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Dyslipidaemia in Behçet's disease as a thrombotic risk factor

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Ann Rheum Dis 2006;**65**:1248–1249. doi: 10.1136/ard.2005.049551

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.

Leiba *et al.*¹ however, stated that hypertriglyceridaemia was also associated with thrombosis in patients with Behçet's disease after excluding those with arterial occlusions. Other authors⁸ did not find a relationship between thrombosis and serum lipid profile in patients with Behçet's disease. It seems to us, on the basis of the results obtained, that there is no clear association between hyperlipidaemia and venous thrombosis in patients with Behçet's disease.

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Accepted 2 March 2006

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High levels of human anti-human antibodies to adalimumab in a patient not responding to adalimumab treatment

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Ann Rheum Dis 2006;**65**:1249–1250. doi: 10.1136/ard.2005.049858

Adalimumab is an effective treatment for rheumatoid arthritis. However, a substantial proportion of patients with rheumatoid arthritis either do not respond or lose their initial response.¹ We report a patient who initially responded to adalimumab treatment, but in whom disease activity increased as treatment continued. We believe that this lack of response to adalimumab is probably caused by the formation of human anti-human antibodies (HAHAs).

A 69-year-old woman with rheumatoid arthritis (diagnosed in 1991) and progressive joint destruction had active disease despite treatment with methotrexate 10 mg weekly and prednisone 7.5 mg/day. Therefore, treatment with adalimumab, 40 mg every other week, was started, in combination with methotrexate 10 mg weekly.

After 16 weeks of adalimumab treatment, the patient's Disease Activity Score 28 had decreased from 6.65 to 4.78

(table 1).² According to the Eular response criteria, this qualifies as a (moderate) responder.

At week 20, treatment with adalimumab and methotrexate was stopped for 8 and 4 weeks, respectively, for the patient to undergo total knee replacement surgery. Despite restarting adalimumab and methotrexate, disease activity remained high for the subsequent weeks. Hence, from week 35 onwards adalimumab 40 mg was given weekly instead of every other week, but disease activity nevertheless remained high. Therefore, treatment with etanercept was started and this change resulted in a substantial improvement of disease activity. Serum trough levels of adalimumab were measured by enzyme-linked immunosorbent assay, similar to that described for infliximab elsewhere (fig 1).³

Serum levels of HAHAs were detected by a newly developed radioimmunoassay, a specific assay measuring

Table 1 Development of disease activity parameters

Time (weeks)	ESR (mm/h)	CRP (mg/l)	VAS	TJC	SJC	DAS 28
0	89	63	98	5	10	6.65
4	58	38	49	1	8	4.88
16	65	26	19	3	5	4.78
28	71	32	85	2	4	5.53
40	91	77	87	5	6	6.31
4 (Enbrel)	51	5	37	1	3	4.32

CRP, C reactive protein; DAS, Disease Activity Score; ESR, erythrocyte sedimentation rate; SJC, swollen joint count; TJC, total joint count; VAS, Visual Analogue Scale.

Abbreviation: HAHAs, human anti-human antibodies