SHORT REPORTS

Streptokinase and serum enzymes

We have recently observed a rise in the serum transaminase (aspartate aminotransferase, AST; and alanine aminotransferase, ALT) levels in patients who received a 24-hour course of streptokinase. The patterns of this enzyme rise suggests a hepatic source.

Patients, methods, and results

During a controlled trial of fibrinolytic therapy in unstable angina, 20 patients were treated in the acute phase with streptokinase (Streptase). A rise in the serum AST and ALT, occurring from 12 to 96 hours after starting treatment, was found in eight of these patients. All eight patients had received a loading dose of 250 000 units of streptokinase, administered intravenously over 30 minutes, as a solution in physiological saline. This was followed by the infusion of 100 000 units per hour for 24 hours. This regimen produced adequate fibrinolysis as assessed by a thrombin time of 2-4 times normal at four hours after the start of treatment in all eight patients. Serum transaminases were estimated by the Boehringer optimised 37°C method for AST and ALT. (Normal levels with this method are 13-42 IU/l for AST and 11-55 IU/l for ALT.) The results in individual patients are summarised below.

Patient	Maximum AST (IU/l)	Time of maximum rise from start of treatment (hours)	Maximum ALT (IU/l)	Time of maximum rise from start of treatment (hours)	Duration of transaminase rise (hours)
1	92	24	107	24	24-48
2	189	12	199	72	12-96
3	186	24	193	24	12-96
4	185	12	161	12	12-48
5	155	48	242	48	24-96
6	161	24	121	48	24-48
7	96	24	122	48	24-72
8	174	12	200	12	12-48

No significant association was noted between the occurrence of a febrile reaction to streptokinase and a rise in the serum transaminase levels. Steroid therapy as prophylaxis against a febrile reaction to streptokinase had no appreciable effect on the occurrence of a transaminase rise. (Results analysed using the Fisher exact probability test.) None of these patients sustained myocardial infarction during the period of observation nor was there any other apparent cause for the enzyme rise. Two patients had a normal serum creatine phosphokinase level at the time of their peak transaminase rise. In one of the patients a rise in the lactic acid dehydrogenase iso-enzyme LD₅ occurred at the time of the peak transaminase rise. Only in these three patients were these additional enzyme estimations performed.

Necropsy was possible in one of these patients (case 3), who died a sudden, presumably cardiac arrhythmic, death ten days after treatment. There was no evidence of myocardial infarction or pulmonary embolus and microscopic examination of the liver showed focal liver cell necrosis (one every six to seven high power fields) scattered in the lobules. Similar appearances were seen in two patients with pulmonary thromboembolic disease who died soon after the start of streptokinase treatment. Nevertheless, this microscopic abnormality was also noted in three other patients, who had not received streptokinase, dying soon after acute myocardial infarction. Thus no specific histological changes were noted in patients who had received streptokinase treatment.

Discussion

This rise in serum transaminase levels associated with fibrinolytic treatment parallels that recently observed during prolonged heparin treatment.¹ The pattern of enzyme rise, the ALT being consistently higher than the AST, suggests a hepatic course and this is supported by the rise in LD₅ observed in one patient.² In this series of patients there was no evidence of any specific abnormality of the liver cells as assessed by light microscopy. No persisting hepatic impairment was noted in any case. The mechanism of this rise in serum transaminase levels is not clear. An acute hepatitis-like syndrome has been described in a single patient treated with streptokinase.³ Furthermore, patients receiving streptokinase treatment for myocardial infarction were found

to have significantly earlier and higher peak enzyme activities,⁴ this being attributed to improved microcirculation in the myocardium. Finally, in the absence of pretreatment tissue damage, possibly the rise in serum transaminase levels reflects a subsidiary action of fibrinolytic therapy, such as activation of the kinin cascade.⁵

The clinical importance of this unexplained rise in serum transaminase levels during fibrinolytic treatment is apparent. An appreciation that such a biochemical abnormality results from fibrinolytic therapy is important in order to avoid drawing inappropriate conclusions from the results of serum transaminase estimations.

We thank the Department of Biochemistry, Stobhill General Hospital, who carried out the transaminase estimations.

¹ Sonnenblick, M, Oren, A, and Jacobsohn, W, *British Medical Journal*, 1975, **3**, 77.

² Plummer, D T, et al, *Biochemical Journal*, 1963, **87**, 416.

³ Mandel, E E, Minn, S K, and van Voolen, C A, *Abstracts of Vth International Congress on Thrombosis and Hemostasis*, Vienna, p 417.

⁴ Praetorius, F, et al, *Klinische Wochenschrift*, 1973, **51**, 397.

⁵ Lewis, G P, *Journal of Physiology*, 1958, **140**, 285.

