Letters to the Editor

Erosive psoriatic polyarthritis: A report of 2 asymptomatic cases

Sirs,

Psoriatic arthritis (PsA) is characterized by a frequent asymmetrical involvement of the joints, the common localization in the spine and by the tendency to evolving in ankylosis. Painless spondylitis (1, 2), sacroiliitis (3) ed enthesitis (4) have been described in the literature. We report 2 cases of longstanding asymptomatic erosive peripheral PsA, one of which was discovered accidentally because of its association with another painful rheumatic disorder.

Patient 1. In March 1994 a 74-year-old male patient suffering from RS3PE syndrome for one month came under our observation. This disease was localized in the hands and feet and was diagnosed according to the clinical picture and laboratory findings reported by McCarty (5). Ecography revealed soft tissue swelling without tenosynovitis. The patient also complained of guttate psoriasis for 60 years, but he never previously suffered from arthralgias, arthritis, dactylitis or entesitis. Roentgenograms of the hands unexpectedly disclosed a typical picture of PsA characterized by marginal erosions asymmetrically localized in some PIP joints and in several DIP joints. Periostitis was also irregularly distributed. Osteopenia was absent. Feet, spine and sacroiliac joints were undamaged. Neurologic examination and upper limb electromyography were normal; in particular, signs of sensory neuropathy were absent.

A short course of corticosteroid therapy (Deflazacort 12 mg/daily for 2 weeks and 6 mg/daily for a further 2 weeks) induced a complete and persisting remission of the RS3PE symptoms. At the moment there were no clinical signs attributable to PsA. No treatment was instituted. To date the joints, finger functioning, and the ESR and C-reactive protein values remain normal; the radiographic picture is unchanged.

Patient 2. A 69-year-old white woman presented in September 1998 with a 2-month history of mild polyarthralgias and swelling of the right ankle and wrists. Moreover, physical examination revealed asymmetrical shortening and/or ankylosis of several toes. A mild use-related bilateral metatarsalgia was present on walking. Roentgenograms of the feet disclosed a typical picture of longstanding psoriatic arthritis mutilans: erosions, acroosteolysis asymmetrically involving the phalangeal and metacarpal bones, and "telescoping digits". Two PIP and 3 MCP joints were fused. A less severe asymmetrical erosive arthritis was also identified in the hands and wrists. The spine and sacroiliac joints were spared. Some lesions of guttate psoriasis were present on the legs. Neurologic investigation did not show any alteration. The patient had never suffered from arthritis, dactylitis or entesitis and recalled only sporadic episodes of arthralgias sometimes in the spine, sometimes in an upper or lower limb. These data were confirmed by the family doctor. Our extensive examinations showed only a mildly increased ESR (30 mm/1st hour) and C-reactive protein (0.9 mg/dl; normal values < 0.5 mg/dl). We decided to administer sulfasalazine 2 g/daily, which resulted in a complete remission of the arthritis and normalization of the indicators of inflammation in 2 months. Metatarsalgia on walking (due to PsA-induced modifications of the feet) persists. Until recently (sulfasalazine is now administered at the dose of 1.5 g/daily), the remission has been stable and the radiographic findings are unchanged.

Our observations show that in PsA asymptomatic involvement is possible not only in the spine (1, 2), sacroiliac joints (3) and enthesis (4), but also in the peripheral joints. This silent arthritis can occur in a mild and self-limiting form (Patient 1) or with a destructive course (Patient 2). Asymptomatic psoriatic polyarthritis is probably rare but it is very difficult to determine its actual prevalence due to the absence (Patient 1) or late appearance (Patient 2) of the clinical manifestations (pain and articular swelling) that usually lead the patient to consulting a physician. In particular, the diagnosis was accidental in the first case and extremely late in the second case. Both of our patients have guttate psoriasis of the skin (the nails are undamaged); the possible significance of this association should be confirmed.

