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Resolution of sclerodermatous myocarditis after autologous stem cell transplantation

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Cardiac involvement in scleroderma is often subclinical^{1–3} and occurs early in the disease.^{4–5} The myocardium, pericardium and conduction system may be affected, resulting in heart failure or arrhythmia.⁶ Symptomatic pericarditis occurs in 7–20% of patients, whereas histological involvement has been reported to be as high as 70–80% at autopsy.⁶

We believe this is the first report of a man with symptomatic sclerodermatous myocarditis in whom the myocarditis resolved after initial pulse cyclophosphamide treatment followed by autologous stem cell transplantation (ASCT).

A 37-year-old mining electrician developed Raynaud's syndrome, skin thickening and polyarthritis in September 2003. Scleroderma was diagnosed 4 months later. By July 2004, he noted a 22 kg weight loss, night sweats, heartburn, nausea, muscle weakness and exertional dyspnoea. Clinical examination showed marked cachexia, widespread scleroderma (except the back), persistent tachycardia, a fourth heart sound, widespread tendon friction rubs, proximal muscle weakness and tender joints. Respiratory examination was normal. Abnormal investigations included high erythrocyte sedimentation rate (71 mm at the end of the first hour), C reactive protein (41 mg/l; normal <5), creatine kinase (1368 U/l; normal <186), troponin (0.74 ng/ml; normal <0.03), lactate dehydrogenase (454 U/l; normal <225), aspartate transaminase (62 U/l or 109 g/l), antinuclear antibodies (1:640 speckled) and extractable nuclear antigen Scl-70 positive. Renal function was normal. An electrocardiogram showed bifascicular block and low voltage in the frontal leads, with reduced ejection fraction (45%), mild mitral and tricuspid regurgitation and a mildly dilated right ventricle. Myocarditis, myositis, tenosynovitis and synovitis were diagnosed.

Initial treatment comprised methylprednisolone and cyclophosphamide (intravenous, 6 times), cyclosporin (50 mg daily) and captopril (6.25 mg twice daily). The patient remained normotensive.

The synovitis, myositis and cardiomegaly resolved, and his weight stabilised. The myocarditis improved (creatinine kinase, 180 U/l; troponin, 0.14 ng/ml), but the scleroderma worsened (affecting the upper back). The tenosynovitis remained problematic.

He underwent non-manipulated ASCT with high-dose cyclophosphamide (50 mg/kg for four doses) and equine-ATG (500 mg) in January 2005.

By day 5 after transplant, the troponin (0.05 ng/dl) and creatine kinase (84 U/l) had normalised. An echocardiogram (day 14) showed an improved ejection fraction (60–65%), normal left ventricle, slightly increased right ventricle and right atrium; electrocardiogram findings remained unchanged.

The patient's weight loss has resolved since then, the modified Rodnan Skin Score has fallen to 15 (from 28) and levels of cardiac enzymes have remained normal.

The coexistence of cardiomegaly, increased levels of cardiac enzymes, tachycardia, reduced ejection fraction, abnormalities on electrocardiogram, presence of inflammatory features in other organ systems and resolution after intense immuno suppression, in the absence of other causes, was consistent with features of scleroderma myocarditis. The persistent conduction abnormality after ASCT was attributed to conduction pathway fibrosis.

Suggested eligibility criteria for ASCT in scleroderma include recent onset, presence of association of vital organs (lung, heart or kidneys) and, in one ongoing trial, absence of prior occupational silica exposure.⁷

Previous studies have noted the objective clinical changes after ASCT in improving skin scores and stabilising involvement of vital organs.^{8–9} In this patient, skin tightness and myocardial function not only stabilised but also improved despite the presumed persistence of endogenous silica. Some studies showed that early immunosuppressive treatment with high-dose corticosteroids and pulse intravenous cyclophosphamide results in good cardiac outcome in acute lupus myocarditis.¹⁰

This case report highlights the therapeutic benefit of ASCT in the treatment of sclerodermatous myocarditis, and in scleroderma affecting skin, tendon sheaths and skin in a patient with early diffuse scleroderma positive for exposure to silica.

