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THU0439

TOCILIZUMAB IN GIANT CELL ARTERITIS. NATIONAL MULTICENTER STUDY OF 134 PATIENTS OF CLINICAL PRACTICE

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Background: Giant cell arteritis (GCA) can be refractory to corticosteroids^{1–3}. Tocilizumab (TCZ) demonstrated to be effective in two short-term clinical trials.

Objectives: To assess efficacy of TCZ in refractory GCA or with side effects to corticosteroids in clinical practice.

Methods: Multicenter study on 134 patients with GCA in treatment with TCZ due to lack of efficacy and/or unacceptable adverse events of previous therapy.

Results: 134 patients (101 w/33 m); mean age of 73.0±8.8 years. Main clinical features at TCZ onset were: PMR (n=73), constitutional syndrome (n=31), headache (n=70), visual (n=28) and jaw (n=14) affection. Besides steroids, 98 patients also received immunosuppressive agents. table 1 shows evolution during follow-up period. After a median follow-up of 12 [3.7–24] months, it was observed a decrease in: **a)**CRP from 1.7 [0.4–3.2] to 0.1 [0.0–0.3] mg/dL **b)**ESR from 33 [14.5–61] to 4^{2–9} mm/1st hour and **c)** Prednisone dose from 15^{10–30} to 5 [0–7.5] mg/day. Outcome of patients was: **a)**discontinuation of TCZ (n=15) due to sustained remission, **b)**dose reduction due to improvement (n=17) or side effects (n=11), **c)**withdrawal of TCZ because of side effects (n=12) and **d)**same dose that at onset (n=73). TCZ had to be discontinued due to: infections, haematological and cardiovascular alterations, neoplasms and hepatic toxicity among the most frequent.

Table 1:

	Baseline n=134	Month 1 n=132	Month 3 n=122	Month 6 n=99	Month 12 n=71	Month 24 n=39
Clinical improvement % (n#)		93.9% (124/132)	94.2% (115/122)	94.9% (94/99)	92.9% (66/71)	100% (39/39)
Laboratory markers, median [IQR]						
ESR (mm/1 st h)	33 [14.5–61] ** (129)	8 [2–12] ** (102)	4 [2–7.5] ** (116)	4 [2–8] ** (93)	4 [2–8] ** (71)	8 [2–16] ** (39)
CRP (mg/dl)	1.7 [0.4–3.2] ** (131)	0.1 [0–0.5] ** (96)	0.1 [0–0.4] ** (110)	0.1 [0–0.3] ** (92)	0.1 [0–0.3] ** (67)	0.1 [0–0.4] ** (39)
Hemoglobin (g/dl)	12.3 [11.4–13.2] ** (126)	13.2 [12.3–14] ** (104)	13.5 [12.5–14.3] ** (107)	13.6 [12.8–14.1] ** (88)	13.3 [12.5–14] ** (64)	13.1 [12.3–13.9] * (39)
Dose of corticosteroids (mg/day), median [IQR]	15 [10–30] ** (134)	13.7 [7.5–20] ** (115)	8.1 [5–12.5] ** (120)	5 [2.5–7.5] ** (97)	2.5 [0–5] ** (71)	0 [0–5] ** (39)

Improvement in at least one of the clinical features. *p<0.001 **p<0.0001 (test de Wilcoxon).

Conclusions: TCZ leads to a rapid and maintained improvement in patients with refractory GCA and/or with unacceptable side effects related to corticosteroids. However, the risk of neutropenia and infection should be kept in mind.

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THU0440

SOLUBLE CTLA-4 IS ELEVATED IN PATIENTS WITH POLYMYALGIA RHEUMATICA AND CORRELATES WITH VASCULAR INFLAMMATION DETECTED BY PET/CT

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Background: Positron emission tomography has shown the presence of large vessel vasculitis (LVV) in 30%–40% of patients with apparently isolated polymyalgia rheumatica (PMR)^[1], but biomarkers associated with the presence of LVV in PMR patients are still lacking. Anti-cytotoxic T lymphocyte antigen-4 (CTLA-4) and its soluble (s) form, resulting from alternative splicing, are well-known immune checkpoint receptor^[2] and have shown to play a role both in neoplastic^[3] and autoimmune diseases^[4]. The rationale for studying the involvement of CTLA-4 in PMR is provided by the evidence of drug-induced PMR/giant cell arteritis (GCA) in patients treated with ipilimumab, an anti-CTLA-4 antibody^[5].

