Cross cultural adaptation and validation of the Arabic version of the CHAQ for measuring functional status in children with JIA

Sirs,

I have read with great interest the article by El Miedany *et al*. (1), wherein the authors evaluated the validity and reliability of the modified translated version of CHAQ in Arab children with JIA. The cohort included 30 Saudi Arabian children with JIA. With all due respect, as a Pediatric Rheumatologist working at the single tertiary care center for pediatric rheumatic diseases in Saudi Arabia, I found the number of Saudi children is too large to be followed outside the country without our prior awareness and as the authors did not specify the collaborative centers, I would like to know in greater detail the methodology of recruitment of a such large Saudi cohort.

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Reply

Sirs,

The Saudi Arabian children suffering from juvenile arthritis were consecutively recruited for the study from those attending or that had been referred to the rheumatology clinic in the Saudi German Hospital, Jeddah, over the period from 5th of March 1995 till the end of April 1997, as well as the Rheumatology Clinic in the insurance hospital and Dar El Shefaa Hospital, Riyadh, Saudi Arabia over the year 2000 where the first and second authors were working. The patients were diagnosed, assessed and followed up in Saudi Arabia.

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Pulmonary aspergillosis in a patient with rheumatoid arthritis treated by etanercept

Sirs

Etanercept is a fusion protein that binds free TNF-α and has been shown in previous trials to be effective against RA, juvenile arthritis and psoriatic arthritis. Concerns have been raised about the increased risk of infections with immunomodulating agents such as etanercept. However, fungal infections in patients treated with TNF-α antagonists are rare and have only been reported with infliximab therapy. We report a case of pulmonary aspergillosis in a patient with RAtreated with etanercept.

In December 2001 a 55-year-old woman with a 10-year history of severe rheumatoid arthritis (RA) was admitted to hospital because of pulmonary infection. She has been treated with oral methotrexate for 6 years, and then with leflunomide for 6 months. In February 2001 leflunomide was stopped because of refractory disease and etanercept was started at 25 mg twice a week in association with prednisolone 5 mg/day; this led to rapid clinical improvement. Five days before admission, however, she presented high fever, dyspnea and a productive cough. A chest roentgenogram showed basal infiltrates in the left lung with middle bilateral pleuritis. Laboratory tests revealed an increased C-reactive protein concentration (150 mg/l) and leukocytosis. Bronchoalveolar-lavage fluid and pleural fluid puncture yielded *Staphylococus aureus* and treatment with amoxicillin-clavulanic acid was started.

Five days after her admission the patient developed respiratory failure associated with pneumopyothorax. A computed tomography scan was highly suggestive of a fungal ball aspergilloma in the pulmonary cavity of the right lung. Etanercept was stopped and treatment with voriconazole was started (6 mg/kg/day) in association with drainage of the pneumothorax. Culture of pleural fluid yielded *Aspergillus fumigatus* on day 15 and was negative for tuberculosis. A few days after beginning fungal therapy, her clinical condition significantly improved. At month three, the pulmonary aspergilloma has completely disappeared.

The role of TNFα in the immune response is very complex. It may limit the extent and duration of inflammation. Etanercept, a recombinant human tumor necrosis factor alpha (TNFα) inhibitor that binds both soluble and cell-bound TNFα, has been shown to reduce disease activity and inhibit joint destruction when administered to patients with RA. Infliximab, another TNF antagonist, is a chimeric mouse-human monoclonal IgG1 antibody that has been approved for the treatment of RA in combination with methotrexate. The number of patients who have been treated with etanercept or infliximab are quite similar.

Because of the potential immunosuppressive properties of TNFα antagonists, adverse events related to infections are a major concern connected with the use of both agents (1, 2). A role for TNFα in susceptibility to infection is clearly suggested by data from animals models of TNFα inhibition and blockade (3). However, in patients treated with infliximab the incidence of tuberculosis and various opportunistic infections (histoplasmosis, listeriosis etc.) seems to be higher with infliximab than with etanercept (1-4). Possible explanations for the disproportionate number of cases associated with infliximab therapy in comparaison to etanercept may related to the different ways in which the two agents neutralize TNFα (4).

Pulmonary aspergillosis has been reported in patients treated with infliximab; however, as far as we know, there have been no cases reported in etanercept-treated patients. Importantly, our patient had no known risk factors for aspergillosis except for immunosuppressive treatment with etanercept and low dose corticosteroids. She had no underlying respiratory disorder which would have predisposed to pulmonary aspergillosis. This complication occurred more than 9 months after leflunomide was withdrawn, at a time when its residual concentration would have been negligible given the half life of this molecule (5). Although there is no available data regarding the long-term effects of leflunomide on the immune response, it should be mentioned that opportunistic infections have rarely been reported in patients treated with leflunomide (6). Our data strongly suggest an association between treatment with etanercept and the development of aspergillosis in this patient.

In conclusion, physicians prescribing etanercepts such as infliximab should be aware of the risk of opportunistic infection including pulmonary aspergillosis. More rigorous monitoring may be needed for patients prior to and during etanercept therapy.

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