Department of Materia Medica and Department of Pathology, Stobhill General Hospital, Glasgow G21 3UW

J T SHEPHERD, MB, MRCP, registrar

S S RAO, MB, MRCPATH, consultant pathologist

J R LAWRENCE, MB, MRCP, senior registrar

M J BRODIE, MB, MRCP, lecturer

W F M FULTON, MD, FRCP, senior lecturer and consultant physician

Anuria due to cystine stones in a baby

Both anuria, as a presenting clinical feature, and cystine stones are rare in early childhood.¹ Cystinuria and urinary calculi, however, have recently been reported in an infant.² Moreover, cystine calculi, often bilateral, occur in older children and adults.³

Case report

The patient, a normally developed 13-month-old boy, had been well, apart from occasional vomiting, until seven days before admission to hospital. He had then become listless, vomited frequently, and for 24 hours did not pass urine. There was no known family history of cystinuria. Abdominal and loin tenderness were present and catheterisation released only 5 ml of urine. The results of investigations were: haemoglobin 10.2 g/dl, blood urea 58.4 mmol/l (352 mg/100 ml), serum potassium 8.1 mmol/l (8.1 mEq/l). An ECG showed T-wave changes consistent with hyperkalaemia. X-ray examination of the abdomen showed three radio-opaque, "ground-glass" opacities suggestive of porous cystine stones—one overlying the right kidney; another in line with the right ureter, near the renal pelvis; and the third in line with the left upper ureter. No cystine crystals were found in the urine.

In the course of peritoneal dialysis the child began to pass urine. Intravenous pyelography and nephrotomography later showed a functioning, hydronephrotic right kidney with two opacities within the pelvis and an enlarged left kidney. A preoperative film, taken three days after admission, showed a functioning, hydronephrotic left kidney. Surgical removal of two stones from the right pelvis through a pyelotomy and one stone from below the left pelviureteric junction via a ureterotomy was uneventful. The "honey-brown" opalescent appearance of the calculi was characteristic of cystine stones, which were found to contain pure cystine. The child's mother co-operated well in giving him a fluid intake of about 1.5 l/day and a mixture containing potassium citrate and in monitoring the urinary pH. The response to treatment was good.

Discussion

That the anuria was apparently painless yet due to bilateral obstruction of the ureters by calculi is noteworthy. Herring,⁴ in a study of 10 000 urinary calculi, found only 89 to contain cystine, of which about 70% were composed of pure cystine, as in our case. Thus urinary tract calculi may be due to cystinuria even in a young child. Cystinuria⁵ is a recessive or incompletely recessive genetic abnormality. Urinary concentrations of cystine, lysine, arginine, ornithine, and cystine-homocysteine are raised. Cystine, the least soluble of the urinary amino-acids, tends to precipitate when present in excessive concentrations. Cystine stones, however, occur only in some cystinuric patients, who may develop them presumably either in utero or during infancy, but the precise reasons for their formation are uncertain. Predisposing causes such as infection or anatomical abnormalities of the urinary tract are unusual.

Most medical treatments aim at reducing the concentration of urinary cystine. Penicillamine or a "high fluid intake" may cause dissolution of cystine calculi, but the immunological abnormalities induced by penicillamine, hypertension, heart failure, electrolyte disturbances due to fluid and alkali excess, and impaired renal function are important considerations in management. Our aim in this patient is to prevent further stone formation and avoid electrolyte imbalance. We are reluctant to use penicillamine because of its side effects.

¹ Bass, H N, and Emanuel, B, *Clinical Pediatrics*, 1966, **5**, 79.

² Chatys-Gorska, L, and Zawadzki, J, *Wiadomosci Lekarskie*, 1974, **27**, 1657.

³ Dent, C E, et al, *British Medical Journal*, 1965, **1**, 403.

⁴ Herring, L C, *Journal of Urology*, 1962, **88**, 545.

⁵ Crawhall, J C, and Watts, R W E, *American Journal of Medicine*, 1968, **45**, 736.

Hull Royal Infirmary, North Humberside, Yorks

M J FARR, MRCP, consultant nephrologist
D W W NEWLING, FRCS, consultant urologist
A H ELDRISY, MD, DCH, paediatric registrar
G A MIRGHANI, MD, DCH, paediatric senior house officer
R J PUGH, FRCP, consultant paediatrician

IgA deficiency and neutropenia

Immunodeficiencies may be associated with neutropenia.^{1 2} We report here a patient with IgA deficiency and neutropenia whose clinical state and neutropenia responded to corticosteroids. This does not seem to have been reported.

Case report

The patient first presented with thrombocytopenia, lymphadenopathy, and splenomegaly at the age of 10 years. He had had many attacks of "bronchitis." There was no family history of recurrent infections. A full blood count was normal except for thrombocytopenia. An antinuclear factor test was negative. Marrow aspirate showed an active marrow with normal megakaryocytes. After splenectomy the platelet count rose to $390 \times 10^9/l$ ($390\,000/mm^3$) and remained normal. Splenic histology was normal. During the next few years he had recurrent attacks of bronchopneumonia and otitis media.

