LETTERS TO THE EDITOR

From wheels to feet: a dramatic response of severe chronic psoriatic arthritis to etanercept

A 47 year old man presented with seven years of severe psoriatic polyarticular arthritis of progressive, symmetrical, and additive course, affecting the shoulders, elbows, wrists, metacarpophalangeal joints, proximal interphalangeal joints, distal interphalangeal joints, hips, knees, and feet. Also, his skin and nails were completely affected with severe erythroderma. The patient was treated with methotrexate, chrysotherapy, antimalarial drugs, salazopyrine, azathioprine, cyclosporin, minocycline, and intra-articular and systemic corticosteroids. All these treatments consecutively and in combinations failed or were stopped owing to side effects. During 1999 his condition deteriorated further with morning stiffness of more than six hours, active synovitis of more than 20 joints, and systemic symptoms, such as extreme fatigue and weight loss of more than 10 kg. The patient became confined to a wheel chair. His blood tests disclosed increased erythrocyte sedimentation rate (ESR) and C reactive protein (CRP) levels, and normocytic normochromic anaemia (table 1).

In July 1999 etanercept (25 mg) subcutaneously twice weekly was started. A week later the patient reported a dramatic improvement in his general wellbeing, morning stiffness, and joint pain accompanied by a significant decrease in the number of swollen and tender joints and the erythematous component of the skin lesions. His clinical improvement continued during the following six weeks. He regained 6 kg weight; the ESR decreased to 11 mm/1st h and the haemoglobin concentration increased to 120 g/l (table 1).

Etanercept, a recombinant human tumour necrosis factor (TNF) receptor Fc fusion protein (Enbrel, Immunex Corp, Seattle, Washington) is a dimer consisting of the extracellular portion of two p75 receptors fused to the Fc portion of human IgG1.¹ Several trials in patients with active rheumatoid arthritis have shown that etanercept is safe, well tolerated, and produces significant improvement in disease activity.^{2,3}

Many studies have shown that TNF α plays an important part in the pathogenesis of psoriatic skin lesions and psoriatic arthritis.^{4,5}

The dramatic effect of etanercept in the present resistant and extremely severe case of psoriatic arthritis suggests a possible role for this drug also in the treatment of severe psoriatic arthritis.

ORI ELKAYAM
MICHAEL YARON
DAN CASPI

Department of Rheumatology,
Tel Aviv "Sourasky" Medical Centre and
"Sackler" Faculty of Medicine,
University of Tel Aviv,
Israel

Correspondence to: Dr Ori Elkayam, Department of Rheumatology, Tel Aviv Medical Centre, 6 Weizman street, Tel Aviv 64239, Israel
Email: unitel87@netvision.net.il

- Moreland LW, Baumgartner SW, Schiff MH, Tindall EA, Fleischmann RM, Weaver AL, et al. Treatment of rheumatoid arthritis with a recombinant human tumour necrosis factor receptor (p75) fusion protein. *N Engl J Med* 1997;337:141–7.
- Moreland LW, Margolis G, Heck LW, Saway A, Bloch C, Hanna R, et al. Recombinant soluble tumour necrosis factor receptor (p80) fusion protein: toxicity and dose finding trial in refractory rheumatoid arthritis. *J Rheumatol* 1996;23:1849–55.
- Moreland LW, Schiff MH, Baumgartner SW, Tindall EA, Fleischmann RM, Bulkitt KJ, et al. Etanercept therapy in rheumatoid arthritis. A randomized, controlled study. *Ann Intern Med* 1999;130:478–86.
- Etehad P, Greaves MW, Wallach D, Aderka D, Camp RD. Elevated tumour necrosis factor- α (TNF- α) biological activity in psoriatic skin lesions. *Clin Exp Immunol* 1994;1:146–51.
- Partsch G, Wagner E, Leeb BF, Broll H, Dunky A, Smolen JS. T cell derived cytokines in psoriatic arthritis synovial fluids. *Ann Rheum Dis* 1998;57:691–3.

Polymyositis, cranial neuropathy, autoimmune hepatitis, and hepatitis C

Autoimmune disorders are common in hepatitis C virus (HCV) infection, and may be due to dysfunction of both cell and humoral immunity.¹ HCV infection has therefore been associated with essential cryoglobulinaemia, polyarteritis nodosa, leucocytoclastic vasculitis, glomerulonephritis, and idiopathic pulmonary fibrosis.^{2,3} Polymyositis (PM) and dermatomyositis (DM) have more rarely been reported during the course of HCV infection.^{3,7} Previous authors have suggested that HCV infection might be responsible for the formation of autoantibodies and circulating autoimmune complexes, leading to PM/DM manifestations.^{2,3} We observed a new case, which is of particular interest, as the patient with PM and cranial neuropathy developed chronic active autoimmune hepatitis and HCV infection.

