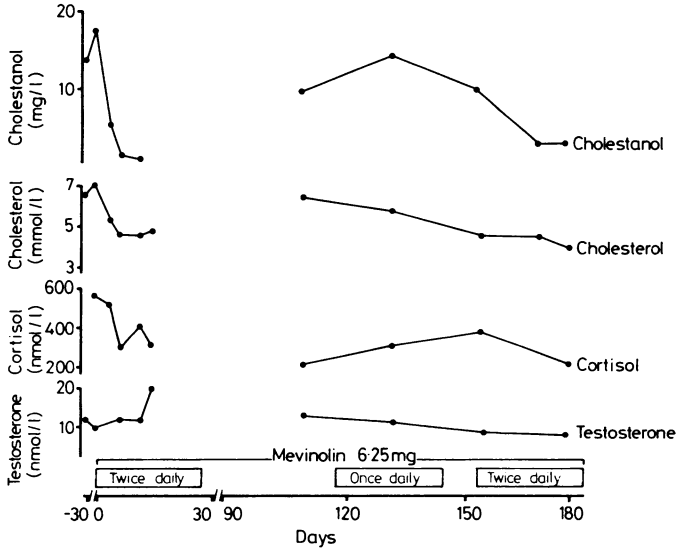
Comment

Cerebrotendinous xanthomatosis is an autosomal recessive lipid storage disease characterised by accumulation of cholestanol and cholesterol in the brain and other tissues.[1] Common manifestations are tendon xanthomas, cataracts, progressive dementia, ataxia, spinal cord signs, and coronary heart disease.[1 2] No effective treatment has been documented.[1]

Cholestanol is a product of the metabolism of cholesterol in mammalian tissues.[3] The first step in normal hepatic degradation of cholesterol to bile acids is dependent on mitochondrial steroid 26-hydroxylase. Absence of this enzyme, first hypothesised by Myant,[3] appears to be the underlying defect[4 5] and may divert sterols from the normal pathways of bile acid synthesis. In view of the serious prognosis in cerebrotendinous xanthomatosis and in the absence of noticeable dementia in our patient treatment was instituted with low dose (6·25 mg twice daily) mevinolin, a competitive inhibitor of hydroxymethylglutaryl coenzyme A reductase. There were no untoward clinical findings. Blood pressure remained unchanged. A biochemical profile of 13 tests and routine haematological studies showed no trends nor deviations from reference ranges. The figure gives the sterol and steroid hormone concentrations. Serum cholestanol



Effects of mevinolin on plasma concentrations of cholestanol, cholesterol, cortisol, and testosterone.

Conversion: SI to traditional units—Testosterone: 1 nmol/l ≈ 0·3 ng/ml. Cortisol: 1 nmol/l ≈ 0·04 μg/100 ml. Cholesterol: 1 mmol/l ≈ 38·6 mg/100 ml.

(Successful use of chenodeoxycholic acid in cerebrotendinous xanthomatosis was reported by G Salen *et al* (*Circulation* 1982;**66**:II-238 (abstract)). In that study mean plasma cholestanol concentration during treatment fell to 8·0 mg/l—that is, reduction was less pronounced than that achieved by mevinolin. Despite this, treatment for one year was associated with improvement in electroencephalographic abnormalities.)

values became normal within four days after beginning mevinolin and decreased further to low normal. Mean plasma cholesterol concentration decreased by 32%; mean high density lipoprotein cholesterol value did not change substantially (1·2 mmol/l (46·3 mg/100 ml) before, 1·4 mmol/l (54·1 mg/100 ml) during treatment), nor did mean plasma triglyceride values change in fasting samples (2·3 mmol/l (204 mg/100 ml) before and during treatment). Plasma cortisol and testosterone concentrations fluctuated within the normal range.

After five months it was too soon to assess the effect of treatment on the neurological disability (computed tomographic scan and electroencephalogram were unchanged), but it is of interest that inhibition of cholesterol synthesis rapidly corrected the high plasma cholestanol concentration. In the first five months of treatment the liver became smaller and the xanthomas showed signs of regression. The reduction in plasma cholestanol was striking and exceeded that in plasma cholesterol; this would be expected if, in the untreated state, tissue concentrations of cholestanol saturated a rate limiting step in its catabolism.

We thank Merck, Sharp and Dohme Ltd for generously supplying mevinolin.

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Anaphylactoid purpura presenting as a medical and surgical emergency

Anaphylactoid purpura, a disease primarily of young children, is a well recognised though infrequent syndrome in the adult.[1] We report a case mimicking gastrointestinal obstruction and pulmonary embolus which was associated with thrombocytosis.

Case report

A 59 year old man presented with pronounced abdominal distension for two days. There was no abdominal pain and he had not passed faeces or flatus for over 24 hours. In addition, four hours previously he had suddenly developed pleuritic type chest pain at the base of his right lung posteriorly with an episode of minimal haemoptysis. Three weeks before admission an uneventful left tibial osteotomy for osteoarthrosis had been performed.