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Dyslipidaemia in Behçet's disease as a thrombotic risk factor

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Leiba *et al*¹ recently suggested that hyperlipidaemia, particularly hypertriglyceridaemia, may be a risk factor for thrombosis in Behçet's disease. Published studies suggest an association between increased levels of plasma lipids and deep-vein thrombosis,^{2–4} although the pathogenic mechanism is controversial. In an ongoing study on the association between thrombophilic defects and thrombotic events in patients with Behçet's disease, we have also evaluated the possible contribution of plasma lipids to the genesis of thrombotic events in these patients. We conducted a case-control study in patients with Behçet's disease recruited from the records of the La Fe, General and Peset University Hospitals in Valencia, Spain, between 1990 and 2005. All patients fulfilled three or more of the International Study Group criteria for the diagnosis of Behçet's disease.⁵ Of the 79 patients, 22 had experienced deep-vein thrombosis or phlebitis and, in addition, one of them had angina pectoris and another had ischaemic stroke. One patient had an ischaemic stroke but no venous thrombosis. The other 56 patients did not experience thrombotic events. The control group (n = 82) was taken from the staff of the La Fe Hospital.

Controls and patients were recruited and studied at the same time. Levels of total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, triglycerides

and glucose were evaluated by enzymatic techniques. Apolipoproteins A I and B were quantified by immunonephelometry, as in previous studies.³

Whereas the difference was not pronounced, in our series there was roughly twice the number of men with thrombosis as women (table 1), as in most series,⁶ although Leiba *et al*¹ found no differences regarding sex. When the lipid profile of patients and controls was compared, the only significant difference seen was in the triglyceride levels (p = 0.003). We observed no differences in the lipid profile when patients were classified according to treatment (no treatment, n = 30; anti-inflammatory drugs alone, n = 13; immunosuppressors with or without anti-inflammatory drugs, n = 36; p > 0.05). Patients with Behçet's disease with and without thrombosis showed similar triglyceride levels (p = 0.769), and we found no differences in any of the lipid parameters analysed. One of the reasons for the difference in our results compared with those of Leiba *et al*¹ may be because Leiba *et al*¹ had a large percentage of patients with arterial events (10%); this is rare in Behçet's disease, in which most thrombotic events are venous.⁷ Clearly, the association of arterial events with dyslipidaemia is well established, which may account for the discrepancy in the results, as in our series 3.8% of the patients with Behçet's disease had had arterial thrombosis.

Table 1 Characteristics of patients with Behçet's disease (with and without thrombosis) and controls

	Patients with Behçet's disease			Controls
	All (n = 79)	With thrombosis (n = 23)	Without thrombosis (n = 56)	(n = 82)
Age (years)	45 (12)	48 (13)	44 (12)	44 (10)
Sex (M:F)	43:36	15:8	28:28	40:42
BMI (kg/m ²)	26 (4)	26 (4.2)	26 (4.6)	25 (3)
Glu (mg/dl)	96 (18)	94 (16)	96 (19)	98 (14)
T chol (mg/dl)	213 (38)	213 (49)	214 (34)	209 (33)
LDL chol (mg/dl)	133 (29)	134 (30)	133 (28)	134 (27)
HDL chol (mg/dl)	55 (14)	57 (17)	55 (14)	56 (11)
TG (mg/dl)	132 (67)*	129 (61)	134 (70)	102 (58)
Apo A (mg/dl)	136 (24)	137 (29)	136 (22)	134 (19)
Apo B (mg/dl)	102 (22)	103 (21)	102 (24)	96 (20)
Apo B:Apo A	0.77 (0.21)	0.77 (0.19)	0.77 (0.22)	0.73 (0.19)

Values are mean (SD).

Apo, apolipoprotein; BMI, body mass index; F, female; Glu, glucose; HDL chol, high-density lipoprotein cholesterol; LDL chol, low-density lipoprotein cholesterol; M, male; T chol, total cholesterol; TG, triglycerides. Student's t test for independent groups was used to compare differences in age, BMI, glucose, lipids and lipoproteins. The χ^2 test was used to determine differences in percentages for sex.

*Difference between patients with Behçet's disease and controls, p ≤ 0.01.