A 48 year old woman presented in March 1997 with a five month history of generalised

muscle weakness and myalgia associated with dysphagia. She had no previous medical history. Examination showed muscle weakness affecting both arms and legs. Muscle power was gauged for eight proximal muscles (that is, neck flexors, trapezius, deltoid, biceps, psoas, maximus and medius gluteus, and quadriceps) by a modification of the British Medical Research Council grading system, resulting in scores ranging from 0 to 11 (theoretical maximum score 88 points). Muscle power of the patient was 65 points. Physical examination also showed dysaesthesias in the area of the left V nerve.

The following laboratory findings were abnormal: erythrocyte sedimentation rate 60 mm/1st h, C reactive protein 70 mg/l (normal <5), creatine kinase 600 U/l (normal 5–130), and aldolase 11.3 U/l (normal 0.5–3.1). Liver tests showed alanine aminotransferase (ALT) 142 U/l (normal 3–21), aspartate aminotransferase (AST) 98 U/l (normal 3–26), γ -glutamyltransferase 210 U/l (normal 5–25), alkaline phosphatase 96 U/l (normal 73–207), and total bilirubin 6 U/l (normal 2–18). Blood electrophoresis yielded total protein 70 g/l, albumin 37 g/l, polyclonal gammopathy with increased IgG at 19 g/l (normal 6–12). An electromyogram showed both low amplitude and polyphasic motor unit potentials affecting muscles of the arms and legs.

Muscle biopsy of the left quadriceps confirmed the diagnosis of PM; microscopic analysis showed inflammatory infiltrates associated with disruption of the muscle architecture and muscle fibre necrosis. Facial electromyogram showed sensorimotor severe impairment affecting both first and second branches of the left trigeminal nerve. Auto-antibody screening was positive for antinuclear antibodies (ANA) >1000; other tests—that is, anti-Jo1 antibody, rheumatoid factors, antineutrophil cytoplasmic antibodies, and cryoglobulin, were negative.

Blood cultures, bacterial (*Mycoplasma pneumoniae*, *Chlamydia*) and parasitic (*Toxoplasma gondii*) serologies were negative. Viral serologies (cytomegalovirus, Epstein-Barr virus, human immunodeficiency virus, coxsackie, parvovirus B19, hepatitis B) were negative, whereas hepatitis C serology was positive. Oesophageal manometry showed a low pressure in the upper oesophageal sphincter and decreased peristalsis within the upper third of the oesophageal body. Pulmonary function tests showed a decrease of carbon monoxide transfer factor (TLCO) 63% of predicted. Other investigations, including thoracic computed tomography, echocardiography, and abdominal ultrasound, were within normal limits. Because of increased aminotransferases (AST and ALT) and positive HCV serology, polymerase chain reaction amplification of HCV RNA was performed on the patient's serum, which was positive. Liver biopsy specimens showed characteristic damage of chronic active autoimmune hepatitis—that is, interface hepatitis. Auto-antibody screening was negative for antimitochondrial, anti-smooth muscle, and anti-LKM1 antibodies.

Steroid treatment, at an initial dose of 1 mg/kg/day, was started. Because of both PM and chronic active autoimmune hepatitis, treatment of hepatitis C with interferon α was not instituted. Both muscular and neurological (that is, dysfunction of the left V nerve) manifestations related to PM improved progressively and disappeared completely in June 1997 (fig 1). Abnormalities of liver tests improved concomitantly (fig 1). At two year

Table 1 Clinical and laboratory variables immediately before (week 0) and after (weeks 1–8) etanercept treatment

	Week 0	Week 1	Week 2	Week 4	Week 6	Week 8
No of swollen joints	22	11	3	2	1	1
No of tender joints	26	16	9	6	3	2
Grip strength (mm Hg)						
Right	43	80	97	88	95	110
Left	38	60	85	78	106	110
ESR* (mm/1st h)	85	45	25	15	11	11
CRP* (g/l)	0.18	ND*	0.02	ND	ND	0.01
Haemoglobin (g/l)	104	101	121	112	131	134

*ESR = erythrocyte sedimentation rate; CRP = C reactive protein (normal range 0–0.01 g/l); ND = not determined.

Figure 1 Course of the patient's polymyositis clinical and biochemical manifestations and virological status with steroids.

follow up the patient remains free of clinical symptoms taking prednisone 9 mg/day. In December 1999 liver tests were normal.

