Letters to the Editor

Role of parvovirus B19 infection in juvenile chronic arthritis. Is more investigation needed?

Sir,

Parvovirus B19 (PBV19), responsible for a common and usually asymptomatic infection in childhood, in adults occasionally causes an erosive arthritis with an unfavorable outcome (1) and it has been shown that it can persist in the synovial fluid and bone marrow of patients with chronic arthritis (2, 3). Joint symptoms have also been described in children, associated or not with erythema infectiosum,commonly consisting of an acute polyarticular, symmetrical arthritis but occasionally of an oligoarticular form or a Still's disease mimicking form (4). Rarely the joint manifestations relapse or persist for months, fulfilling the criteria for Juvenile Chronic Arthritis (JCA) (5-7).

In order to characterize the role of PVB19 infection in the pathogenesis of JCA, we studied the prevalence of PVB19 infection in a prospective study, enrolling 41 children (31 F/10 M, mean age 5.9 years, range 1.3-14) who presented inflammatory arthritis lasting for more than 3 months. During 1 year follow-up, 35 out of 41 (mean age 5.9; range 2-14 years) patients developed JCA diagnosed according to the 1987 criteria of the American College of Rheumatology (8). All the blood samples have been tested for PVB19, EBV, HSV, CMV, Rubella, Toxoplasma and Coxachie. Ninety-three sex-matched healthy children,homogeneous for age distribution were analyzed as controls.

IgM and IgG anti-PVB19 were assayed in the serum by ELISA-kit (DAKO). Viral DNA was extracted from serum on columns (QUIAGEN) and nested PCR was performed as described by Fridell in 1992, including a PVB19 positive serum as control.

Data were analyzed using Student's t-test for non-paired samples and Pearson's correlation test. The relative risk was calculated with EPIINFO 6 software.

We found that 16/35 (45.7%) children who developed JCA were positive for anti-PVB19 IgG compared to 23/93 (24.7%) healthy controls. The difference in PVB19 infection prevalence between JCA and control group was statistically significant ($p = 0.02$) (Table I). Stratification by age (1-5,6-10 and >10 years) showed that this difference was more evident in the patients between 6-10 years of age ($p < 0.05$). Children affected by arthritis with previous PVB19 infection had an increased risk of developing JCA (1.85; CI: 1.1-3.07).

One out of the 6 patients who did not fulfill the criteria for JCA was positive for anti-PVB19 IgG, a 6-year-old child with self-limiting arthritis involving both hands and feet and a history of a previous episode resembling erythema infectiosum.

Table I. Serological markers of PVB19 infection and PVB19 genome detection in patients and controls (*p = 0.02).

Cohorts	Total No.	IgG+/IgM-	IgG-/IgM-	Viral DNA
JCA patients	35	16 (45.7%) *	19 (54.3%)	neg
Monoarticular		1 (6.25%)	8 (42.1%)	
Pauciarticular		8 (50%)	6 (31.5%)	
Polyarticular		5 (31.2%)	5 (26.3%)	
Systemic		2 (12.5%)	-	
Non -JCA patients	6	1 (16.6%)	5 (83.4%)	neg
Total patients	41			
Controls	93	23 (24.7%)	70 (75.3%)	neg

As expected, the age at disease onset was significantly higher (7.4 years, range 2.1-14) in the PVB19 positive group of children than in the remaining negatives (4.4 years, range 1.25-11.5) ($p < 0.001$). The anti-PVB19 IgG prevalence was higher in the pauciarticolar and systemic form, but it was not possible to analyze it due to the small number of patients in each group. Sera of all children were negative for anti-PVB19 IgM and for genomic PVB19 DNA (Table I). No increased prevalence of antibodies against any of the other investigated viruses has been observed, as compared to healthy pediatric populations reported in the literature.

It is interesting that we did not find any evidence of recent or persisting infection, since none of the patient was positive for anti-PVB19 IgM and/or viral genome. This could be explained in the context of an autoimmune mechanism, which might require some time to determine a symptomatic joint inflammation. The mean age of the PVB19 positive JCA children was significantly higher compared with the PVB19 negative (7.4 vs 4.4). Since the increase of PVB19 infection prevalence over time might lead to errors in the interpretation of the data, a careful recruitment of controls was essential.

In conclusion, according to other reports supporting the linkage between PVB19 infection and chronic arthritis (9,10), this study support the hypothesis of a cause-effect relationship between Parvovirus B19 infection and juvenile chronic arthritis. Although, the absence of correlation with the severity of the clinical picture or with specific laboratory parameters, and the observation of a stronger association in older children, suggest that PVB19 infection is only one of the players implicated in the pathogenesis of JCA. We therefore encourage aiming for a better definition of Parvovirus joint disease in children since further study might provide insights into its complex mechanisms.

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