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A single course of rituximab does not abrogate anti-infliximab antibodies in patients with rheumatoid arthritis

The development of anti-infliximab antibodies in 8% to 43% of infliximab-treated patients is associated with decreased efficiency and increased risk of adverse effects.[1–3] An intervention that can diminish anti-infliximab antibody formation is therefore warranted. Rituximab, a chimeric monoclonal antibody that selectively depletes CD20-positive B lymphocytes, could potentially inhibit the human antibody response against infliximab. Therefore, we assessed the proportion of patients with rheumatoid arthritis (RA) in which treatment with rituximab resulted in the depletion of anti-infliximab antibodies.

Consecutive patients with RA with detectable anti-infliximab antibodies, who were initiated on treatment with either rituximab or adalimumab, were included in this prospective controlled cohort study. There were no exclusion criteria other than the regular contraindications. Baseline assessment included measurement of disease activity, demographic and clinical data. Patients received rituximab (2×1000 mg intravenously, day 0 and 15) or adalimumab at a dosage of 40 mg subcutaneously every other week. Anti-infliximab antibody measurements before the first administration of rituximab and after 16 and 24 were compared with patients treated with adalimumab as control group. Serum anti-infliximab antibody levels were determined by a previously described radioimmunoassay.[3]

The baseline characteristics of the included 32 patients (17 rituximab and 15 adalimumab) are depicted in table 1. Although the baseline anti-infliximab antibody levels tended to be higher in the adalimumab group (100 (interquartile range (IQR) 28 to 416 AU/ml) compared to the rituximab group (29 (IQR 19 to 127)), this difference did not reach statistical significance ($p = 0.2$). A negative trend was found between baseline anti-infliximab antibody levels and the interval between the last administration of infliximab and start of the present therapy ($r = -0.32$, $p = 0.07$).

Table 1 Baseline characteristics of patients

	Rituximab group (n = 17)	Adalimumab group (n = 15)
Age (years)	56 (12)	53 (12)
Women (n, %)	8 (47)*	13 (87)*
Disease duration (years)	15.7 (9.1)	15.8 (7.8)
Previous DMARDs (n)	6.5 (2.6)*	3.7 (2.1)*
Previous biologicals (n)	2.5 (0.9)*	1.3 (0.5)*
Rheumatoid factor positive (n, %)	17 (100)	13 (87)
Disease activity (DAS28) at baseline	6.0 (1.6)	5.0 (1.4)
Interval between last infliximab infusion (months) and present therapy (median (p25–p75))	25 (7.2 to 36)*	5.8 (2.5 to 25)*
Concomitant DMARD at baseline (n, %)	15 (88)	13 (87)
Methotrexate (n, %)	11 (65)	13 (87)
Dose (mg/week)	13.6 (6.3)	16.9 (9.4)
Azathioprine (n, %)	2 (12)	0
Leflunomide (n, %)	1 (6)	0
Oral corticosteroids at baseline (n, %)	10 (59)	5 (33)
Dose (mg/day)	9.3 (2.9)*	4.9 (1.9)*

Variables are expressed as mean (SD) unless stated otherwise.
*$p<0.05$.
DAS28, 28-joint Disease Activity Score; DMARD, disease-modifying antirheumatic drug.

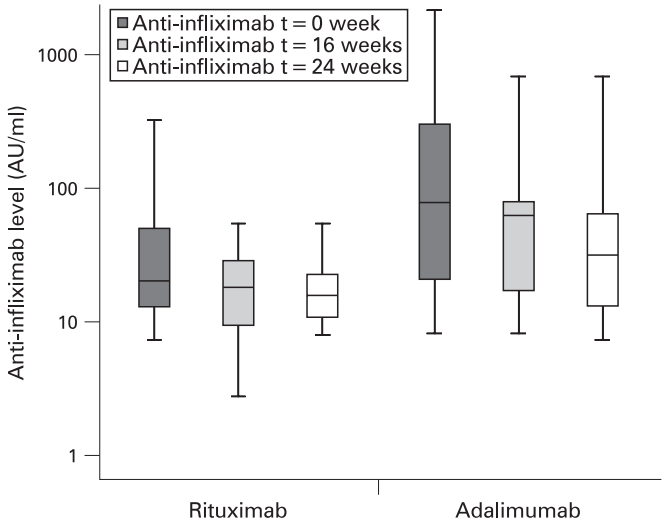

Figure 1 Anti-infliximab antibody levels (AU/ml) prior to treatment with rituximab or adalimumab (t = 0) and 16 and 24 weeks after treatment.

After 24 weeks, the median serum anti-infliximab antibody levels in the rituximab group and adalimumab group decreased from 29 AU/ml to 23 AU/ml and from 100 AU/ml to 44 AU/ml, respectively (fig 1). The mean (SD) decrease in anti-infliximab antibody levels was not more pronounced in the rituximab group (20% (38%) reduction) compared to the adalimumab group (36% (52%) reduction). Rituximab treatment did not lead to seroconversion of anti-infliximab antibodies in any of the patients. One adalimumab-treated patient had anti-infliximab levels below the cut-off level of 12 AU/ml. A linear regression association model showed that baseline anti-infliximab antibody levels did not act as a confounder on the relation between decrease in anti-infliximab antibodies and received treatment.

The results presented here show that rituximab neither abrogates anti-infliximab antibodies nor modulates the change of existing anti-infliximab antibody levels compared to adalimumab. Non-selective inclusion, broad inclusion criteria, blinded assessment of anti-infliximab antibody levels, the use of a comparable control group and the application of linear regression to detect possible confounders, all supported an adequate internal validity of the study. Although our data show that anti-infliximab antibody levels do not seem to be affected by rituximab, this does not necessarily imply that rituximab will not affect the production of anti-infliximab antibodies in the presence of infliximab. Conceivably, reintroduction of infliximab in patients with anti-infliximab antibodies previously treated with rituximab could lead to decreased formation of anti-infliximab antibodies by short-lived plasma cells.

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High-resolution MRI for assessment of middle meningeal artery involvement in giant cell arteritis

Giant cell arteritis (GCA) typically involves the superficial cranial arteries, the aorta and its branches. It has been discussed to which extent the vasculitic changes of the cranial arteries continue into the intracranial region. Autopsy findings have indicated that the characteristic signs of arteritic inflammation of GCA end after crossing the dural border.[1] In a recent review of several published cases it was concluded that intracranial/intradural involvement in GCA is rare and represents a small subset of GCA that is non-responsive to corticosteroids and has a fatal course.[2]

Contrast-enhanced, high-resolution MRI allows non-invasive assessment of mural inflammation in the extracranial, superficial arteries in giant cell arteritis.[3] Here, we report MRI findings suggestive of intracranial vasculitic involvement in patients with GCA. High-resolution MRI of 50 patients with GCA (15 men, 35 women, mean age 70.4 years) and signs of cranial arteritis in MRI scans acquired at 1.5 and 3 Tesla were retrospectively evaluated by 2 radiologists. Imaging parameters of the applied contrast enhanced, fat saturated multislice T1-weighted spin echo (SE) sequence have been reported elsewhere.[4 5]

Utilising the above-mentioned MRI protocol, mural thickening and contrast enhancement of the intracranial but extradural course of the medial meningeal artery (MMA), most likely representing mural inflammatory changes, was depicted in 16 patients (32%) (fig 1). These findings were bilateral in nine patients and unilateral in seven patients.

In 32 patients the diagnosis of GCA was established by positive temporal artery biopsy (TAB). In 6 of the other 18 patients TAB was negative. In these cases, as well as in the 12 cases in which no TAB was performed, GCA was established

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