Methotrexate treatment of polymyalgia rheumatica/giant cell arteritis-associated large vessel vasculitis

Sirs,

Polymyalgia rheumatica (PMR) and giant cell arteritis (GCA) are frequently overlapping diseases. About one third of patients with "pure" PMR and two thirds of those with GCA show involvement of different large arteries, including the aorta and its branches (1, 2). These findings have been detected mainly in studies performed with positron emission tomography (PET), a sensitive imaging method for large vessel inflammation (3, 4). We have previously shown that a third of PMR patients with steroid-resistant disease have large vessel vasculitis (5). Steroid resistance was defined as the impossibility to withdraw prednisolone treatment before 2 yrs and to taper its dosage to <7.5mg daily without exacerbations (6).

The three patients from the original paper (5) and two additional ones, who also showed steroid resistance, were treated with methotrexate (MTX) 10 to 15 mg/week in addition to the ongoing dose of prednisone (7.5–18.75 mg/day). The five women had a median age of 73 years (range 52–75 years). Four of them had several symptoms possibly suggesting the coexistence of giant cell arteritis (slight headache, transient pain during chewing) but none had a palpable, hard, painful, or pulseless temporal artery; biopsy was performed in only one patient and resulted negative. PET-CT was performed before and after a median of 10.7 months (range 6-16 months) of MTX treatment (Fig. 1). Two different methods were used to calculate vascular uptake. The first (**A**), suggested by Blockmans *et al*. (1), evaluates vascular FDG uptake as negative (0) or positive, further scored semiquantitatively as 1=minimal but not negligible, 2 =clearly increased, and 3=very marked FDG uptake; the second (**B**), suggested by Walter *et al*. (7), scores the uptake with the same grading but relates values to liver uptake in terms of 0=no uptake present, 1=low-grade uptake, lower than liver uptake, 2=intermediate-grade uptake, similar to liver uptake, 3=high-grade uptake, higher than liver uptake. Each of the seven vascular regions cited in Table I contributed to the Total Vascular Score (TVS), which ranges between 0 and 21. Joint involvement due to synovitis and/or bursitis was calculated with a semiquantitative score, ranging from 0 (absent) to 2=clearly increased in three areas including shoulders, hips, and the spine (1). The corresponding Total Joint Score (TJS) was comprised between 0 and 6. Two readers (DC and SM) evaluated each 140 arteries (7 arteries before and after treatment, in 5 patients, with 2 methods) and 30 joints. Intraclass correlation coefficient (ICC) was 0.75 for vasculitis and 0.92 for synovitis/bursitis. In case of discordance, final scoring was obtained after consensus between the readers.

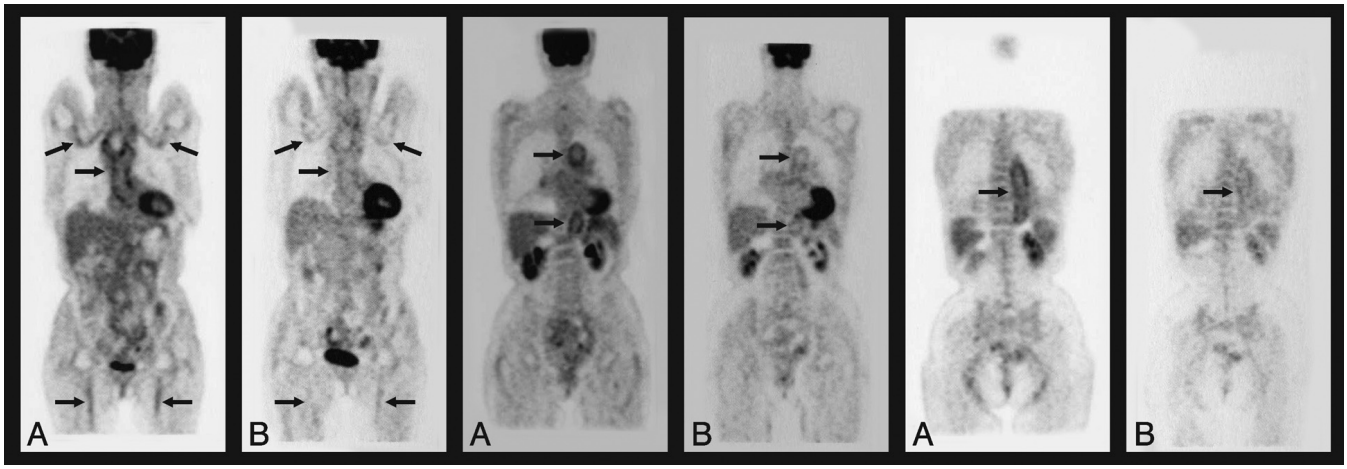

Fig. 1. PET-CT uptake of (18F) fluorodeoxyglucose in the large vessels (arrows) of a patient with polymyalgia rheumatica and vasculitis before (**A**) and after (**B**) the addition of methotrexate to the standard steroid treatment.