He was readmitted at the age of 14 with fever and cough. Laboratory findings were as follows: leucocyte count $3.1 \times 10^9/l$ ($3100/mm^3$), neutrophils 8%, lymphocytes 74.5%, monocytes 15%, and eosinophils 1.5%; platelet count $161 \times 10^9/l$ ($161\,000/mm^3$); Paul-Bunnell and extended Widal tests negative; bone marrow aspirate showed active myelopoiesis; IgG 10.8 g/l, IgA 0.3 g/l, IgM 7.5 g/l; 51% of lymphocytes formed spontaneous rosettes with sheep red cells (normal 50%-60%); lymphocyte response to phytohaemagglutinin stimulation normal; surface immunofluorescence staining test showed IgG in 6.4% lymphocytes (control 13.3%), IgM in 5.2% (control 11%), IgA in 2.7% (control 6%), and a slightly reduced B-cell population. Assay of antibody to *Escherichia coli* and antibody response to primary antigenic challenge with pneumococcal polysaccharide were negative. Mantoux test (1/1000) was also negative although the patient had been vaccinated with BCG. Platelet agglutinin and complement fixation test for incomplete platelet antibodies were negative. Leucocyte agglutinin was positive. Tests for other antibodies, including antinuclear antibodies, smooth muscle antibodies, and mitochondrial antibodies, were all negative.

The patient was given cephaloridine 6 g/day for seven days with no effect.

Prednisone 40 mg/day was then started. The fever lysed within 24 hours, and the neutrophil count rose from $0.18 \times 10^9/l$ to $1.71 \times 10^9/l$ (180 to $1710/mm^3$) over 20 days. Over the next five years attempts to withdraw the steroid were unsuccessful. Every time he would become neutropenic and feverish and would respond only to an increase in prednisone dosage. He also developed eczema. He was last admitted at the age of 21 with pneumococcal septicaemia. His leucocyte count then was $6.2 \times 10^9/l$ ($6200/mm^3$), neutrophils 81%, lymphocytes 12%, monocytes 7%; IgG 6 g/l, IgA 0.39 g/l, and IgM 1.98 g/l. Necropsy showed generalised lymphadenopathy with bilateral pleural effusion and no evidence of lymphoma.

Immunoglobulin levels in members of the immediate family were normal.

Discussion

This patient had low IgA, normal IgG, and high IgM serum concentrations. B-cells were slightly reduced, and the number and function of T-cells were probably normal. Recurrent bronchopneumonia, otitis media, thrombocytopenia, neutropenia, eczema, and a raised level of IgM are not unusual in selective IgA deficiency.³ IgA deficiency is associated with autoimmune phenomena and with the presence of various autoantibodies.³ Furthermore, immunodeficiency may be associated with neutropenia,^{1 2} but the cause of this is not clear. The beneficial effect of prednisone on our patient's neutropenia and infection, and their exacerbation when prednisone was withdrawn, pointed to an immunologically mediated destruction of his polymorphs, in which the leucocyte agglutinin might have been implicated. His immune deficiency was unlikely to have been the result of splenectomy in childhood, since after splenectomy children usually have low serum IgM but normal IgA and IgG concentrations.⁴ We therefore think that his IgA deficiency was probably congenital and the neutropenia was due to the presence of a leucocyte antibody which was controlled with prednisone.

We thank Dr K L G Goldsmith of the Lister Blood Group Reference Laboratory for doing the tests on platelet and leucocyte agglutinins, and Dr A D B Webster, Clinical Research Centre, Immune Deficiency Referral Laboratory, for the tests on B-cell marker and antibodies response to *E coli* and pneumococci.

¹ Hitzig, W H, and Schlapfer, A, *Abstracts of the 10th Congress of the International Society of Haematology*. Stockholm, Munksgaard, 1964.

² Stiehm, E R, and Fudenberg, H H, *American Journal of Medicine*, 1964, **40**, 805.

³ Hong, R, and Ammann, A J, *American Journal of Pathology*, 1972, **69**, 490.

⁴ Schumacher, M J, *Archives of Disease in Childhood*, 1970, **45**, 114.

Department of Clinical Haematology, University College Hospital Medical School, London WC 1

R P NG, MB, MRCP, senior lecturer in haematology
T A J PRANKERD, MD, FRCP, professor of haematology

Acute dilatation of stomach as late complication of drug overdose

To our knowledge acute dilatation of the stomach complicating severe drug poisoning has not been reported.

Case report

A 16-year-old girl was admitted to hospital four hours after taking an unknown quantity of amitriptyline, orphenadrine, and flurazepam. Her pupils were widely dilated and she was deeply unconscious showing no response to painful stimuli. The heart rate was 120 per minute and the systolic blood pressure only 80 mm Hg. A cuffed endotracheal tube was passed and a minimal amount of tablet fragments was recovered by gastric lavage. Subsequently convulsive episodes occurred and an electrocardiogram showed an idioventricular rhythm. Supportive measures were instituted and cardiac monitoring showed resumption of sinus rhythm four hours after admission.

Her general condition gradually improved and after 48 hours she was fully conscious and superficially well, the pulse rate being 90 per minute and the blood pressure 120/75 mm Hg. On the third day, however, she