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Rheumatology 2015;54:371–372
doi:10.1093/rheumatology/keu435
Advance Access publication 5 December 2014

Treatment of systemic sclerosis with tocilizumab

SIR, SSc has a highly variable clinical picture and different levels of severity. Despite innumerable attempts to identify potential drugs, there is a lack of effective immunomodulatory therapies [1, 2]. IL-6 overexpression and pathogenicity in SSc have been demonstrated [3], and the effects of IL-6 in the SSc fibrotic response *in vitro* are concentration dependent [4], thus providing the rationale for its antagonization with tocilizumab (TCZ) [5]. Two cases of SSc treated with TCZ have been published [6]. In addition, TCZ has been demonstrated to be effective in SSc-polyarthritis in a trial that enrolled 15 patients treated with TCZ [7]. We report a mini-series of three patients with refractory SSc (patients 1, 2 and 3), treated with TCZ (8 mg/kg every 4 weeks). They were all female, and age at the time of SSc diagnosis was 52 (patient 1), 34 (patient 2) and 53 (patient 3) years old. The time lapse since diagnosis was 3 years, 8 years and 1 year, respectively. At baseline, the manifestations were as follows: skin thickening in face, hands (patients 1, 2 and 3), forearms, trunk (patients 1 and 2) and lower legs (patient 2); facial telangiectasias (patients 1–3); RP (patients 1, 2 and 3); digital ulcers in PIP joints (patient 1 with three ulcers and patient 2 with eight ulcers); arthralgias of PIP joints, wrists, elbows (patients 1 and 2), shoulders (patients 2 and 3) and MCP joints (patient 3), with synovitis only in PIPs and MCPs of patient 3; gastro-oesophageal reflux (patients 1 and 2), malabsorption syndrome (patient 1); intestinal infarction (patient 2); non-specific interstitial pneumonia, according to the scoring system proposed by Wells [8] (patient 1 with

TABLE 1 Evaluated parameters at baseline and after the first tocilizumab infusion

Parameter	Patient	Baseline	6 months	9 months
mRSS	1	17	11	–
	2	41	25	–
	3	7	5	–
Digital ulcers, *n*	1	3	0	–
	2	8	0	–
	3	0	0	–
Weight, kg	1	35	47	–
	2	49	57	–
	3	70	62	–
Patient global assessment (0–100)	1	70	40	–
	2	70	30	–
	3	60	10	–
Haemoglobin, g/dl	1	9.5	11.5	–
	2	11.8	13.3	–
	3	14.2	14.7	–
ESR, mm/h	1	86	55	–
	2	46	5	–
	3	3	3	–
CRP, mg/dl	1	8.1	1.9	–
	2	1.75	0	–
	3	0	0	–
DLCO, %	1	47.8	50	–
	2	72.1	75	–
	3	78	63	–
Chest CT (Wells' score)	1	Global disease extent 40% Reticular 40% Ground glass 60%	–	No change
	2	Global disease extent 15% Reticular 20% Ground glass 80%	–	No change
	3	Global disease extent 20% Reticular 10% Ground glass 60%	–	Global disease extent 25% Reticular 15% Ground glass 85%

mRSS: modified Rodnan Skin Score; DLCO: diffusing capacity for carbon monoxide.

extensive disease, patients 2 and 3 with limited disease); decreased diffusing capacity (DLCO) with normal lung volumes (patient 1, 47.2%; patient 2, 72.1%; patient 3, 78%); detectable right ventricular systolic pressure (patient 1, 28 mmHg; patient 2, 22 mmHg); anaemia (patient 1, haemoglobin 9.5 g/dl; patient 2, haemoglobin 11.8 g/dl), raised ESR (patient 1, 86 mm/h; patient 2, 46 mm/h), raised CRP (patient 1, 8.1 mg/dl; patient 2, 1.75 mg/dl). The immunology profile showed ANAs (patients 1, 2 and 3), anti-topo I antibodies (patients 2 and 3) and anti-PMscl 100 antibodies (patient 3). Patient 3 was also positive for RF and anti-CCP2 antibodies.

Patient 1 received treatment with iloprost, bosentan, CYC, AZA, HCQ and steroids. An initial response was seen, but 2 months after completing CYC and on AZA, lung involvement worsened, with an increased extent of ground glass appearance and fibrosis on chest CT. Digital ulcers reappeared at this point and the patient had a steep weight loss. Patient 2 was refractory to steroids, bosentan, CYC and AZA. Patient 3, with an overlap of SSc and RA, was treated with MTX, HCQ, steroids and etanercept, which was switched to adalimumab after an injection site reaction. She had poor control of arthritis and progression of lung involvement. The decision was to administer TCZ in all three of the patients.

Overall, TCZ was well tolerated, and all the patients experienced a general improvement in coping with normal daily activities. Clinical and laboratorial parameters and pulmonary function tests were reassessed 6 months after the first administration, and chest CT was repeated after 9 months (Table 1). The patient global assessment improved by 30 (70 to 40), 40 (70 to 30) and 50 (60 to 10) in patients 1, 2 and 3, respectively. Skin thickness evaluated with the 17 site modified Rodnan skin score improved in patient 1 (from 17 to 10) and patient 2 (from 41 to 25). Patient 3 varied from 7 to 5. Simultaneously, the two patients with digital ulcers showed complete healing. An increase in haemoglobin levels and body weight was also noted, which was accompanied by a decrease in ESR and CRP levels and thus reflected the anti-inflammatory effects of TCZ. There was a halt in the progression of lung disease in patient 1 (no progression on CT; DL_{CO} 50%) and patient 2 (no progression on CT; DL_{CO} 75%) and only a slight CT worsening and decrease in DL_{CO} to 65% in patient 3. All the patients had an important and long-standing lung involvement with fibrosis, and therefore the potential benefits of TCZ (or lack of) should be considered with caution. Patient 3 had RA/SSc overlap syndrome, with previous treatment with MTX and active synovitis that ameliorated after treatment with TCZ (DAS28 decreased from 3.82 to 2.87 in 6 months), which is consistent with previous evidence. Our mini-series suggests that TCZ might be a valuable treatment for SSc. These results reinforce the need for clinical trials using TCZ in diffuse SSc.

Rheumatology key message

- TCZ could be a valuable option for the treatment of SSc.

Funding: No specific funding was received from any funding bodies in the public, commercial or not-for-profit sectors to carry out the work described in this manuscript.

Disclosure statement: The authors have declared no conflicts of interest.

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Accepted 16 September 2014
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Rheumatology 2015;54:372–373
doi:10.1093/rheumatology/keu353
Advance Access publication 8 September 2014

Comment on: Induction treatment of ANCA-associated vasculitis with a single dose of rituximab

SIR, In their report of 19 ANCA vasculitis patients, Turner-Stokes and colleagues [1] present interesting data on remission induction treatment with a single dose of rituximab. The authors conclude that the efficacy of the