INSTRUCTIONS FOR LETTERS TO THE EDITOR

Editorial comment in the form of a Letter to the Editor is invited. The length of a letter should not exceed 800 words, with a maximum of 10 references and no more than 2 figures or tables; and no subdivision for an abstract, methods, or results. Letters should have no more than 4 authors. Financial associations or other possible conflicts of interest should be disclosed.

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Sensitivity and Specificity of the CASPAR Criteria for Psoriatic Arthritis in a Family Medicine Clinic Setting

To the Editor:

Psoriatic arthritis (PsA) is an inflammatory arthritis associated with psoriasis with an estimated prevalence in the United States of 0.25%[1]. The prevalence of PsA in patients with psoriasis is 30%[2]. Since the prevalence of psoriasis in North America is 2%, the estimated population prevalence of PsA of 0.25% is probably an underestimate[3]. PsA is thus underdiagnosed. This may be due to the lack of recognition of the condition in family practice and dermatology practice.

The original diagnostic criteria of Moll and Wright are the simplest and the most frequently used[4]. In order to make the diagnostic criteria more specific a number of classification criteria were developed, but none were widely agreed upon or validated[5,6]. The ClASsification of Psoriatic ARthritis (CASPAR) study group published new criteria for the classification of PsA derived from patients attending rheumatology clinics[5]. The sensitivity and specificity of the CASPAR criteria in the original study were 91.4% and 98.7%, respectively[5]. Subsequently, we have shown that the criteria have a sensitivity of 99.1% in early PsA[7]. The performance of the CASPAR criteria outside specialty rheumatology clinics has not been investigated. The authors of the original study felt that it was not possible to apply the results of the study to the general population or to other clinic populations (e.g., dermatology clinic populations) as the study was conducted in patients with known inflammatory articular disease[5]. The authors recommended that the criteria be tested in the general population[5]. We therefore conducted the present study to evaluate the criteria in patients attending a Family Medicine clinic.

The CASPAR criteria were applied to consecutive consenting patients attending a Family Medicine clinic attached to the Toronto Western Hospital. All patients were assessed by a rheumatologist according to a standard protocol, based on which a diagnosis of PsA was made. The protocol was based on the University of Toronto PsA clinic protocol, and included questions about inflammatory joint symptoms and a complete physical examination including detailed musculoskeletal assessment[8]. All patients were tested for antinuclear antibodies and for rheumatoid factor. Other laboratory tests and radiographs were done when clinically indicated. The diagnosis was subsequently confirmed by a rheumatologist acknowledged to be an expert on PsA. The CASPAR criteria were applied to all patients participating in the study and in a subgroup with inflammatory musculoskeletal symptoms, and the sensitivity and specificity determined[5].

Table 1. Demographic and disease characteristics of all study participants (n = 175).

Characteristics	No. (%) or ± SD
Female/male	112/63
Mean (± SD) age, yrs	41.2 (± 14.3) years
Subjects with psoriasis (%)	8 (4.6)
Subjects with inflammatory joint symptoms and/or signs (%)	37 (21)
Psoriatic arthritis	2
Ankylosing spondylitis	1
Undifferentiated spondyloarthritis	1
Rheumatoid arthritis	1
Systemic lupus erythematosus	1
Gout	1
Inflammatory joint symptoms/signs	28
Tender joints	15
Inflammatory back pain	9
Enthesitis	2
Tender joints and inflammatory back pain	1
Tender joints and enthesitis	1

A total of 175 subjects were evaluated. Their demographic and disease characteristics are given in Table 1. Thirty-seven (21%) had inflammatory musculoskeletal symptoms and/or signs at the time of evaluation. The disease characteristics of these 37 patients are also given in Table 1. Two subjects had PsA. Twenty-eight subjects had various musculoskeletal symptoms and/or signs, but a specific diagnosis was not made.

The CASPAR criteria for classification of PsA were applied to the entire group of 175 subjects. Both subjects with PsA satisfied the CASPAR criteria. Thus the sensitivity was 100%. Of the 173 subjects who did not have PsA, 171 did not satisfy the criteria. The specificity thus was 98.8%. The criteria were applied to the subgroup of subjects with inflammatory musculoskeletal symptoms/signs. Both patients with PsA satisfied the criteria (sensitivity 100%). Of the 35 subjects without PsA, 33 did not satisfy the criteria (specificity 94.3%). Two patients without PsA satisfied the CASPAR criteria. One had psoriasis and ankylosing spondylitis and the other had psoriasis and inflammatory back pain.

Thus, our study shows that the CASPAR criteria have a sensitivity of 100% and specificity of 98.8% (94.3% if restricted to patients with inflammatory musculoskeletal symptoms/sign) in a family practice setting. After further validation in primary care, early arthritis clinics, and general rheumatology clinics, the criteria may be used as both diagnostic and classification criteria. This will greatly help research on the epidemiology and genetics of PsA, and will also facilitate early diagnosis of this condition in clinical practice. The prevalence of inflammatory articular symptoms/signs in the study subjects was high (21%). The estimated prevalence of self-reported arthritis/rheumatism in Canada is 17.63%[9]. Our figures are higher, even though we have included patients with inflammatory musculoskeletal symptoms only. The higher prevalence could be explained by the fact that the clinic is attached to a major university teaching hospital dealing primarily with rheumatology and neurological sciences.

The results of our study show that CASPAR criteria are highly sensitive and specific when applied to subjects attending a family medicine clinic. The criteria thus have the potential to be used as diagnostic criteria for PsA and as a tool in epidemiological studies on the prevalence of PsA.

VINOD CHANDRAN, MBBS, MD, DM; CATHERINE T. SCHENTAG, MSc; DAFNA D. GLADMAN, MD, FRCPC, University of Toronto Psoriatic Arthritis Clinic, Centre for Prognosis Studies in the Rheumatic Diseases, Toronto Western Hospital, Toronto, Ontario, Canada. Address reprint requests to Dr. Gladman; E-mail:dafna.gladman@utoronto.ca

Vinod Chandran is supported by a Krembil Psoriatic Arthritis Fellowship. The University of Toronto Psoriatic Arthritis Program is partially supported by the Krembil Foundation.

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Dr. Taylor replies

To the Editor:

Classification criteria are very helpful in identifying a group of people with meaningful homogeneity with respect to a particular disease, syndrome, or health condition. The more closely the criteria concur with the true state of the patient and the more specific contexts in which this is demonstrated, the more useful the criteria. The CASPAR criteria for psoriatic arthritis (PsA) are the most robust and accurate classification criteria yet demonstrated for any rheumatic disease[1]. The criteria remain accurate in the context of early disease and, as shown by Dr. Chandran and colleagues, in undifferentiated patients presenting to a family medical clinic. This is possibly unprecedented in rheumatology.

Yet some caveats remain. Chandran and colleagues propose that the excellent performance of the CASPAR criteria across different contexts constitutes evidence for "diagnostic criteria." This is a more challenging concept than "classification criteria." First, diagnosis is a process in which all available information is processed, interpreted, and synthesized. Data beyond those listed in classification criteria may be important in the final diagnostic analysis. For example, in some patients, magnetic resonance imaging findings may be important to aid diagnosis, yet these are not listed in current classification criteria. Second, classification criteria are supposed to be applied to groups of people, in which probabilistic terms such as sensitivity and specificity or positive and negative predictive value have meaning. In the case of an individual, who either has the disease or not, such probabilistic statements are of limited value. The usefulness of a probability statement when applied to an individual patient depends not only on the absolute value of that probability but also on the consequences of error[2]. Greater likelihood of misdiagnosing a person as having the disease when they do not may be acceptable when the diagnosis leads to relatively innocuous treatment, for example. It is rarely possible to be able to specify in advance the "costs" associated with making a correct or incorrect diagnosis. It may be the case that "diagnostic criteria" can only be meaningful when the criteria define the disorder, so that it is logically impossible for the disease to be present when the criteria are not met and logically impossible for the disease not to be present when the criteria are met. An example of this could be synovial uric acid crystals for the disease of gout. At this time, such a pathognomic feature for PsA is more elusive, and until it is found perhaps we should be more circumspect about claims for "diagnostic criteria."

The other difficulty with the CASPAR criteria that may limit direct application to nonrheumatology settings, despite their accuracy, is the requirement of "inflammatory articular disease." The presence of this item was determined by a rheumatologist in the study reported by Chandran, *et al*. It is unclear whether nonrheumatologists can confidently or accurately judge the presence of inflammatory articular (joint, entheseal, spinal) symptoms and signs, although there is evidence that examinations of joints and for dactylitis are as reliable (or unreliable) among dermatologists as rheumatologists[3]. Nonetheless, further evidence for the broader application of CASPAR criteria might come from testing nonrheumatologist accuracy in determining whether the criteria are met or not.

WILLIAM J. TAYLOR, PhD, MBChB, FAFRM, FRACP, Department of Medicine, University of Otago, Wellington, New Zealand.
E-mail: will.taylor@otago.ac.nz

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Subclinical Atherosclerosis in Patients with Psoriatic Arthritis

To the Editor:

In the May 2008 issue, Eder, *et al* reported the presence of subclinical atherosclerosis, determined by high-resolution carotid ultrasonography, in 40 unselected patients diagnosed with psoriatic arthritis (PsA)[1]. The authors concluded that subclinical atherosclerosis in PsA may not be attributed solely to the presence of traditional cardiovascular (CV) risk factors[1].

We entirely agree with this assumption. In this regard, in 2007 we described the presence of endothelial dysfunction, considered as an early development in the atherogenesis process[2], in patients with PsA without previous history of CV events or traditional CV risk factors[3]. More important, using high-resolution carotid ultrasonography, in the same year we found evidence of subclinical atherosclerosis, manifested by increased carotid intima-media thickness, in 59 PsA patients without history of CV events or traditional CV risk factors compared to matched controls[4].

Although it is now clear that rheumatoid arthritis (RA) is associated with accelerated atherosclerosis and increased CV mortality[5], information about PsA is still limited. However, epidemiologic studies performed by highly experienced investigators support that CV is one of the leading causes of death in PsA patients[6,7].

