HLA-DR and DQ antigen frequencies observed in SLE patients and controls from Singapore

Antigen	SLE (n = 26)		Controls (n = 77)	
	n	%	n	%
DR1	0		0	
DR2	7	26.9	21	27.3
DR3	7	26.9 *	12	15.6
DR4	7	26.9	17	22.1
DR7	0		7	9.1
DR8	7	26.9	13	16.9
DR9	9	34.6	19	24.7
DR10	1	3.8	4	5.2
DR11	2	7.7	12	15.6
DR12	5	19.2	20	26.0
DR13	1	3.8	3	3.9
DR14	1	3.8	9	11.7
DQ2	6	23.6	13	16.9
DQ4	4	15.3	9	11.7
DQ5	7	26.9	18	23.4
DQ6	15	57.7	33	42.8
DQ*0601	10	38.4	23	29.9
DQ*0602	3	10.7	7	9.1
DQ*0603-8	2	7.6	3	3.9
DQ7	7	26.9	31	40.3
DQ8	5	19.2	8	10.4
DQ9	8	30.7	25	32.5

* $\chi^2 = 0.99$; odds ratio 2.0; 95% confidence interval 0.51 to 7.83; $p = 0.09$.

also a non-significant increase in DR8.⁴ However, our most striking finding was the absence of a DR2 association with SLE, as this had been found in the studies from Hong Kong and Korea^{4,5} and in a further study from Kuala Lumpur, Malaysia.⁶

One possible explanation for these differences could be genetic admixture in the Singapore Chinese population, as there has been some intermarriage with Malays, Indians, and Europeans since the seventeenth century. In contrast, Hong Kong Chinese rarely marry non-Chinese. This could explain the presence in the Singapore SLE patients of the typical white population SLE susceptibility haplotype carrying DR3 and DQ2. Another explanation could be ethnic heterogeneity among the southern Chinese. In Singapore, for example, approximately 75% of the Chinese migrated from Fujian Province, whereas 90% or more of the Hong Kong Chinese came from Guangdong Province. Unfortunately, the HLA distributions in these populations are not well characterised, but there may be significant differences which could have implications for the relative frequencies of MHC haplotypes (particularly DR2) predisposing to SLE in these populations.

MARTIN RUDWALEIT
KATHRYN GIBSON
PAUL WORDSWORTH

Nuffield Department of Clinical Medicine,
John Radcliffe Hospital, Oxford, United Kingdom
KEVIN PILE
Queen Elizabeth Hospital, Woodville, Adelaide 5011,
Australia
VERNON OH
National University Hospital, Singapore 0511

Correspondence to: Dr P Wordsworth, Nuffield Department of Clinical Medicine, John Radcliffe Hospital, Oxford OX3 9DU, United Kingdom.

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Treatment of refractory reflex sympathetic dystrophy with pamidronate

Reflex sympathetic dystrophy (RSD) is a condition affecting part or the whole of a limb, and is characterised by pain, vasomotor disturbance and trophic changes. RSD can persist for months or years and be severely disabling.¹ On radiographs, it is characterised by local osteoporosis, which corresponds to osteoclast hyperactivity. Calcitonin, an anti-osteoclastic drug, has been shown to help some patients.² Pamidronate, a second generation bisphosphonate, is a potent anti-osteoclastic agent,³ which is the rationale for using it in the treatment of RSD.

In an open prospective study, we evaluated the efficacy of pamidronate in the treatment of refractory RSD. Eleven patients (three men and eight women; mean age 51.3 (SD 12.8) years) suffering from RSD of at least six months duration (mean of 14.6 (10.3) months), refractory to calcitonin and physical therapy, were included. All patients fulfilled Doury's criteria for the diagnosis of RSD.⁴ The involved sites were the foot (n = 5), the hand (n = 2), the upper limb (n = 2), the knee (n = 1), the lower limb (n = 1). In eight cases, the RSD was related to local injury. Six patients had had to stop work because of RSD.

