was 0·94 g/l, haptoglobins 0·12 g/l, and lactate dehydrogenase 1664 U/l. A methaemalbumin test was positive. Her haemoglobin concentration was 10·8 g/dl but subsequently fell to 5·3 g/dl. Her plasma bilirubin concentration was 26 μmol/l, (1·56 mg/100 ml), but other liver function tests remained normal and methaemoglobin was not detected. The direct Coombs test was positive with an anti-IgG antibody titre of 1 in over 800. A weak autoantibody without rhesus or other major blood group specificity was found in her serum by the automated enzyme technique of Marsh.[4] Red cell glucose-6-phosphatase dehydrogenase activity and haemoglobin electrophoresis were normal.

Her platelet count fell to 46×10^9/l (46 000/mm^3) on the third day, but there was no other evidence of definite disseminated intravascular coagulation. Immunoglobin and complement concentrations were normal and the result of an autoantibody screen including antinuclear factor was negative. The presence of nomifensine in her plasma and urine was confirmed by gas liquid chromatography. No other drugs were detected on screening the urine. Her plasma urea and creatinine concentrations rose from 3·0 mmol/l (18 mg/100 ml) and 99 μmol/l (1·1 mg/100 ml) respectively on admission to 45 mmol/l (270 mg/100 ml) and 1045 μmol/l (11·9 mg/100 ml) four days later. Urine tests for protein, haemoglobin, and urobilinogen were strongly positive. She became anuric and haemodialysis was required on six occasions before the diuretic phase began 10 days later. A renal biopsy specimen obtained 10 days after admission showed acute tubular necrosis with no evidence of disseminated intravascular coagulation. At this time the Coombs test had become negative and the platelet count had returned to normal. Improvement was maintained and she was discharged home one month after taking the nomifensine. Two months later her haemoglobin, platelet count, and plasma urea and creatinine concentrations were all normal. Twenty months after the overdose she remained well with a haemoglobin concentration of 14·5 g/dl and a normal blood film.

Comment

Acute haemolysis and tubular necrosis occurred in this patient after overdosage of nomifensine and possibly nitrazepam and chlordiazepoxide. In our experience of many thousands of cases of benzodiazepine poisoning we have never encountered these complications, and we are unaware of any such reports. There is much less experience of nomifensine overdosage, but in 28 reported cases there was no serious toxicity[1-3] and haemolysis was not encountered in preclinical toxicity studies in animals (P Stonier, personal communication). Bournerias and Habibi,[5] however, described immune haemolytic anaemia and impaired renal function in a patient taking therapeutic doses of nomifensine intermittently. Our case is very similar and there was no other obvious cause for haemolysis. Unlike these investigators, we were unable to demonstrate nomifensine-dependent agglutination of red cells in response to the antibody and, unfortunately, studies with red cell eluates were not carried out. The low serum antibody titre with a strongly positive Coombs test in our patient suggests that the antibody was of high affinity and strongly bound to erythrocytes. Probably she developed autoantibodies to red cells while taking nomifensine intermittently and subsequently suffered massive haemolysis after an overdosage. Although serious, such reactions to nomifensine seem to be very uncommon.

We thank Dr S H Davies, Department of Haematology, Royal Infirmary, Edinburgh, and Dr P Stonier (Hoechst UK Ltd) for advice and information about nomifensine.

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(*Accepted 30 September 1980*)

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Pathogenesis of papilloedema and raised intracranial pressure in Guillain-Barré syndrome

Papilloedema and raised intracranial pressure are rare but well-recognised complications of the Guillain-Barré syndrome. The pathogenesis is unknown. If the mechanism were increased accumulation of cerebrospinal fluid large ventricles becoming smaller with clinical improvement would be expected, but if the mechanism were brain swelling the reverse would be true. We have therefore measured ventricular volume from computed tomographic (CT) scans[1 2] of a patient with the Guillain-Barré syndrome (*a*), when headaches and papilloedema were present and (*b*) after recovery.

Case report

A 16-year-old schoolboy was admitted to hospital in April 1980 with a two-week history of weakness in both legs. The weakness then spread to the arms, face, and bulbar and respiratory muscles. He also complained of tingling in his fingers and toes. Examination showed a thin youth with pronounced facial bulbar and proximal limb weakness. The limbs were hypotonic and areflexic with flexor plantar responses. Sensation was not impaired and the fundi were normal.