A remaining question regards the increased incidence of subclinical

atherosclerosis observed in PsA patients without traditional CV risk factors[3,4]. In RA this may be explained by the persistence of a chronic inflammatory status. An association between the mean values of C-reactive protein in patients with longstanding RA without classic CV risk factors and the presence of subclinical atherosclerosis was found[8]. Pathogenic mechanisms similar to those leading to accelerated atherosclerosis in RA, in particular the presence of chronic inflammation, may possibly account for the development of subclinical atherosclerosis in PsA. In keeping with that, we also observed a positive association between the duration of PsA and the presence of subclinical atherosclerosis[4].

Based on these considerations, we feel that patients with PsA must now be considered as individuals who are at high risk for CV events.

MIGUEL A. GONZALEZ-GAY, MD, PhD; TOMAS R. VAZQUEZ-RODRIGUEZ, MD, Rheumatology Division; CARLOS GONZALEZ-JUANATEY, MD, PhD, Cardiology Division, Hospital Xeral-Calde, Lugo; JAVIER LLORCA, MD, PhD, Division of Preventive Medicine and Public Health, School of Medicine, University of Cantabria, Santander, Spain.

Address reprint requests to Dr. Gonzalez-Gay.
E-mail: miguelaggay@hotmail.com

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Dr. Eder, *et al* reply

To the Editor:

We thank Gonzales-Gay, *et al* for their interest in our article[1]. Their letter reinforces our conclusions and further elaborates on the subject.

The data regarding the prevalence of atherosclerosis in psoriatic arthritis (PsA) is still sparse. However, several recent reports, immediately before and since the publication of our study, have concurred with our results by finding an increased prevalence of subclinical atherosclerosis, determined by ultrasound of the carotid arteries, in patients with PsA[2,3]. These findings support the notion that atherosclerosis is indeed more prevalent in PsA.

These findings, however, may not be entirely analogous to the situation present in rheumatoid arthritis, where increased mortality, largely due to cardiovascular disease, is apparently restricted to rheumatoid factor-positive patients[4]. Obviously that would not be the case in PsA. Additional larger cohort studies are needed to further assess the clinical and disease-associated risk factors for atherogenesis in PsA.

Recent reports have suggested that anti-tumor necrosis factor agents can decrease the progression of atherosclerosis in rheumatoid arthritis[5,6]. An interesting future area of investigation would be to assess the influnce of these agents on atherogenesis in patients with PsA.

LIHI EDER, MD; DEVY ZISMAN, MD; DORON RIMAR, MD, Department of Internal Medicine, Carmel Medical Center and Rheumatology Clinic, Lin Medical Center; MENASHE BARZILAI, MD, Ultrasound Unit; MICHAL RAHAT, PhD, Immunology Research Center; ARIE LAOR, MD; HAIM BITTERMAN, MD, Department of Internal Medicine, Carmel Medical Center; MICHAEL ROZENBAUM, MD; ITZHAK ROZNER, MD, Department of Rheumatology, Bnai Zion Medical Center; JOY FELD, MD, Rheumatology Clinic, Lin Medical Center, and Department of Rheumatology, Bnai Zion Medical Center, Haifa, 31048 Israel.

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Interferon-γ Is Associated with Vascular Endothelial Dysfunction in Patients with Rheumatoid Arthritis

To the Editor:

Rheumatoid arthritis (RA) is a chronic inflammatory condition resulting in excessive cardiovascular (CV) mortality, irrespective of classic CV risk factors[1]. Population-based studies have highlighted the importance of inflammatory mediators within atherosclerotic plaques, suggesting that chronic inflammation acts independently or synergistically with other fac-

Table 1. Selected clinical characteristics of 23 patients with RA, allocated in tertiles according to the magnitude of absolute change in flow-mediated vasodilation (FMV). Except for proportions, results are expressed as median (interquartile range).

Data	1st Tertile, n = 8	2nd Tertile, n = 7	3rd Tertile, n = 8
Age, yrs	53 (32–56)	41 (39–55)	54 (40–60)
Disease duration, yrs	10 (6–13)	7 (3–10)	12 (8–24)
Gender (F/M)	7/1	6/1	7/1
Weight, kg	67.4 (57–76)	60 (48–71)	57.5 (55–68)
Systolic blood pressure, mm Hg	115 (110–126)	113 (105–119)	126 (106–150)
Diastolic blood pressure, mm Hg	74 (72–76)	70 (61–76)	79 (73–82)
Antihypertensive drugs (%)	12.5	14	37.5
Diabetes mellitus (%)	12.5	0	25
Rheumatoid nodules (%)	12.5	14	25
Bone erosions (%)	87.5	85.7	100
Prednisone ≤ 10 mg/day (%)	25	42.8	12.5
Anticytokine antibodies* (%)	38	57	38
Costimulatory blocker** (%)	62	43	62
Tender joint count	6 (5.7–7.7)	4 (1–8.5)	6.5 (4.5–9.2)
Swollen joint count	3 (1.5–4.5)	4 (0.5–5)	4 (2.5–5.5)
C-reactive protein, mg/l	7.57 (4.9–10.9)	6.2 (0.6–8)	3.97 (3.3–17.4)
DAS28 index	4.04 (3.7–4.2)	3.6 (2.6–4.04)	3.8 (3.6–4.5)
Rheumatoid factor (%)	100	71.4	100
Basal artery diameter, mm	3.7 (3.5–3.8)	3.2 (2.9–3.3)	3.4 (3–3.8)
Post-hyperemic diameter, mm	3.9 (3.8–4.1)	3.8 (3.6–4.1)	4.8 (3.9–5.2)
Absolute change of FMV, mm	0.32 (0.26–0.37)	0.74 (0.58–0.79)†	1.12 (1.05–1.31)††#

* Anti-tumor necrosis factor or anti-IL-6 monoclonal antibodies. ** CTLA4-Ig fusion protein. † vs 1st tertile, p = 0.0003; †† vs 1st tertile, p = 0.0002; # vs 2nd tertile, p = 0.0003.

Table 2. Serum levels of selected biomarkers, allocated in tertiles according to magnitude of absolute change in flow-mediated vasodilation (FMV).

Biomarker	1st Tertile	2nd Tertile	3rd Tertile
Anti-CCP, U/ml			
Median (IQR)	251 (133–312)	55 (33–534)	273 (79–539)
Mean ± SD	253 ± 181	266 ± 300	309 ± 273
IFN-γ, pg/ml*			
Median (IQR)	601 (374–970)	0 (0–1165)	16 (0–244)
Mean ± SD	971 ± 1234	1321 ± 2568	170 ± 268
IL-6, pg/ml			
Median (IQR)	201 (0–687)	99 (55–347)	178 (120–412)
Mean ± SD	394 ± 480	276 ± 365	347 ± 418
IL-4, pg/ml			
Median (IQR)	101 (67–206)	53 (0–239)	27 (0–117)
Mean ± SD	249 ± 397	475 ± 1033	347 ± 849
IL-10, pg/ml			
Median (IQR)	1782 (913–3280)	1779 (0–7725)	1245 (778–4512)
Mean ± SD	2292 ± 2009	9632 ± 18440	3079 ± 3984
sVCAM-1, ng/ml			
Median (IQR)	235 (187–441)	182 (155–202)	213 (195–248)
Mean ± SD	398 ± 335	180 ± 42	234 ± 92
sE-selectin, ng/ml			
Median (IQR)	34 (23–84)	33 (22–54)	34 (25–72)
Mean ± SD	73 ± 86	37 ± 21	50 ± 36

* 1st vs 3rd tertile, p = 0.03. CCP: citric citrullinated peptide; IFN-γ: interferon-γ; IL-6: interleukin 6; sVCAM: soluble vascular cell adhesion molecule.

tors in the pathogenesis of atherosclerosis[1,2]. Vascular endothelial dysfunction (ED) precedes atherosclerosis and represents an early sign of vascular damage[2].

Prospective and cross-sectional studies have demonstrated higher ED in patients with RA than in healthy subjects[2,3], and that different antiinflammatory therapeutic strategies can dramatically improve endothelial

function[4,5]. However, a consistent finding is the persistence of ED in a significant subset of patients despite a successful antiarthritic response. Clinical and serological factors underlying this persistence of ED remain poorly understood.

Our pilot exploratory observational study was performed to investigate if different inflammatory markers are associated with persistence of ED. Protocols were approved by our local ethics committee. For inclusion, patients must have fulfilled the 1987 American Rheumatism Association (American College of Rheumatology) classification criteria for RA[6], therapy with ≥ 2 disease modifying antirheumatic drugs (DMARD) plus a biological agent for at least 1 year, and an improvement ≥ 1.2 on Disease Activity Score-28 after initiation of biologic therapy (to define successful antiarthritic response). Use of prednisone ≤ 10 mg/day, angiotensin-converting enzyme inhibitors, beta-blockers, and calcium-antagonists at the time of study was allowed. Patients were excluded if they had a history of cardiovascular/cerebrovascular disease, smoking within previous year, other rheumatic disease (except Sjögren's syndrome and fibromyalgia), use of insulin, nitrates or thiazolidinediones, or active infectious disease or neoplasm was present.

Sera were tested for high-sensitivity C-reactive protein (hsCRP) and rheumatoid factor (RF) by nephelometry, as well as anti-cyclic citrullinated peptide-2 (anti-CCP2) antibodies, interferon-γ (IFN-γ), interleukin 6 (IL-6), IL-4, IL-10, and soluble E-selectin and soluble vascular cell adhesion molecule-1 by ELISA. Flow-mediated vasodilation (FMV, a validated surrogate marker for endothelial function) was measured by high resolution ultrasound with a 10 MHz linear-array transducer (Hewlett Packard SonoS5500), in accord with guidelines of the International Brachial Artery Reactivity Task Force[7]. Differences were estimated by Kruskal-Wallis and post-hoc analysis using Mann-Whitney tests. Proportions were assessed by Fisher's exact tests, and Spearman's rank coefficient was used for correlations.

Twenty-three patients (20 women; mean age 50 yrs, range 25–77) were included. According to absolute change in brachial artery diameter, 8 patients were allocated into the first tertile (0.32 mm), 7 in the second (0.74 mm), and 8 in third (1.12 mm). There were no differences in demographics, clinical features, inflammatory status, concurrent diseases, or treatment (including DMARD, biologic agent, and antihypertensive drugs; Table 1). Median IFN-γ concentration (Table 2) in patients with lowest FMV (first tertile) was 601 pg/ml [interquartile range (IQR) 374–970]; it was only 16 in those with highest FMV (IQR 0–244; $p = 0.03$). No differences for other cytokines, adhesion molecules, or autoantibodies were found. Analyses of correlation did not attain statistical significance (data not shown).

