

Letters to the Editor

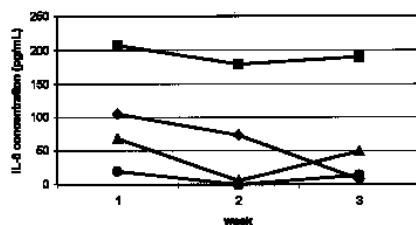


Fig. 1. IL-6 concentration before (week 1) and after 2 and 3 weeks from the administration of i.v. steroid boli in the 4 patients with recent onset polymyalgia rheumatica. The mean IL-6 concentration plus 3 standard deviations in 43 healthy age- and sex-matched controls was < 4 pg/mL.

much as 65% of patients (1). Therapeutic approaches proposed to reduce the incidence of steroid-related side effects include different administration schemes of steroids or alternative drugs with a possible steroid-sparing effect. Steroids have been used by shoulder injection (2) or weekly depot injections (3). Steroid-sparing therapies studied so far include methotrexate (4), azathioprine (5), and tenidap (6), but their efficacy is not clear.

Our hypothesis was that steroid pulses administered in the early phase of the disease could induce remission by aborting inflammation. The recently described mechanisms of action, such as inhibition of nuclear factor- B resulting in decreased transcription for expression of pro-inflammatory genes (7) and non-genomic physicochemical actions (8), are probably active only when steroid pulses are used. Steroid pulses are not associated with the side effects commonly reported with chronic administration. In this pilot study, administration of pulse steroids to PMR patients, at doses roughly equivalent to those assumed in the first 2 months of standard therapy, was attempted. Four patients affected by untreated PMR (9) (mean disease duration 64.8 days, range 49-90 days) were studied. The study was performed according to the declaration of Helsinki and was approved by the relevant ethical committees. PMR recurrences and relapses were defined as signs or symptoms of the disease associated with increased ESR or CRP appearing, respectively, during treatment or after its discontinuation. ESR, CRP, and IL-6 (R&D Systems, Minneapolis, MN, USA) were evaluated before treatment and after 7 and 15 days from the first corticosteroid bolus. Bolus i.v. injections of methylprednisolone (250 mg in 250 cc of saline) were administered on 3 consecutive days. If PMR relapsed, oral prednisone was given with the rapidly decreasing dosage previously used in a controlled trial on the efficacy of methotrexate as steroid-sparing agent (4). End points of the study were the time between the last steroid

bolus and the relapse of PMR, if any, as well as the dosage of steroids eventually needed after the 3-day course. In addition, the number of recurrences and relapses occurring during and after oral steroid treatment respectively was calculated and compared with those of the control group of the previously cited therapeutic trial, consisting of 31 patients with PMR treated with prednisone alone (4).

PMR symptoms disappeared and laboratory signs of inflammation improved in 3/4 patients during i.v. treatment, but recurred in all patients after a mean time of 6.4 days (range 3-14 days) from the last steroid bolus. The mean dosage of oral prednisone taken after the boli was 2237 ± 213 mg, a value which was not different from the 2832 ± 750 mg taken by controls. Recurrences were seen in 1 out of 4 (25%) patients in the first group and in 22 out of 31 (71%) patients in the second group (ns). The median follow-up period after the initiation of steroid treatment was 19 months (range 12-22 months). After completion of the treatment, no pulse-treated patient suffered relapses in comparison with 10/31 (32.3%) controls (ns). IL-6 concentrations dramatically decreased after the bolus treatment but returned to the initial values 2 weeks later in all but one patient (Fig.1). This patient did not improve after the boli and therefore received oral steroids earlier than the other patients, a fact that probably kept the IL-6 concentration low.

In conclusion, 3 pulses of i.v. methylprednisolone failed to induce remission in PMR and to show any steroid-sparing effect in our small, uncontrolled study. Similarly, no significant corticosteroid-sparing effect has been described after a single pulse with 240 mg of methylprednisolone in patients with GCA (10).

M.A. CIMMINO, MD F. CANTINI², MD
P. MACCHIONI¹, MD L. PULSATPELLI³, MD
L. BOIARDI¹, MD C. SALVARANI¹, MD

Clinica Reumatologica, D.I.M.I., Università di Genova; ¹Divisione di Reumatologia, Arcispedale S. Maria Nuova, Reggio Emilia; ²Divisione di Medicina Interna, Ospedale di Prato, ³Laboratorio di Immunologia e Genetica, Istituto Rizzoli, Bologna, Italy.

Address correspondence to: Marco A. Cimmino, MD, Clinica Reumatologica, D.I.M.I., Università di Genova, Viale Benedetto XV no. 6, 16132 Genova, Italy. E-mail: cimmino@unige.it

References

1. GABRIEL SE, SUNKU J, SALVARANI C, O'FALLON WM, HUNDER GG: Adverse outcomes of anti-inflammatory therapy among patients with polymyalgia rheumatica. *Arthritis Rheum* 1997; 40: 1873-8.
2. SALVARANI C, CANTINI F, OLIVIERI I et al.: Corticosteroid injections in polymyalgia rheumatica: a double blind, prospective, randomized, placebo controlled study. *J Rheumatol* 2000; 27: 1470-6.