Nerve conduction studies showed slowing of velocities (common peroneal nerve 30 m/s) consistent with the Guillain-Barré syndrome. Lumbar puncture yielded cerebrospinal fluid at 160 mm H_2O and containing protein 2·2 g/l and no cells. Paul-Bunnell test gave a negative result, serum lead concentration was normal, and no excess of porphyrins was detected in serum, urine, or faeces. Complement fixation tests showed raised titre against measles virus (1024/1024), and complement components C4 and factor B were very low. Over the next few weeks bulbar and respiratory function improved but severe limb girdle weakness persisted.

Ten weeks after presentation the patient developed nausea, vomiting and headache, and bilateral papilloedema. CT scan showed no evidence of any mass lesion, and the ventricular volume was 18·6 ml. Cerebrospinal fluid pressure was 330 mm H_2O with a protein concentration of 3·6 g/l and 2×10^6 white cells/l (2/mm^3). The headaches improved after the lumbar puncture, and a course of six plasma exchanges resulted in a dramatic improvement in strength.

When reviewed in September he was well with no headaches and the papilloedema had resolved. CT scan showed subjectively smaller ventricles with a volume of 5·2 ml.

Comment

Both decreased absorption of cerebrospinal fluid[3] and cerebral oedema[4] have been suggested to explain the raised intracranial pressure that may occur in the Guillain-Barré syndrome. The sometimes inconsistent relationship between raised intracranial pressure and cerebrospinal fluid protein concentration, the inability to produce an animal model by injecting protein into the intrathecal space, and the rarity of raised intracranial pressure as a complication of the syndrome militate against increased cerebrospinal fluid protein as a cause of decreased absorption.[5] Brain swelling appeared to be an attractive hypothesis, especially after Joynt's[4] case report with biopsy findings that he considered to be in keeping with cerebral oedema.

In our patient the reduction of ventricular volume from 18·6 ml to 5·2 ml with resolution of the papilloedema suggests that symptoms had been caused by an accumulation of cerebrospinal fluid. That absorption of cerebrospinal fluid is impaired by excess protein alone is disputed, so an alternative mechanism must be sought. In four other patients with Guillain-Barré syndrome without papilloedema we found no abnormalities in the serum complement. In our patient possibly an immunological disturbance with activation of the classical and alternative complement pathways resulted in impaired cerebrospinal fluid absorption at the arachnoid villi or, alternatively, increased production of cerebrospinal fluid at the choroid plexus. This would suggest that patients with Guillain-Barré syndrome who have a relapsing course and develop papilloedema are immunologically different from patients with conventional symptoms of polyneuropathy alone.

We thank Miss Margaret Matheson, senior physicist, without whose invaluable help the ventricular volumes could not have been measured.

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(*Accepted 29 September 1980*)

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Measuring glycosylated haemoglobin concentrations in a diabetic clinic

The glycosylated haemoglobin (HbA_1) concentration is a useful index of diabetic control.[1 2] Measuring the concentration by chromatography on cation exchange columns, however, requires a skilled technician and controlled temperatures, and the result is not immediately available. We have therefore evaluated a new method (Corning Medical Ltd, Halstead, Essex) that offered accuracy, simplicity, and speed. We assessed the method in our diabetic clinic over six weeks by (*a*) comparing it with a chromatographic method run concurrently, (*b*) examining the feasibility of obtaining a result in time for the patient's consultation, and (*c*) estimating the value of the result.

Patients, methods, and results

On arrival all patients have their urine tested, are weighed, have their eyesight tested (yearly), and give a finger-prick blood sample for glucose and HbA_1 estimations. Often an hour or more passes after arrival before the patient sees the doctor. Some patients arrive well before the clinic starts to minimise this time, and finger-prick sampling was begun on these before 1 pm, so that the first results were available by 2 pm. Also by seeing mainly new patients first, who need more doctor-time, we hoped to achieve a good flow.