On admission he was pyrexial (38·2°C), tachypnoeic, and centrally cyanosed. His pulse was regular at 100/min and the jugular venous pressure was raised. There was decreased air entry at both lung bases with coarse crepitations. The abdomen was distended with minimal generalised tenderness and high pitched obstructive bowel sounds.

Initial investigations showed: haemoglobin concentration 16·5 g/dl; white cell count $26{\cdot}1 \times 10^9$/l (26 100/mm³); erythrocyte sedimentation rate 114 mm in first hour; platelet count 700×10^9/l (700 000/mm³); blood urea and serum electrolyte concentrations normal; arterial blood gases, Po_2 6·4 kPa (48 mm Hg), Pco_2 5·1 kPa (38·3 mm Hg), hydrogen ion 36 mmol/l. Chest *x* ray films showed bilateral basal consolidation with atelectasis in the right mid-zone suggesting infarction. Erect and supine abdominal *x* ray films confirmed large bowel gaseous distension with several fluid levels.

Pulmonary embolus was suspected and he was treated with intravenous heparin and high flow oxygen. The asymptomatic abdominal signs persisted, developing into frank gastrointestinal obstruction five days later with constipation, copious vomiting, severe central colicky abdominal pain, and generalised guarding. He developed pain in both wrists and a maculopapular rash on the extensor surface of the thighs and calves, which progressed within 24 hours to palpable purpura and superficial necrotic areas of up to 1 cm² in diameter.

The initial leucocytosis returned to normal; the thrombocytosis, however, increased to 1010×10^9/l (1 010 000/mm³). Tests for faecal occult blood were consistently negative although microscopic haematuria and proteinuria developed. Other investigations, including screening tests for organ specific autoantibodies, antinuclear factor, and sputum pneumococcal capsular antigen, were negative. The only biochemical abnormalities were an increase in serum alanine aminotransferase and alkaline phosphatase (liver origin) reaching peaks of 108 IU/l (normal range = 10-40 IU/l) and 236 IU/l (normal

range=40-100 IU/l) respectively. Tests for hepatitis B surface antigen were negative. Ultrasonography of liver and gall bladder was normal.

Anaphylactoid purpura was diagnosed and treatment with intravenous hydrocortisone 100 mg four times daily started. Respiratory and abdominal symptoms resolved completely within 18 hours. The patient was discharged home nine days later taking a gradually decreasing dose of prednisolone. He remained well six weeks later and steroid treatment was stopped. All haematological and biochemical indices were within normal limits.

Comment

Gastrointestinal symptoms are found in 44% of adults with Henoch-Schönlein purpura but are the presenting complaint in only 8%. Colicky abdominal pain is a prominent symptom in 78% of those presenting with gastrointestinal symptoms.[1] To our knowledge there have been no reports of this condition in patients presenting with gross abdominal distension, absolute constipation, obstructive bowel sounds, and the total absence of abdominal pain. Massive gastrointestinal haemorrhage associated with the disease may be controlled by corticosteroids, when the possibility of intussusception has been excluded[2 3]; this indicates the prognostic importance of early diagnosis and treatment.

Respiratory symptoms, simulating pneumonia or pulmonary emboli, are present in 6·5% of cases,[1] and in our patient it is likely that the pulmonary features were another facet of the anaphylactoid purpura. The rapid relief of symptoms within 18 hours of corticosteroid treatment also supports this view. We assumed that the gut and lung abnormalities were due to small vessel vasculitis in these organs. As transient abnormal liver function has been reported in other forms of systemic arteritis, such as temporal arteritis,[4] the abnormal liver function tests were probably a manifestation of vasculitis. Thrombocytosis has been reported as a rare event in paediatric cases.[5] This seems, however, to be the first reported association of thrombocytosis with anaphylactoid purpura in an adult. The mechanism is unknown.

In summary, this case of anaphylactoid purpura merits description because of its unusual presentation with painless gastrointestinal obstruction, respiratory symptoms, abnormal liver function tests, and thrombocytosis.

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Maintenance of remission in ulcerative colitis with 5-amino salicylic acid in high doses by mouth

Oral 5-amino salicylic acid coated with an acrylic based resin (Eudragit S) is released in the colon[1] and has a similar clinical effect to sulphasalazine in maintaining remission in patients with ulcerative colitis.[2] We determined whether higher doses of 5-amino salicylic acid were more effective in preventing relapse compared with conventional doses of sulphasalazine and also measured serum concentrations of the metabolites during a six month trial.

