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SHORT REPORTS

Reticulo-endothelial phagocytosis in patients with nephritis

The reticuloendothelial system (RES) plays an important part in removing circulating immune complexes, particularly those which are large and fix complement.¹ Such circulating complexes lead to nephritis and various forms of vasculitis.² We therefore thought it important to assess the clearance capacity of the reticuloendothelial cells in different types of nephritis. Salky, Mills, and diLuzio³ have reported an increased RES clearance for an artificial lipid emulsion in many immunological diseases such as rheumatoid arthritis, and systemic lupus erythematosus, and in rheumatic fever with polyarthritis, but it is more convenient to measure the clearance of heat-aggregated iodinated human serum albumin. We used this method for studying RES function in renal transplant recipients,⁴ and heat-aggregated human serum gammaglobulin for studying renal glomerular mesangial cell phagocytosis in animals with experimental nephritis.

Methods and results

Patients attending the outpatient clinic with nephritis were asked to volunteer for the study. Ward patients convalescing from myocardial infarction were the normal controls, and gave informed consent. Aggregated human serum albumin, containing a tracer quantity of iodinated human serum albumin (Radiochemicals, Amersham), was prepared.⁴ For each test patients were given an intravenous dose of 150 mg sodium iodide to block the thyroid gland, and 10 minutes later they were given intravenously through a Venflon needle iodinated aggregated albumin, 5 mg per kg body weight. Thereafter 2.0 ml blood samples were taken with precise timing at two-minute intervals for 12 minutes, and again at 15 and 20 minutes, into EDTA anticoagulant. The value for each patient was expressed as the half-time of the clearance in minutes (T_{50}).

The overall results are presented in the figure, which also illustrates the activity of individual cases. An increased RES clearance capacity, as judged by a shorter half-time of clearance of aggregated albumin, was present in patients with proliferative and membranous nephritis, and also in those with

mesangial IgA disease and with active Henoch-Schönlein disease. Patients with active disease were those with increased RES phagocytosis, even among the patients with focal nephritis whose mean values were in the normal range. Patients with lipodystrophy gave clearance values within the normal range, and three patients with lipodystrophy and mesangiocapillary nephritis had clearances close to the normal values.

Discussion

Increased RES activity in proliferative and membranous nephritis probably reflects the occurrence of circulating immune complexes or continued antigenic stimulation. Unfortunately there is no way in man for measuring the activity of the mesangial cells, as is the case in animals. Nevertheless, a test for whole body RES phagocytic activity should be useful for assessing the effects of anti-inflammatory drugs.

The finding of increased RES activity in mesangial IgA disease is important since it explains in part why IgA is found in this condition. Mesangial IgA disease probably forms part of a spectrum of disease which merges with the Henoch-Schönlein syndrome, and our results (see figure) certainly support this statement. Indeed, probably the mesangial uptake of IgA is part of a generalised increase of RES activity, which in turn may be due to some alteration of the IgA molecule.

In mesangiocapillary nephritis there is manifest mesangial activity. Nevertheless, none of our cases showed any significant increase of overall RES activity. Moreover, the slower clearances in this group were in patients who also have lipodystrophy. Since at necropsy lipodystrophy patients are found to have Kupffer cells laden with lipid, this is a possible explanation of the findings. Alternatively, the receptor sites on the Kupffer cells are blocked by some other means.

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The figure shows the distribution of aggregated albumin half-lives (T_{50}) in the various categories of nephritis and also whether the patients had active, subacute, or inactive disease at the time of study. (The mean values for patients with proliferative and membranous nephritis and for mesangial IgA disease and Henoch's nephritis were all significant at $P < 0.001$.)

Attempted suicide in labour

While suicide in pregnancy is uncommon, attempted suicide seems as prevalent in pregnant as in non-pregnant women.¹ But two reviews of attempted suicide in pregnancy^{1,2} found that attempts were uncommon in the third trimester and none had occurred in labour.

Case report

The patient, a 20-year-old unmarried English girl, had a past history of petit mal epilepsy, intermittent depression, and premenstrual tension.

In February 1974 she stopped taking an oral contraceptive because of irregular bleeding. She soon became pregnant, although she did not realise the implications of the amenorrhoea and went ahead with a yellow fever vaccination preparatory to a visit abroad. Eventually, at 18 weeks, she booked in for hospital confinement. The pregnancy was uneventful until 37 weeks, when she was admitted for rest because of a blood pressure of 150/100 mm Hg. She was prescribed diazepam 10 mg three times a day and amylorbarbitone 200 mg at night. Eight days after admission she spontaneously went into labour. Two hours after its onset she was found deeply unconscious, responding only to deep pain. Her locker was found to contain a hoard of 13 diazepam and 2 amylorbarbitone tablets. Her plasma barbiturate level was 0.1 mmol/l (2.2 mg/100 ml). The labour progressed normally and the fetal heart was monitored. Five hours after the onset of labour she began to recover consciousness and after eight hours was delivered of a live boy weighing 2325 g. In the puerperium she confessed that she had been told by a neighbour that the yellow fever injection would cause a malformed baby. This fear had evidently haunted her throughout the pregnancy and she took her carefully hoarded tablets when she recognised the onset of labour. Thereafter she made good progress. She was followed up in psychiatric outpatients, but had no overt evidence of depression.

