocytopenic purpura may follow infusion of plasma alone.[5] Our patient's recovery cannot be attributed to one particular treatment, but prolonged PGI_2 infusion, either by controlling hypertension, reversing platelet consumption, or restoring an important deficiency, may have contributed to it. This form of treatment warrants further study in conditions associated with platelet consumption, especially when prostacyclin is deficient. The sensitivity of the blood pressure to PGI_2 infusion was of particular interest.

We thank our colleagues who helped in the management of this patient. Prostacyclin was supplied by Dr J O'Grady of the Wellcome Foundation Ltd.

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(*Accepted 18 April 1980*)

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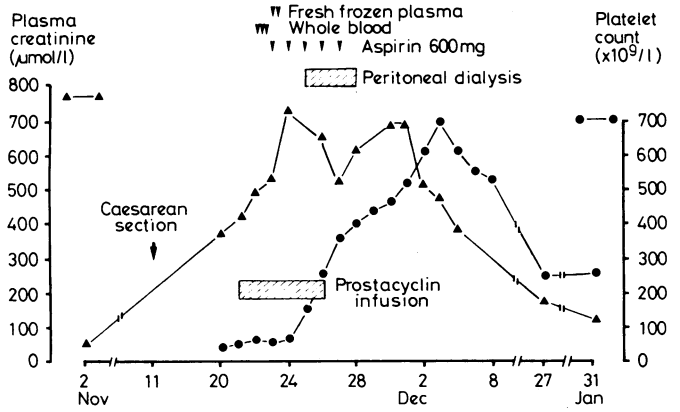


Clinical course of patient with prostacyclin deficiency and haemolytic-uraemic syndrome. Abscissa is date, 1979-80, ordinates plasma creatinine concentration and platelet count.

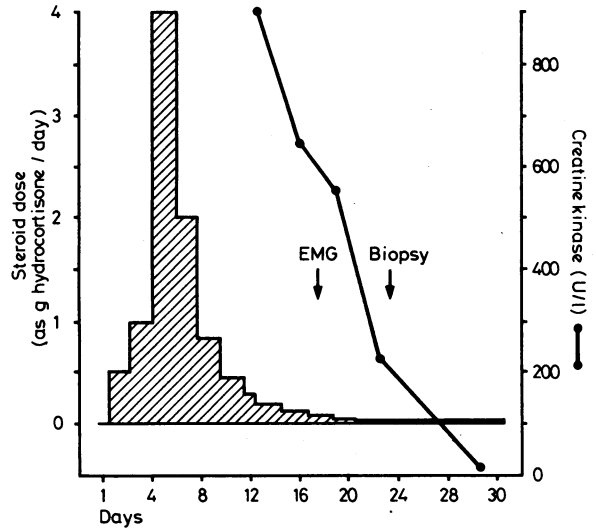
Acute hydrocortisone myopathy

Potent synthetic corticosteroids can cause a myopathy that is usually insidious in onset and proximally distributed. We describe a patient who developed an acute generalised myopathy after receiving high doses of hydrocortisone for status asthmaticus. This is the second such case to be reported, and the clinical picture differs strikingly from the myopathy caused by other steroids.

Case report

A 37-year-old housewife was admitted to hospital with a four-day history of increasing breathlessness after an upper respiratory tract infection. She had been asthmatic since childhood but had been satisfactorily maintained on inhaled sympathomimetics and occasional short courses of prednisolone by mouth. She was allergic to penicillin and to pyelographic contrast medium. She had had recurrent urinary tract infections. On admission she was cyanosed with intense bronchospasm. She was treated with intravenous aminophylline, a salbutamol infusion, and hydrocortisone 1 g six-hourly.

Despite these measures she required mechanical ventilation and was subsequently transferred to the Queen Elizabeth Hospital. Artificial ventilation was continued for a total of six days, during which time she received subcutaneous terbutaline 0·25 mg six-hourly and a reducing dose of hydrocortisone, later changed to oral prednisolone (figure). She also required soluble insulin for transient hyperglycaemia and intravenous heparin for an axillary vein thrombosis. The plasma potassium concentration was reduced to 2·0-3·0 mmol(mEq)/l during sympathomimetic treatment but returned promptly to normal when this was stopped.



Steroid dosage and serum creatine kinase concentrations in case of acute hydrocortisone myopathy. Day 1 is day of initial presentation. Timing of electromyography (EMG) and muscle biopsy indicated.

