High frequency of parvovirus B19 in patients tested for rheumatoid factor

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Symptomatic adult parvovirus B19 infection typically causes a brief arthritis, often with a rash. Persistent symptoms may occur,¹ and B19 has been linked with many rheumatic diseases. Virus specific IgM is detectable for about three months after infection, leaving a narrow window in which to make a diagnosis when chronic symptoms arise. Since blood samples from patients with musculoskeletal disease are frequently tested for rheumatoid factor we sought B19 DNA by polymerase chain reaction in such samples in order to identify any relation between chronic symptoms and parvovirus infection.

Subjects, methods, and results

Remaining serum from 503 consecutive samples submitted for a rheumatoid factor test was collected prospectively between December 1992 and February 1993. Samples from blood donors (348) and from inpatients requiring blood transfusions (333), also collected during these months, served as controls. Clinical data were obtained retrospectively from records. B19 DNA was identified using a method for screening large numbers of samples.²

Parvovirus DNA was found in 23 test samples and two control samples. Samples submitted from general practitioners were more likely to be positive (table). All samples positive for B19 DNA and 48 negative samples were tested for IgG and IgM by an indirect fluorescent antibody technique.³ The proportion of samples positive for rheumatoid factor ($\geq 1/16$) was similar in B19 DNA positive patients (3) to that for B19 negative patients (53) ($P=0.98$).

Of the 23 patients with B19 DNA 17 had typical joint pain resolving within one month (seven also had a rash); two, known to have longstanding intermittent seronegative arthritis, experienced an exacerbation and were both IgM positive; one had an illness lasting four months diagnosed as myalgic encephalitis; one had carpal tunnel syndrome; one had intermittent fatigue and neutropenia over many months; and one was lost to follow up. Clinical diagnoses for samples

sent from the rheumatology department were: rheumatoid arthritis 29%; osteoarthritis 15%; no diagnosis 11%; and 45% miscellaneous disorders.

Comment

Parvovirus infection diagnosed on the basis of clinical features, IgM, and presence of DNA occurred frequently in individuals seen in general practice who were tested for rheumatoid factor. This reflects early testing for rheumatoid factor in patients who subsequently have a short lived illness. A definite clinical diagnosis was made in only one case, although in most cases the illness was recognised as viral. Failure to identify a specific infection in this situation matters since parvovirus is an important cause of fetal death in the second trimester⁴ and many patients were women of child bearing age. It may also matter for those with persistent symptoms. B19 is highly infectious and often asymptomatic.⁵ Viraemia is rarely detected in symptomatic individuals except by polymerase chain reaction, and isolation of patients is unlikely to prevent further infections.

An epidemic cannot explain the frequency of infection since only 40 infections were reported to the infectious disease surveillance unit in Scotland between December 1992 and February 1993. Two patients with parvovirus DNA and prolonged symptoms were IgM negative. It is difficult, in retrospect, to be certain that symptoms in these cases were due to persistent infection. Two patients with an established seronegative polyarthritis were IgM positive. These patients probably developed a coincidental acute parvovirus infection rather than an exacerbation of their underlying disease. It does not imply any relation between B19 and seronegative arthritis. Parvovirus was rarely found in samples sent from the rheumatology department. Since we relied on clinical records to assess symptom duration we may have underestimated chronicity. Virus specific IgM, found in some samples that were negative for B19 DNA, showed that we were underestimating the frequency of infection by polymerase chain reaction alone. It is clear that serological tests will identify most parvovirus infections and that this infection is often not recognised in general practice.

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Details of patients and controls, presence of B19 DNA, and results of serological testing

	Subjects		B19 DNA positive		Serology (IgM: IgG) in DNA positive samples
	No	Mean age (yr)	No	Mean age (yr)	
Patients tested for rheumatoid factor	503		23*		21†:23
Men	156	45.6	2	30	
Women	347	45.0	21	35.5	
Source					
General practitioners	297		20†		20:20
Rheumatology	118		1		IgM and IgG
Orthopaedics	22		1		IgG only
Others	66		1		IgG only
Blood donor samples	348		1		
Men	204	37			
Women	144	33			
Blood transfusion samples	333		1		
Men	117	61			
Women	216	52			

* $P<0.001$ when compared with controls. Odds ratio 18 (95% confidence interval 4.2 to 76.7).

†Odds ratio 5 (1.5 to 17); $P=0.01$ when compared with samples from other sources.

‡ $P<0.001$ when compared with 48 sera that were negative for B19 DNA (two of the negative sera were IgM positive; both patients had an illness typical of B19 infection).