Our study confirms that a subset of patients with RA persists with ED even when successful antiarthritic therapy has been achieved. Additionally, our findings suggest this persistence is associated with IFN-γ (albeit a dose-dependent effect was not seen), but not with other cytokines or prognostic markers of RA (bone erosions, rheumatoid nodules, RF, anti-CCP2).

The rationale to implicate IFN-γ in the disturbed FMV emerges from CD4+ T-cells lacking CD28 expression[8]. CD4+CD28^{null} T-cells represent a pool of prematurely senescent lymphocytes resulting from chronic activation, implicated in autoimmune phenomena because of their proinflammatory activity[8,9]. CD4+CD28^{null} cells produce large amounts of IFN-γ, a T_H1-cytokine closely involved in both rheumatoid synovitis and atherosclerosis[9,10]. IFN-γ is the main trigger for production and release of reactive oxygen species in endothelium; additionally, it inhibits collagen synthesis and facilitates production of matrix metalloproteinases in plaque's fibrous cap[10]. These effects seem to play a key role not only in the formation of plaques but most importantly in ED and its consequent instability and rupture. Accordingly, Aubry, *et al* compared autopsies of patients with RA and non-RA controls matched for sex and CV risk factors[11], finding that among subjects with CV disease, 54% of controls had grade 3–4 lesions versus 7% of patients; nevertheless, vulnerable plaques and inflammatory changes in media/adventitia artery layers were significantly more common in patients than in controls. These findings suggest that patients with RA have less chronic atherosclerosis but more inflammation and plaque instability than controls. Recently, Kerekes, *et al* reported that levels of IFN-γ were significantly higher in patients with RA and low FMV ($r = 0.51$, $p = 0.014$) than in those with high FMV[12].

Although in the recommended range for a crossover design evaluating FMV (at least 20–30 patients)[7], our small sample prevented us from adjusting groups for traditional CV risk factors, limiting any other inferences. However, our study supports the implementation of longitudinal studies of larger numbers of patients.

In our study, the subgroup of patients with aggressive RA that persisted with ED despite successful antiarthritic therapy showed high serum concentrations of IFN-γ.

LUIS M. AMEZCUA-GUERRA, MD, Department of Immunology, Instituto Nacional de Cardiología Ignacio Chávez, LaSalle University School of Medicine; RICARDO MÁRQUEZ-VELASCO, BSc, Department of Immunology; RICARDO HERNÁNDEZ-ÁVALOS, MD, Department of Echocardiography; ANGÉLICA VARGAS, MD, Department of Rheumatology, Instituto Nacional de Cardiología Ignacio Chávez; RAFAEL BOJALIL, MD, PhD, Department of Immunology, Instituto Nacional de Cardiología Ignacio Chávez, Department of Health Care, Universidad Autónoma Metropolitana-Xochimilco, Mexico City, Mexico. Address reprint requests to Dr. R. Bojalil, Department of Immunology, Instituto Nacional de Cardiología Ignacio Chávez, Juan Badiano 1, Sección XVI, Tlalpan, 14080, Mexico City, Mexico. E-mail: bojraf@yahoo.com

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Neuromuscular Involvement in Rheumatic Patients Treated with Anti-Tumor Necrosis Factor Therapy – Three Examples

To the Editor:

Tumor necrosis factor-α (TNF-α) blocking agents are widely used for treatment of various rheumatic diseases. Neurologic complications such as demyelination and axonal degeneration have been rarely reported in patients undergoing this therapy[1,2], and neuromuscular changes only once — a case of polymyositis (PM)[3].

We have accumulated experience with anti-TNF agents in our hospital; we describe 3 patients with inflammatory rheumatic diseases who developed clinically relevant neuromuscular involvement while being treated with TNF-α blockers (Table 1).

Case 1. A 40-year-old man with active ankylosing spondylitis (AS) had improved on therapy with adalimumab 40 mg biweekly when he felt pain in both quadriceps, subsequently spreading to the upper limb. Creatinine kinase (CK) was mildly elevated to 300 U/l (normal < 150 U/l). After withdrawal of adalimumab, his complaints resolved and laboratory values returned to normal. Because of persistent disease activity he restarted adalimumab 3 months later. The pain recurred, with CK 1062 U/l. Neurologic examination revealed decreased tendon reflexes of the lower limb in the presence of mild sensory loss in his soles. A muscle biopsy revealed degeneration and mild neurogenic atrophy without loss of myelinated nerve fibers. A diagnosis of axonal neuropathy associated with muscle damage due to denervation was made. Adalimumab was discontinued, with subsequent complete resolution of his symptoms.

Case 2. A 46-year-old man with longstanding AS developed diffuse pain in the limbs in January 2005, one week after his fifth infusion of infliximab (3 mg/kg). The immunosuppressive therapy was initially started in October 2004 because of high disease activity (Bath AS Disease Activity Index = 6). The initially elevated laboratory markers of inflammation, which had normalized during anti-TNF therapy, were now elevated again. Neurologic examination showed difficulty walking on heels. Tendon reflexes were normal apart from bilaterally absent ankle jerks. Magnetic resonance imaging showed inflammation of the left soleus muscle. Histologically mild interstitial myositis and predominantly demyelinating neuropathy were found. Infliximab was discontinued in January 2005, and treatment with high-dose corticosteroids (100 mg prednisolone for 4 days) was initiated and then gradually tapered. This resulted in marked improvement of muscle pain and weakness.

Table 1. Patient characteristics.

Characteristics	Patient 1	Patient 2	Patient 3
Age, yrs	40	46	57
Sex	M	M	F
Diagnosis	AS	AS	RA
Disease duration	16	17	26
Disease status	BASDAI 4.3	BASDAI 6	DAS-28 4.7
Previous therapy	NSAID, sulfasalazine	NSAID, sulfasalazine	All available DMARD
TNF blocker medication	Adalimumab	Infliximab	Etanercept
Onset	March 2004	October 2004	June 1999
Neuromuscular involvement, onset	May 2004/July 2004	January 2005	January 2003
Symptoms	Pain in m. quadriceps	Diffuse pain in the limbs	Initial mild myalgia developed to progressive muscle weakness
Neurologic examination	No deficit (May 2004)/DTR + sensory loss (July 2004)	Difficulty walking on heels	Muscle weakness (MRC scale 3)
CK, mg/dl, normal < 174 mg/dl	300 (May 2004)/1062 (July 2004)	Normal	400 (January 2003)/1067 (January 2004)
ANA	Negative	Negative	1:160 (1999)/1:2560 (2003)
Inflammatory markers	No elevation	CRP 17.5 mg/dl (normal < 1 mg/dl) ESR 97 mm/h	CRP 8.6 mg/dl, ESR 36 mm/h
Electromyogram	Normal	Normal	Increased insertional activity (m. tibialis anterior)
Nerve conduction studies	Reduced amplitudes/distal delay	Demyelination	Normal
Magnetic resonance imaging (T1 weighted)	Normal (upper arm)	Inflammation of the left m. soleus	Widespread edema in right m. vastus medialis
Muscle biopsy	Mild neurogenic atrophy, no MHC class I expression	Focal inflammatory infiltrates, mild expression of MHC class I	Necrosis of fibers, focal inflammatory infiltrates (diffuse expression of MHC class I)
Diagnosis	Axonal neuropathy	Interstitial myositis with demyelinating neuropathy	Necrotizing myositis
Treatment	Discontinuation of adalimumab	Discontinuation of infliximab, High-dose corticosteroids	Discontinuation of etanercept, High-dose corticosteroids, IV cyclophosphamide pulse
Outcome	Complete resolution	Marked improvement of weakness	Death

DTR: decreased tendon reflexes; DMARD: disease modifying antirheumatic drugs; NSAID: nonsteroidal antiinflammatory drugs.

Case 3. A 57-year-old woman with severe erosive seropositive rheumatoid arthritis (RA) had been successfully treated with etanercept 25 mg twice weekly. After some years she presented with mild myalgia without neurologic symptoms. CK was 400 U/l despite discontinuation of statins. Etanercept had to be discontinued in November 2003 because of an infection of the right toe. After 4 weeks of appropriate intravenous (IV) antibiotic therapy the infection was clinically cured. Measurement of CK revealed increased values between 400 and 800 U/l. Due to a significant flare, she was urged to restart anti-TNF therapy. Six weeks later she reported diffuse pain in the upper limbs and progressive symmetrical muscle weakness, mainly in the pelvic and shoulder region. This was accompanied by dyspnea under exposure. Antinuclear antibodies (ANA) were now found to be positive and CK peaked to 1067 U/l. A muscle biopsy revealed necrotizing myositis without signs of infection (Figure 1). Etanercept was stopped and high-dose prednisolone and IV cyclophosphamide (500 mg/m^2) were given. The muscle weakness improved considerably, but the patient developed leukopenia and acute respiratory distress syndrome (ARDS); she died of sepsis due to *Pneumocystis jiroveci* (carinii) pneumonia.

Muscle pain and weakness may be due to defined rheumatic diseases such as PM, but can also be caused by antirheumatic drugs[4]. The latter should be considered if (1) there is no history of muscular symptoms, and (2) there has been a symptom-free period between start of therapy and onset of myopathy; and if (3) symptoms are reversible on discontinuation of the drug.

Only 2 cases of PM as a potential side effect of anti-TNF therapy have been reported[3,5]. Mild myopathic changes have been described in the biopsy specimens of patients with neurologic side effects of anti-TNF-α therapy[2].

We describe patients with muscle pain and neuromuscular involvement upon undergoing therapy with TNF-α blockers. One patient had only muscle changes, the other 2 also had neuropathy.

Neurological symptoms reported in association with the use of TNF-α blockers have mainly been those of demyelination[1]. The role of TNF-α in the pathogenesis of myelin-specific autoimmunity is unclear, but myelin-specific T cells may become activated by anti-TNF-α therapy[6]. Elevated expression of TNF-α has been reported in patients with myositis and Duchenne muscular dystrophy, but rarely in neurogenic disorders[7]. The precise role of TNF-α in muscles is not known. However, there are more reports of refractory PM and dermatomyositis responding to anti-TNF therapy than there are of myopathy suggestive as a side effect of these agents[8].

