histological changes of sarcoidosis. She was followed for a further four years without further incident. At no time during the 11 years that she was under supervision was evidence found to suggest a sarcoid lesion anywhere else than in her right lung and right breast.

Comment

Goldman has recently drawn attention to the rare occurrence of tuberculosis in breast tissue.² This case may help to remind clinicians of the need to consider granulomas in the differential diagnosis of mammary disorders.

I thank Dr R I K Elliott for providing the photomicrograph.

- ¹ Scadding, J G, *Sarcoidosis*, p 385. London, Eyre and Spottiswoode, 1967.
² Goldman, K P, *Tubercle*, 1978, **59**, 41.

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Transient myeloid and erythroid aplasia associated with infectious hepatitis

Bone marrow aplasia is an uncommon but serious sequel to acute infectious hepatitis. This form of aplasia occurs predominantly in teenagers and young adults, typically running a protracted course with a mortality of 85% during the first 16 months in 174 cases reported up to 1975.¹ Early bone marrow transplantation has been advocated because of this ominous prognosis.² We have, however, observed a case of marrow depression associated with acute infectious hepatitis which displayed features departing considerably from the reported pattern: the aplasia did not affect megakaryocytes, and complete haematological recovery occurred after four weeks of myeloid and erythroid aplasia.

Case report

A 26-year-old woman in the third trimester of her second pregnancy developed polyarthralgia, malaise, and maculopapular rash, followed after five weeks by features of acute hepatitis. The liver was moderately enlarged and there was no splenomegaly or lymphadenopathy. Sole exposure to drugs had been penicillin administered during the preceding week. Plasma concentration of bilirubin was 20 $\mu\text{mol/l}$, alkaline phosphatase 370 IU/l, and

aspartate transaminase 220 IU/l. Radioimmunoassay showed no hepatitis B surface antigen or antibody. IgA antibody to hepatitis A was detected, but there was no IgM antibody, indicating past but not recent infection with hepatitis A.³ No rise in titre occurred in antibodies to toxoplasma or cytomegalovirus, and no antinuclear factor or heterophile antibody was detected. Antibody to Epstein-Barr virus was not determined. Liver function deteriorated further, and three weeks later a healthy premature infant was delivered. At this time the patient developed fever, and severe neutropenia was detected. Marrow aspiration and trephine showed considerable erythroid and complete myeloid depression but normal numbers of megakaryocytes. Severe neutropenia persisted for 27 days and was associated with high fever. Treatment consisted of intravenous antibiotics, bowel sterilisation, and 17 leucocyte transfusions. Extensive postpartum haemorrhage secondary to clotting factor deficiency was treated successfully with fresh frozen plasma. The platelet count remained normal throughout the illness except for a transient fall during the haemorrhage, and was attributed to effects of transfusion with 26 units of blood in four days. Weekly studies showed no change in the bone marrow until neutrophils reappeared in peripheral blood on day 27. The aspirate then showed 33% erythroblasts and 62% granulocyte precursors. The fever resolved, and normal blood counts were permanently restored after two days. Resolution of abnormal liver function required three months before serum alkaline phosphatase became normal. Needle biopsy of the liver on day 28 showed a picture consistent with resolving acute viral hepatitis.

Comment

Marrow depression is a well-recognised sequel to acute infectious hepatitis, but this case indicates that there may be greater variability in the marrow injury and its course than had been appreciated.^{1,2} No explanation for the deviation from the usual pattern of protracted aplasia affecting all cell series was evident from the features of the preceding hepatic illness, which satisfied accepted criteria.^{1,2} Serological evidence indicated that the hepatitis was not due to hepatitis B, which was consistent with previous experience,¹ but due to non-A, non-B viral hepatitis.³ The spontaneous recovery of haemopoiesis clearly indicates that progression to protracted aplasia is not inevitable, and that in our patient early marrow transplantation would have been inappropriate. In one other case aplasia affected only myeloid series, but death from sepsis supervened,⁴ so that it remains to be established whether persistence of one or two cell series predisposes to earlier haemopoietic recovery.