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Expression of Fas antigen (CD95) on peripheral blood lymphocytes in Behçet's disease

Sirs,

Behçet's disease (BD) is a chronic, inflammatory disorder affecting various organ systems (1). The etiology and pathogenesis of BD are unknown, but there is considerable data indicating that immunological abnormalities are important (2,3). Numerous kinds of infectious microorganisms have been postulated as causative agents of BD in genetically susceptible individuals (4, 5). The complex interaction of genetic and enviromental factors seems to be responsible for immunological dysregulation, and an inflammation triggered by immunological mechanisms causes the disorder. Apoptosis is important in the regulation and functioning of the immune system and plays significant roles in the control of the immune response (6). The Fas Ag (CD95) is a 45 kDa cell-surface protein belonging to the tumour necrosis factor (TNF) family. Interaction of Fas Ag (CD95) with its specific ligand triggers the apoptotic death of T and B lymphocytes (7). Therefore, in order to analyze the possible role of apoptosis in BD, we studied the expression of Fas antigen on peripheral blood lymphyocytes from BD patients.

Our study group consisted of 62 patients (34 patients with active BD and 28 patients with inactive BD) and 29 age and sex-matched healthy adults as controls. The diagnosis of BD was estabilished using the criteria of the International Study Group for BD (8). Disease activity was based on clinical findings at the time of venipuncture. Patients lacking any clinical signs were categorized as having inactive disease. Patients with major oral aphthae and genital ulcerations, arthritis, ocular manifestations, neurologic manifestations and/or large vessel involvement constituted the group with active disease. At the time of the study, 46 patients were taking only colchicine and the remaining 18 were taking no drugs.

Whole blood samples were directly stained with two or three-color monoclonal antibodies (Becton Dickinson, San Jose, CA) and analyzed by a FACSort flow cytometer (Becton Dickinson). Blood samples were collected in EDTA tubes and used within 2 hrs of storage at room temperature. In order to

stain the cells, 100 µl blood was mixed with 10µl fluorescein isothiocyanate(FITC)-labeled anti-CD95 and phycoerythrin (PE)-labeled anti-CD45RO in 2 separate tubes. Then peridinin isothocyanate(PerC-P)-labeled anti-CD4 was added to one of the tubes and PerC-P-labeled anti-CD8 was added to the other. On addition, we mixed the blood FITC-labeled anti-CD95 and PerC-P-labeled anti-CD19 in another tube. Following 20 min incubation, the erythrocytes were removed by lysis. The cells were then washed twice with cell wash and analyzed immediately for fluorescence using a FACSort flow cytometer and Cell Quest software. Isotype-matched FITC, PE, and PerC-P-labeled antibodies were used as negative controls. Three-colour analysis was performed for the T cell subset as described previously (9). A gate for the lymphocyte population was defined by forward and side light scatter characteristics, and FL3 PerC-P-strongly positive areas were further gated as CD4 or CD8 T cell population for subsequent two-colour analysis. FITC/PE labeled-anti-CD45/CD14(leucagate), FITC/PE labeled-anti-CD3/CD4 and anti-CD3/CD8 were also used to determine the percentage of the corresponding subpopulation.

First, expression of Fas Ag (CD95) on CD4+, CD8, CD19+ cells was examined (Table I). The one-tailed variant test was used for statistical comparisons. There was no significant difference in the percentage of Fas-positive cells within CD4+ and CD8+ T cells between active BD, inactive BD and the controls ($p > 0.05$). Although Fas staining of the B cells was somewhat weaker than that of the T cells, there was no significant difference between the groups ($p > 0.05$).

