Clinical and Immune Peculiarities of Pseudotuberculous Polyarthritis Against a Background of Chronic Opisthorchiasis

Sir—In recent years, there has been a heightened interest by investigators in the arthritic forms of Yersinia infection. In the territory of Siberia, 50–60% of patients develop yersiniosis against a background of chronic opisthorchiasis because this area is a prominent natural breeding ground of Opisthorcis (liver fluke). It causes changes in the clinical manifestation and problems with diagnosis and treatment. It is generally known that some infectious diseases (typhoid, dysentery, brucellosis and viral hepatitis) with accompanying chronic opisthorchiasis have a more serious outcome with a tendency towards chronicity [1–4]. Outcomes of yersiniosis, and especially pseudotuberculosis, in association with chronic opisthorchiasis have not been sufficiently investigated. This investigation set out to explore clinical and immunological indices in patients with pseudotuberculous polyarthritis (PTP) and accompanying chronic opisthorchiasis (CO).

Twenty-seven patients aged from 18 to 50 yr with acute to moderate forms of PTP were divided into two groups: with accompanying CO (Group I: four men and eight women) or without (Group II: six men and nine women). The criteria for inclusion in these groups were determined according to age, sex and the absence of other accompanying diseases. Examination of these patients established no evidence of brucellosis, Chlamydia infection, Lyme borreliosis, tuberculosis or joint disease. A diagnosis of pseudotuberculosis infection in all patients was confirmed serologically by indirect haemagglutination (RIHA) with titres ranging from 1:100 to 1:64 000. Yersinia pseudotuberculosis was isolated by coproculture from five patients out of 27 (18.5%).

Clinical assessment of affected joints was carried out in order to avoid additional injury. Radiography confirmed the diagnosis of polyarthritis. Diagnosis of CO was confirmed by finding ova in faeces and bile.

In patients with PTP, and also in 25 patients with CO and 25 healthy people (control groups), the following indices of cellular and humoral immunity were analysed: circulating blood levels of T and B lymphocytes and subpopulations of theophylline-resistant (TRL) and theophylline-sensitive (TSL) T lymphocytes; reactive lymphocyte blast transformation indices (RLBT) after stimulation with phytohaemagglutinin (PHA) and measurement of serum levels of IgA, IgM, IgG and IgE. Four basic clinical manifestations of joint disease [5] were also measured using: a pain index (revealed by active and passive motion); joint index (pain on palpation of the joints); phlogistic index (by degree of expression of exudate); and duration of morning stiffness.

According to all the indices measured, patients with mixed pathology showed a greater level of phlogistic activity in the joints. Pathological joint changes in the compared groups were symmetrical and plural, but in patients of Group I a greater number of joints were involved in this process than in Group II. The duration of PTP with CO was longer than for groups without helminthiasis; this averaged 38.2 days for patients in Group I and 26.3 days for those in Group II. Recurrence of arthritis was noted in 33.3% of patients in Group I and 13.3% in Group II. It was evident that PTP with CO had a pronounced tendency to chronicity. Analysis of RIHA titres established that diagnostic titres appeared later in patients with mixed pathology than in those with a monoinfection.

Immunological examination of the patients with PTP was conducted at 2 (height of the disease), 3 and 4–5 weeks after the onset of pseudotuberculosis, and also at 3 and 6 months after discharge from hospital. In patients with CO alone (control group), there was evidence of T lymphopenia, but the B-cell counts and indices for TRL and serum immunoglobulin levels (IgA, IgM and IgG) were normal with increased TSL and a lowering of RLBT. These immune changes can be ascribed to pathogenic changes associated with helmint infections. There were also additional tissue changes consistent with a chronic inflammatory process in the bile ducts and gall bladder. As is known, T lymphopenia and a decrease in PHA stimulation of RLBT are observed in patients with chronic liver diseases, e.g. hepatitis, cholangitis, cholecystitis and cirrhosis [6–10]. In addition, prolonged circulation of metabolic products of Opisthorcis in the blood exerts toxic and allergic influences on the human organism [11]. Thus, depression of T lymphocytes in people with CO may be the manifestation of chronic inflammation of the liver, bile ducts and gall bladder, and also the result of protracted intoxication and modified allergic responses in the body.

