Discussion

Measles giant-cell pneumonia has mainly been described in children with immunological deficiencies,[1 2] although a paper describing Kenyan children with measles and pneumonia concluded that most cases of pneumonia were viral.[3] In adults two cases of measles pneumonia have been reported, both fatal. One patient had a malignant reticulosis,[4] and the other, also a 28-year-old woman, had an unclassified blood dyscrasia since childhood.[5]

The case I describe had no significant past history or gross immunological deficiency. Giant-cell measles pneumonia is a histological diagnosis not usually made during life, but the clinical picture, specific rise in antibody titre, and lack of bacterial growth lead us to consider this such a case.

I thank Dr J F Dow for permission to report on a patient under his care, and Dr J C Batten, Dr M J Boyd, and Dr J G Collier for their help and advice. Virological investigations were undertaken by Professor H Stern.

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Delayed healing of varicose ulcer with levamisole

Levamisole (L-tetramisole), an anthelmintic drug, has been reported to restore delayed hypersensitivity reaction in patients with cancer.[1] The possible role of cell-mediated immunity in the pathogenesis of rheumatoid arthritis has been summarised by Yu and Peter.[2] Huskisson *et al*[3] and Veys *et al*[4] reported encouraging results of levamisole in patients with rheumatoid arthritis, whereas Dinai and Pras[5] found no improvement and in some patients the arthritis even became worse. We have recently studied the effect of levamisole in rheumatoid arthritis. In one patient a healed varicose ulcer broke down and healed only with withdrawal of the drug. Since this possible complication has not apparently been reported we thought that it would be of interest.

Case history

A 67-year-old woman was seen first in May 1975 with a six-month history of polyarthritis. She had had morning stiffness and enlargement of several joints. She had been treated with salicylate, phenylbutazone, indomethacin, naproxen, ibuprofen, and more recently benorylate. Ten years earlier her varicose veins had been surgically stripped, and she had had a recent varicose ulcer which had completely healed. The results of laboratory tests included haemoglobin 9·5 g/dl, erythrocyte sedimentation rate 88 mm in first hour, and rheumatoid factor strongly positive at a titre of 1/2048. *X*-ray films of joints showed erosive changes typical of rheumatoid arthritis in many joints. The final factor of relevance was a history of penicillin allergy.

Treatment was begun in September 1975 with levamisole 50 mg, three times daily. One month later the patient complained of headache, dizziness, and vomiting, which she attributed to levamisole. She had also noticed that the healed varicose ulcer had started to break down. In December 1975 her arthritis had improved but the ulcer remained broken. Zinc sulphate, 660 mg daily, was begun. In February 1976 the patient developed purpuric rash on both forearms which disappeared after two weeks when levamisole medication was given on only two days each week. Nevertheless, the ulcer deteriorated and became larger and septic despite antibiotic ointment and Viscopaste dressings.

In June 1976 the patient developed mouth ulcers. The varicose ulcer reached 6 cm in diameter and had an irregular margin and purulent discharge, while satellite ulcers appeared round its edge. Levamisole was stopped; the ulcer healed completely in one month; and the mouth ulcers, headache, and anorexia disappeared.

Discussion

Rash, fever, anorexia, nausea, giddiness, mouth ulcers, granulocytopenia, tremor, disturbance of taste, neurosensory irritability, and transient gastralgia have been the side effects of levamisole reported so far.[3-5] In our patient treatment with levamisole was accompanied by the breakdown of a previously healed gravitational ulcer which promptly healed when the drug was discontinued. It is extremely difficult to be certain whether or not levamisole can be implicated as the cause of the breakdown of the ulcer, but it is surprising that not only did the ulcer continue to increase in size the longer the drug was prescribed, but satellite ulcers also appeared. The ulcer measured about 6 cm in diameter when levamisole was discontinued and had healed completely after only one month.

One would have to challenge the patient with a further course of levamisole to see whether the same events occurred to be certain of the causal relationship, but this we consider ethically unjustified. The post hoc, ergo propter hoc is a common fallacy in clinical medicine. Though we cannot prove this causal relationship, we know of no effect of levamisole on collagen turnover and wound healing other than its effect on cellular immunity.

