Cardiac pacing has not been found beneficial, although adrenaline has a temporary effect.[7] Chronic cardiac effects have rarely been described, although Hughes *et al*[8] reported two cases in which cardiac muscle was clinically affected. In one a cardiac vacuolar myopathy similar to that of the more commonly affected skeletal musculature was confirmed histologically at necropsy. Affected cardiac muscle has been found more often in experimental work on animals. The electrocardiographic changes usually found in cases of chronic intoxication are the non-specific changes in ST and T waves of generalised myocardial damage. Complete heart block has not been reported.

Pre-existing cardiac conduction disturbance is a contraindication to the use of chloroquine in rheumatic disorders. Patients receiving high-dose chloroquine treatment should undergo baseline and further, periodic electrocardiographic assessment as frequently as ophthalmological examination—that is, about every six months.

Permanent pacing was instituted in this case because of life-threatening dysrhythmias and the belief that the conduction disturbance was due to chloroquine and probably irreversible; that this is so has not yet been proved.

We thank Mr R Daniel, consultant ophthalmic surgeon, for giving us his opinion on the retinal lesions, and Dr J L Thirkettle, consultant physician at Crawley Hospital, Sussex, for referring the patient.

[1] Martindale, W, *Extra Pharmacopoeia*, ed Ainley Wade, 27th edn, p 344. London, Pharmaceutical Press, 1977.
[2] Rodnan, G P, McEwen, C, and Wallace, S, *Journal of the American Medical Association*, 1973, **224**, 662.
[3] Scherbel, A, *et al*, *New England Journal of Medicine*, 1965, **273**, 360.
[4] Kiel, F W, *Journal of the American Medical Association*, 1964, **190**, 398.
[5] Manku, M S, and Horrobin, D F, *Lancet*, 1976, **2**, 1115.
[6] Charles, D, *et al*, *Bulletin de la Société Médicale d'Afrique Noire de Langue Française*, 1975, **20**, 7.
[7] Michael, T A D, and Aiwazzadeh, S, *American Heart Journal*, 1970, **79**, 831.
[8] Hughes, J T, *et al*, *Quarterly Journal of Medicine*, 1971, **40**, 85.

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# SHORT REPORTS

## Renal failure due to glomerulonephritis in sarcoidosis

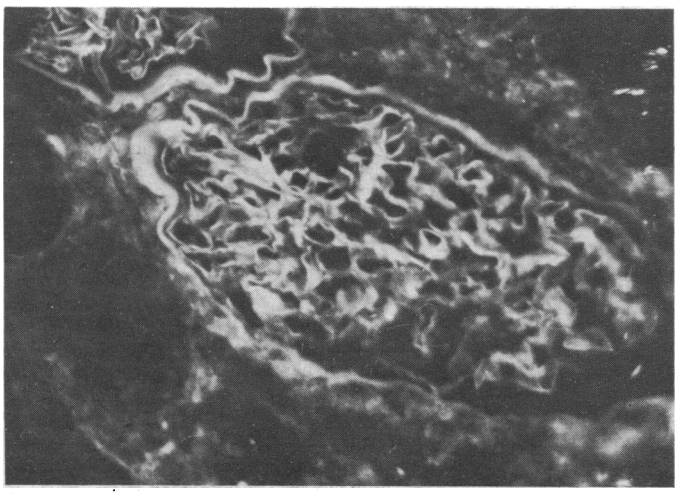
Renal failure in sarcoidosis is uncommon and may be due to hypercalcaemia,[1] lesions of the kidney itself (the typical non-caseating granulomata),[2] or, rarely, glomerulonephritis.[3] We report a case of sarcoidosis in which severe renal failure was associated with mesangioproliferative glomerulonephritis.

### Case report

A 43-year-old married woman had been well until 1959, when she presented with weight loss and exertional dyspnoea. Sarcoidosis was diagnosed after open lung biopsy and her symptoms improved with a course of oral steroids. She remained well until June 1977, when she returned with a seven-week history of lassitude, anorexia, weight loss, and joint pains. She was emaciated and pale with a uraemic coloration and acidotic breathing. A few axillary lymph nodes were palpable, and atrophic scars with a faint macular rash on the limbs were present. Her pulse was 100/min and blood pressure 140/80 mm Hg, with a soft, apical, midsystolic murmur. She had moderate enlargement of the liver and spleen and a calcified ovarian cyst. The remaining findings were normal.