The baby cried at birth and required only routine resuscitation. His cord blood barbiturate level was 0.07 mmol/l (1.3 mg/100 ml), but he remained cold, hypotonic, and areflexic. His breathing was shallow and irregular and he had to be fed by tube because his sucking reflex was absent. After 48 hours he improved and bottle-feeding was gradually introduced.

Comment

In attempted suicide in labour two individuals rather than one are poisoned. Barbiturates pass freely from mother to fetus across the placenta and the blood levels equilibrate within minutes after an intravenous injection. Some fetal depression is to be expected if oral amylorbarbitone is given between 30 minutes and 6 hours before delivery.³ Cord blood barbiturate levels, however, do not correlate well with the degree of neonatal depression.⁴ Since in the present case the mother took the tablets about seven to eight hours before delivery the prolonged neonatal depression in the baby was presumably due to the diazepam. This accords with the findings of McCarthy *et al.*,⁵ who found rising fetal blood levels of diazepam over the first 30-48 hours after large doses by mouth to the mother in labour because of massive storage of the drug initially in the fetal tissues. Diazepam is commonly given in current obstetric practice, and nursing staff should ensure that the drugs issued are actually taken by any patient who might possibly take an overdose.

I am indebted to Mr David Cowie for his help and advice.

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Myxoedema and hydrocele

Serous effusions have been recognised as an uncommon complication of hypothyroidism for many years,^{1,2} pleural and pericardial effusions and ascites being most commonly described. Only one previous report has appeared in which hypothyroidism was associated with hydroceles, which resolved on treatment with thyroxine.³ We describe here a similar patient seen recently.

Case report

A 66-year-old retired hospital porter had been unwell for a year. During the six months before admission he had suffered from dryness of the skin; intolerance to cold; constipation; shortness of breath; hoarseness; and

slowing of his movements, speech, and thought processes. He felt dizzy and had had frequent falls. In addition he had had a large swelling of the right testicle. Recently he had spent most of the day asleep. Admission was precipitated by an upper respiratory tract infection. On examination he had classical gross myxoedema. His temperature was 34.4°C, his blood pressure 220/120 mm Hg, and there was evidence of airways obstruction and mild cardiac failure. There was a right scrotal swelling about 10 cm by 8 cm, which felt hard and smooth and was not easy to transilluminate (fig 1a).

(a) Appearance before treatment (urinary catheter in situ). (b) Appearance after four months' treatment.

Investigations showed a serum thyroxine of <10 nmol/l (normal range 58-128) and an effective thyroxine ratio of 0.78 (normal range 0.86-1.05). Thyroglobulin antibodies were positive at a dilution of 1/5000, and thyroid microsomal antibodies at 1/6 500 000. The chest x-ray film showed bilateral pleural effusions and cardiomegaly, and the results of echocardiography was consistent with a small pericardial effusion.

Treatment was started with ampicillin, physiotherapy, and L-thyroxine, 0.05 mg daily. Despite treatment his general condition deteriorated and four days later he was unrousable and in respiratory failure, and was transferred to the intensive therapy unit for assisted ventilation. He gradually improved and was finally discharged six weeks after admission on L-thyroxine, 0.2 mg daily. The scrotal swelling was treated conservatively and slowly decreased in size. Four weeks after discharge it was much smaller and easily transilluminable.

After four months' treatment, he was much improved, normotensive, and clinically euthyroid. His chest x-ray film was clear. A small hydrocele persisted on the right side, and in addition a second small hydrocele could be palpated on the other side (fig 1b). These caused the patient no problem and no other form of treatment was required.

Discussion

Pleural, pericardial, peritoneal, synovial, middle ear, and uveal effusions have been recorded in hypothyroidism. The subject has recently been reviewed and the first documented case of hypothyroidism associated with bilateral hydroceles recorded.³ This patient was a 51-year-old man, who, as in our case, had severe autoimmune hypothyroidism, and whose hydroceles resolved after three weeks treatment with thyroxine. This initial report made us suspect that our patient's large hard scrotal swelling was in fact a tense hydrocele, and that expectant treatment was justified. The fact that resolution on treatment was incomplete suggests that our patient may have had small bilateral hydroceles initially, one of which became grossly enlarged in association with the development of hypothyroidism. The occurrence of these two cases within a short period may indicate that the association is not rare and that previous cases have been overlooked. Both reports suggest that aspiration of hydroceles in hypothyroidism is unnecessary, and treatment of the underlying disease with thyroxine should cause adequate resolution.

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