One possible pathogenic mechanism is an autoimmune process initiated by viral infection and directed against haemopoietic tissue,⁵ although this case provided no supportive evidence as recovery occurred in the absence of glucocorticoid or cytotoxic immunosuppressive treatment.

We thank Dr B Dwyer for referring this patient.

¹ Hagler, L, *et al*, *Medicine*, 1975, **54**, 139.

² Camitta, B M, *et al*, *Blood*, 1974, **43**, 473.

³ Lehman, N I, and Gust, I D, *Medical Journal of Australia*, 1977, **2**, 731.

⁴ Dische, F E, and Golding, J R, *British Medical Journal*, 1957, **2**, 738.

⁵ Royal Marsden Hospital Bone-Marrow Transplantation Team, *Lancet*, 1977, **2**, 742.

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Course of peripheral blood indices relative to time of delivery.

Intermittent ophthalmoplegia

Intermittent severe ophthalmoplegia with complete normality between attacks occurred over several years in a woman. We present evidence of an unrecognised part of the range of dysthyroid eye disease, and the case shows the initial diagnostic confusion that may occur.

Case report

A 35-year-old housewife was referred to us in 1975 with a two-year history of recurrent episodes of ophthalmoplegia with painful, red, oedematous eyes;

ptosis; and diplopia. An episode affected either or both eyes and lasted one to three weeks. The patient was completely normal between attacks. She had had a partial thyroidectomy when aged 19 years for hyperthyroidism with exophthalmos. There had been complete recovery, and no thyroid medication was given. A sister aged 50 years had also had hyperthyroidism. There were no recent symptoms of thyroid, muscular, or neurological disease. Throughout two and a half years of observation by us the patient remained clinically euthyroid. Changes comprising eye pain, swelling of eye muscles, redness and oedema of conjunctivae, and severe ophthalmoplegia affected one or both eyes to differing extents in different episodes. The most usual restriction of eye movement was upwards, but sometimes lateral or medial deviation was the more severe abnormality. During a representative period without treatment consecutive attacks came at intervals of 29, 32, 18, 8, 3, 23, 55, 21, 10, 13, 17, and 25 days. They were not associated with menstruation or changes in body weight. There was no myasthenia, and Tensilon testing was normal on three occasions. There was no exophthalmos, maximum Hurtle reading at 100 mm separation being 16 mm.

Serum thyroxine (T4) and triiodothyronine (T3) have been normal on nearly all occasions (figure). Serum thyroid stimulating hormone (TSH) was

or improvement over months or years.¹ In our patient eye symptoms fluctuated relatively rapidly, with complete remissions between attacks, but over the four years before prednisone was started the severity had not changed. We believe that we have witnessed an unrecorded part of the range of dysthyroid eye disease.

We thank Drs K Mashiter and A Goolden for thyroid hormone estimations, Professor D S Munro for LATS and LATS-P assays, Professor Deborah Doniach for antibody studies, and Dr G B Hollings for referring the patient.

¹ Rundle, F F, *The Thyroid Gland*. London, Butterworths, 1964.

² Lawton, N F, *Proceedings of the Royal Society of Medicine*, 1977, **70**, 698.

³ Gorman, C A, in *Clinics in Endocrinology and Metabolism*, vol 7, No 1. London, W B Saunders, 1978.

⁴ Doniach, D, *Proceedings of the Royal Society of Medicine*, 1977, **70**, 695.

⁵ Dirmikis, S, Kendall-Taylor, P, and Munro, D S, *Thyroid Research*. New York, Excerpta Medica, 1976.

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Measurement in case of intermittent ophthalmoplegia. Normal ranges are hatched. Arrows show peak serum TSH response (normal < 25 mU/l) after TRH 200 µg intravenously.