At all periods of disease, the patients in Group I had T lymphopenia, lowered RLBT, normal quantities of B cells and TRL, and increased TSL counts which did not return to normal until 3 months after discharge from hospital. In contrast, Group II patients with PTP, but no helminthiasis, had normal T-cell levels during the period of convalescence and for 3 months after. Also in this group, B-cell levels were increased in week 2 of their illness, but TSL and RLBT levels were normal after 3 months. Thus, the presence of T lymphopenia, changes in the functional activity of T cells and the response of RLBT to PHA were typical for patients with PTP. It is likely that lipopolysaccharides of Y. pseudotuberculosis had an immunosuppressive effect. The influence of CO on the indices of cellular immunity in patients with PTP was only...
revealed during convalescence just prior to or after discharge from hospital when the levels of T cells and RLBt were decreased in patients with mixed pathology (as well as in patients with CO only), whereas levels in patients with PTP only were normal.

The patients in Group I also showed an increase in IgG in the second week of disease, which returned to normal in the third week. The serum IgA level was increased throughout the time course of the disease and took a further 3 months to return to normal. Serum IgM showed a transient increase at 3 and 4–5 weeks of illness, before returning to normal after 3 months. The serum IgE levels in patients of both Group I and Group II remained constantly high, and after 6 months only approached normal levels in Group II. This prolonged high level of IgE was more pronounced in patients with accompanying CO.

It is considered that these immunological changes reflect clinical differences found in patients with PTP and CO, and can be ascribed to the allergic responses generated by an accompanying helminthiasis.

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Successful Child Bearing During Intravenous Cyclophosphamide Therapy in a Patient with Systemic Lupus Erythematosus

Sir—Recently, SLE patients have received immunosuppressive agents that can induce ovarian failure and/or teratogenicity [1–3], although the outcome of pregnancy in such patients has rarely been reported.

We experienced a successful child bearing in an SLE patient who became pregnant during the course of cyclophosphamide (CYC) therapy.

A 23-yr-old woman developed butterfly rash, arthralgia, and proteinuria in 1992. Laboratory findings included: ANA 1280 dils, positive results for LE cell preparation and anti-Sm antibody, and diffuse proliferative glomerulonephritis (WHO class IVa). She responded well to prednisolone (20–30 mg/day) until June 1994 when she exhibited lupus nephropathy (pre-tribial oedema and proteinuria 4.6 g/day). High-dose methylprednisolone therapy (1000 mg for 3 successive days) failed to improve her renal function. After initiating i.v. CYC therapy (750 mg/M), her clinical and laboratory findings improved. She had therefore been treated with CYC therapy since November 1994.

She first became pregnant in February 1995, during i.v. CYC therapy. Because of disease activity and possible teratogenicity, she obtained an abortion at the 12th gestational week. After the exacerbated disease state had improved, the dose of CYC was decreased by June 1995 (750 mg/2M). She became pregnant again because of her definite will to bear her child; she became pregnant 10 days after the last CYC treatment. Further CYC therapy was discontinued. In January 1997, she bore a healthy boy at full term (birth weight 3010 g, Apgar score 9).

Continuous CYC treatment during pregnancy, especially in the first trimester, has resulted in congenital anomalies [4–6]. Successful child bearing in patients in whom CYC had been stopped 3 yr before labour has been reported [2]. Two of four had a good outcome: one laboured pre-term at 34 weeks, and the other one went full term with a child who was small for date. These outcomes suggested that CYC influenced fetal development minimally when its use was discontinued 3 or more years before pregnancy. Our patient became pregnant during the course of CYC treatment. The interval between the last CYC treatment and pregnancy is at most 2 or 3 weeks. In the extremely early period of pregnancy, CYC cannot reach the fetus because of the unestablished placenta. In addition, CYC was metabolized rapidly [7]. This length of ‘wash-out’ period can bring minimal influences on fetal development.

