LETTER

Rheumatoid arthritis after human parvovirus B19 infection

Polyarthropathy associated with human parvovirus B19 (B19) is usually transient, but often resembles rheumatoid arthritis (RA).¹⁻³ However, B19 DNA screened by polymerase

chain reaction (PCR) may be positive not only in autoimmune diseases, but also in non-arthropathy.⁴ To study whether or not RA occurs after acute B19 infection, we conducted a prospective study of patients with acute onset polyarthritits. Sixty seven cases showing acute inflammatory polyarthritits from January 1990 to June 1990 were examined and followed up for six years. Among them, 12 (9 female and 3 male) exhibited IgM anti-B19 antibodies.⁵ PCR, followed by a Southern blot analysis⁶ also showed the presence of B19 DNA in all 12 cases with IgM anti-B19 antibodies, but did not in the remainder. Initially, rheumatoid factor (RF) was negative in all B19 positive cases except

one, but became positive in four, two to four months after the infection (table 1). Among RF positive cases, three (MI, RM, and TY) developed active polyarthritits with destructive changes in the joints including fingers, wrists or elbows, and rheumatoid nodules. These patients were diagnosed as typical RA fulfilling the 1987 American College of Rheumatology (ACR) criteria for the diagnosis of RA⁷ as shown in table 2. No cases in the B19 negative group met the ACR criteria for RA during six years of follow up. Figure 1 shows that B19 DNA was no longer detected in blood samples from the patients MI, RM, and TY four months after the initial episodes. It was, however, positive in bone marrow and synovial tissue. Both in situ hybridisation (ISH) and immunofluorescence (IF) study^{8,9} also revealed the presence of B19 DNA/RNA as well as VP-1 antigen in mononuclear cells of bone marrow samples (fig 2). Examination of peripheral mononuclear cells by the stimulation with B19 antigen, showed significantly higher proliferative responses to recombinant VP-1 in patients MI, RM, and TY compared with others (p<0.002).

Clinically, three patients with RA were in an active stage and, therefore, treated with a high dose (20 g/day) of gammaglobulin for 10 days (fig 1) after a variety of anti-rheumatic drugs including gold, D-penicillamine or methotrexate became ineffective. The treatment caused a reduction in multiple joint pain and swelling, and a decrease in the C reactive protein value (from 0.8 to 0.3 for patient MI and from 3.6 to 2.0 for patient RM). The number of VP-1 positive cells in bone marrow markedly decreased after the treatment (from 3.6% or 2.6%, to undetectable values or 0.5% in MI and RM respectively).

Table 1 Prevalence of joint involvement and RF after the initial episode

Clinical finding	Group*	No of positive cases/no of total cases		
		Initial episode	4 months after	6 years after
Joint pain	B19 negative	52/52 (100)	4/52 (7.7)**	2/52 (3.6)**
Joint pain	B19 positive	12/12 (100)	4/12 (33.3)**	4/12 (33.3)**
Positive RF	B19 negative	3/52 (5.8)	3/52 (5.8)**	3/52 (5.8)**
Positive RF	B19 positive	1/12 (8.3)	5/12 (41.6)**	4/12 (33.3)**

*Each group was divided into two groups based on the evidence of IgM anti-B19 antibody at beginning of the study. **p<0.01.

Table 2 Profile of patients who developed RA after acute B19 infection

Age (y)	40	42	44
Sex	Male	Female	Male
Morning stiffness	++	++	++
Arthritis of three or more joint areas	+(10)*	+(14)	+(9)
Arthritis of hand joints	++	++	++
Symmetric arthritis	+	+	+
Rheumatoid nodules	++	-	+
Serum rheumatoid factor	+	+	+
Radiographic changes	+	+	++
Class	2	2	3
Stages	III	III	III

*Number of affected joints.

Figure 1 Clinical course of patients MI (A) and RM (B). MTX; methotrexate, CRP; C reactive protein, ESR; erythrocyte sedimentation rate, RF; rheumatoid factor.

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