Radiographs of the affected sites showed osteopenia in all cases. The patients were given 30 mg of intravenous pamidronate in 500 ml of saline over four hours, daily, for three consecutive days. The patients received no standard treatment for their RSD from one month before the administration of pamidronate until three months after it. Patients were assessed by the same observer at baseline and after one and three months. Evaluation consisted of a visual analogue scale for pain (VAS), and a physician global assessment (no improvement, moderate, significant or excellent improvement) based on objective signs on clinical evaluation (hyperhidrosis, vasomotor changes, joint stiffness). Blood cell count and serum calcaemia (corrected with serum albuminaemia) were measured before, during, and one and

three days after the administration of pamidronate.

The mean VAS decreased from 58.8/100 (20.2) before therapy, to 41.1/100 (26.8) at one month ($p < 0.05$; Wilcoxon paired test) and 33.8/100 (29) at three months ($p < 0.01$). In the physician global assessment, the results were: no improvement (n = 4), moderate improvement (n = 1), significant improvement (n = 3), and excellent improvement (n = 3) at one and three months. Three of the six patients who had had to stop work had returned to work after three months. We were unable to find predictive factors for efficacy (age, gender, affected site, degree of osteopenia). Pamidronate was well tolerated, apart from classical minor adverse effects: two patients had a transient fever, two patients had brief, asymptomatic hypocalcaemia (2.05 mmol/l) and one patient had hypocalcaemia (2 mmol/l) associated with perioral paraesthesia which resolved rapidly with oral calcium treatment (1 g/day).

It is not possible to say whether the observed improvements were attributable to the treatment, the natural history of the disease, or psychological factors, as pamidronate was not compared with placebo in a double blind trial. However, more than 50% of the patients suffering from chronic disease, previously refractory to treatment, showed significant or excellent improvement while taking pamidronate, suggesting that it was effective.

In conclusion, this study suggests that pamidronate is a safe and effective drug for the treatment of some refractory cases of RSD. Further double blind trials are required to confirm these results.

JEAN FRANCIS MAILLEFERT
CHRISTINE CHATARD
SUSANNAH OWEN
THIERRY PEERE
CHRISTIAN TAVERNIER
Department of Rheumatology,
Hôpital Général, Dijon, France

JACQUES TEBIB
Department of Rheumatology,
Centre Hospitalier Lyon-Sud,
Pierre Benite, France

Correspondence to: Dr J F Maillefert, Service de Rhumatologie, Hôpital Général, 3 rue du Fb Raines, 21000 Dijon, France.

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Pericardial tamponade preceding cutaneous involvement in systemic sclerosis

Cardiac involvement in systemic sclerosis may be primary, or secondary to involvement of other organ systems. Primary cardiac involvement in systemic sclerosis may be manifested as pericardial disease, myocardial disease, conduction system abnormalities, or cardiac arrhythmias.¹ Cardiac symptoms do not usually appear until late in the disease, but exceptionally may precede the recog-

nition of scleroderma.² We report a patient with acute pericarditis and pericardial tamponade preceding cutaneous involvement in systemic sclerosis.

A 62 year old woman presented with precordial non-pleuritic pain and fever. She had a 25 year history of Raynaud's phenomenon. Physical examination disclosed a pericardial friction rub and a 20 mm Hg paradoxical pulse. The electrocardiogram showed a low voltage and non-specific ST-T wave abnormalities. Chest radiograph showed cardiomegaly with small bilateral pleural effusions. Routine laboratory studies were normal except for the erythrocyte sedimentation rate (ESR) (86 mm/1st h) and antinuclear antibodies (ANA) (positive (1/320), with a homogeneous immunofluorescence pattern). Viral titres were negative. An echocardiogram showed a large anterior and posterior echo free space with right atrial collapse. The haemodynamic study confirmed the presence of pericardial tamponade.

Pericardiocentesis yielded 400 ml of fluid containing protein 52 g/l (normal <30 g/l), glucose 4.2 mmol/l (normal 1.9–2.8 mmol/l), lactate dehydrogenase 2130 IU/l (normal <450 IU/l) and adenosine deaminase 13 IU/l (normal <45 IU/l). The pericardial fluid cultures were negative, including Lowenstein culture.