Concerning the maternal aspects, the prevalence of ovarian failure is reported to increase with age [8]. Our patient did not show ovarian failure and became pregnant at the ages of 21 and 22 yr. Her disease did not exacerbate during pregnancy and the periperium. In SLE patients in remission, the disease does not flare in pregnancy, as seen in our patient [9]. Our observation suggested that even during CYC treatment, patients with inactive SLE during their younger ages might bear a child under stringent monitoring, although birth control should be required for such patients.

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Fluoroquinolones as a Cause of Tendon Disorders in Patients with Renal Failure/Renal Transplants

Sir—In recent years, an increase in the incidence of tendinopathies, particularly in renal transplant patients, has been reported [1, 2]. Fluoroquinolones have been accused of being a responsible factor. We report on four patients with tendon disorders following treatment with these agents.

Case no. 1 was a 55-yr-old white male who received a kidney transplant in 1986. In 1995, bilateral tendinitis of the extensor hallucis longus occurred 3 days after initiation of ciprofloxacin (250 mg b.d.). Risk factors for tendinopathies were chronic renal failure with a creatinine clearance of 22 ml/min [3] and 9 yr of prednisone therapy [4–6].

Case no. 2 was a 65-yr-old white male who obtained a kidney transplant in 1981. In 1995, bilateral Achilles tendinitis occurred after a 2-d exposure to fleroxacin (250 mg b.d.). Risk factors for tendinopathies were advanced age over 60 yr [1, 5, 7, 8], chronic renal failure with a creatinine clearance of 15 ml/min [3] and 14 yr of prednisone therapy [4–6].

Case no. 3 was a 58-yr-old white female who obtained a kidney transplant in 1996. In 1996, rupture of the left Achilles tendon following bilateral tendinitis occurred 5 days after a second course of ciprofloxacin (250 mg b.d.). Risk factors for tendinopathies were renal failure with a creatinine clearance of 40 ml/min [3] and 1 month of high-dose prednisone [4–6].

Case no. 4 was a 37-yr-old white male who had been undergoing chronic haemodialysis since 1976. In 1995, rupture of the right quadriceps tendon occurred 2 months after initiation of ciprofloxacin therapy (250 mg b.d.). Risk factors for tendinopathies were chronic renal failure [3], insulin-dependent diabetes mellitus and severe secondary hyperparathyroidism [3, 6].

Six major reports concerning fluoroquinolone-induced tendinopathies appeared from 1992 to 1995 [1, 2, 4, 5, 7, 8], as summarized in Table I. Interestingly, the overwhelming majority of patient reports originated from France [5, 8]. In the USA, only one case has been published [9] and no single case of tendon problems was found in 2122 patients who had received fluoroquinolones [10].

In conclusion, fluoroquinolones represent an important cause of tendinitis and tendon rupture. However, the evidence for this causality is based purely on epidemiological data.

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<table>
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<th>Reference</th>
<th>Year</th>
<th>Number of patients (tendinitis/rupture*)</th>
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<th>Reported risk factors</th>
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<td>Ribard et al. [7], 1992</td>
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<td>7 (4/3)</td>
<td>1–35 days</td>
<td>Advanced age</td>
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<tr>
<td>Leray et al. [1], 1993</td>
<td></td>
<td>5 (not stated)</td>
<td>Not stated</td>
<td>Advanced age</td>
</tr>
<tr>
<td>Donck et al. [2], 1994</td>
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<td>11 (9/2)</td>
<td>Not stated</td>
<td>Duration of haemodialysis, secondary hyperparathyroidism</td>
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<tr>
<td>Royer et al. [8], 1994</td>
<td></td>
<td>100 (69/31)</td>
<td>1–90 days</td>
<td>Male sex, advanced age, steroids (?)</td>
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<tr>
<td>Szarfman et al. [4], 1995</td>
<td></td>
<td>25 (0/25)</td>
<td>2–42 days</td>
<td>Advanced age, steroids, long-term dialysis</td>
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<tr>
<td>Pierfitte [5], 1995</td>
<td></td>
<td>421 (340/81)</td>
<td>10 days (tendinitis) &gt;15 days (tendon rupture)</td>
<td>Advanced age, steroids</td>
</tr>
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</table>