Investigations showed a normochromic normocytic anaemia (Hb 7·9 g/dl); the serum concentration of urea was 38·7 mmol/l (232 mg/100 ml), potassium 5·8 mmol(mEq)/l, calcium 2·6 mmol/l (10·4 mg/100 ml), and albumin 3·3 g/l (3·3 mg/100 ml). Her creatinine clearance was 3 ml/min, and urinary protein excretion 0·5–1 g/24 h. The results of the antistreptolysin-O titre, sheep cell agglutination test, latex test, antinuclear factor, and lupus erythematosus cell preparation were all negative. She had normal serum immunoglobulin and complement concentrations. Despite the presence of normal liver function tests, a liver biopsy showed typical sarcoid granulomata. Acid- and alcohol-fast bacilli were not isolated from sputum, urine, or liver, and the result of the Mantoux test was negative, 1/100. A chest *x*-ray film showed right apical nodules. An intravenous pyelogram showed bilateral small, smooth kidneys with no nephrocalcinosis. A renal biopsy specimen showed a mesangioproliferative glomerulonephritis with diffuse, global, granular, and linear deposits of C3, IgG, and IgA in basement membranes and mesangia on immunofluorescence (see figure). No calcification and no sarcoid granulomata were seen.

Initial peritoneal dialysis appreciably improved her condition. Nevertheless, her condition did not stabilise and she was started on prednisolone, 60 mg reducing to 15 mg per day. Her renal function improved and six weeks later the creatinine clearance had risen to 48 ml/min. Her ovarian cyst was removed and she has since remained well.



Fluorescent IgG showing granular deposits largely confined to the mesangial regions and linear staining of the capillary basement membranes (×300).

### Comments

Lebacq *et al*[1] found that renal failure was most conspicuous in the 11% of patients with sarcoid and hypercalcaemia. Nevertheless, our patient's serum calcium concentration was not appreciably raised. Direct involvement of the kidney by sarcoid tissue[2] seems unlikely in this instance in the absence of biopsy evidence, even given the problems of sampling. Thus the cause of the renal failure here is uncertain, although similar pathological findings have been described in sarcoidosis.[3] In two of these cases,[3] as in this instance, both linear and granular immunofluorescence was present.

Although the aetiology of sarcoidosis remains unknown, many of its clinical manifestations such as arthralgia, erythema nodosum, and uveitis are thought to be due to circulating immune complexes, and, using the platelet aggregation technique, Hedfors and Norberg found such complexes in six out of 26 patients.[4] If, as is commonly believed, such glomerular lesions are due to trapped immune complexes, this case would provide further evidence of the importance of immune complexes in sarcoidosis. The factors responsible for these remain unknown, but may result from other immunological disturbances occurring in sarcoidosis.[5]

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[1] Lebacq, E, Verhaegen, H, and Desmet, V, *Postgraduate Medical Journal*, 1970, **46**, 526.
[2] Bolton, W K, *et al*, *Clinical Nephrology*, 1976, **5**, 88.
[3] McCoy, R C, and Tisher, C C, *American Journal of Pathology*, 1972, **68**, 339.
[4] Hedfors, E, and Norberg, R, *Clinical and Experimental Immunology*, 1974, **16**, 493.
[5] James, D G, Neville, E, and Walker, A, *American Journal of Medicine*, 1975, **59**, 388.

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# HLA patterns and diabetic retinopathy

The major cause of morbidity in insulin-dependent diabetic patients is vascular complications—particularly microangiopathy, as reflected by retinopathy and nephropathy. The factors influencing the development of these complications remain poorly understood. Studies in diabetic identical twins have suggested that genetic factors may have a role not only in the liability to diabetes but also in the likelihood of diabetics developing retinopathy.[1] The pattern of HLA antigens is genetically determined and an association between the HLA pattern and several diseases, including insulin-dependent diabetes, has been well established. This investigation aimed at seeking an association between the HLA pattern and liability to or protection from severe diabetic retinopathy in insulin-dependent diabetic patients. Because of a recent report in abstract form,[2] we directed our attention to the antigens HLA-A1 and HLA-B8.