RA can be associated with autoimmune myopathies such as PM. This is mostly not associated with ANA titer as in our patient. However, the muscle biopsy in that case did not show characteristic T cell infiltrates, but did reveal extensive necrosis[9]. Autoimmunity was considered as a possible

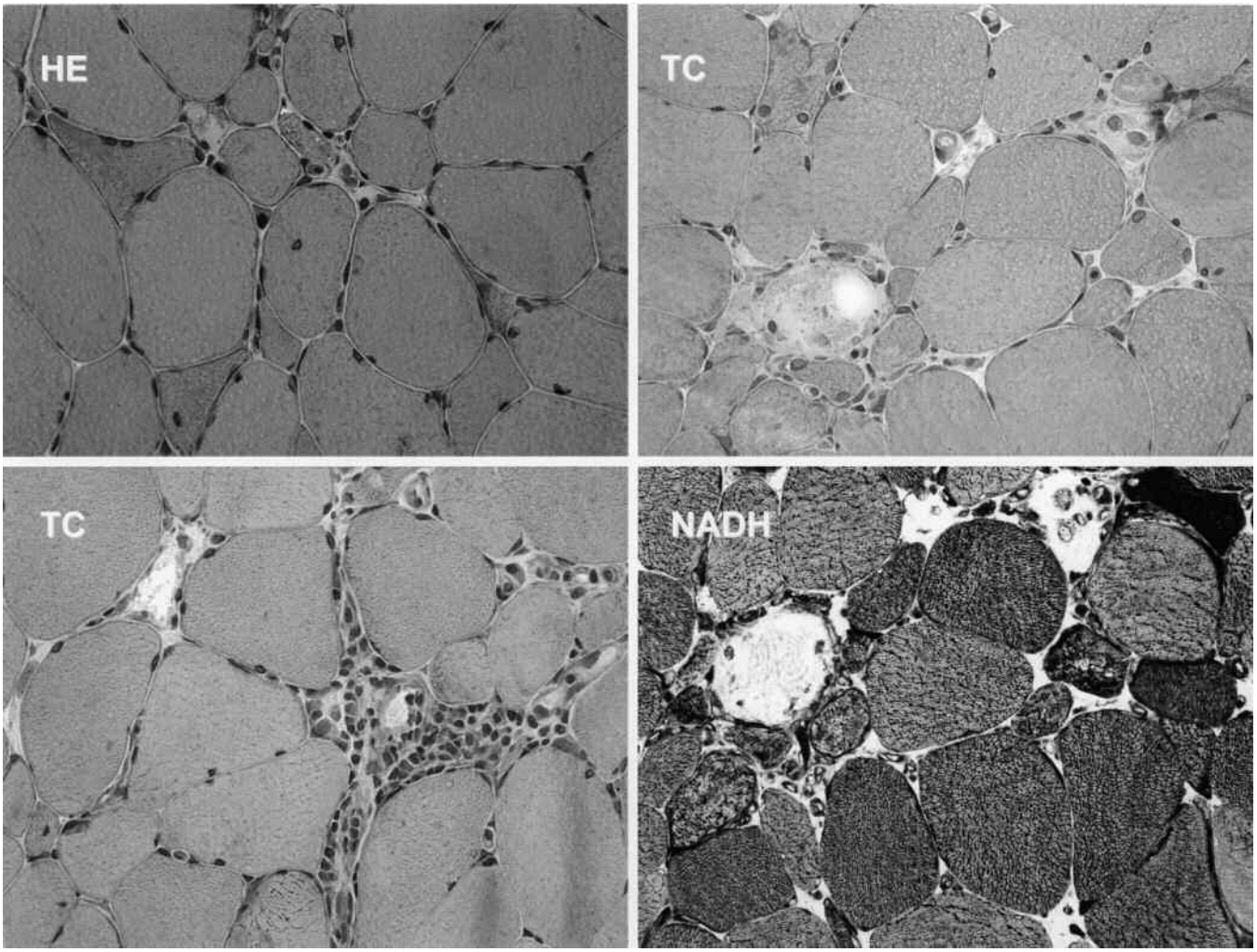

Figure 1. Patient 3: transverse section of muscle biopsy from the vastus lateralis. Hematoxylin-eosin (HE) stain shows variation in fiber size and many basophilic regenerating muscle cells. Modified Gomori trichrome (TC) stain shows 2 muscle-cell necroses and a mild perivascular inflammatory infiltration. NADH dehydrogenase stain reveals a dark regenerating fiber and 2 necrotic fibers devoid of oxidative reaction (original magnification ×20).

explanation, whereas a statin-induced myopathy[10] was unlikely. The death due to ARDS of our patient with RA was probably related to immunosuppression[11].

Myopathy is a rare feature of AS and there is no association with autoimmune muscle diseases. Patient 1 had muscle complaints and an elevated CK, but axonal neuropathy was diagnosed because neurogenic changes were seen histologically. In Patient 2, mild interstitial myositis and demyelinating neuropathy were diagnosed. Elevated acute-phase indicators are rare in inflammatory myopathy, and muscle enzymes may well be normal[12].

Together, these data suggest that TNF-α blockade may induce neuromuscular symptoms in patients who do not have preexisting neurological symptoms.

UTA KILTZ, MD; CLAAS FENDLER, MD; JURGEN BRAUN, MD, Rheumazentrum Ruhrgebiet, St. Josefs-Krankenhaus, Landgrafenstrasse 15, 44652 Herne, Germany. Address reprint requests to Dr. Kiltz. E-mail: kiltz@rheumazentrum-ruhrgbiet.de

We thank Prof. M. Vorgerd, Bochum, Germany, for his help with interpretation of neurological findings and for providing Figure 1.

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An Unusual "Gouty" Case of Back Pain and Fever

To the Editor:

A 53-year-old woman was referred to the rheumatology service after presenting to a local medical unit with severe low back pain, fever, and malaise. She had been discharged from a surgical unit 2 weeks previously, where she had been investigated for low back pain, pyrexia, and urinary symptoms. She had undergone a magnetic resonance imaging (MRI) scan of her lumbar spine that had shown only degenerative changes with no nerve root or cord lesion. C-reactive protein (CRP) had been elevated at 122 mg/l and urine culture was positive for coliforms. She was treated with oral antibiotics and discharged with the diagnoses of mechanical back pain and urinary tract infection (UTI). The back pain had persisted. Closer questioning determined her pain was mainly in the right buttock region, and she was unable to bear weight. She complained of nausea, anorexia, and fever. Her only significant history was of hypertension, for which she took atenolol. There was no relevant family history, and no history of rash or psoriasis. She was pyrexic (38.5°C) and tachycardic (102 beats/min). Blood pressure was 135/91 mm Hg. She was clinically dehydrated. She was exquisitely tender in the region of her right sacroiliac (SI) joint. Examination also revealed evidence of a mild peripheral joint synovitis, and a small right knee effusion. Systematic examination was otherwise unremarkable.

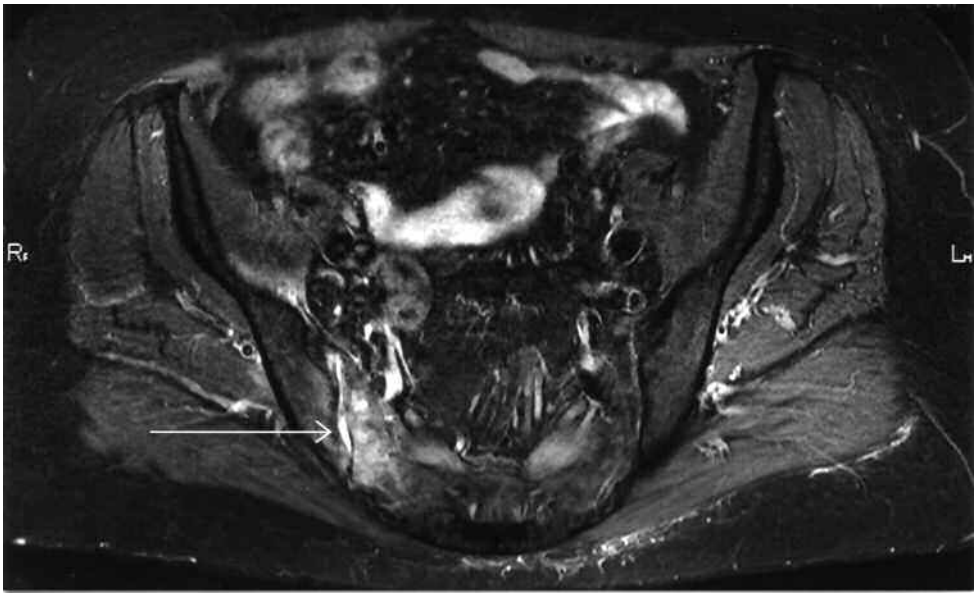

Figure 1. MRI of the SI joints: axial short-tau inversion recovery sequence.

The working differential diagnoses were septic arthritis of the right SI joint, or an acute inflammatory spondyloarthropathy. She was transferred to the rheumatology unit, where she received intravenous fluids and analgesia. Initial investigations revealed CRP 392 mg/l, white blood cell count 16.3×10^9/l, neutrophils 11×10^9/l, hemoglobin 10.6 g/dl, mean corpuscular volume 86 fl, erythrocyte sedimentation rate 120 mm/h. She had mild impairment of renal function, with creatinine 101 µmol/l. The remainder of her biochemical profile was normal. Urate was 0.44 mmol/l. Cultures of blood and urine were taken. Fluid (9 ml) was aspirated from her right knee and sent for culture and crystal analysis. Plain radiography of her pelvis was unremarkable.

An MRI scan of her pelvis was urgently requested (Figure 1). This revealed an effusion within the right SI joint. There was cortical irregularity on both sides of it and an area of edema within the sacrum measuring 2 cm × 1 cm maximum diameter. In addition there was a small extension of fluid anteriorly at the superior aspect of the joint, in keeping with an abscess measuring 1 cm maximum diameter. The signal from the remainder of the pelvis was within normal limits.