*Some patients with tendon ruptures also had preceding tendinitis.
Successful Response to Angioplasty in a Patient with Upper Limb Ischaemia Secondary to Giant Cell Arteritis

Sir—Upper limb ischaemia is an uncommon complication of GCA [1–3]. The treatment of patients with this complication includes steroids and reconstructive surgery in refractory cases [4]. We describe a patient with GCA presenting with upper limb ischaemia who responded well to angioplasty performed prior to the onset of steroid therapy.

A 69-yr-old woman was admitted to the vascular surgery service of our hospital because of acute left upper limb ischaemia. An urgent humeral arteriotomy was performed, and embolectomy was attempted with a Fogharty’s catheter, but no thrombotic material was obtained. After that, pain and pallor improved, but the distal pulses remained absent. A selective arteriography of the aortic arch and its branches revealed two smooth left humeral artery stenoses. The lesion was treated with percutaneous transluminal angioplasty, with favourable morphological and haemodynamic results. Owing to persistent fever since admission, a more thorough study was requested to our department. The patient recalled having morning stiffness and pain in the shoulders, upper arms and thighs since 3 months. Physical examination revealed a fever of 38°C and pain on shoulder movements. Laboratory studies showed a mild normocytic anaemia with normal leucocyte and platelet counts. The ESR was 107 mm/h. Coagulation tests, routine biochemistry profile, antinuclear antibodies, rheumatoid factor and antinuclear antibodies, as well as chest radiograph, electrocardiogram and echocardiogram, were negative or normal. Blood and urine cultures were negative. A biopsy of the left temporal artery revealed a typical GCA arteritis in acute stage. Treatment with prednisone 1 mg/kg/day was started. Fever remitted and polymyalgia symptoms improved shortly thereafter.

Upper limb ischaemia is an uncommon presentation of GCA, its incidence ranging from 5 to 8% in previous reports [1, 5]. Subclavian and axillary arteries are most commonly involved, but humeral stenosis, as in our case, has been described [4]. Moreover, it can be the only manifestation of the disease [6]. Steroid therapy rapidly improves upper limb vascular symptoms in GCA patients, although angiographic evidence of stenosis usually persists for years [4, 7]. Invasive therapeutic approaches are restricted to cases with severe persistent ischaemia despite steroid treatment [4]. In this case, the diagnosis of GCA was not initially considered, and angioplasty was performed early with good morphological and clinical results, before steroid treatment was initiated. These data suggest that angioplasty could be a valuable procedure in non-responding cases, rendering reconstructive surgery unnecessary. In addition, this case emphasizes the importance of adequate clinical history taking and implies that a temporal artery biopsy should be considered in the study of unexplained upper limb vascular symptoms, especially if other findings such as polymyalgia and fever are present.

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First-Time Manifestation of Generalized Wegener’s Granulomatosis Despite Methotrexate

Sir—Recently, several studies showed methotrexate (MTX) to be an effective treatment of systemic vascul-
itis. The first reports concerned patients with Takayasu arteritis [1, 2]. In the meantime, MTX has been used in patients with generalized Wegener’s granulomatosis [3–5]. Patients with life-threatening disease were not included. In the study by Hoffman et al. [3], MTX was effective at inducing remission in up to 71%. However, a significant relapse rate during MTX occurred [4]. Another study confirmed these results recommending MTX as a suitable therapy to maintain remission [5]. In this study, the activity score decreased further in patients who had a partial remission at the beginning of the study. Side-effects were rare. We report two patients who developed generalized Wegener’s granulomatosis while treated with MTX for other presumed conditions.