## Patients, methods, and results

Two highly-selected groups of unrelated Caucasian insulin-dependent diabetics were studied. All had developed diabetes at 30 years or less, and the mean age of onset of diabetes was not significantly different between the groups. Group A consisted of 16 patients who had developed obvious severe proliferative retinopathy (recurrent vitreous haemorrhages, fibrous tissue proliferation, or grossly evident neovascularisation) within 25 years of the onset of diabetes. Many also had nephropathy and neuropathy, but the group was defined in terms of the retinopathy. Group B consisted of 14 patients who had survived for at least 25 years after the onset of diabetes without clinical evidence of definite retinopathy, or other microvascular complications. In 12 of these 14 patients the absence of retinopathy was confirmed by fundal photography. Occasional microaneurysms were accepted in patients in this group, but more definite evidence of retinopathy led to their exclusion. The normal controls for the HLA studies were 586 Caucasian blood donors, healthy subjects undergoing multiphasic screening, and laboratory personnel.

*Frequency of absence of HLA–A1, presence of HLA–B8, and pattern HLA–B8 without A1 in the two groups of diabetic patients and in the non-diabetic controls*

| | HLA-A1 negative | HLA-B8 positive | HLA-A1 negative and B8 positive |
|---|---|---|---|
| Group A: proliferative retinopathy (n = 16) | 12 (75%) | 12 (75%)* | 9 (56%)† |
| Group B: no diabetic complications (n = 14) | 7 (50%) | 6 (43%) | 1 (7%) |
| Non-diabetic controls (n = 586) | 68% | 27% | 4% |

*P = 0·03 cf group B, and P < 0·001 cf controls.
†P = 0·005 cf group B, and P < 0·001 cf controls.

HLA typing was performed by standard lymphocytotoxic techniques,[3] and statistical comparison between the two groups of diabetic subjects was performed individually for the antigens A1 and B8 and for the combination B8 without A1, using Fisher's exact test. Comparison of group A with the non-diabetic controls was performed by the $\chi^2$ test (two by two).

The recorded increased prevalence of HLA-B8 in the insulin-dependent diabetic patients was found in both groups of diabetic patients, though significantly more frequently in group A. In addition, the unusual HLA pattern B8 without A1 was greatly increased in frequency in group A patients compared with group B patients and the controls.

## Discussion

Linkage disequilibrium leads to a strong association between the HLA antigens A1 and B8. Thus the pattern B8 without A1 is uncommon, occurring in only 4% of non-diabetic Caucasians. Our study has shown a strong association between this unusual HLA pattern (B8 without A1) and severe proliferative retinopathy in insulin-dependent diabetic patients. Although the number of patients in each group was small, the groups were carefully chosen to represent the extreme ends of the range of liability to diabetic retinopathy. Another report,[4] in which no association between HLA patterns and diabetic microangiopathy was shown, considered a heterogeneous group of diabetic patients of varying duration, type of treatment, and severity of diabetic complications; this may have obscured the relationship.

The strong association of an uncommon HLA-pattern with severe diabetic retinopathy suggests that genetic factors linked to the HLA system may have a dominant role in determining the development of or protection from diabetic complications. This study throws no light on whether this association is secondary to different degrees of metabolic control, hormone levels, immune responses, or other factors possibly associated with the HLA system.

Any consideration of the factors responsible for the development of microvascular complications in insulin-dependent diabetic patients should include a consideration of genetically determined characteristics. In addition, HLA typing allows the identification of a group of patients at particular risk of developing severe retinopathy.

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[1] Pyke, D A, and Tattersall, R B, *Diabetes*, 1973, **22**, 613.
[2] Shin, D, *et al*, *Diabetes*, 1977, **26**, suppl No 1, p 417.
[3] Teresaki, P I, Vredevoe, D L, and Mickey, M R, *Transplantation*, 1967, **5**, 1957.
[4] Chuck, A L, and Cudworth, A G, *Diabetologia*, 1977, **13**, 387.

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# Paget's disease and primary hyperparathyroidism

First described by Albright in 1934,[1] hyperparathyroidism in association with Paget's disease is rare. There has been no report in which the diagnosis of the hyperparathyroidism was made as the result of a raised serum parathyroid hormone concentration.

## Case report

A 73-year-old woman was seen as an outpatient in December 1973 with dizziness, falling attacks, and severe pain and deformity of her right leg. Radiology showed gross Paget's disease localised to the proximal half of the right femoral shaft. No abnormality was seen in a skull *x*-ray film. Serum concentrations were as follows: calcium 3·6 mmol/l (14·4 mg/100 ml), phosphate 0·6 mmol/l (1·9 mg/100 ml), total protein 68 g/l (6·8 g/100 ml),