Conversion: SI to traditional units—T4: 1 nmol/l ≈ 0.78 ng/ml. T3: 1 nmol/l ≈ 0.65 ng/ml.

usually at or slightly above the upper limit of normal, both basally and after thyrotrophin releasing hormone (TRH) 200 µg intravenously. Free thyroxine index, neck uptake of technetium, and T3 suppression were all normal. Long-acting thyroid stimulator (LATS) and LATS-protector were not detected. Thyroid antibodies were positive (tanned red cells titre 640, cytoplasm haemagglutination titre 6400). Serum complement, full blood count, and ESR were always normal and there were no circulating immune complexes. Radiology of the optic foramina, pituitary fossa, and orbital veins was normal. An EMI scan showed slightly enlarged eye muscles. In May 1977 prednisone 10 mg/day was started empirically. There was a reduction in severity but not frequency of symptoms. We have titrated the dose of prednisone against the severity of symptoms and found 10 mg/day to be the lowest reasonably effective dose.

Comment

The history, family history, and antibody studies all implicate the thyroid gland. Alternative diagnoses such as myasthenia gravis, orbital tumour, multiple sclerosis, and ethmoiditis are now excluded. Ophthalmoplegia and other eye signs occur in association with both hyper- and hypo-thyroidism,¹⁻³ but the pathogenesis remains enigmatic. An association with abnormal thyroid antibodies directed against orbital tissues has been proposed.⁴ In hyperthyroidism either LATS or LATS-protector are detectable in 90% of patients.⁵ The natural time course of dysthyroid eye disease is of gradual worsening

Hashimoto's thyroiditis presenting as T3 toxicosis

In the early phases of Hashimoto's thyroiditis the patient may have the clinical features of hyperthyroidism,¹ usually associated with increased secretion of thyroxine. We describe here a case of Hashimoto's thyroiditis presenting with hyperthyroidism associated with increased secretion of triiodothyronine rather than thyroxine, and this particular patient shows elegantly the progression from T3 toxicosis to hypothyroidism.

Case report

A woman aged 43 was referred to the endocrine clinic in July 1977 complaining of loss of 3.5 kg in weight and a fine tremor of her fingers that interfered with her work as an artist. She was taking no medication. Her mother had suffered from Graves's disease, but there was no other relevant family history. On examination she was fidgety and had lid-lag without exophthalmos and a fine tremor of the fingers. The thyroid gland was not enlarged. The serum thyroxine (T4) concentration was normal but the serum triiodothyronine (T3) concentration was raised (table). Thyroid microsomal antibodies were detected by immunofluorescence (+ ±) but no antibodies to thyroglobulin were detected by the immunofluorescent or tanned red cell techniques.

During the next seven months no treatment was given. The tremor and lid-lag persisted but the weight remained virtually constant. The serum concentration of T4 remained normal and that of T3 was persistently raised. The serum concentration of thyroid stimulating hormone (TSH) was low, and the thyrotrophin-releasing hormone (TRH) test showed a flat response (basal TSH < 1, at 20 min 1.4, and at 60 min < 1 mU/l). In April 1978 the patient said she felt distinctly better, with loss of her tremor and some weight gain.

Serial measurements of serum thyroxine (T4), triiodothyronine (T3), and thyroid stimulating hormone (TSH) concentrations in case of Hashimoto's thyroiditis presenting as T3 toxicosis

	T4 (nmol/l)	T3 (nmol/l)	TSH mU/l	Weight (kg)
July 1977	127	3.35	<1.0	58.00
Sept 1977	141	3.40		58.25
Oct 1977	121	3.55		58.65
Feb 1978	107	3.20		58.93
April 1978	61	1.30	1.3	59.70
May 1978	40	1.60	40.0	61.85
June 1978	37	1.60	50.0	62.70
Normal range	70-160	1.08-2.61	<1-3.5	

Conversion: SI to traditional units—Thyroxine: 1 nmol/l ≈ 0.08 µg/100 ml. Triiodothyronine: 1 nmol/l ≈ 0.06 ng/100 ml.