Case 1 was a 56-yr-old woman who was diagnosed with rheumatoid arthritis according to the ACR criteria in 1994. She presented with a symmetrical synovitis of the wrists, MCP and PIP joints. Both knees and the MTP joints were also affected. The ESR was 42 mm and rheumatoid factor was present. The morning stiffness lasted for 2 h. Radiographs of the hands and feet showed no erosions. Within the first year, she developed remitting fever and a small-vessel vasculitis of the skin on both lower legs as proven by histology. First she was treated with steroids alone at a median dosage of 20 mg prednisone/day. At the beginning of 1996, the polyarthritis worsened. MTX was added (15 mg/week). Nine months later, she complained of chronic sinusitis, weight loss and fatigue. In December 1996, she was admitted to the hospital with dyspnoea and fever. Radiographs of the chest disclosed bilateral infiltrates. A histological specimen of the nose confirmed the diagnosis of Wegener’s granulomatosis. In the laboratory, the ESR was 80 mm. Rheumatoid factor was still detectable at 125 U/ml. For the first time, the patient was cANCA positive (anti-proteinase 3 positive). Radiographs of the hands and feet documented the non-erosive character of the inflammatory joint involvement. The treatment was changed immediately from MTX to daily cyclophosphamide. In March 1997, the patient had improved markedly, the pulmonary infiltrates were no longer present.

Case 2 was a 43-yr-old man admitted for removal of an intracranial tumour of the right skull base in July 1993. The patient complained of fatigue, depression and focal neurological symptoms according to the affection of several cranial nerves. The histology of the tumour showed the unexpected pattern of a giant cell arteritis. In addition, a temporal biopsy was performed with negative result. At that time, the ESR was 40 mm, rheumatoid factor was positive and ANCA were negative. The patient was treated with 20 mg prednisone/day. Under this therapy, the patient was in remission and the ESR returned to normal. After 1 yr of treatment, the patient developed fatigue and depression again. The ESR increased to 60 mm. MTX was started at a dosage of 20 mg/week in addition to 15 mg prednisone/day. Again all symptoms resolved. The ESR returned to 10 mm. Fifteen months later, the patient presented with sinusitis, severe temporal headache, fever, weight loss and depression. Red casts were detectable in the urine. Histology of the nose and kidney confirmed the diagnosis of Wegener’s granulomatosis. The cANCA test was positive now with anti-proteinase 3 specificity. The histology of the intracerebral tumour was reviewed by a vasculitis expert who confirmed the initial diagnosis. Treatment with oral cyclophosphamide was initiated and a remission achieved within 9 months.

Follow-up studies of patients with Wegener’s granulomatosis suggest that the disease starts as a localized vasculitis, often ANCA negative. The initial presentation may be puzzling and mimic other rheumatic conditions. The shift to the typical generalized feature may take years [6]. Treatment with daily cyclophosphamide and steroids is effective at inducing remission in the majority of patients [6]. Unfortunately, the rate of therapy-related morbidity and mortality is significant [6]. Therefore, MTX was investigated in patients with moderate disease activity or as a second-line treatment [3–5]. Our case reports demonstrate that the progression of a vasculitis to the generalized stage of Wegener’s granulomatosis was not prevented by MTX. The dosage used in the two patients described was the same as that used in the Wegener’s granulomatosis MTX studies (0.3 mg/kg/week) [4, 5]. In conclusion, the treatment of Wegener’s granulomatosis with MTX may not be sufficient to prevent progression of the disease. These limitations of MTX treatment have to be kept in mind when using the drug in vasculitis patients. Therefore, close follow-up is necessary in order to recognize increasing disease activity early and to be prepared to change the immunosuppressive treatment.