Objectives: To evaluate the concentration of sCTLA-4 in PMR patients and to correlate it with vascular and joint inflammation.

Methods: Forty consecutive patients with of PMR, of whom 9 also had also GCA, underwent a standardised clinical examination and a PET/CT scan. Arterial and joint uptake of FDG were scored relative to liver and then summed up to obtain a total vascular score (TVS) and a total joint score (TJS). Patients were further subdivided into three groups for the analysis of the correlation with joint and vascular uptake: "vasculitic patients" (with grade-3 uptake in at least one vascular district), patients with intermediate uptake (excluded from this set of analyses), and patients without vasculitis. sCTLA-4, was evaluated by ELISA. Patients without autoimmune diseases served as controls.

Results: sCTLA-4 serum levels were significantly higher in PMR patients than in controls (p<0.001, figure 1), although their concentrations did not significantly differ between patients with and without vasculitis. However, sCTLA-4 showed a positive correlation with TVS (r=0.35, p=0.025), figure 1. Panel A: comparison of serum level of sCTLA-4 in patients with PMR and controls (HD: healthy donors). Panel B: correlation between sCTLA-4 and total vascular score.

Conclusions: The present study provides the first evidence that serum sCTLA-4 concentration is elevated in PMR patients, and that it correlates with TVS. Although the exact mechanisms underlying the upregulation of sCTLA-4 remain

elusive, we feel that aberrant production of cytokines, or abnormal activation of intercellular signalling pathways can be involved.

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THU0441 ENDOTHELIAL DYSFUNCTION IN POLYMYALGIA RHEUMATICA

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Background: Polymyalgia Rheumatica(PMR)is an inflammatory disease that affects people over 50 years old, characterised by pain and functional limitation of shoulder and hip, acute phase reactant elevation and a dramatic response to low doses of steroids.

Atherosclerosis is a chronic inflammatory process that affects the arterial vessels of multiple districts. Endothelial dysfunction is an early event of the atherogenic process. Chronic inflammatory diseases have an increased risk of accelerated atherosclerosis and cardiovascular disease.

A study on 41 subjects with giant cell arteritis with and without PMR showed an increased mean-intimal thickness, suggesting a pro-atherogenic role of PMR. However there are no studies that evaluated endothelial dysfunction which is a more precocious marker of subclinical atherosclerosis in PMR patients

Objectives: Aim of the study was to compare endothelial function among PMR patients to a control population. Moreover, the trend of endothelial dysfunction was evaluated over time in relationship to the improvement of clinical, laboratory and instrumental parameters.

Methods: The study involved 16 treatment-naive patients with a new PMR diagnosis.

Every 3 months routine visits were performed;at each visit laboratory and clinical data and the endothelial function at the brachial artery were evaluated.

The endothelial function was evaluated at the brachial artery level after 15 min of rest; the brachial artery diameter and the basal flow was measured at baseline and after the positioning of sphygmomanometerfor 5 min to induce the forearm ischemia. The flow was measured again 15 s after deflation of the sleeve and 60–90 s after the diameter of the artery reassessed to obtain flow-mediated dilatation (FMD). The FMD, which represents endothelium-dependent vasodilatation was expressed as percentage increase to the starting diameter after stimulation

Results: 16 PMR patients(mean age 73.9±5.8, 7 Female)were compared with a population of 16 healthy controls age-matched(70.8±8.1,p=ns).

The two groups differed for the values of Erythrocyte Sedimentation Rate(ESR) (61.1±28 vs 19.3±16 mm/h, p<0.001)and C-Reactive Protein (CRP)(35.6 ±28.1 mg/L vs 2.4±0.4 mg/L, p<0.001).

At the sixth month of follow-up ESR was 31.2±29.9 mm/h while CRP was 8 ±5.9 mg/L; at the twelve month of follow-up ESR was 22.7±13.6 and CRP was 9.1±8.2 mg/L

In PMR patients group 11 patients had hypertension, 5 dyslipidemia, 1 diabetes and 5 patients were smokers, while in control group 9 had hypertension, 10 dyslipidemia, 6 were smokers and no one had diabetes. Healthy subjects matched by age, sex and comorbidity were chosen as controls.

