Infliximab in refractory sarcoidosis: the ild care experience

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Introduction

Sarcoidosis has a substantial impact on patients' lives. Sarcoidosis patients with chronic disease often require prolonged treatment. Although alternatives to corticosteroids have been frequently administered in this disease, corticosteroids remain the mainstay of treatment. However, disabling side effects which accompany prolonged treatment can necessitate the use of alternative, steroid-sparing agents. The tumor necrosis factor (TNF) inhibitors can be useful in treating chronic sarcoidosis.[1] Among the biologic agents which inhibit TNF, infliximab has been studied most extensively in sarcoidosis. In one double blind randomized study evaluating the effect of the anti-TNF-α drug Infliximab in sarcoidosis it was found that the more severe the disease, the more likely the patient will respond to therapy.[2] The observation that more significant improvement occurred in those with patients with lower initial vital capacities (FVC) was supported by another randomized trial by Rossman et al.[3] More recently, Elfferich et al. demonstrated that anti-TNF-α therapy had a positive effect on cognition, fatigue, and other symptoms related to sarcoidosis.[4]

Aim

The aim of this study was to report our experience with infliximab in refractory sarcoidosis patients.

Methods

From 2003 till 2010 in 77 refractory sarcoidosis patients (55 male; Chest X-ray stage 0-I: n=28; stage II-II: n=31 and stage IV: n=18) treatment with infliximab was initiated as they did not respond to corticosteroids and/or methotrexate (MTX), or suffered from severe side effects. The indication varied from respiratory functional impairment, small fiber neuropathy (SFN) to neurosarcoidosis. The dose was 5mg/kg (402±54 mg); the dose interval 4.5±0.6 weeks (range 3-5). Additionally, they used prednisone (4.5±6.5; range 0-25mg daily) and MTX 4.8±4.4; range 0-15mg once a week). Clinical data were gathered and they all completed the Fatigue Assessment Scale (FAS) and the small fiber neuropathy screening list (SFNSL). Retrospectively, the data were analysed after a follow-up period of one year.

Table 1. Summary of inflammatory laboratory parameters, lung function test results and HRCT score according to Oberstein[5] of the sarcoidosis patients studied and the effect on these clinical manifestations after 12 months treatment with infliximab.

	Baseline total population (n=77)	After 12 months (n=70)
CRP (2-9 μg·mL^{-1})	5.5±11.0	2.6±3.0*
ACE (9-25 U·L^{-1})	20.6±13.8	16.5±6.4*
sIL-2R (240-3154 pg·mL^{-1})	2970±3150	1498±765*
FVC, % predicted	93.0±16.1	95.8±16.3
DLCO, % predicted	76.8±16.7	80.2±19.3
HRCT (Oberstein total score; n=28)	7.9±3.1	6.1±3.6*

All values are presented as mean ± SD; *p<0.01.

Figure 1. HRCT before and after one year treatment with 5 mg/kg infliximab showing a reduction of the parenchymal lesions.

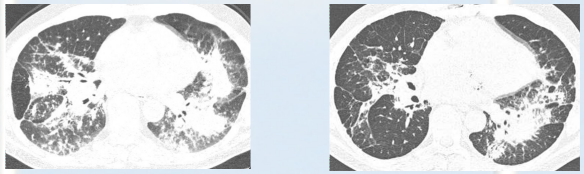
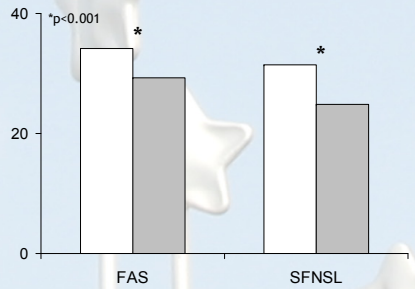


Figure 2. Fatigue Assessment Scale (FAS) score and Small Fiber Neuropathy Screenings List (SFNSL) score of the studied sarcoidosis patients before (white bars) and after 12 months treatment (gray bars) with 5 mg/kg infliximab.



Results

The treatment period was 1.8±1.3 (range: 0-7yrs). After one year follow-up the signs of inflammation in the peripheral blood improved, as well as the radiological features (Table 1 and Figure 1). Fatigue was less prominent (FAS score: 29.9±7.8 vs 34.1±7.5; p<0.001), and the SFN related symptoms improved (SFNSL 23.1±14.7 vs 28.5±15.0; p<0.001; Figure 2). The exercise capacity (6 minute walking distance) and fatigue improved in >70% of the patients, 20% were stable. Seven cases (9%) had to stop due to antibody formation, 31 are still on treatment.

Conclusions

Infliximab appeared successful in more than 70% of the sarcoidosis patients with refractory chronic sarcoidosis demonstrating:

- a reduction of fatigue and symptoms related to small fiber neuropathy
- a reduction of the inflammatory markers of disease activity
- an improvement of HRCT features

Even severe cases with Chest X-ray stage IV responded well.

A dose interval of 4-5 week seemed to be the most appropriate.

References

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