3. DASGUPTA B, DOLAN AL, PANAYI GS, FERNANDES L: An initially double-blind controlled 96 week trial of depot methylprednisolone against oral prednisolone in the treatment of polymyalgia rheumatica. *Br J Rheumatol* 1998; 37: 189-95.

4. CAPORALI R, CIMMINO MA, FERRACCIOLI GF, GERLI R, SALVARANI C, MONTECUCCO C: Can methotrexate be used as a steroid-sparing agent in the treatment of polymyalgia rheumatica? Preliminary results of a randomized, double blind, placebo-controlled study. *Arthritis Rheum* 2001; 44 (Suppl.): S383.
5. DE SILVA M, HAZLEMAN BL: Azathioprine in giant cell arteritis/polymyalgia rheumatica: a double blind study. *Ann Rheum Dis* 1986; 45: 136-8.
6. LITTMAN BH, BJARNASON D, BRYANT G et al.: Steroid sparing activity of tenidap in patients with polymyalgia rheumatica: A multicenter double blind randomized placebo controlled study. *J Rheumatol* 1995; 22: 1097-103.
7. BOUMPAS DT: A novel action of glucocorticoids - NF- B inhibition. *Br J Rheumatol* 1996; 35: 709-10.
8. BUTTGEREIT F, WEHLING M, BURMESTER GR: A new hypothesis of modular glucocorticoid actions. Steroid treatment of rheumatic diseases revisited. *Arthritis Rheum* 1998; 41: 761-7.
9. JONES JG, HAZLEMAN BL: Prognosis and management of polymyalgia rheumatica. *Ann Rheum Dis* 1981; 40: 1-5.
10. CHEVALET P, BARRIER JH, POTTIER P et al.: A randomized, multicenter, controlled trial using intravenous pulse of methylprednisolone in the initial treatment of simple forms of giant cell arteritis: a one year follow-up study of 164 patients. *J Rheumatol* 2000; 27: 1484-91.

β -thalassaemic trait and systemic lupus erythematosus

Sirs,

The coexistence of haemoglobinopathies and connective tissue disorders has rarely been investigated and published data relating to this matter are only anecdotal. In 1975 we demonstrated that the incidence of the β -thal trait in patients with RA coming from an area in which haemoglobinopathy is endemic, such as Ferrara and Rovigo (the Po Delta, northern Italy), is higher than would be expected based on its occurrence in the general population (19.8% vs 13.1% of a random population from the same two areas) (1).

In SLE, varying degrees of anaemia are quite a common finding but only rarely has the issue of concomitant haemoglobinopathies been addressed. To the best of our knowledge 16 reported cases have described

Table I. Prevalence of Beta-thalassaemic trait in patients with RA and SLE compared to the control population (data referring to the Ferrara and Rovigo areas of Italy).

Total no. subjects	Expected prevalence of -thal in the geographic area studied	Observed prevalence of -thal	Ratio of -thal observed/-thal expected
RA	146	13.1%	19.8%
SLE	177	13.1%	9.6%

ed the coexistence of sickle cell disease (SCD) and SLE (2), but only Kaloterakis *et al.* (3) described a case of sickle cell/ -thalassaemia in a SLE patient.

In a study conducted by Montecucco *et al.* (4) it was stated that the prevalence of the -thal trait in patients with connective tissue diseases and seronegative spondyloarthropathies is similar to that expected for the whole population according to their geographic distribution, but the conclusion was not supported by consistent data.

Previously we observed a markedly lower incidence of the -thal trait among a lupus population born in Ferrara and Rovigo areas compared to a control population coming from the same two areas (5). However, these findings were historical and remained unpublished because of the lack of a rigorous methodological approach to gathering and analysing the data.

We have now prospectively studied the prevalence of -thal minor in 177 consecutive SLE patients from the Ferrara and Rovigo areas (32 males and 145 females, mean age 54 years, range 20-89) diagnosed according to the 1997 revised ACR criteria (6, 7) and followed by our Department from 1998 to the present. Their -thal status was suspected based on findings of a low mean corpuscular volume, low haemoglobin value, and increased number of red blood cells; the condition was confirmed in all the cases by haemoglobin electrophoresis. In this patient population we found 17 SLE patients (all female, mean age 53 years, range 20-88) with -thal minor (9.6% of the cases). This prevalence was 0.7 times lower than the expected rate of 13.1% of the control population and almost half of the prevalence previously observed in RA patients (19.8%) coming from the same areas (Table I).