At baseline FMD of patients was lower than controls(6.6±3.4 vs 10.7±2.3, p<0.001). After 6 months of steroid therapy the difference between the two groups remained significant(6.1±2.7 vs 10.7±2.3 p=0.001), while at the twelfth month the two groups achieved comparable FMD values(8.7±3.6 vs 10.7±2.3,p=0.067). The FMD values show an inverse correlation with values of ESR(R=−0.42 p=0.019)and CRP(R=−0.56 p=0.001)at baseline.

Conclusions: Endothelial dysfunction in patients with PMR appears early during the course of the disease and is related to levels of acute phase reactant; steroid therapy gradually improves these values;only after a year of therapy comparable values are observed between patients and healthy controls.

Disclosure of Interest: None declared

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THU0442 IS BEHCET'S SYNDROME GETTING Milder? A RETROSPECTIVE ANALYSIS OF INITIAL PRESENTATION FINDINGS THROUGHOUT 4 DECADES

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Background: There is some evidence that incident Behcet's syndrome (BS) might be becoming less severe.¹

Objectives: We compared clinical findings at presentation of BS patients registered in a large, long standing dedicated multidisciplinary outpatient clinic at 4 time points during a 40 years period.

Methods: There were 4 groups. Group 1 included patients registered in 1979–1981, Group 2 those registered in 1990, Group 3 in 2000 and Group 4 in 2010. Only demographic and clinical findings at initial presentation were recorded.

Results: As shown in table 1, over 4 decades, male/female ratio decreases gradually. While mean age at presentation does not change, the median disease duration got shorter. Almost all clinical manifestations except genital ulcers and neurological involvement tended to decrease in frequency. This was also true when genders were separately analysed. Importantly the severity of vascular and eye disease decreased (table 1,2). The slope of vascular disease was more obvious.

Abstract THU0442 – Table 1. Initial demographic and clinical characteristics of cohorts

	Group 1 1979–81 cohort n=211	Group 2 1990 cohort n=170	Group 3 2000 cohort n=225	Group 4 2010 cohort n=270	P
Male/Female	140/71	110/60	142/83	150/120	0.069
Male/Female ratio	1.97	1.83	1.71	1.25	
Mean age at disease onset	31.5±8.3	30.9±9.0	30.7±9.3	32.3±9.6	NS
Median disease duration	2.5 [1.0–6.0]	2.0 [1.0–5.0]	1 [0.5–3]	1 [0.6–4]	0.06
Mucocutaneous inv., n (%)					
Genital ulceration	187 (88.6)	137 (80.6)	184 (81.7)	220 (81.4)	NS
Papulopustular lesion	174 (82.5)	130 (76.5)	187 (83)	185 (68.5)	<0.001
Erythema nodosum	132 (62.6)	88 (51.8)	101 (44.8)	112 (41.4)	<0.001
Ocular involvement, n (%)	107 (50.7)	107 (62.4)	97 (43.1)	129 (47.7)	0.001
Vascular involvement, n (%)	49 (23.2)	29 (17.0)	41 (18.2)	31 (11)	0.008
Large vessel involvement, n (%)	21 (42.9)	11 (38.0)	13 (31.7)	7 (22.5)	<0.001
Neurologic involvement, n (%)	7 (3.3)	6 (3.5)	5 (2.2)	10 (3.7)	NS
Arthritis, n (%)	79 (37.4)	37 (21.8)	53 (23.6)	56 (20.7)	<0.001

Abstract THU0442 – Table 2. Severity of ocular involvement at presentation

Ocular involvement	Group 1 1979–81 cohort n=107	Group 2 1990 cohort n=106	Group 3 2000 cohort n=97	Group 4 2010 cohort n=129	p
Visual acuity<0.1 in bilateral eyes, n (%)	17 (15.7)	8 (7.5)	6 (6.5)	9 (6.9)	0.03*
Visual acuity<0.1 in unilateral eye, n (%)	23 (21.3)	19 (17.9)	18 (19.7)	22 (17)	
Visual acuity>0.5 in bilateral eyes	39 (36.1)	54 (55.6)	55 (60.4)	73 (56.6)	

*Group 1 vs 4 and Group 1 vs 3