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Symptomatic Antiphospholipid Syndrome Induced by Chlorpromazine

Sir—A 42-yr-old woman treated for borderline personality disorder with chlorpromazine 260 mg/day presented with a sudden onset of right-sided weakness, numbness and headache. There was no history of arthritis, skin rashes, mouth ulcers, recurrent miscarriages or Raynaud’s phenomenon. There was a family history of cerebrovascular disease, her mother having died following a stroke at the age of 41 yr. She smoked 30 cigarettes per day. Other medication on admission was moclobemide 150 mg twice/day and ranitidine 300 mg/day.

Examination confirmed upper motor neurone signs affecting the right arm, leg and face with hemiplegia and hemiparaesthesiae. She was normotensive and examination was otherwise unremarkable.

An MRI of the brain showed widespread abnormality in the subcortical white matter consistent with small-vessel angiopathy (Fig. 1).

Further investigation revealed that the ESR (Westergren) was elevated at 40 mm/h with a normal CRP. Haematology and biochemistry, including blood glucose and lipids, were normal. Autoantibody screening showed a positive ANA with an IgG titre of 50 and an IgM titre of 1600. Double-stranded DNA was negative, as was extractable nuclear antibody and the VDRL. Complement and immunoglobulins were normal. Chest radiograph, ECG and echocardiogram were unremarkable.

Anticardiolipin antibody was positive with an elevated IgM titre of 24.1 (normal <9). Screening for lupus anticoagulant was positive with a prolonged activated partial thromboplastin time at 48 s (control 31) which only corrected to 40 s with 50:50

Test: Normal plasma. Clotting factor, protein C and protein S concentrations were all within the normal range.

A diagnosis was made of antiphospholipid syndrome possibly secondary to chlorpromazine. The chlorpromazine was stopped and she was anticoagulated to an International Normalized Ratio (INR) of between 3.0 and 3.5. Her weakness resolved and she made a full recovery.

Since discontinuation of the chlorpromazine, the anticardiolipin antibody titres have fallen progressively to within the normal range. Warfarin was, therefore, discontinued and there have been no further cerebrovascular events.

The antiphospholipid syndrome, a disorder of vascular thrombosis associated with elevated levels of antiphospholipid antibodies [1], may occur in the context of SLE or as a primary disorder [2]. The antibodies, which may be IgG, IgM or IgA, also occur in various infections, other connective tissue diseases and with certain drugs such as the phenothiazines (e.g. chlorpromazine) [3]. The presence of IgM anticardiolipin antibodies associated with chlorpromazine is well described, but not thought to be associated with clinical features [4]. Some work has suggested that the reason antibody presence does not correlate with thrombotic events is because phenothiazines themselves exert an antithrombotic effect [5].

This case is of interest because it appears that the patient developed symptomatic antiphospholipid syndrome, with IgM anticardiolipin antibodies, secondary to chlorpromazine. It is possible that the serological changes may have assumed greater relevance in the presence of the other risk factors (smoking and a family history of cerebrovascular disease). It is also

Fig. 1.—MRI of the brain showing extensive areas of high signal intensity (arrowed) involving predominantly the subcortical white matter. The features are consistent with small-vessel angiopathy and subsequent ischaemic demyelination. There is associated mild cerebral atrophy.
noteworthy that both the symptoms and the serological findings resolved following discontinuation of the phenothiazine treatment.

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Acrodermatitis atrophicans (ACA)  
Yes. — Acrodermatitis chronica atrophicans (ACA) is a tick-borne dermatological infection caused by Borrelia burgdorferi [1]. Borrelia burgdorferi sensu lato has been subdivided into three main genospecies (B. burgdorferi sensu stricto, B. garinii, B. afzelii) and a hitherto unnamed genospecies termed group VS 116 [2]. Borrelia afzelii has proved to be responsible for ACA [3]. Besides skin lesions affecting mainly the extremities, the joints located underneath the skin lesions may be involved [4]. The condition can easily be mistaken for other rheumatic diseases, and a correct diagnosis is all the more important since it is curable, as will be seen in the following case report.