Patients and methods

Sixty seven patients (36 men and 31 women) were admitted to the trial. All were in remission with ulcerative colitis or proctitis and had passed three or less stools daily without blood or slime during the previous month. Admission to the trial depended on normal sigmoidoscopic findings. All patients gave informed consent before admission to the six month trial and were seen 12 and 24 weeks after admission. Diary cards recording the daily frequency of stools and any blood loss were completed throughout, and sigmoidoscopic examination was repeated at the end of the trial or in patients with recurrent symptoms. Relapse was defined as a recurrence of symptoms with sigmoidoscopic changes including contact or spontaneous mucosal haemorrhages, pus, or ulceration.

The study was randomised and double blind using identical placebo tablets for both sulphasalazine and 5-amino salicylic acid. All patients were given two sets of tablets, either active 5-amino salicylic acid and placebo sulphasalazine or placebo 5-amino salicylic acid and active sulphasalazine. The number of trial tablets was based on the patient's usual dose of sulphasalazine. Tablets of 5-amino salicylic acid each contained 400 mg which is equivalent to 1 g of sulphasalazine; at least six tablets of 5-amino salicylic acid were taken daily (2·4 g) with an increase of two tablets for each gram of sulphasalazine above the entry dose of 2 g in those patients taking high doses of sulphasalazine. The mean dose of 5-amino salicylic acid taken was 2·7 g (range 2·4-4·4 g) and of sulphasalazine 2·3 g (range 2-4 g); this mean dose of sulphasalazine is equivalent to 0·9 g of 5-amino salicylic acid. Fifty one patients who helped with our first trial were entered into the current study and their treatment was crossed over. Compliance was checked at each hospital visit.

The 5-amino salicylic acid was obtained from Aldrich Chemicals Limited and the tablets were coated with Eudragit S to a thickness of between 100 and 130 μm. 5-Amino salicylic acid and acetyl 5-amino salicylic acid were analysed by high pressure liquid chromatography using a modification of the method described by Shaw *et al.*[3] The analysis was performed on a LiChrosorb 10 RP 18 bonded dilica reversed phase column (Merck). The mobile phase was acetonitrile-0·05 mol potassium dihydrogen phosphate solution (15:85), pH 7·4, containing 0·1% tetrabutyl ammonium hydroxide. 5-Amino salicylic acid and acetyl 5-amino salicylic acid were detected using a fluorescent spectrometer (excitation 360 nm, emission 425 nm). Serum was treated with an equal volume of acetonitrile to precipitate proteins, and after centrifugation the supernatant was injected on to the chromatograph. Concentrations of 5-amino salicylic acid were read off a calibration curve which was linear over the ranges of 5-amino salicylic acid and acetyl 5-amino salicylic acid measured. The lower limit of sensitivity for measurements of 5-amino salicylic acid was 0·1 μg/ml and for acetyl 5-amino salicylic acid 0·2 μg/ml.

Results

Ten of the 67 patients (six women and four men) were withdrawn from the study; four failed to take treatment regularly, one became pregnant, one had an unrelated problem, and four developed severe headaches. The four who developed headaches were later found to be taking sulphasalazine. Of the remaining 57 patients, 12 had a clinical relapse and 45 completed the trial (table). Seven of the 32 patients taking 5-amino salicylic acid (22%) and five of the 25 patients taking sulphasalazine (20%) relapsed; this difference was not statistically significant. Serum concentrations of acetyl 5-amino salicylic acid were significantly higher than those for 5-amino salicylic acid. Concentrations of these two metabolites were consistently higher in patients taking high doses of the enteric coated 5-amino salicylic acid preparation compared with those in patients taking lower doses of sulphasalazine.

Details of 57 patients treated with 5-amino salicylic acid or sulphasalazine during a six month trial period excluding 10 patients who were withdrawn

	5-Amino salicylic acid	Sulphasalazine
No of patients	32	25
Sex (M/F)	19/13	13/12
Mean (SD) age (years)	48·6 (16·2)	43·9 (14·1)
Mean (SD) duration of disease (years)	8·8 (6·2)	7·5 (5·9)
Mean (SD) time since last attack (years)	2·15 (2·3)	1·8 (1·2)
No of patients with:		
Proctitis	15	11
Left sided disease	7	9
Extensive disease	10	5
No (%) of relapses	77 (22·1)	5 (20·1)
Median (range) serum 5-amino salicylic acid concentration (μg/ml) at three months	0·7 (<0·1-6·5)*	<0·1 (<0·1-0·2)†
Median (range) serum 5-amino salicylic acid concentration (μg/ml) at six months	0·8 (0·1-5·3)*	0·1 (<0·1-0·3)†
Median (range) serum acetyl 5-amino salicylic acid concentration (μg/ml) at three months	1·8 (<0·2-12·0)*	0·3 (<0·2-1·4)†
Median (range) serum acetyl 5-amino salicylic acid concentration (μg/ml) at six months	2·5 (0·2-7·8)*	0·5 (<0·2-2·2)†

* 20 patients.
† 17 patients.