Aspiration of the right SI joint under fluoroscopic guidance was attempted. Although no significant aspirate was obtained, 1 ml of saline was injected and aspirated and sent for laboratory analysis. The MRI appearance was felt to represent sepsis, therefore intravenous antibiotics were started, initially flucloxacillin, fusidic acid, and also ciproxin (in view of the recent UTI). She made slow progress, although her pain became more controllable and her renal function improved (with more fluid and after stopping her nonsteroidal antiinflammatory drugs). The results of knee and SI aspirates then became available; there was no growth on culture of either sample. Monosodium urate (gout) crystals were isolated from both her right knee and right SI joint. Blood and urine cultures were negative. Her diagnosis was changed to acute polyarticular gout.

Antibiotics were discontinued and colchicine (500 µg BD) and prednisolone (40 mg/day) were added. She responded rapidly and within 7 days she had become asymptomatic; her CRP fell to 7 mg/l. She was discharged on a reducing course of oral steroids. At review 1 month later she remained well and oral allopurinol was added. Plain radiographs of her feet revealed a "punched out" erosion of her left first metacarpal head in keeping with gout.

Gout is a common cause of acute inflammatory arthritis. Although often presenting initially in peripheral joints, especially of the feet, gout may also present with SI joint involvement[1,2]. Our case highlights a number of important points: (1) Targeted history-taking localized her symptoms to the SI joint, even though she was complaining of "back pain." (2) Detailed clinical examination confirmed the SI tenderness and also the peripheral joint involvement (which she had not complained of), allowing investigation to be directed to the correct areas. (3) The importance of attempting joint aspiration: gouty crystals were seen in washings from the SI joint, although no free fluid was obtained. (4) Plain radiographs of the SI joints may appear normal, despite significant MRI abnormalities. Also, plain radiographs of the feet may reveal erosions typical of gout, even when there is no history of attacks.

CLAIRE M. RIDDELL, MRCP(UK), Rheumatology Specialist Registrar, Department of Rheumatology; MARK ELLIOTT, FRCR, Consultant Radiologist, Department of Radiology; ANDREW P. CAIRNS, MD, FRCP, MFSEM, Consultant Rheumatologist, Department of Rheumatology, Musgrave Park Hospital, 20 Stockman's Lane, Belfast, Northern Ireland, BT9 7JB. Address reprint requests to Dr. Riddell;
E-mail: clairemriddell@gmail.com

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Differential Response of Psoriatic Onycho-Pachydermo-Periostitis to 2 Anti-Tumor Necrosis Factor-α Agents

To the Editor:

Psoriatic onycho-pachydermo-periostitis (POPP) syndrome is a rare form of psoriatic arthritis (PsA), with 16 documented cases[1-13]. The significant clinical features of this syndrome include psoriatic onychodystrophy, connective tissue thickening, and periostitis of the distal phalanges, producing a drumstick-like deformity[1,13]. The great toe is generally affected, although other toes and fingers may also be involved. Patients with POPP syndrome experience pain in the thickened distal phalanges that may result in severe functional impairment. The treatment of this condition has been generally unsatisfactory until the introduction of anti-tumor necrosis factor-α (TNF-α) agents[13]. We describe a patient with POPP who was successfully treated with infliximab after failing to respond to etanercept.

A 53-year-old French–Canadian man presented in January 2003, with a 6-month history of left foot pain. There were no significant past illnesses. Examination revealed psoriatic lesions behind his right ear and on the dorsum and soles of both feet, and diffuse discoloration of the toes of the left foot. The distal phalanges of the left great, second, and fourth toes were thickened, and there was onycholysis of all fingernails and toenails, with tenderness and swelling of the distal interphalangeal (DIP) joints of middle, ring, and little fingers (Figures 1A, 2A, 3A).

There was radiological evidence of a periosteal reaction of the shaft of the proximal phalanx of the left second toe (Figure 4A). A diagnosis of POPP syndrome was made based on these findings. The tests for rheumatoid-factor antinuclear antibodies were positive and HLA-B27 was negative.

He was given methotrexate (MTX) 12.5 mg per week for 5 months, which was subsequently increased to 25 mg weekly for an additional 2 months, with no response. Leflunomide, 20 mg daily, was then added to the MTX in November 2003. This combination was continued until June 2005, without improvement. He lost 11.4 kg in weight and his functional capacity deteriorated. He could no longer make a fist, or walk more than 1 block even when assisted by a cane. He was forced to give up his used truck dealership.

He was then prescribed etanercept 50 mg subcutaneously once weekly. This was terminated in December 2005 due to lack of response. His Health Assessment Questionnaire (HAQ) was 2.7 (maximum score of 3) and C-reactive protein (CRP) was 28 mg/l (upper limit 8 mg/l).

Infliximab treatment was initiated in January 2006 (5 mg/kg intravenously on week 0, 2, and 6 and q 6 weeks thereafter, and MTX 25 mg weekly). Upon reevaluation in July 2006, there was no evidence of synovitis of the DIP joints of the fingers. Moreover, the pain and thickening of the distal phalanges of the toes had diminished. The skin lesions had improved, but some onycholysis of his fingernails and toenails persisted (Figures 1B, 2B, 3B).

The HAQ score had diminished from 2.7 to 1.3. The CRP had declined from 28 mg/l to 3.1 mg/l and the erythrocyte sedimentation rate (ESR, Wintrobe method) from 48 mm/h to 10 mm/h. CRP and ESR values declined further to 2.3 mg/l and 8 mm/h, respectively, in early 2007. He was able to resume many normal activities of daily living, including his hobby of hunting. Figures 1C, 3C, and 3D, taken after 10 months of infliximab therapy, show resolution of his onycholysis. Results of a radiological study of the left foot are illustrated in Figure 4B. There is resolution of the periostitis. However, joint fusion and phalangeal destruction remain. Figure 4C shows the typical "pencil-in-cup" deformity of the right thumb. His improved functional capacity has been maintained and he continues to receive infliximab 5 mg/kg intravenous infusions at 6–7 week intervals.

This is the seventeenth reported case of POPP syndrome[13] and it conforms to the ClASsification criteria for Psoriatic ARthritis (CASPAR)[14]. MTX as monotherapy or in combination with leflunomide was ineffective in controlling our patient's disease, consistent with previous observations that the traditional treatments for PsA have been ineffective in POPP syndrome[13]. Whereas the anti-TNF-α agent, etanercept, also yielded no improvement in his condition, infliximab provided an excellent remission of his synovitis, psoriasis, onycholysis, and distal phalangeal thickening.

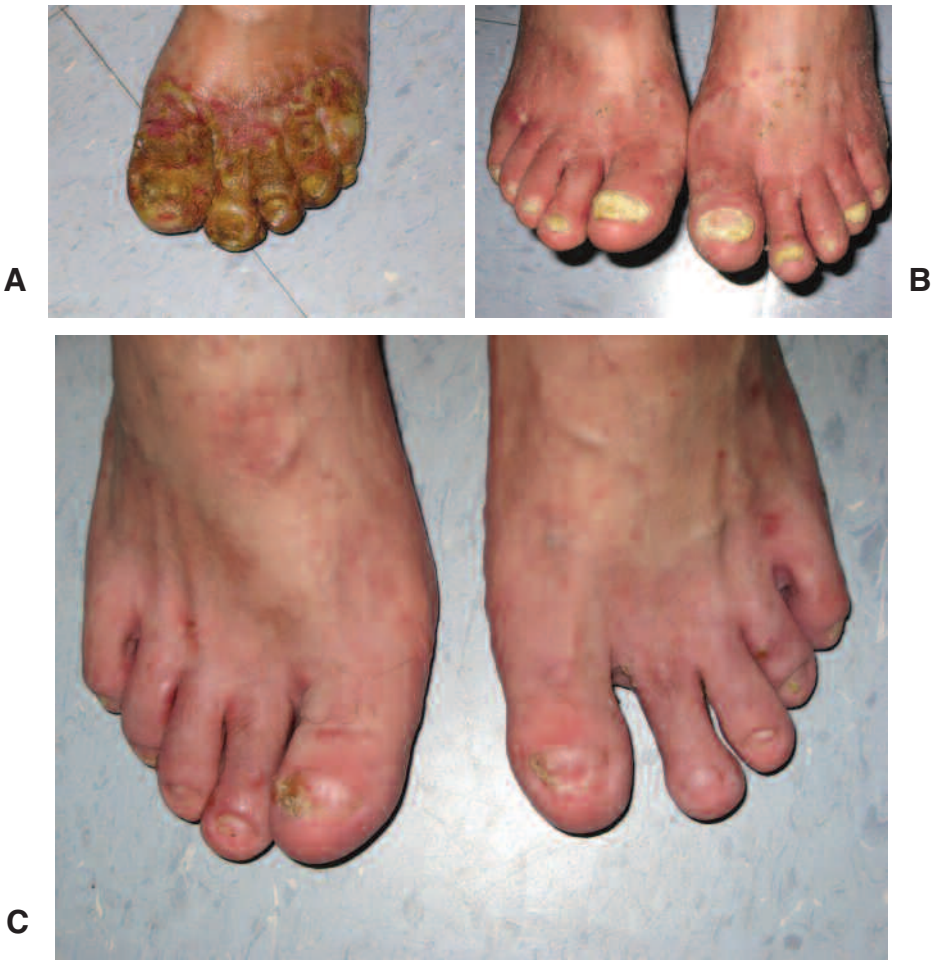

Figure 1. A. Before treatment with infliximab: left foot shows onycholysis and skin lesions of all toes. The left great, second, and fourth toe demonstrate enlargement of the distal phalanx. B. Seven months following treatment with infliximab: note improvement in skin lesions and partial improvement of thickening of the distal phalanges. C. Ten months following treatment with infliximab: dorsum of both feet showing improvement of onycholysis and skin lesions. Residual thickening of the distal phalanges with drumstick deformity is noted.