After pericardiocentesis the clinical improvement was immediate, the ESR was 47 mm/1st h, and the patient was discharged some days later.

Three years after discharge, the patient presented with a three month history of progressive hardening of the skin of the fingers, hands, and forearms. Physical examination revealed microstomia, sclerosis of the skin of the fingers, hands, and forearms, and also hardening of the skin of the trunk. Bibasilar rales and an intense second heart sound were present.

The chest radiograph was normal, as was the echocardiogram. Examination of the nailfold capillaries showed dilatation of capillary loops, tangled formations, and capillary loss. Oesophageal manometry showed oesophageal aperistalsis and a functional respiratory test disclosed mild restrictive disorder. Routine laboratory studies were normal and ANA were positive (1/1280) with a homogeneous immunofluorescence pattern; anti-Scl-70 antibodies

were positive by immunoblotting assay; anti-centromere antibodies were negative by immunofluorescence test with human epithelial (HEp)-2 cells. Diffuse systemic sclerosis was diagnosed and treatment with penicillamine was started.

Systemic sclerosis affects the heart in several ways. Postmortem studies demonstrated cardiac involvement in up to 80% of patients with the disorder.² The incidence of pericardial disease is 33–71%,^{2,3} with or without pericardial effusion. Echocardiographic studies have revealed disease in 21–41% of subjects.⁴

Most pericardial involvement in patients with systemic sclerosis is subclinical and does not directly affect prognosis. Symptoms of pericarditis are reported in only 7–20% of patients.³ Haemodynamic signs and pericardial tamponade secondary to pericardial effusion are relatively uncommon in these patients, but have been associated with a poor prognosis.¹

Two clinical patterns of pericardial disease in systemic sclerosis have been described: acute pericarditis, and chronic pericardial effusion.³ The presence of pericardial effusion and congestive failure was associated with the subsequent development of renal failure.^{1,3}

McWhorter *et al*³ described three patients with systemic sclerosis who had signs of pericardial tamponade, but none of these required pericardiocentesis. Uhl *et al*⁵ reported three patients with diffuse systemic sclerosis who required pericardiocentesis to relieve hypotension secondary to pericardial tamponade; all presented with symptoms and signs of acute pericarditis. More recently, two cases of limited systemic sclerosis associated with acute pericarditis and pericardial tamponade that required pericardiocentesis have been reported.^{6,7}

The patient reported now had a pericardial tamponade three years before the appearance of skin sclerosis. It is exceptional for cardiac symptoms to precede the more obvious skin sclerosis and, when they do, the cause is rarely diagnosed at the time.² We have not identified any other case of pericardial tamponade preceding other manifestations of scleroderma.

Among the five reported cases of systemic sclerosis associated with acute pericarditis and pericardial tamponade that required pericardiocentesis,^{5–7} only one patient

underwent histological investigations; these revealed pericardial fibrosis.⁵ It is conceivable that, with the relative incapacity for distension in scleroderma complicated by pericardial fibrosis, only a small volume of pericardial fluid may precipitate pericardial tamponade.

The cases of systemic sclerosis associated with pericardial tamponade were all of the acute pericarditis type. It is difficult to differentiate between this type of pericardial disease in systemic sclerosis and idiopathic or viral pericarditis.³ In common with the previously described cases of systemic sclerosis associated with acute pericarditis and pericardial tamponade,^{5–7} the patient we describe showed certain features that suggest a relationship between acute pericarditis and systemic sclerosis, such as the presence of Raynaud's phenomenon for some years before the pericarditis appeared, and the existence of ANA (titre 1/320) with a homogeneous immunofluorescence pattern during the acute episode of pericarditis.

C PEREZ-BOCANEGRA

V FONOLLOSA

C P SIMEON

J CANDELL

R SOLANS

A GOMEZ

M VILARDELL

Internal Medicine Department,

Hospital General Universitario Vall d'Hebron,
Barcelona, Spain

Correspondence to: Dra C Perez-Bocanegra, Servicio de Medicina Interna 3ª P (Dr VilardeLL), Hospital General Vall d'Hebron, Pº Vall d'Hebron 119–129, 08035 Barcelona, Spain.

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