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Retinitis pigmentosa and autoimmune endocrine abnormalities in identical twins

We report the concurrence of retinitis pigmentosa with autoimmune diseases in identical twin sisters, an association not previously described.

Case reports

Case 1—a 59-year-old woman, deaf and dumb since birth, was admitted to hospital with suspected gastroenteritis. She was found, however, to have hyperthyroidism; there were no ocular signs, but ophthalmoscopy showed retinitis pigmentosa.

The diagnosis of hyperthyroidism was confirmed biochemically, the serum thyroxine-iodine being 244 nmol/l (3·1 ng/ml) (normal range 60-140 nmol/l (1-1·8 ng/100 ml)) and the serum triiodothyronine 9 nmol/l (6 ng/ml) (normal range 1·25-3·75 nmol/l (0·8-2·4 ng/ml)). The 4-hour thyroid uptake of ^{132}I was increased at 83% and a thyroid scan showed a moderate goitre of the Graves's type. The serum cortisol concentrations before and after tetracosactrin stimulation were within the normal range and the resting plasma corticotrophin concentration was normal at 23 pg/l. The thyroglobulin red-cell agglutination titre was 1/25 000.

Immunofluorescence tests showed the presence of thyroid colloid and microsomal antibodies, and adrenocortical antibodies (twice, strongly positive) but gastric parietal cell, intrinsic factor, and mitochondrial and smooth muscle antibodies were not detected. Test results for rheumatoid and antinuclear factors were negative. The patient was given carbimazole

and subsequently treated with radioactive iodine (^{131}I). She made a good recovery.

Case 2.—This patient, who was the only sibling of patient 1, died at another hospital at the age of 52. According to relatives the two sisters were identical twins. She had been admitted with a short history of vomiting and fainting. She had congenital deaf mutism and retinitis pigmentosa with generalised pigmentation of the Addisonian type. She became severely hypotensive and died.

At necropsy no adrenal tissue was found on the left side, and the right adrenal was grossly atrophic. There was no other evidence of endocrine disease or tuberculosis. The diagnosis was Addison's disease.

Comment

Retinitis pigmentosa is often genetically determined, the mode of inheritance being dominant, recessive, or X-linked—for example, Usher's syndrome (retinitis pigmentosa with nerve deafness) usually behaves as an autosomal recessive trait.[1] In Graves's disease hereditary factors are well recognised, although the mode of inheritance is controversial. The tendency to form thyroid autoantibodies is heritable, however, and probably under polygenic control.[2] In patient 1, autoantibodies to both thyroid (colloid and microsomal) and adrenal cortex were present. Although no results of immunological tests were available for patient 2 both adrenal and thyroid antibodies probably would have been present as adrenal atrophy and chronic thyroiditis frequently coexist.[3] Otherwise the family history of our two patients was non-contributory. There was no history of visual abnormalities, congenital deafness, or of endocrine disease in any of their near relatives, nor of consanguinity in their parents. Probably, however, their predisposition to nerve deafness, retinitis pigmentosa, and endocrine disease was genetically determined. It would be valuable to assess the prevalence of autoantibodies and of autoimmune disorders in other patients with retinitis pigmentosa. The recent finding of raised concentrations of immunoglobulins in this condition[4] adds further impetus to such a study.

We are indebted to Dr R A Thompson, Regional Immunology Laboratory, East Birmingham Hospital, for the adrenal antibody studies and to Dr J C Davies, University of Liverpool Subdepartment of Endocrine Pathology, for carrying out the corticotrophin estimation. We thank Dr I Goldberg for suggestions and advice and Dr R M Evans for permission to report details of Case 2. The ophthalmological diagnosis in Case 1 was confirmed by Dr H M Rose.

