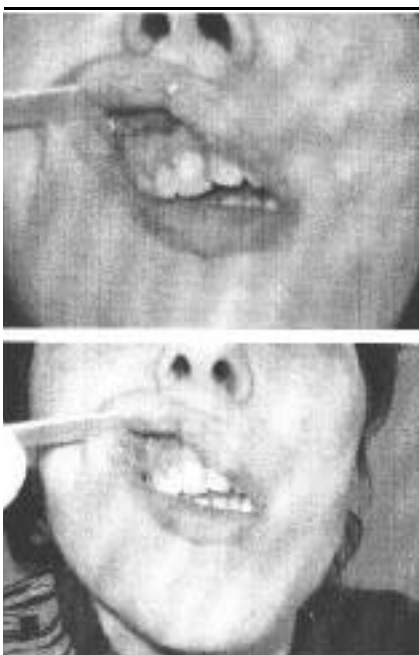


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## Successful treatment of resistant Behçet's disease with etanercept

Sirs,  
Behçet's disease (BD) is a chronic, inflammatory vasculitis characterized by oral and genital ulcerations, ocular and skin lesions, arthritis and neurological involvement (1). We report the case of a resistant BD patient who was successfully treated with etanercept.

A 32-year-old woman was admitted at the Rheumatology Unit of the L. Sacco University Hospital in December 2002 for polyarthritis involving the right wrist, left knee, right elbow, proximal interphalangeal joints of the fingers and metatarsophalangeal joints. She also reported an occasional headache. She had a history of recurrent oral and genital aphthous ulcerations, and papulopustular skin lesions (PPL) which started when she was 26 years old. Physical examination revealed a slight fever (37.1°C) and a blood pressure of 120/70 mmHg. She had lost 3 Kg during the last few months. Laboratory findings were as follows: haemoglobin 10g/dl, WBC 6.500/mm<sup>3</sup>, ESR 55 mm/h, CRP 2.8 mg/dl. The liver and the renal functions were normal.



**Fig. 1.** Oral ulcers in a patient with Behçet disease before and after treatment with etanercept.

RF, ANA and anti-DNA antibodies were negative. Hepatitis B and C, cytomegalovirus, parvovirus B19 and HIV virologies were negative. Anticardiolipin and c and p-ANCA were negative. HLA-B51 was present. Pathergy was negative. Ophthalmological examination detected an anterior uveitis with hypopion. A radiography revealed narrowing of the joint space in the left knee and in the right elbow, erosive changes of the proximal interphalangeal joints, and bone destructive changes in the wrist. Sacroiliac joint involvement was negative.

The diagnosis of BD based on the International Study Group criteria for BD (2) was made and she was treated with oral prednisolone (10 mg/day), methotrexate (MTX) (15 mg/week), and anti-inflammatory agents (NSAIDs). The patient did not tolerate MTX. In April 2003 the disease was severely active. The patient presented with fever, oral ulcers, and polyarthritis; ESR was 99 mm/h, CRP was 5.3 mg/dl. Prednisolone (25 mg/day) and cyclosporin A (CsA) (250 mg/day) were introduced. The treatment was well tolerated by the patient and the corticosteroid dose was tapered.

Four months later the patient presented a PPL on the lower extremities and on the face. Three weeks later the patient presented with acne on the lower extremities, on the face and on the trunk, and oral ulcers. CsA was stopped. An improvement of PPL was observed, but in October 2003 the patient presented with a severe episode of oral and genital aphthae associated with polyarthritis. Treatment with prednisolone 25 mg/day was started. PPD test was negative and chest radiograph did not show any nodular infiltrates. Treatment with etanercept, 25 mg subcutaneously twice a week was started (3). After 4 weeks the lesions disappeared and the polyarthritis improved. At present the patient is in clinical remission (Fig. 1). The current therapy is: MTX (15 mg/week), steroids (7.5 mg/day) and etanercept 25 mg (2 sc weekly injections). The joint symptoms in BD are present in 40-75% of cases of BD (4, 5). According to Vernon-Roberts *et al.* (6) and Nanke *et al.* (7) joint deformities and destruction have been reported in a few cases. In our case the patient had polyarthritis involving the right wrist, left knee, right elbow, proximal interphalangeal joints of the fingers and metatarsophalangeal joints. The treatment with NSAIDs, corticosteroids and MTX was started as a first-line therapy for BD. MTX is efficacious for arthritis, but this patient did not tolerate it. The patient was treated with CsA but a severe PPL associated with an episode of oral ulcers made it necessary to stop the treatment.

Treatment with anti-TNF- may be useful for the oro-genital ulcerations of BD and for erosive arthritis (8,9). Our findings appear to be the first case in which anti-TNF- is beneficial in the treatment of genital

ulcerations and uncommon erosive arthritis (10).

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## Can characterization by traditional Korean medical criteria help in our understanding of patients with rheumatoid arthritis ?

Sirs,

Traditional Korean Medicine (TKM) is an ancient discipline that classifies individuals with musculoskeletal problems using very different terms than Western medicine (1-3). TKM relies more on the clinician's reading of the patient's symptoms and signs with little attention to details of joint findings. The relationship between TKM diagnoses and Western concepts of rheumatoid arthritis (RA) have not been previously ex-

# Letters to the Editor

amed.