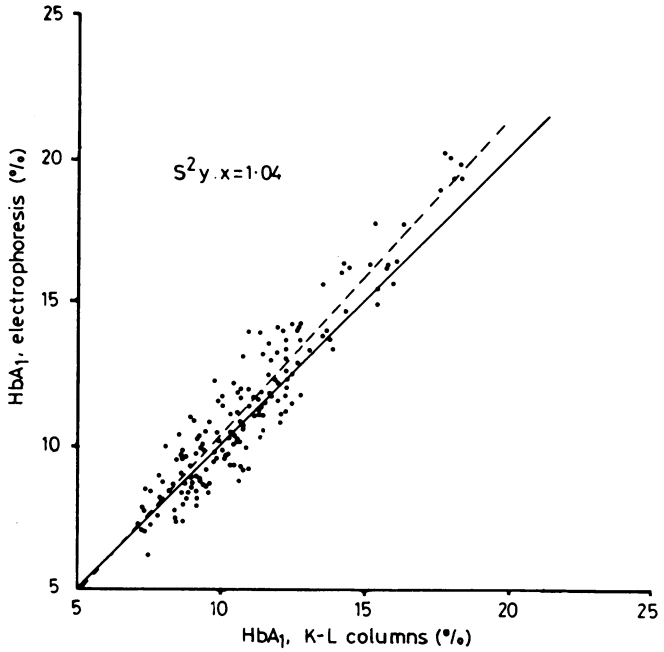
Blood obtained by finger-prick (10 μl) was haemolysed in 30 μl 0·1% saponin, 0·05% EDTA. Aliquots of haemolysate (1 μl) were analysed by electrophoresis and endosmosis on agar gels for 40 minutes and the percentage of HbA_1 determined by scanning densitometry. Standard deviation for replicate samples was 0·5%. Details of our chromatographic method have been published.[3] The value of the measurements was assessed by questionnaire. After seeing each patient the doctor looked at the HbA_1 result, decided what advice to give the patient, and then answered four questions: Does this alter your management? Was the result as expected? Do you think it usefully reinforced the advice you have given? Did it alter the timing of further follow-up? Questionnaires were collected at the end of each clinic. Equipment fitted on a standard trolley, and it was found convenient to run the system in the clinic, reagents being non-toxic. The technician took about 30 minutes to learn the method.

The results were closely similar to those of chromatography (figure). In week 1 about half the results were available in time for the consultation. Week 2 was less satisfactory, but by week 3 and thereafter most results were obtained in time. A total of 259 questionnaires were answered. Haemoglobinopathy was identified in 10 cases, which we excluded from analysis. As a result of the measurements patient management was changed in 17% of cases (ranges 10-25% over the six weeks and 11-26% for the six doctors). The result was unexpected in 26% of cases (ranges 20-33% and 18-36% respectively) and was thought usefully to reinforce the advice given in 45% (ranges 38-56% and 14-75%) and to alter timing of follow-up in 12% (ranges 5-23% and 2-23%). When the first, third, and fourth questions were combined a positive answer was obtained in 135 (54%) cases.

Comment

Measuring HbA_1 by electrophoresis/endosmosis was simple, accurate, and rapid compared with column chromatography, and most results were obtained during clinic time. Nevertheless, there was some extension of waiting time and overcrowding in our just adequate waiting area, and longer term some adjustments will be necessary. Patients may need to be re-educated into considering a clinic visit as an opportunity for advice partly based on preliminary checks (including HbA_1) rather than a visit to the doctor preceded by a long wait.

As a result of measuring HbA_1 almost one-fifth of patients had their management changed, which is substantially more than after many tests. In over half the measurement was thought to be useful. Further studies will identify patients in whom HbA_1 measurement is most valuable.



Relation between HbA_1 concentrations measured by electrophoresis/endosmosis and our own modified Kynoch-Lehmann (K-L) columns[3] (n=192). HbA_1 by electrophoresis = 1·10 × HbA_1 by K-L − 0·64 (——Line of identity. - - - Regression line).

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(*Accepted 8 October 1980*)

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Spontaneous biochemical remission in parathyroid carcinoma

Spontaneous remission is an unusual but recognised feature of primary hyperparathyroidism associated with adenoma, and is then attributed to infarction of, or haemorrhage into, the affected gland. A remission seems not to have been described in parathyroid carcinoma. We describe the case of a patient with parathyroid carcinoma who had a spontaneous but temporary biochemical remission which may have been related to tumour infarction.

Case report

The patient, a man aged 60, was well until June 1976, when he developed pain in the lower lumbar region. He also noticed ankle swelling and had lost 7 lb (3·18 kg) in weight. There was no significant medical history. He was found to have hypercalcaemia and was referred to the metabolic unit, Manchester Royal Infirmary, for further investigation. Clinical examination gave normal findings apart from congenital finger clubbing. Serum concentrations were: calcium 3·75 mmol/l (15 mg/100 ml), inorganic phosphate