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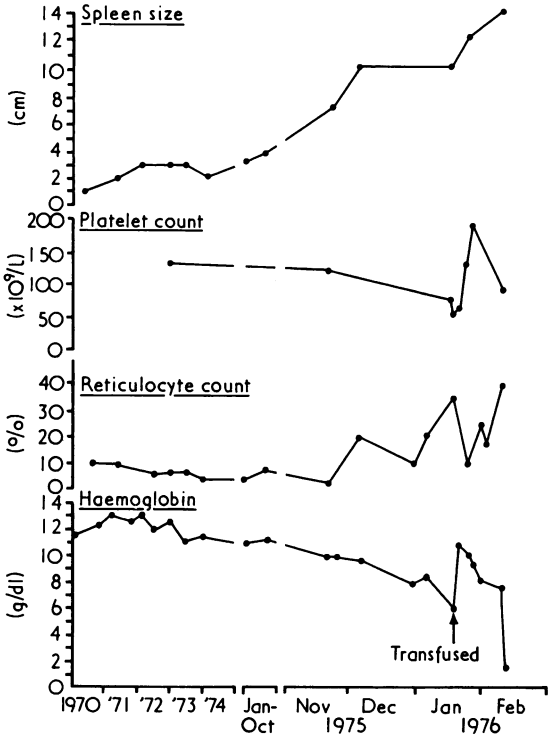
Acute splenic sequestration crisis preceded by hypersplenism in haemoglobin SC disease

Fatal splenic sequestration crises may occur suddenly in homozygous sickle cell anaemia (HbSS),[1] haemoglobin SC disease (HbSC),[2] and sickle thalassaemia (HbS/Thal).[3] In reported cases there has been no mention of warning signs. We, therefore, report such a crisis in a patient with HbSC who had recently developed hypersplenism.

Case report

A 12-year-old West Indian girl with HbSC was admitted only twice for painful crises between 1966 and 1974. Her haemoglobin concentration remained between 11 and 13 g/dl and her spleen 3 cm below the costal margin during these years (figure). Between November 1975 and January 1976 she was admitted four times and her haemoglobin level fell from 10·3 g/dl to 6·1 g/dl. During the fourth admission, precipitated by a minor chest infection, her platelet count was 70×10^9/l, reticulocytes 16%, and white cells $5{\cdot}1 \times 10^9$/l. Bleeding, clotting, partial thromboplastin and prothrombin times, and fibrin degradation products were normal, thus excluding consumption coagulopathy. A serum bilirubin of 25 μmol/l made haemolysis unlikely. She was transfused, but over the next two weeks her haemoglobin concentration fell again to 8·3 g/dl. Her spleen had gradually enlarged to 13 cm below the costal margin over the preceding two months (figure).



Clinical course in patient

Hypersplenism was diagnosed and we decided to transfuse her weekly to a haemoglobin concentration of 12 g/dl to suppress production of sickle haemoglobin before splenectomy. On 10 February 1976 her haemoglobin was 7·7 g/dl and transfusion was planned for two days later. Nevertheless, after only 24 hours she was admitted moribund and suffered an immediate cardiac arrest. Resuscitation was unsuccessful and final laboratory tests showed a haemoglobin concentration of 1·4 g/dl, and white cell count $52{\cdot}3 \times 10^9$/l.

Necropsy showed pallor of all organs except the spleen, which was congested and weighed 2210 g (normal 200 g). Histological examination showed considerable sickling in the red pulp of the spleen and sinusoids of the liver. The sinusoids of both organs were packed with nucleated cells, many of which contained phagocytosed red cells.

Discussion

Palpable splenomegaly occurs in at least half of patients with HbSC disease (present in nine of our eighteen paediatric patients) and life-threatening sudden splenic sequestration crisis may occur in young patients with HbSS and HbSC before splenic infarction has led to fibrosis. Seeler and Shwiaki[4] reported 20 episodes of sequestration crisis in children aged between 6 and 55 months; four died and four had one or more recurrences. They found platelet counts below 150×10^9/l in 11 of the 16 patients in whom platelets were measured, and we have also observed thrombocytopenia in a 2-year-old girl with HbSS with splenic sequestration; her haemoglobin concentration was 2·0 g/dl, platelets 31×10^9/l, white cells $27{\cdot}7 \times 10^9$/l. Thus thrombocytopenia is an important indicator of splenic sequestration since, although septicaemia may also induce thrombocytopenia, in 15 of 16 anaemic crises *not* due to sequestration the platelet count was normal.[5] Splenectomy as prophylaxis against recurrent sequestration crisis in young children carries a risk of overwhelming bacteraemia