Myopathy first became evident when the patient was slow to resume spontaneous respiration despite resolution of her bronchospasm. She was unable to raise her limbs from the bed, both proximal and distal muscle groups being profoundly weak. There were no sensory or reflex changes and the cranial nerves were intact. Serum creatine kinase concentration 888 U/l (normal female range 0-65 U/l) and aspartate transaminase 168 U/l (normal range 5-30 U/l). Serum bilirubin, creatinine, and thyroxine concentrations were normal. The subsequent slow fall in creatine kinase concentration is shown in the figure. Electromyography showed no specific abnormalities. A biopsy specimen of the left deltoid muscle showed vacuolar changes in all fibre types and regenerating basophil fibres throughout the specimen. There was no evidence of denervation. Results of routine histochemical tests were normal. The major electron microscopic feature was the presence of large numbers of glycogen granules in the intermyofibrillar spaces, both within lysosome-like vesicles and free in the sarcoplasm.

Muscle power slowly improved. Recovery was almost complete after six months despite the continuation of prednisolone 5-10 mg daily to control her asthma. Detailed inquiry elicited no evidence of preceding or familial muscle disorder.

Comment

The clinical features of the only other reported case of myopathy attributable to hydrocortisone[1] were remarkably similar to those described here. Both patients required ventilation for status asthmaticus and were given several grams per day of intravenous hydrocortisone. Both developed an acute myopathy that took several months to resolve, and distal limb muscles were as severely affected as proximal. It may be relevant that both patients were given intravenous beta-stimulants in addition to hydrocortisone, though only one of them became hypokalaemic. We suggest that hydrocortisone myopathy is an entity distinct from other forms of steroid myopathy but closely resembling experimental cortisone myopathy. Massive glycogen accumulation is a characteristic ultrastructural feature in the animal model[2] and has been occasionally reported in human steroid myopathy due to other agents.[3 4] It is probably an early change. The pathogenesis of the muscle damage is unknown. Possibly hypoxia or beta-adrenergic stimulants were contributory factors in the two cases described.

Although an accurate dose-response curve would be hard to construct, there is evidence that for an adult of average size the optimal dose of hydrocortisone is not more that 1 g 24 hours by continuous infusion.[5] Higher doses are probably unnecessary and potentially hazardous.

We thank Dr GW Pearce for reporting on the muscle biopsy specimen and for his helpful comments on the case.

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(*Accepted 21 April 1980*)

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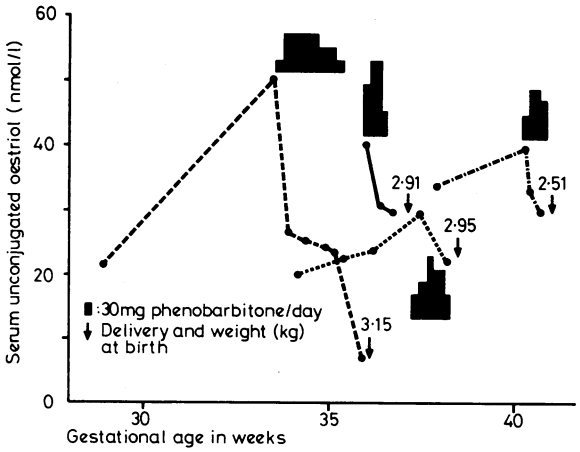
Phenobarbitone and serum unconjugated oestriol concentrations in four pregnant women with hypertension

In most cases studied over one year kit method serum unconjugated oestriol estimations (IM 94, Radiochemical Centre, Amersham, UK) proved to be valuable and reliable indicators of fetoplacental function in "at risk" pregnancies. Oestriol concentrations that fall or fail to rise normally have generally been associated with additional clinical evidence of either fetal distress or an unfavourable outcome of the pregnancy at term, or both.



Serial serum unconjugated oestriol concentrations in four hypertensive pregnant patients receiving phenobarbitone.
Conversion: SI to traditional units—Oestriol: 1 nmol/l ≈ 28·8 ng/100 ml.

Patients and results

We have observed falling oestriol concentrations in four patients with severe hypertension shortly after they began treatment with phenobarbitone (figure); in only one of these (small-for-dates baby and meconium-stained amniotic fluid) was there evidence of impaired fetoplacental function. Neither we nor previous workers[1] have recorded falls of this kind in patients with hypertension, either untreated or receiving alternative treatment,