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Adalimumab: a new modality for Behçet's disease?

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Aberrant T cell function,¹ subsequently accompanied by increased tumour necrosis factor α (TNF α) levels, induces inflammatory symptoms in patients with Behçet's disease (BD).² Subsequently, treatment usually involves T cell-directed immunosuppressive or anti-TNF α treatment in patients with severe disease.^{3–7} Administration of the new human monoclonal TNF α antibody adalimumab has only been described in three patients with BD with uveitis.⁸ We analysed

the effects of adalimumab on severe and often chronic disease in six heavily pretreated patients with BD in whom immunosuppressive therapy had failed (table 1).

These patients were treated in the past with infliximab.⁹ Indications for anti-TNF α treatment were uveitis (patients 2 and 4), CNS disease (patients 3 and 5), colitis (patient 6) and severe oral ulcers and arthritis (patient 1), and are further presented in table 1. Symptoms were scored retrospectively

Table 1 Clinical effects in patients treated with infliximab or adalimumab for Behçet's disease

	1		2		3		4		5		6	
Age/gender	43/M		40/M		41/F		36/M		43/F		34/M	
Gifts of infliximab	1		16		9		6		6		10	
Comedication adalimumab*	—		P(15), MTX		D, Cys, Pf		P(10), MP		P(10), A(100)		Cys, Th, P(30), MTX	
Tapering of comedication	—		P(2.5–10)		Cys		P(5)		P(7.5)		Cys, Me, B	
Symptoms and response† before and after anti-TNF α treatment.												
Symptoms and indications for anti-TNF α treatment	I	A	I	A	I	A	I	A	I	A	I	A
Uveitis	pr	po	pr	po	pr	po	pr	po	pr	po	pr	po
Oral ulcers	—	—	—	—	1	½	1	½	—	—	—	—
Genital ulcers	1	0	1	½	1	0	1	0	—	—	1	0
Skin	1	0	1	0	1	½	1	0	—	—	—	—
Colitis/oesophageal ulcers	—	—	—	—	—	—	—	—	—	—	—	—
CNS involvement	—	—	—	—	—	—	1	0	—	—	1	0
Arthritis or arthralgia	1	0	1	0	1	½	1	0	—	—	—	1
Total#	4	0	4	1	5	2	5	1	3	0	2	½
Duration (mean 530/427) (days)	30		>327		943		>576		318		>395	
Rate of relapse (mean 128/–) days57	—		81		—		289		—		201	

–, none; A, adalimumab; B, budesonide; CNS, central nervous system; Cys, ciclosporin; D, dexamethasone; F, female; I, infliximab; M, male, Me, mesalazine; MP, monthly high dose of 1g methylprednisolone; MTX, methotrexate; P, prednisone; Pf, pentoxifylline; po, post; pr, prior; Th, thalidomide; TNF, tumour necrosis factor. Only symptoms preceding anti-TNF α treatment are mentioned. Treatment schedules: infliximab: 3–5 mg/kg every 1–3 months intravenously according to disease intensity and response; adalimumab: 40 mg subcutaneously every 2 weeks.

Relapse rate after cessation of anti-TNF α treatment.

*Immunosuppressive therapy that was combined at the start of adalimumab, dose in milligrams between paraphrases.

†Complete response was defined as being free of symptoms. Incomplete response indicates subjective response and reduction in frequency of symptoms. Visual acuity was assessed according to local ophthalmological guidelines. Symptoms before anti-TNF α was indicated were allocated 1; incomplete remission and complete remission were ½ and 0, respectively.

#Cumulative score, ½ counted as 0.5, complete response as 0.

since no official scoring system such as the Behçet's Disease Current Activity Form (BDCAF) was available at the start of anti-TNF α treatment in our centre.

It is unknown how long anti-TNF α treatment must be given, but anti-TNF α treatment in patients with rheumatic arthritis is continued for >2 years and continued until there is a settled response.¹⁰ In our patients, infliximab was discontinued after complete response of >3 months or acceptable improvement of (eye) symptoms. In five of the six patients, relapses after infliximab did not necessitate immediate restart of anti-TNF α treatment. In this period (mean duration 562, range 136–1093 days), immunosuppressive therapy could be adjusted until the symptoms required a restart of anti-TNF α treatment. Adalimumab was considered to be equal potential, but more convenient, and was added in cases of severe relapse with patients' informed consent. In addition, formation of auto-antibodies to infliximab when restarted was considered. All patients responded and most of them showed dramatic and quick improvement. Subsequently, immunosuppressive therapy could again be tapered (table 1).

Patient 6 had a severe BD-associated colitis and was periodically treated with infliximab and other immunosuppressive agents for nearly 3 years. Despite intensified immunosuppressive therapy, the colitis worsened and became refractory and life threatening. Subsequently, a high dose of adalimumab 40 mg/week was started subcutaneously, yielding a complete response of >1 year. Adalimumab was briefly combined with 30 mg of prednisone, which was tapered rapidly to prevent central retinal serosa ablation that developed in a previous period in which steroids had been used. Later, mesalazine and rectal budesonide were also given. Apart from some minor flares, the patient remained stable for nearly 2 years. Until now, all patients are receiving adalimumab, except patient 5 who discontinued 4 months after complete remission was achieved (table 1). In general, few side effects were observed. Three patients (1, 3 and 6) developed lichenoid-like lesions that were treated with local steroids by a dermatologist.

This report on patients with treatment refractory BD indicates that adalimumab treatment is promising and can be prescribed safely for a prolonged period. To our knowledge, this is the first case series in which patients with BD with systemic

disease treated with adalimumab are presented. More studies on this subject are warranted.

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Autosplenectomy: rare syndrome in autoimmunopathy

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Autosplenectomy has been described in association with systemic lupus erythematosus (SLE).¹ Although in patients with SLE small or atrophic spleens are usually seen, the complete absence of the spleen has been observed rarely. Here, we report a patient with an 18-year history of autoimmunopathy who developed anatomical asplenia during the disease.

A 51-year-old Caucasian woman was first diagnosed in 1988 as having autoimmunopathy of incompletely defined aetiology with antinuclear antibodies (ANA) positivity and immunocomplexes in conjunction with reduced complement levels and serositis. The patient presented with massive pleural and pericardial effusions.

Laboratory studies showed normal blood counts. Antibodies to extractable nuclear antigens or to phospholipids (lupus anticoagulant and anti-cardiolipin antibodies) could not be detected. Although suggestive of having SLE, the patient did not fulfill the classification criteria for the disease at any given time.² Notably, the spleen was normal in all respects as confirmed by ultrasound and CT scan, at the time of initial contact. Treatment was initiated with glucocorticoids and plasmapheresis, with good clinical response. Because of unresponsiveness to or unbearable toxicity

Abbreviations: AIH, autoimmune hepatitis; ANA, antinuclear antibody; SLE, systemic lupus erythematosus