PM/DM are systemic inflammatory disorders affecting the skeletal muscles and other organs, notably the gastrointestinal tract.⁸ The prevalence of oesophageal impairment in patients with PM/DM has therefore been reported to be as high as 60%.⁸ Involvement of the liver is less recognised, and is considered to be rare in PM/DM where it is usually due to immunosuppressive treatment. To date, only a few investigators have described liver manifestations in patients with PM/DM; liver impairment in these patients was related to associated conditions—that is, primary biliary cirrhosis⁹ and HCV infection.³⁻⁷

We report, to our knowledge, the first case of a patient with PM associated with autoimmune hepatitis and HCV infection. In this instance, the diagnosis of autoimmune hepatitis could be made, because the patient fulfilled all the criteria for autoimmune hepatitis—namely, (a) increased ALT and AST, with alkaline phosphatase less than threefold the normal value; (b) total gammaglobulin or IgG levels >1.5 times the upper limit of normal; (c) ANA titres >1/80; and (d) characteristic histological liver damage.

Our findings raise the question of an association between PM and autoimmune hepatitis as part of a continuum, suggesting that autoimmune hepatitis should be included within the spectrum of liver manifestations of

PM/DM and may be due to immunity dysfunction. From a practical point of view, these data indicate that the diagnosis of autoimmune hepatitis may be suspected in patients with PM/DM presenting with cytolytic hepatitis. However, autoimmune hepatitis might also be related to HCV infection in our patient. As previous authors have recently shown that the prevalence of HCV infection was similar in patients with autoimmune hepatitis and the general population, they concluded that HCV could be excluded as a cause of autoimmune hepatitis.¹⁰ Further prospective trials are required to evaluate the prevalence of autoimmune hepatitis in patients with PM/DM, with and without HCV infection. Finally, our unusual case is reminiscent of one reported by Ferri *et al.*,³ who described a patient with cranial mononeuritis associated with PM and HCV infection. In our experience the diagnosis of PM related left V nerve palsy could be made as both neurological and muscle manifestations completely resolved concomitantly with steroid treatment.

I MARIE

H LEVESQUE

H COURTOIS

Department of Internal Medicine,

Centre Hospitalier Universitaire de

Rouen-Boisguillaume,

76031 Rouen Cedex, France

A FRANÇOIS

Department of Pathology and Cytology

G RIACHI

Department of Gastroenterology

Correspondence to: Dr Isabelle Marie

- 1 Pawlotsky JM, Ben Yahia M, Andre C, Voisin M-C, Intrator L, Thoraval FR, *et al.* Immunological disorders in C virus chronic active hepatitis: a prospective case-control study. *Hepatology* 1994;19:841-8.
- 2 Johnson RJ, Gretch DR, Yamabe H. Membranoproliferative glomerulonephritis associated with hepatitis C virus infection. *N Engl J Med* 1993;328:465-70.
- 3 Weisendaal D, Imam T, Holyst MM, King PD, McMurray RW. Polymyositis, pulmonary fibrosis, and hepatitis C. *Arthritis Rheum* 1995;38:437-9.
- 4 Ferri C, La Civita L, Fazzi P, Pasero G, Zignego AL. Polymyositis, lung fibrosis, and cranial neuropathy in a patient with hepatitis C virus infection. *Arthritis Rheum* 1996;39:1074-5.
- 5 Gomez A, Solans R, Simeon CP, Seva A, Garcia F, Fonollosa V, *et al.* Dermatomyositis, hepatocarcinoma, and hepatitis C. *Arthritis Rheum* 1997;40:394-5.
- 6 Nishikai M, Miyairi M, Kosaka S. Dermatomyositis following infection with hepatitis C virus. *J Rheumatol* 1994;21:1584-5.
- 7 Ueno Y, Kondo K, Kidoroko N, Kobashi R, Kanaji K, Matsumura T. Hepatitis C infection and polymyositis. *Lancet* 1995;346:319-20.
- 8 Marie I, Hachulla E, Levesque H, Reumont G, Ducrotte P, Cailleux N, *et al.* Intravenous immunoglobulins as treatment of life threatening esophageal involvement in polymyositis and dermatomyositis. *J Rheumatol* 1999;26:2706-9.
- 9 Boki KA, Dourakis SP. Polymyositis associated with primary biliary cirrhosis. *Clin Rheumatol* 1995;14:375-8.
- 10 Lohse AW, Gerken G, Meyer zum Büschenfelde K-H. Autoimmune hepatitis and hepatitis C virus infection. *Curr Stud Hematol Blood Transfus* 1998;62:152-60.