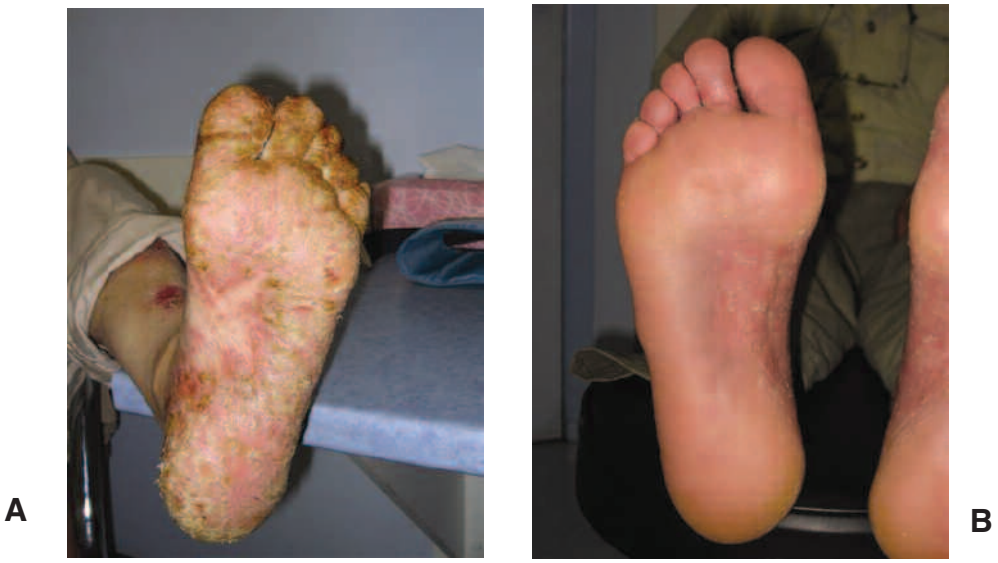

Figure 2. A. Before treatment with infliximab: the patient's left foot. Both feet had similar psoriatic lesions. Note enlargement of distal phalanges. B. Seven months after treatment with infliximab, showing good improvement in skin lesions.

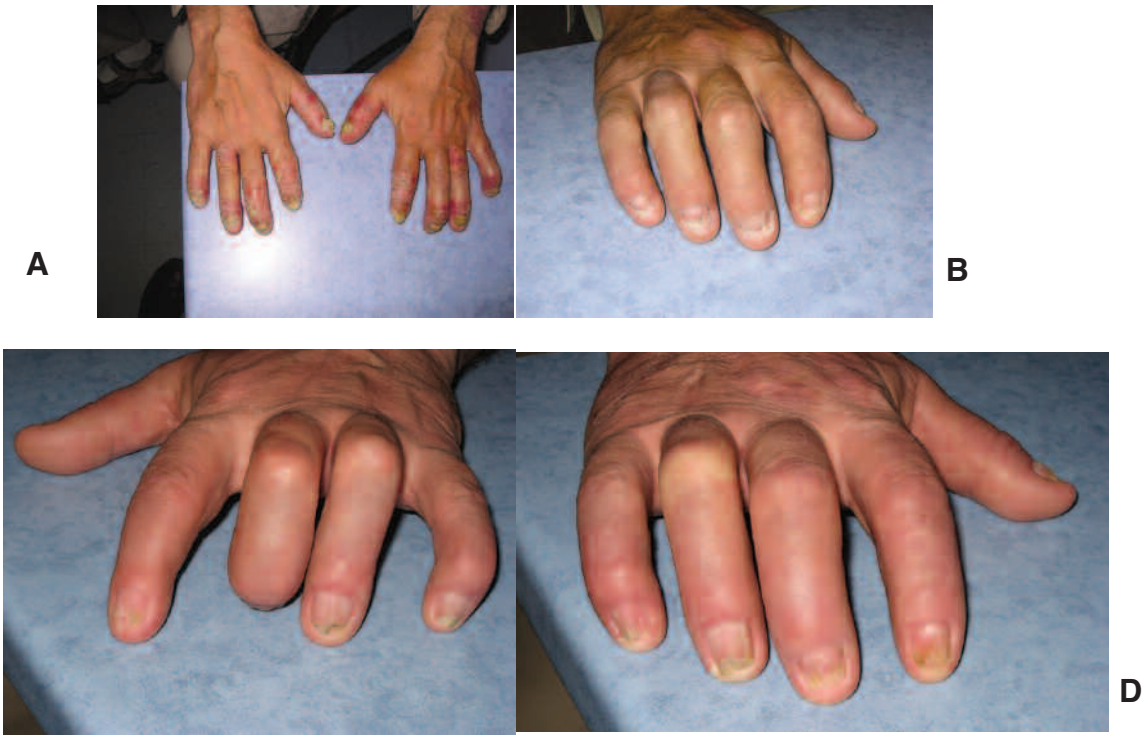

Figure 3. A. Hands before treatment with infliximab; note swelling of DIP joints of middle, ring, and little fingers, as well as onycholysis and skin lesions. B. Seven months after infliximab therapy: improvement of skin lesions and synovitis. C. Ten months after treatment with infliximab: left hand showing good resolution of onycholysis. D. Ten months after treatment with infliximab: right hand showing resolution of onycholysis.

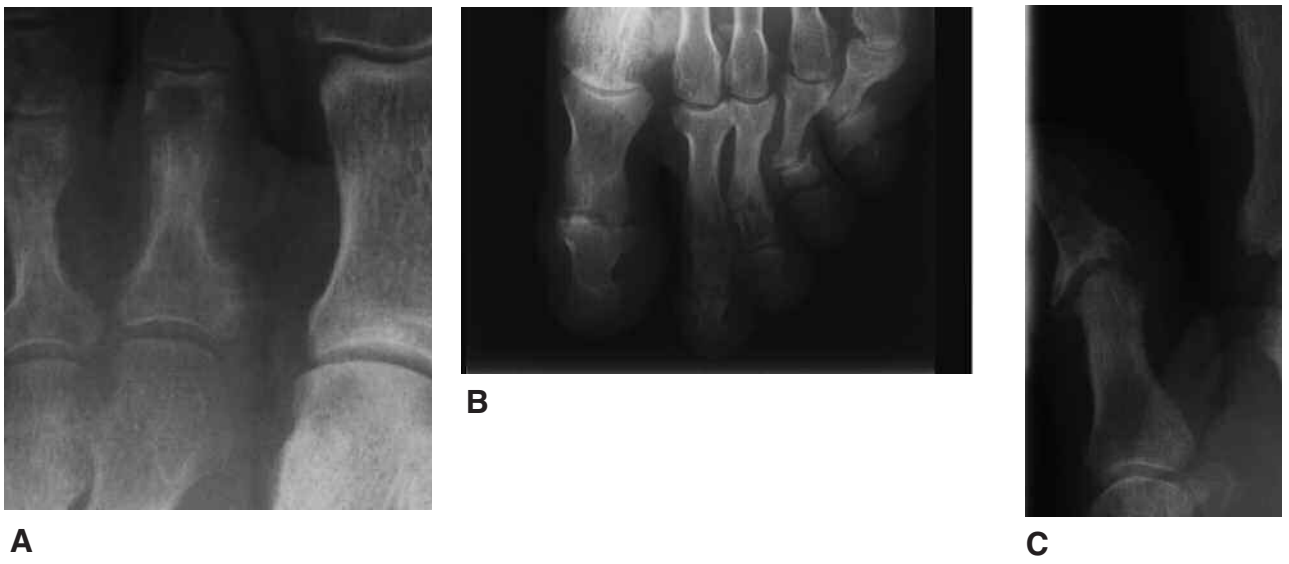

Figure 4. A. Before treatment with infliximab: periostitis involving the proximal phalanx of the left second toe. B. Ten months after treatment with infliximab: the left foot in May 2007 shows fusion of DIP joints of the left first and second toes as well as destruction of phalanges in the left fourth and fifth toes. There was no periostitis. C. Twelve months after treatment with infliximab: the right thumb in July 2007 shows the typical "pencil-in-cup" deformity of PsA.

This is the second report of successful treatment of POPP syndrome with an anti-TNF-α agent. The first success was reported with adalimumab[13]. The question arises why the POPP syndrome responded to infliximab and adalimumab, but not to etanercept. Etanercept is a soluble receptor and is structurally distinct from infliximab and adalimumab, which are monoclonal antibodies[15-17]. The complexes that infliximab and adalimumab form with both soluble and membrane-bound ones are significantly more stable than those formed with etanercept[17,18]. This could enhance the clearance of circulating TNF-α. In addition, infliximab and adalimumab, unlike etanercept, have the capacity to induce cell lysis (apoptosis) after reacting with membrane-bound TNF-α[16-19].

It remains to be determined whether the effectiveness of infliximab and adalimumab as compared to etanercept in POPP syndrome may be due to their better binding kinetics for soluble TNF-α, and/or their enhanced capacity to bind to TNF-α at the tissue level, with resultant cell lysis. These differences remain the subject of active research[19].

MORTON ALLAN KAPUSTA, MD, FRCPC, FACP, Associate Professor of Medicine, McGill University, Department of Medicine, Division of Rheumatology, Sir Mortimer B. Davis–Jewish General Hospital, Montreal; CHARLES DUMONT, MD, FRCPC, Senior Physician, Department of Internal Medicine, Lakeshore General Hospital, Pointe-Claire, Quebec, Canada. Address reprint requests to Dr. M. Kapusta, 5885 Cote des Neiges Road, Suite 205, Montreal, Quebec H3S 2T2. E-mail: kapustamorton@netscape.net

ACKNOWLEDGMENT

We thank Marilyn Krelenbaum, MSc, for her invaluable assistance, and Dr. G. D'Ignazio and the team at Source Unique, Hawkesbury, Ontario, for excellent care of the patient.

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Alemtuzumab (Campath-1H) for Treatment of Refractory Polymyositis

To the Editor:

We describe a 48-year-old woman with polymyositis refractory to conventional therapy who responded to alemtuzumab (Campath-1H). This humanized lymphocytotoxic monoclonal antibody recognizes the cell-surface glycoprotein CD52, abundantly expressed by B and T lymphocytes, monocytes, and natural killer cells.

Our patient presented in 1996 with seropositive, antinuclear antibody-negative, nonerosive rheumatoid arthritis, which was treated with sulfasalazine 2 g daily. In 1998 she developed generalized muscle pains; investigations showed creatine kinase (CK) was > 5000 U/l, anti-Jo-1 antibody was positive; muscle biopsy and electromyography confirmed an inflammatory myopathy. There was no evidence from this or subsequent biopsies to suggest an inclusion body myositis. She was initially treated with prednisolone 45 mg daily and azathioprine 150 mg daily but these failed to control her myositis. Over the next 8 years various other agents were prescribed, singly and in combination, and prednisolone was continued (Table 1).

