The impact of abatacept treatment on the vasculature in patients with rheumatoid arthritis

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Rheumatoid arthritis (RA) is chronic inflammatory musculoskeletal disease characterised by an increased risk for cardiovascular disease (CVD). RA can be treated using disease-modifying anti-rheumatic agents (DMARDs), but not all patients respond sufficiently well to DMARDs. Anti-tumour necrosis factor-alpha (anti-TNF-α) is a first line biological treatment and can reduce the occurrence of cardiac events and improve endothelial function (1). In patients who fail anti-TNF-α, newer biologics may be utilised, with studies in RA reporting beneficial effects of rituximab and tocilizumab on the vasculature (1, 2). Conversely, little is known about the cardiovascular effects of abatacept – a modulator of the co-stimulatory signal for T cell activation, with only one study reporting increased arterial stiffness following treatment (3). T-cells are upstream regulators of inflammation in both RA (4) and CVD (5), and have been shown to accelerate *in vitro* atherosclerosis (6). A recent seven-year prospective study revealed that abatacept is safe and improves physical function, quality of life and disease activity in RA (7). Similar findings were apparent in group of patients with amyloid A amyloidosis secondary to RA (8). We report for the first time the effect of abatacept treatment on endothelial function in the microvessels and large vessels of a young female with severe RA.

A 32-year-old female with seropositive RA (disease duration: 11 years) who had previously been treated with anti-TNF-α agent etanercept (50 mg) for one year was switched to abatacept, as per standard guidelines. The patient received 3 infusions of abatacept which were each separated by four weeks. The patient continued receiving 25 mg methotrexate, 7.5 mg prednisolone, 20 mg leflunomide and 200 mg hydroxychloroquine throughout treatment. Assessment of microvascular endothelial function was conducted using laser Doppler imaging with iontophoresis of the vasodilator agonist acetylcholine (ACh), and in the large vessel using brachial artery flow-mediated dilatation (FMD). Both techniques have been described in detail previously (1). The assessments were conducted at pre-treatment baseline, 2 weeks and 3 months after initiation of treatment.

The disease activity score in 28 joints was elevated at pre-treatment baseline but was markedly reduced at all time points following treatment (Table I). Pre-treatment erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) remained low at baseline and at 2 weeks following treatment but increased at 3 months. Microvascular endothelial function was reduced at 2 weeks before increasing to pre-treatment values at 3 months. In the large vessels, endothelial function showed a consistent decline at both follow-up visits.

Table I. Patient characteristics.

	Pre-treatment	2-weeks	3-months
Abatacept			
ESR (mmhr)	2	2	9
CRP (mg/l)	3	3	16
DAS28	4.95	2.30	3.80
Microvascular endothelial function (%)	300	202	311
Flow-mediated dilatation (%)	12	10	9

ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; DAS28: disease activity score in 28 joints.

Our preliminary findings are the first to indicate that abatacept treatment results in a transient worsening of microvascular endothelial function and a prolonged decrease in endothelial function of the large vessels. Similarly, Mathieu and colleagues reported increased arterial stiffness following 6 months of abatacept treatment in 21 RA patients (3), and partly attributed their findings to a worsening lipid profile. Indeed, in hypercholesterolemic mice, abatacept treatment results in a significant decrease in atherosclerosis (6). These findings suggest that T cell co-stimulatory pathways could modulate endothelial function via alterations in classical CVD risk factors. Interestingly, improvements in the vasculature following biological treatment in RA could be mediated by classical CVD risk factors (9, 10). Further large-scale studies examining the impact of abatacept on endothelial dysfunction in patients with RA are needed.

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