SHORT REPORTS

IgA deficiency during D-penicillamine treatment

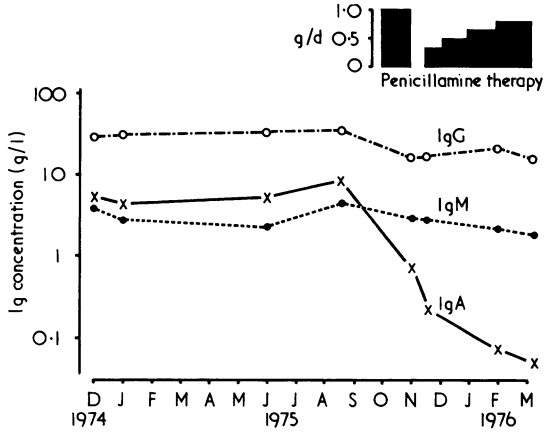
The most common immunodeficiency is a selective lack of IgA, which is found in about 1/700 in the general population.[1] In some instances family cases are found, but usually IgA deficiency seems to be isolated. Against this background it is of great interest to note that IgA deficiency can be induced by phenytoin.[2 3] Recently we observed in a girl with Wilson's disease diminishing IgA levels during treatment with penicillamine. This suggests that exogenous factors have a role in IgA deficiency.

Case report

The patient was a 12-year-old previously healthy girl presenting with haemolytic anaemia, succeeded by macroscopic haematuria, oedema of the legs, and severe liver dysfunction with low serum albumin (23 g/l) and definitely raised immunoglobulin concentrations (IgG 28, IgA 9, and IgM 4·2 g/l). Complement factors were depressed: C3 <0·15 g/l and C4 45%. There were also signs of impaired renal function. Blood haemoglobin, leucocytes, and differential counts were normal but the platelet count was reduced to 60-100 $\times 10^9$/l. Wilson's disease was diagnosed from the findings of low serum ceruloplasmin concentration (0·025 g/l); the presence of a prominent Kayser-Fleischer ring; a "sunflower" cataract; and a high excretion rate of urinary copper.

D-penicillamine treatment, 1 g daily, was started in October 1975 but was withdrawn after one month because of extensive skin erythema. The drug was reintroduced in a low dose after two weeks together with pyridoxine. The D-penicillamine dosage was slowly increased, but after four months at 0·75 g daily, thrombocytopenia—a platelet count down to 13×10^9/l—appeared. A new attempt is now being made to restart D-penicillamine together with corticosteroids.

During D-penicillamine treatment the IgG and IgM concentrations decreased moderately (see figure), whereas the reduction in IgA concentration was drastic. This reached very low levels (0·075 g/l) after four months' treatment. IgE was 24 U/ml at that time. The patient had 55% T-lymphocytes (sheep red-cell-rosette forming cells) and 21% B-lymphocytes (membrane-Ig positive cells). The results of stimulation of the patient's lymphocytes with PHA, ConA, PWM, PPD, and Candida antigen were normal. The last two antigens also induced lymphocyte-mediated inhibition of leucocyte mobility. There was a normal development of Ig-containing cells after PWM stimulation. IgA-containing cells also appeared. The patient had no detectable antibodies against IgA.



Immunoglobulin concentrations in relation to treatment with D-penicillamine.

Discussion

Our suspicion that the D-penicillamine treatment may have caused the IgA deficiency in this case is strengthened by a recent report by Strickland and Leu,[4] where low IgA levels were found in six out of 40 patients with Wilson's disease, most of whom had been treated with D-penicillamine. IgA deficiency was also suggested by Rimbaud *et al*[5] on the basis of immunoelectrophoretic analysis in a patient with Wilson's disease treated by D-penicillamine. On the other hand, we found normal IgA levels in eight patients with Wilson's disease who had been treated with D-penicillamine for up to 14 years (samples kindly supplied by Dr Irmin Sternlieb, Albert Einstein College of Medicine, New York).

Since penicillamine is being increasingly used in treating conditions other than Wilson's disease—for example, rheumatoid arthritis—it may be of importance to analyse further its possible relationship to IgA deficiency.

[1] Bachmann, R, *Scandinavian Journal of Clinical and Laboratory Investigation*, 1965, **17**, 316.
[2] Aarli, J A, and Tönder, O, *Scandinavian Journal of Immunology*, 1975, **4**, 391.
[3] Seager, J, *et al*, *Lancet*, 1975, **2**, 632.
[4] Strickland, G T, and Leu, M-L, *Médicine*, 1975, **54**, 113.
[5] Rimbaud, P, *et al*, *Mèdecine et Chirurgie Digestives*, 1973, **2**, 3.

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Meningitis due to Escherichia coli 09 in a patient with uraemia

Escherichia coli causes meningitis in infants but rarely in adults,[1] in whom it is usually secondary to trauma to the central nervous system[1] and occasionally caused by bacteraemia.[2] We describe a fatal case of meningitis caused by *E coli* 09, a known urinary pathogen, in a Zambian woman with pyelonephritis.

Case report

A young Zambian woman was admitted to the University Teaching Hospital with a history of vomiting and bloody diarrhoea for three days and of a generalised seizure immediately before admission. She was febrile and comatose, responding only to painful stimuli, and had mild dehydration and deep rapid respiration. There was severe neck rigidity with bilateral extensor plantar responses but no focal neurological signs. The results of laboratory investigations on admission were: haemoglobin 10·5 g/dl; white cell count $14·6 \times 10^9$/l (14 600/mm^3); serum sodium 137 mmol(mEq)/l; potassium 4·8 mmol(mEq)/l; chloride 98 mmol(mEq)/l; urea 69 mmol/l 415 mg/100 ml); cerebrospinal fluid contained red blood cells 7×10^9/l (7000/mm^3), white blood cells 4×10^9/l (4000/mm^3) (polymorphs 80%, lymphocytes 20%), protein 2·8 g/l (280 mg/100 ml); glucose 2·2 mmol/l (40 mg/100 ml). The urine contained moderate amounts of albumin, and innumerable pus cells and red blood cells in the sediment. *E coli* was grown on culture of both the cerebrospinal fluid and the urine. Stool culture showed no pathogens. The *E coli* isolated from the specimen of cerebrospinal fluid and the urine were identical—serogroup 09 motile but H untyped.

The meningitis was treated initially with a high dose of ampicillin, to which gentamicin was added after 36 hours. The blood urea concentration rose steadily, and the patient became increasingly acidotic. Peritoneal dialysis was started 72 hours after admission. This successfully corrected her metabolic abnormalities, but her neurological condition deteriorated despite antibiotic treatment, and the patient died five days after admission.

At necropsy the meninges were found to be thickened and covered with a purulent exudate. The brain was soft, and the cut surface showed congestion and oedema. The ventricles were filled with pus. Both kidneys were small (l 46 g, r 45 g) with a finely granular surface and adherent capsule. The cortex and medulla were both small, and the renal substance contained several small pus-filled cavities. Histologically the kidneys showed features of membranoproliferative glomerulonephritis with an acute on chronic pyelonephritis. The bladder was small with features of chronic nonspecific