Despite these regimes her CK always remained above 3000 U/l and she became progressively weaker. Prior to treatment with alemtuzumab in 2006, she required a wheelchair and assistance to rise from sitting. Muscle power was 3/5 MRC grade in the proximal lower limbs, 4– or 4/5 in the upper limb and distal muscle groups. She became increasingly breathless and hypoxic (pO_2 7.7 kPA inspiring room air), with reduced alveolar diffusing capacity (KCO 1.09; predicted 1.51). Further investigations revealed significant pulmonary arterial hypertension (PAH) at right-heart catheterization with mean pulmonary artery pressure 44 mm Hg (normal 10–17 mm Hg), pulmonary vascular resistance 10.09 Wood units (normal 2–4 Wood units), and pulmonary artery wedge pressure 8 mm Hg (normal 5–13 mm Hg). A high resolution computerized tomography chest scan showed interstitial fibrosis with a nonspecific interstitial pneumonia pattern. In addition there was respiratory muscle weakness (sniff nasal inspiratory pressure 21

Table 1. Drug therapy used prior to alemtuzumab therapy. Prednisolone was continued at varying doses; medications listed were also used in combination. Methotrexate was avoided because of patient's respiratory disease.

Drug Therapy	Duration, mo	Reason for Cessation
Azathioprine 150 mg	3	Inefficacy
Cyclosporine 200 mg	34	Inefficacy
Intravenous immunoglobulin 0.5 mg/kg (monthly)	3	Inefficacy
Chlorambucil 2 mg daily	12	Inefficacy
Adalimumab 40 mg alternate weeks	3	Inefficacy
Adalimumab 40 mg weekly	3	Inefficacy
Mycophenolate mofetil 2 g	24	Inefficacy
Tacrolimus 2 mg daily	12	Inefficacy
IV cyclophosphamide 15 mg/kg; methylprednisolone 700 mg, 6 pulses at 3 weekly intervals	18	Inefficacy

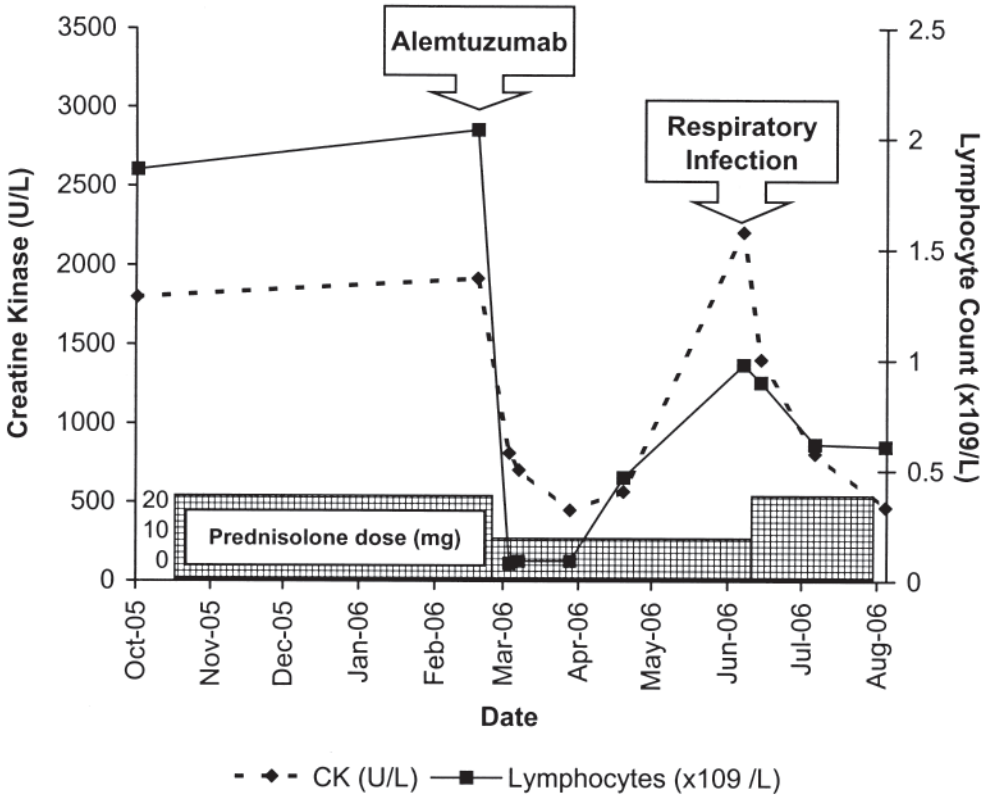

Figure 1. Changes in CK, absolute lymphocyte count, and prednisolone dose with time.

mm Hg; predicted 84 mm Hg). The PAH was considered to be out of proportion to her interstitial lung disease and she was given sildenafil, as a targeted pulmonary vasodilator for connective tissue disease-associated PAH.

In March 2006 she received 120 mg alemtuzumab intravenously over 4 days, with glucocorticoid premedication on Day 1. She experienced a "first-dose" reaction consisting of fever, rigors, and bronchospasm, but there were no other adverse effects. Following therapy she received oral cotrimoxazole, acyclovir, and nystatin for 1 month as prophylaxis against infection, and her prednisolone dose was immediately reduced to 10 mg. Her muscle power improved over a few weeks. Functionally she was now able to rise from sitting and walk independently, and there was an increase to 4–/5 MRC grade in the proximal lower limbs, and to 4 or 4+/5 in the upper limb and distal muscle groups on objective assessment. Biochemical and hematological responses are illustrated in Figure 1. A lower respiratory tract infection 3 months after receiving alemtuzumab corresponded with a clinical and biochemical relapse of her myopathy. Mycophenolate mofetil (MMF) was restarted at 1 g bd, and her prednisolone dose was increased again to 20 mg, with subsequent improvement. Unfortunately there was no improvement in respiratory function following Campath-1H and, despite treatment with sildenafil, the patient died in June 2007. The most recent CK prior to her death was 150 U/l (May 2007).

Polymyositis is an idiopathic inflammatory myopathy diagnosed by the combination of proximal muscle weakness, elevated muscle enzymes, and an invasive T cell infiltrate on muscle biopsy, in the absence of features suggestive of inclusion body myositis. There are few randomized, controlled trials to guide decisions on treatment[1]. Conventionally, oral corticosteroids are used initially. Other immunosuppressive drugs are added if there is insufficient response or as steroid-sparing agents. Reports of therapies that are effective in polymyositis refractory to standard treatment are limited to case reports, case series, and uncontrolled studies[2].

Our patient responded to alemtuzumab when other treatments, including cyclophosphamide and IV immunoglobulin, had failed. Autologous stem-cell transplant was considered, but would have been too hazardous due to her cardiorespiratory disease. The appearance of numerous T cells and few B cells on her muscle biopsy led us to use alemtuzumab rather than rituximab. Alemtuzumab is potently lymphocytotoxic for both B cells and T cells and is licensed for the treatment of certain types of chronic lymphocytic leukemia. It has also been used effectively to treat refractory autoimmune and inflammatory diseases including systemic vasculitis[3,4], ocular inflammation[5], multiple sclerosis[6], and rheumatoid arthritis[7]. After administration to our patient there was a rapid decline in lymphocyte count, matched by a precipitous fall in CK. Both rose transiently at the time of a respiratory infection several weeks later, but notably, CK was subsequently controlled with MMF, which had previously proved ineffective. It also proved possible to reduce her prednisolone dose. Sadly, her pulmonary function did not improve, presumably reflecting irreversible fibrosis in the lung parenchyma and pulmonary arteries.

Our patient had previously refractory polymyositis with lymphocytic infiltrates, and her muscle disease responded rapidly to a single course of treatment with alemtuzumab. A subsequent flare of symptoms was controlled with MMF, a previously ineffective drug. We advocate further investigation of alemtuzumab in this type of setting.

BEN THOMPSON, MRCP, Arthritis Research Campaign Educational Research Fellow, Rheumatology SpR, Musculoskeletal Unit, Newcastle-upon-Tyne Hospitals NHS Foundation Trust; PAUL CORRIS, FRCP, Professor of Thoracic Medicine, Institute of Cellular Medicine, Newcastle University; JAMES A.L. MILLER, PhD, MRCP, Consultant Neurologist, Department of Neurology, Newcastle-upon-Tyne Hospitals NHS Foundation Trust; ROBERT G. COOPER, MD, FRCP, Consultant, Honorary Reader in Rheumatology, University of Manchester Rheumatic Diseases

Centre, Salford Royal Hospital NHS Trust; JOHN P. HALSEY, FRCP, Consultant Rheumatologist, Department of Rheumatology, University Hospitals of Morecambe Bay NHS Trust; JOHN D. ISAACS, PhD, FRCP, Professor of Clinical Rheumatology, Musculoskeletal Research Group, Institute of Cellular Medicine, Newcastle University. Address reprint requests to Dr. B. Thompson, Musculoskeletal Unit, Level 2, Freeman Hospital, Newcastle-upon-Tyne, NE7 7DN, UK.
E-mail: b.thompson@ncl.ac.uk

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Early Callus Formation in Human Hip Fracture Treated with Internal Fixation and Teriparatide

To the Editor:

Osteoporosis is becoming a serious public health problem in Asian countries. Hip fractures represent the most significant osteoporotic fractures. Except under conditions of extremely poor health status, treatment with surgical intervention and early mobilization remains the gold standard for treating hip fractures. Recently, teriparatide, recombinant parathyroid hormone (PTH 1-34), has been approved for treatment of osteoporosis. We describe an enhanced callus formation phenomenon in a patient with hip fracture who was treated by internal fixation and daily PTH 1-34 injection.

A 62-year-old woman with liver cirrhosis experienced sudden right groin pain when undertaking rehabilitation. Radiographs revealed a basal neck fracture (Figure 1a). The fracture was immobilized with a percutaneous cannulated screw. Due to her severe osteoporotic condition, daily PTH 20 μg injection (Eli Lilly, Indianapolis, IN, USA) with calcium 1500 mg and vitamin D 400 IU supplement were also prescribed. Protected weight-bearing with the use of double crutches was suggested for her postoperative program.