A 63-yr-old woman had been bitten by several ticks in the area of Lausanne in 1988. There was no skin lesion or systemic illness associated with the tick bites. Since 1990, she had been suffering from an erythematous rash on her nose and the malar region. Since 1993, she had also been complaining of progressive pain and swelling of the fingers (mainly the third and fourth), all symmetrical, and of numbness and dysesthesiae in all of her digits. She also noted a nodule growing above her left elbow. The third and fourth fingers became stiff and red over a year, with a flexion deformity of thePIP joints. There was no pruritus.

On clinical examination in May 1995, she had facial erythema, a tender firm nodule (2.5 × 2 cm) above the left olecranon and no psoriasis. The third and fourth fingers, which were tender at palpation, had a boutonnière reducible deformity and an oedematous swelling. The skin above the DIP of the third and fourth fingers of both hands was purplish, thin and shining (Fig. 1a). There were no Heberden’s or Bouchard’s nodes. The MCP and the wrist joints were slightly tender, but not swollen; Tinel’s and Phalen’s tests were negative.

The laboratory results, including the antinuclear factor, were normal or negative. No synovial fluid could be obtained by aspiration from the small joints of the hands. A biopsy of the cutaneous lesions was not performed. Standard X-rays of the hands revealed only subluxation of the PIP and DIP joints of the third and fourth fingers. Tc99 m bone scintigraphy was normal. Antibodies to Borrelia, measured by ELISA, were strongly positive for IgG, but normal for IgM. Immunoblot confirmed the specificity of these reactions. The immunoblots carried out to assess immunoreactivity against the four genospecies of B. burgdorferi [5] clearly revealed a stronger intensity and higher number of bands against B. afzelii (Fig. 2).

The patient was treated with doxycycline for 3 months. There was a dramatic response: the numbness of the fingers disappeared within 10 days, the arthralgias and swelling of the fingers subsided within 2 months; after 8 months, the olecranon nodule was no longer present and the skin on her fingers was almost normal. Only a reducible symmetrical boutonnière deformity of the fingers persisted (Fig. 1b). Serological follow-up showed a sharp decrease in reactivity against many Borrelia sp. antigens (Fig. 2).

After the initial examination, the differential diagnosis for this patient consisted essentially of nodular seronegative rheumatoid arthritis and systemic lupus erythematosus. It was owing to the history of several tick bites in an endemic area [6], the presence of cutaneous changes characteristic of ACA and the detection of a specific immune reaction to B. afzelii that the diagnosis of Lyme borreliosis was made. The patient’s response to antibiotics was excellent within 2 months.

Rheumatic manifestations associated with ACA have previously been described in Germany. They were referred to as acrodermatitis atrophicans arthropathica [7, 8], in which olecranon nodules, facial erythema and scleroderma-like lesions may occur [1, 8]. In a cohort of 50 cases of ACA in Sweden, 11 presented dislocation of the small joints of the hands or feet [4]. In our case, the residual joint damage closely resembled

**Fig. 1.** (a) Sausage-like appearance of the middle and ring fingers (left hand). The skin is atrophic. (b) Boutonnière deformities of the fingers 5 months after the antibiotic treatment had been stopped. The right hand has the same residual deformities.
Jaccoud’s arthropathy with boutonnière deformities of the fingers, which were voluntarily reducible but without radiological erosions. Furthermore, the joint involvement in our case seems to be periarticular rather than articular, consistent with the definition of Jaccoud’s arthropathy. Recognition of ACA is important since pain and swelling of the fingers in this patient showed a positive reaction, and lip biopsies showed reticulo-nodular infiltration and transbronchial lung biopsies demonstrated the presence of lymphoid IP.