Secondly, we evaluated the relationship between CD45RO and Fas Ag(CD95) expression on CD4+ and CD8+ T cells. Three-color immunofluorescence analyses demonstrated that Fas Ag(CD95) was mainly expressed by CD45RO+ memory T cells from BD patients as well as from healthy individuals. The percentage of CD95+CD45RO+ cells within T4 cells were as follows; active BD: 54.09 ± 11.28, inactive BD: 53.87 ± 11.93, controls: 54.97 ± 9.29 and percentage of CD95+CD45 RO+ cells within T8 cells were as follows; active BD: 38.61 ± 12.44, inactive BD 40.26 ± 13.49, controls 38.25 ± 11.20.

The results of most immunological studies suggest a central role for T cells in the pathogenesis of BD. It has been shown that T cells in this disease proliferate vigorously in response to a specific peptide derived from both mycobacterial and human 65-kD shock proteins (hsp) (10) Recently, the observation that T cell oligoclonal expansion correlated with disease activity suggested a possible role of antigen-specific T cells in the pathogenesis of BD (11). Apoptotic cell death is an important mechanism for regulating the fate of lymphocytes following encounters with self and foreign antigens. Defective Fas/FasL interaction may cause failures in T cell apoptosis after a normal immune response. It is known that the expression of Fas on T and B lymphocytes increases after antigen receptor-mediated activation and the activation-induced death of mature T cells occurs through Fas and Fas-Ligand interactions (12, 13). In our study, there was no increase in Fas antigen expression on T cells from active BD patients. Therefore, it may be hypothesized that activated T cells could fail to undergo apoptosis following antigen activation and they may produce cytokines contributing to inflammation.

There have been few studies conducted to determine the role of apoptosis in the pathogenesis of BD. Nakamura *et al.* (14) also found that there was no difference in the proportion of CD4+ or CD45RO+ cells with Fas between active uveoretinitis patients and controls, although the proportion of CD8+ cells with Fas was significantly higher in BD patients with active uveoretinitis. Hamzou1 *et al.* (15) reported high levels of bcl-2 protein in the T lymphocytes of patients with BD. These findings and those of our study suggest that some dysfunctioning in the regulatory mechanism of apoptosis in T cells may have a role in the pathogenesis of BD. Apoptosis is a complex process involving many regulatory mechanisms. Therefore, the multiple and sequental dysregulation of apoptosis involving different cell types, such as T cells, can possibly occur in BD. Further studies are needed to determine the role of apoptosis in the pathogenesis of BD. The susceptibility of Fas-mediated apoptosis should be analyzed by functional studies using anti-Fas-mAb or recombinant FasL in addition to the determination of expression of FasL Our findings in this study could assist such future studies.

Table I. Percentages of Fas-positive cells within various lymphocyte subpopulations.

		Fas-positive cells in (%)		
	(n)	CD4+ cells	CD8+ cell	CD19+ cells
Active Behçet's disease	(34)	55.82 ± 10.75*	54.17 ± 15.42	12.25 ± 5.18
Inactive Behçet's disease	(28)	55.19 ± 12.14	56.95 ± 13.35	11.13 ± 4.83
Controls	(29)	56.10 ± 9.17	51.39 ± 13.35	10.30 ± 4.28

*The result is presented as the mean ± standard deviation of the percentage of Fas Ag (CD95)-positive cells from each lymphocyte population.

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Calf muscular infarction in a diabetic patient

Sirs,

Diabetic muscle infarction (DMI) is a rare complication of diabetes mellitus. The thigh is commonly affected. Calf muscles are exceptionally involved (1-4). We report a case of DMI presenting as a painful calf mass and review the data in the literature on its diagnosis and management.

A 36-year-old woman presented with a 4-month history of pain and swelling of the right calf. She had a 10-year history of diabetes mellitus, poorly controlled and complicated by proliferative retinopathy, nephropathy and sensory neuropathy. Physical examination showed a firm, tender mass in the right posterior-medial calf. There were no associated systemic symptoms or signs indicative of infection, and no discoloration of the skin suggesting cellulitis, gangrene or deep venous thrombosis. Laboratory tests indicated: erythrocyte sedimentation rate 113 mm/hr, blood glucose 1.03 g/l, serum creatinine 60 mg/l, and serum creatinine kinase 144 UI/L. Ultrasonography of the posterior portion of the calf demonstrated an area of heterogeneous decreased echogenicity. Magnetic resonance imaging showed in the T2-weighted image a high signal intensity within the soleus and plantaris musculus (Fig. 1).