One month after surgery and PTH treatment, an external callus formation was noted around the fracture site (Figure 1b), which became more solid 3 months later (Figure 1c). The fracture line became invisible and the patient was pain-free 6 months postoperatively (Figure 1d). At 1-year followup, she had resumed previous activity (swimming, bicycle riding) without difficulty or pain.

Estrogens, bisphosphonates, and selective estrogen receptor modulators (SERM) are used in treatment of osteoporosis as inhibitors of bone resorption[1]. Cao, *et al* reported that use of antiresorptive agents suppressed callus remodeling in ovariectomized rats[2].

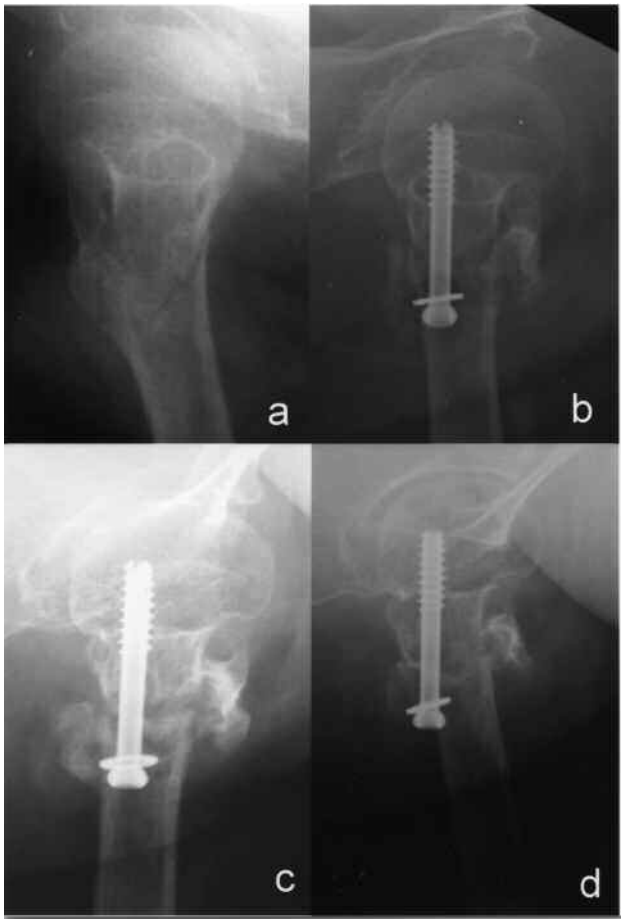

Figure 1. (a) Preoperation roentgenogram showing complete basal neck fracture. (b) One month after operation, showing callus formation. (c) Three months after operation, the amount and density of callus had increased. (d) Six months after operation, callus was consolidated and the fracture line is scarcely visible.

PTH is a calcium homeostasis regulator[3]. Low extracellular calcium level stimulates PTH secretion, which promotes calcium reabsorption in kidney and bone resorption[4]. Continuous infusion of PTH was reported to cause osteopenia, probably due to greater acceleration of bone resorption than bone formation; whereas intermittent PTH treatment has been shown to increase bone formation and bone mass, leading to improved compressive strength. The mechanisms of the diverse actions of the hormone on bone remain obscure, and may be caused by differences in intracellular signaling mechanisms[5]. Animal studies with intermittent PTH also showed a significant cancellous bone mass increase in ovariectomized models[6]. Skripitz and Aspenberg demonstrated that PTH treatment will increase the amount of new bone formation and implant fixation strength in normal rats[7,8].

We describe the first case of enhanced callus formation after daily teriparatide injection in a patient with hip fracture. Based on experience of other hip fractures treated during the same period, it is a reasonable presumption that early callus formation was due to usage of PTH. To our knowledge, enhanced callus formation by PTH in fracture has not been reported before. Intermittent PTH therapy seems to be a promising adjuvant therapy of fracture healing. Randomized controlled clinical trials are required, focused on the effect of different doses or duration of teriparatide treatment.

CHEN-TUNG YU, MD; JUI-KEI WU, MD, Department of Orthopedics; CHIUNG-CHIUNG CHANG, RN, Department of Nursery; CHIU-LIANG CHEN, MD, Department of Orthopedics, Changhua Christian Hospital, Changhua; JAMES CHENG-CHUNG WEI, MD, PhD, Institute of Medicine, Chung Shan Medical University, Division of Allergy, Immunology and Rheumatology, Chung Shan Medical University Hospital, Taichung, Taiwan. Address reprint requests to Dr. J.C-C. Wei, Division of Allergy, Immunology and Rheumatology, Chung Shan Medical University Hospital, No. 110, Sec. 1, Jianguo N. Rd., South District, Taichung City 40201, Taiwan. E-mail: wei3228@gmail.com

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Evaluation of a Knee and Shoulder Arthrocentesis Training Program for Primary Care Providers

To the Editor:

Referrals to rheumatologists for rather routine knee and shoulder arthrocenteses are common. Such referrals might be decreased if primary care providers (PCP) were more comfortable doing these procedures. Residents in internal medicine and family practice do have opportunities for procedures during their training but the few reports evaluating the effect of any such training suggest that physicians do not feel confident after residency[1,2].

A few evaluations on the influence of arthrocentesis training for residents and hospital staff have suggested that at least in the short term increased confidence was achieved[3-5]. We describe the effects of a series of 5 training programs to PCP on arthrocentesis techniques.

We evaluated effects of a series of free programs conducted at Pri-Med meetings in 5 different cities. Half-hour sessions were provided for 4 trainees at each session by 1 of 5 experienced rheumatologists for each session. In addition to the physician authors, trainers at the 5 sites are listed in the acknowledgment below.

Sessions covered indications for arthrocentesis, contraindications, supplies needed to be prepared, materials to inject, and importance of synovial fluid analysis. We reviewed the anatomy and the joint aspiration procedures in detail, providing hands-on experience with knee and shoulder models (Sawbones®, Pacific Research Laboratories, Vashon, WA, USA).

Table 1. Average number of knee aspirations or injections per 3-month period.

	Prior	After Training
More than 11, n (%)	9 (6.9)	12 (9)
6–10, n (%)	11 (8.4)	23 (17)
1–5, n (%)	76 (58)	81 (62)
0, n (%)	35 (26.7)	15 (11)

Table 2. Average number of shoulder aspirations or injections per 3-month period.

	Prior	After Training
More than 11, n (%)	4 (3.0)	6 (4.7)
6–10, n (%)	8 (6.1)	21 (16)
1–5, n (%)	60 (45.8)	68 (53)
0, n (%)	59 (45)	34 (26)

Participants also palpated shoulder landmarks on each other. Instructions included both glenohumeral and subacromial bursal procedures with demonstration and practice on both anterior and posterior approaches to the glenohumeral joints. Knee practice included both medial and superolateral retropatellar approaches.

Simple satisfaction questionnaires were completed by all attendees at the conclusion of their half-hour session. A more detailed questionnaire was mailed to all attendees 3 months after their training.

A total of 1969 individuals attended the 5 programs. Family and general practitioners were 38%, internists 24%, nurse practitioners 22%, physician assistants 7%, and others 9%. Seventy-one percent of all people attending had never done joint aspirations or had done none since training.

On the initial satisfaction questionnaire virtually all (99%) reported that they found the training useful. Seven percent, or a total of 131, responded to the more detailed followup questionnaire at 3 months. Of these responders, 96% reported that they felt more comfortable aspirating joints and administering injections.

Respondents at 3 months were much more likely to have done aspirations than the 29% of the whole group. Table 1 shows numbers of reported knee aspirations or injections per 3-month period before and after the training. Table 2 shows similar figures for shoulder procedures. Twenty responders at 3 months, who had done no procedures before, now did knee procedures and 15 did shoulder aspirations or injections.

These results provide the first, although still limited, evidence on the reported effect of training of PCP about joint aspiration and injection. A project with similar models for residents and faculty reported by Jolly, *et al* described only greater comfort with procedures[4]. Vogelgesang, *et al*[3] trained residents with a lecture and practice on a model. Those so trained did better on a quiz and reported more confidence than a control group given only a normal clinic rotation.

In addition to procedures done we asked for comments. A few felt that they still needed a mentor to do the first few actual patients. Most were using the training to give injections rather than for diagnosis. Many wanted instruction about other sites for injections. Others felt that the hectic practice pace left no time for procedures.

There are some limitations made evident by our study. We had only a 7% response rate at 3 months. Information from initial nonresponders to the 3-month survey would be helpful. Comparison with programs with actual use in patients or different models would be important. Despite instruction and handouts on synovial fluid analysis, we did not receive any responses about this helping with diagnosis. We have no information on the

true effect of this brief training on patient care[6]. How should we evaluate quality and effect on patient care of these procedures by PCP?

H. RALPH SCHUMACHER, MD; LAN X. CHEN, MD, PhD, University of Pennsylvania and Veterans Administration Medical Center, Philadelphia, Pennsylvania; LESLEY GLICK, MD, Phase Five Communications, New York, New York, USA. Address reprint requests to Dr. H.R. Schumacher, VA Medical Center, 151K University & Woodland Aves., Philadelphia, PA 19104.

Supported in part by an investigator initiated grant from TAP Pharmaceuticals.

ACKNOWLEDGMENT

We thank additional trainers: Alan Marks, Robert Zurier, Sharon Katz, and Christine Kovacs at Boston; Filemon Tan, Sean Xiang Tao, Francis Williams, and George Duna at Houston; David Alboukrek, Jeffrey Kaine, Robert Levin, David Makover, Ira Pardo, and Adam Rosen at Fort Lauderdale; Darcy Majka, Prya Damaraju, Eric Gall, Lori Siegel, and Calvin Brown Jr at Rosemont; and Gail Kerr, Raymond Flores, Sean Whelton, Mark Gourley, Kenneth Austin, Charles Via, and Violet Rus at Baltimore.

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Correction

Khan AA, Sándor GKB, Dore E, et al. Canadian consensus practice guidelines for bisphosphonate associated osteonecrosis of the jaw. J Rheumatol 2008;35:1391-7. Professional affiliations of 2 authors on page 1392 should read as follows; S. Sutherland, DDS, MSc; N. Blanas, DDS, FRCDC, Sunnybrook Health Sciences Centre, and Faculty of Dentistry, University of Toronto. We regret the error.