**Effect of Low-dose Cyclosporin Treatment on Interstitial Pneumonitis Associated with Sjögren’s Syndrome**

Sit—Cyclosporin (CSA) is an immunosuppressive agent with a well-established profile that is widely used in the field of organ transplantation [1], and is also effective in treating a spectrum of immune-mediated diseases [2–8]. In general, similar doses of CSA to those administered following transplantation (5–15 mg/kg) have been employed in the treatment of autoimmune rheumatic diseases and related interstitial pneumonitis (IP) [2–6]. However, the optimum dose of this drug for autoimmune disorders has not yet been established because of a scarcity in the number of patients treated with CSA in these diseases. We recently encountered two cases of steroid-resistant IP associated with Sjögren’s syndrome (SS) which were treated effectively with an extremely low dose of CSA (1 mg/kg/day).

Case 1 was a 62-yr-old man and case 2 was a 54-yr-old woman. Both patients were admitted to our hospital with the chief complaints of cough and dyspnoea. Their chest X-ray and CT findings indicated a diaphragmatic hernia with the chief complaints of cough and dyspnoea recurred during the process of tapering PSL. Although PSL treatments partly contributed to these improvements, the patients were diagnosed as having IP associated with SS and initially underwent treatment with prednisolone (PSL). Although PSL treatments were effective in both patients, their PaO2 levels fell and dyspnoea recurred during the process of tapering the PSL (Fig. 1). In response to exacerbation of IP, CSA (1 mg/kg/day = 50 mg/day) was added to their PSL therapy. After CSA treatment, the resting PaO2 of these patients increased, and chest X-ray and CT findings also showed a marked improvement, although PSL therapies partly contributed to these improvements.

Since adverse effects associated with CSA are dependent on the size of the dose and the duration of treatment [9], and CSA-mediated nephropathy has been reported as having occurred at even relatively low doses (< 5 mg/kg/day) [6], the lowest effective dosage should be administered. In some patients with...
autoimmune-mediated diseases such as psoriasis [7] and systemic lupus erythematosus (SLE) [8], low doses of CSA treatment (2.5–3.0 mg/kg/day) were reported to be effective in reducing the disease activities. Our cases indicate that lower dose of CSA than previously recommended may be worthwhile for exacerbation of IP associated with autoimmune rheumatic diseases, such as SS, which have shown resistance to steroid therapy and may reduce the adverse effects associated with CSA. They also indicate that this therapy may be helpful in regard to tapering of the steroid dose, although long-term CSA treatment, even if very low dose, ought to be monitored carefully for the induction of lymphoma.

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Pneumocystis carinii Investigation in Patients with Wegener’s Granulomatosis

Sirs—Wegener’s granulomatosis (WG) is distinguished from other necrotizing vasculitides by its predilection to affect the respiratory tract; moreover, airway inflammation has been shown to occur in essentially autoimmune-mediated diseases such as psoriasis [7] and systemic lupus erythematosus (SLE) [8], low doses of CSA treatment (2.5–3.0 mg/kg/day) were reported to be effective in reducing the disease activities. Our cases indicate that lower dose of CSA than previously recommended may be worthwhile for exacerbation of IP associated with autoimmune rheumatic diseases, such as SS, which have shown resistance to steroid therapy and may reduce the adverse effects associated with CSA. They also indicate that this therapy may be helpful in regard to tapering of the steroid dose, although long-term CSA treatment, even if very low dose, ought to be monitored carefully for the induction of lymphoma.

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HIV patients [6]. Second, patients with connective tissue disease (CTD) are at risk for *P. carinii* infections because of the use of immunosuppressive therapy, but this increased risk of infection is greater in WG than in other CTD [7, 8]. Third, co-trimoxazole, the treatment of choice for PCP, reduces the incidence of relapses in patients with WG in remission [2]; this effect has not been achieved with other antimicrobial drugs. This finding suggests that the drug exerts its protective effect by preventing infections, although some investigators have postulated that co-trimoxazole may have anti-inflammatory effects [9] or immunosuppressive properties [2].

In spite of these arguments, our results suggest that *P. carinii* infection is not implicated in the pathogenesis of WG. Nevertheless, further studies are needed to confirm these findings.

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