The MRI features were most consistent with a muscular infarction or myositis. A limited muscle biopsy showed necrotic areas compatible with infarction, thrombosis of the vessels, necrosis of the vessel walls, intravascular inflammation and signs of muscle regeneration. A diagnosis of idiopathic muscular infarction was retained. The patient was treated with bed rest and analgesics. Her pain and swelling gradually improved over about 4 months.

Muscle infarction is a rarely reported complication of diabetes. DMI is usually seen in patients with long-standing poorly controlled diabetes mellitus, with a mean duration of 17.4 years; most patients also have multiple end-organ microvascular complications. The cause of diabetic muscle infarction appears likely to be diabetic microvascular disease, since most patients with DMI have multiple end-organ microvascular diabetic complications (5). The characteristic clinical presentation is the acute onset of severe pain. The calf is exceptionally involved. On clinical examination, there is usually a palpable, painful mass with swelling and induration of the surrounding tissue. Muscular enzyme levels (creatine kinase and aldolase) may be elevated. Standard radiographic films are rarely helpful, except to exclude bony abnormalities or soft tissue calcification. CT studies may demonstrate muscle swelling, but this is a non-specific and inconstant finding. Areas of muscle infarction are seen on MR images as marked muscle swelling that is isointense on T1-weighted images and hyperintense compared with skeletal muscle on T2-weighted, inversion-recovery, and gadolinium-enhanced MR images. Nevertheless, MR changes are not specific for DMI, and also accompany the edema of tumor or inflammatory disease (2, 6-8).

The radiologic differential diagnosis of diabetic muscle infarction includes soft-tissue abscess, pyomyositis, necrotizing fasciitis, and other causes of myositis (dermatomyositis, focal myositis, nodular myositis, and proliferative myositis). The diagnosis of diabetic muscle infarction remains a clinical and radiographic diagnosis and, at times, may require histopathologic confirmation. Focal myositis, proliferative myositis, and nodular myositis are not individually distinguishable on clinical examination or MR imaging, and muscle biopsy is necessary to identify the characteristic histologic features.

Clinical treatment is predominantly symptomatic and conservative, although some have suggested a role for anticoagulation therapy.

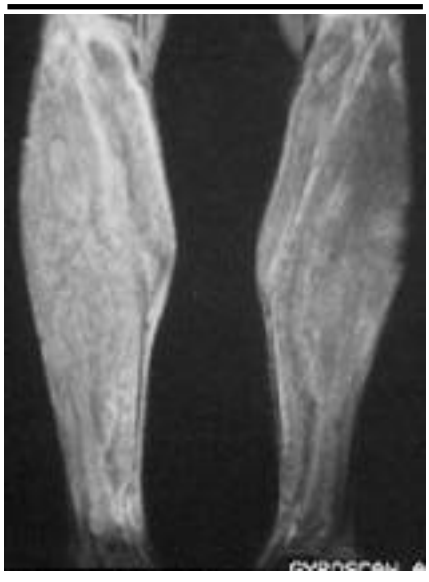

Fig. 1. Magnetic resonance imaging showed on the T2-weighted image a high signal intensity within the soleus and plantaris musculus.

The symptoms of diabetic muscle infarction resolve over several weeks (8, 9). Recurrence in the same or another location may be relatively frequent (1, 10).

While there have been only a small number of cases reported, DMI may be mistaken for other disorders and is probably under-recognized. Careful consideration of the clinical, radiologic and if necessary, biopsy features of the syndrome will distinguish it from the other neuro-muscular complications of diabetes and other causes of leg pain.

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