Table I. PET-CT uptake of (18F) fluorodeoxyglucose and laboratory parameters of inflammation in 5 patients with steroid-resistant PMR/GCA before (baseline) and after (follow-up) the adjunct of methotrexate to the current steroid treatment. The vascular score was calculated by two methods A and B (see text for the details). (TVS: Total Vascular Score, TJS: Total Joint Score).

	Patient 1				Patient 2				Patient 3				Patient 4				Patient 5			
	baseline		follow-up		baseline		follow-up		baseline		follow-up		baseline		follow-up		baseline		follow-up	
ARTERY	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B
thoracic aorta	3	3	1	2	3	2	1	1	2	2	2	2	1	2	1	1	2	2	1	1
carotid	1	1	1	1	0	0	0	0	1	2	0	0	1	2	0	0	1	1	1	1
subclavian	2	1	1	1	1	1	0	0	3	3	2	2	1	1	1	1	1	1	0	0
axillary	2	2	1	1	0	0	0	0	2	2	1	1	0	0	0	0	1	1	0	0
abdominal	2	3	0	0	0	0	0	0	2	2	1	1	0	0	0	0	0	0	0	0
iliac	0	0	0	0	1	1	0	0	1	1	0	0	0	0	0	0	0	1	0	0
femoral	1	2	0	0	1	1	1	1	1	1	0	0	3	3	1	1	1	1	1	1
TVS	11/21	12/21	4/21	5/21	6/21	5/21	2/21	2/21	12/21	13/21	6/21	6/21	6/21	8/21	3/21	3/21	6/21	7/21	3/21	3/21
SYNOVITIS/BURSITIS																				
hip	1		0		1		0		1		1		2		1		1		0	
shoulder	1		0		2		2		2		1		2		1		0		0	
spine	1		0		0		0		0		1		2		0		2		0	
TJS	3/6		0/6		3/6		2/6		3/6		3/6		6/6		2/6		3/6		0/6	
ESR (mm/h)	89		41		57		41		50		24		116		16		56		22	
CRP (mg/dL)	87		21		28		22		24		4		95		6		7		4	

The combined treatment with MTX and steroids markedly improved the clinical condition of all patients allowing mean prednisone tapering from 13.1 mg/day to 7.9 mg/day. In the same period, median ESR declined from 57 mm/h (range 50–116 mm/h) to 24 mm/h (range 16–41 mm/h) (p=0.06), and median CRP from 28 mg/dL (range 6.6–95.4 mg/dL) to 6 mg/dL (range 2–22.5 mg/dL) (p=0.06). After MTX treatment, the median TJS changed from 3 (range 3–6) to 2 (range 0–3) (p=0.12); the median TVS declined from 6 (method A, range 6–12) and 8 (method B, range 4–13) to 3 (range 2–6) and 3 (range 2–6), respectively (both p=0.06) (Table I). All statistical calculations were performed with the Wilcoxon test for paired samples. The two scoring methods did not differ from each other. No correlation was found between TJS, TVS, ESR, and CRP.

In our patients with PMR-related symptoms and underlying vasculitis, the traditional PMR steroid treatment was insufficient, but co-administration of MTX improved control of inflammation. Clinical, laboratory, and imaging features of inflammation declined, although not significantly, most probably because of the small sample considered. The two semiquantitative methods used to evaluate (18F) fluorodeoxyglucose uptake proved to be equivalent, although scores obtained with method B were slightly higher. A more objective and reliable method could be to place ROIs on selected arteries and calculate their mean SUV. MTX has shown efficacy and steroid sparing effect in both PMR (8) and GCA (9), although these results have been questioned. Our results support the utility of MTX in vasculitis; they further suggest that MTX may be especially effective in the subset of patients with PMR or GCA who are also affected by large vessel vasculitis.

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