These data suggest that -thal subjects exhibit a particular immunological reactivity of different circulating lymphocyte T-cells subpopulations. If we consider that RA is a prevalently Th1-oriented disease and SLE is a prevalently Th2-oriented disease, it could be argued that -thal might modify the immunological profile of circulating T cells through a different immune reactivity. Obviously confirmation of this hypothesis will require further studies on T-cell subpopulations and their functioning in

-thal subjects.

On the basis of these data we conclude that the prevalence of the -thal trait is higher in our RA patients and lower in our SLE patients compared with the normal population. The reasons for this different frequency and the way in which the -thal trait interferes with the clinical characteristics of RA and SLE remains a matter of discussion. Large prospective epidemiologic studies will be necessary to determine if the prevalence of serologic and clinical features of immune complex diseases such as SLE is influenced by the coexistence of a haemoglobinopathy.

G. CASTELLINO, MD F. TROTTA, MD
M. GOVONI, MD

Unità Operativa di Reumatologia,
Dipartimento di Medicina Clinica e
Sperimentale, Università degli Studi di
Ferrara, Italy

Corresponding author: Dr. Gabriella
Castellino, Cattedra e Unità Operativa di
Reumatologia, Dipartimento di Medicina
Clinica e Sperimentale, Università degli
Studi di Ferrara, Azienda Ospedaliera-
Universitaria "S. Anna", Corso Giovecca
203, 44100 Ferrara, Italy.
E-mail: gabriella_castellino@yahoo.it

References

1. MARCOLONGO R, TROTTA F, SCARAMELLI M: Beta-thalassaemic trait and rheumatoid arthritis. *Lancet* 1975; i: 1141.
2. SAXENAVR, MINAR, MOALLEM HJ, RAO SP, MILLER ST: Systemic lupus erythematosus in children with sickle cell disease. *J Pediatr Hematol Oncol* 2003; 25: 668-71.
3. KALOTERAKIS A, FILIOTOU A, HAZIYANNIS S: Sickle cell/ -Thalassaemia and systemic lupus erythematosus. *Lupus* 1999; 8: 778-81.
4. MONTECUCCO C, CAPORALI R, ROSSI S, EPIS O: Rheumatoid arthritis in beta-thalassaemia trait. *Br J Rheumatol* 1999; 38: 1021-2.
5. CASTELLINO G, GOVONI M, TROTTA F: Rheumatoid arthritis in -thalassaemia trait. *Rheumatology* 2000; 39: 1286-87.
6. HOCHBERG M: American College of Rheumatology revised criteria for the classification of systemic lupus erythematosus. *Arthritis Rheum* 1997; 39: 403-4.
7. TAN EM, COHEN AS, FRIESHE *et al.*: The 1982 revised criteria for the classification of systemic lupus erythematosus. *Arthritis Rheum* 1982; 25: 1271-7.

Monolateral coxitis as a unique osteoarticular manifestation of Parvovirus B19 infection

Sirs,

Since its discovery (1), human parvovirus B19 (B19) has been linked with a broad spectrum of clinical syndromes, the most common of which are erythema infectiosum, aplastic crisis complicating chronic hemolytic anemia and hydrops fetalis (2). The articular manifestations, though less commonly recognised, have received increasing attention recently. The recent studies have shown that B19 infection can cause acute arthritis both in children and adults, although its prevalence in adults with arthralgia and acute arthritis has been reported to be 80% (3) while in children it is 21.2% (4) or 21.6% (5). In order to provide further insights into the various clinical manifestations of acute arthritis in children with B19 infection we would like to report a 13-year-old male child with monolateral coxitis.

The patient was admitted to our unit because of remittent fever lasting for 20 days associated with pain and restricted left hip motion. The boy held his left hip flexed and abducted, with no internal rotation and no objective evidence of local inflammation. Laboratory investigations revealed leukocytosis (13,600 cells/ml) with normal neutrophils (60%), high ESR levels (62/hr) and positive C reactive protein CRP(20.7 mg/l; normal range 0-3 mg/l).

ANA, nDNA, HLA-B27, ASO, the Mantoux test and serologic tests for Cytomegalovirus, Epstein-Barr virus, rubella, *Mycoplasma pneumoniae* and brucella were all negative. B19 infection was diagnosed on the basis of the specific presence of IgM antibody (enzyme immunoassay: IgM 92.5 U/ml; normal < 30 U/ml) and was confirmed by seroconversion during a 6-month follow-up. Ultrasound evaluation and computerized tomography of the left hip confirmed the presence of synovial fluid. After 2 days of treatment with Flurbiprofene (5 mg/kg/day) the fever disappeared and the articular symptomatology slowly improved; after 15 days of therapy CRP and leucocytosis were normalized. Flurbiprofene therapy was continued for 3 months, with final normalization of the ESR and complete recovery of hip motion.

According to a very recent pediatric study, the most frequently involved joints associated with B19 infections are the knee, wrist, ankle and interphalangeal joints, whereas the elbow, shoulder and cervical vertebrae are less frequently affected (5). To the best of our knowledge coxitis had never been reported hitherto in the literature. Another atypical finding in the present case is the mo-