Sasang constitutional medicine is a major branch of TKM. Disease susceptibility and drug response of individuals are presumed to be different depending on their constitutional traits. Four constitutions described in Sasang medicine refer to Tae-Yang, Tae-Yin, So-Yang, and So-Yin. Tae-Yang can be translated as a high Yang energy person, while So-Yin could be a low Yin energy person etc., using the Chinese concepts of Yin and Yang (Table I). These are felt to explain the individual differences in vulnerability to pathologies and propose guidelines for the safe and effective use of medicinal herbs depending on individual traits. Patients are also classified by four symptom patterns ("Wind Damp/Cold Damp", "Heart Heat", "Phlegm/Blood Stagnation", and "Liver Kidney function Deficiency")

We investigated the relative frequency of TKM syndromes in patients with RA and looked for associations between disease characteristics as determined by a Western rheumatologist and TKM characterization of the same patients.

An expert in Traditional Korean Medicine (TKM) from a TKM faculty in Seoul, Korea performed an examination including the pulse and tongue, and then administered a TKM questionnaire to 35 patients with RA seen in clinics in two teaching hospitals in

the USA. All patients met the ACR criteria for RA. Patients were classified by the 4 TKM constitutional types and 4 symptom patterns. These data were analyzed for their relationship to disease activity and disability on 0-3 point Likert scales, the presence of rheumatoid factor, and medications being used, as recorded by a Western-trained academic rheumatologist.

The Tae-Yin constitutional type patients tended to have the most active RA. This was seen in 20%. These patients were viewed as gentle and fearful and would be encouraged to use aerobic exercise and sauna as well as herbs to prevent "blood stagnation", with an anti-inflammatory effect as well. Most RA patients were of the So-Yang constitutional type (54%). Patients of the So-Yang constitution most often had "liver/kidney function deficiency". These patients were more anxious and hot tempered and in TKM therapy would be advised to use yoga, meditation and herbs which would be used to cool the "Heart Heat" and stimulate "Kidney function". These patients had less active arthritis but were most often on anti-TNF therapy and so presumably previously had more active RA (Table I).

Only 5 patients were considered to have the "Wind Damp/Cold Damp", a symptom complex which TKM would only treat with analgesic herbs. None of these had severe

RA and only one required anti-TNF therapy. The most common TKM symptom description for these RA patients was "Liver Kidney Deficiency" (40%) which is related in TKM theory to bone and cartilage diseases. There was no significant relationship between this TKM symptom pattern and RA activity, disability or medications.

The most common TKM diagnostic syndrome found in this rheumatoid arthritis patient population was the So-Yang constitutional type and "Liver Kidney function deficiency". TKM diagnoses in the patients had little correlation with the Western assessment except for identifying a small group of patients who had less active RA but were also more likely to be on anti-TNF therapies. Treatment makes one-time small-scale studies such as this one very difficult to interpret. This pilot study thus suggests that any future study should also compare TKM characterization and more complete Western disease descriptions before treatment.

Based on the 4 different constitutional type patients, TKM emphasized background aspects which would perhaps direct attention to how patients cope and adjust. This individualized approach may address components of care that are not consistently addressed in Western medicine. Very few studies published in Western journals have examined the effects of traditional Asian diagnosis and therapy in RA (4, 5).

We propose that the additive effects of components of TKM diagnoses and therapy are worth examining in patients before and after they are treated with standard Western regimens.

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**Table. I.** Features of four types of Sasang constitutional medicine (1), the proportion of patients with RA and reported in the general Korean population, and disease status of the patients with RA.

	Tae-Yang Type	Tae-Yin Type	So-Yang Type	So-Yin Type
General figure	Developed nape of the neck Slender waist	Thick waist Weak nape of the neck	Developed chest Small hips	Developed hips Weak chest
Face	Large and thin Shiny eyes Wide	Rounded Looks hard	Small Thin lips Narrow jaws Protruding	Smart
Skin	Soft	Solid	Dry and thin	Tender
Walking		Heavy and gentle	Unstable	Stable
Characters	Creative Positive Progressive Charismatic Heroic Rash mind	Gentle Commercial Endurable Humorous Looks foolish Coward Fearful mind	Unstable Easily gets bored Outside-oriented Sacrificing Righteous Easily acceptable Hot tempered Anxious mind	Neat Negative mind Inside-oriented Intelligent Systematic Selfish Jealous Narrow-minded Nervous mind
Healthy sign	Urination	Perspiration	Bowel movement	Digestion
Pulse		Long and tight	Rapid and floating	Smooth and weak
Proportion of general population (%)	Very rare	50%	30%	20%
Proportion of RA population (%)	0%	20%	54%	26%
Mean of joint activity score (0-3 scale)		1.66	1.15	1.22
Rheumatoid factor (%)		100%	78.9%	88.8%
Mean of function score (0-3 scale)		1.42	1.21	1.22
Anti-TNF therapy (%)		8%	37.5%	9%