Human parvovirus B19 infection among patients with chronic blood disorders

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ABSTRACT

Objective: In a normal host, parvovirus infection can be asymptomatic or can result in erythema infectiosum or arthropathy. Patients with underlying hematologic and immunologic disorders who become infected with this virus are at risk for aplastic anemia. This small study attempts to confirm this relation between the human parvovirus B19 infection as one of the predisposing factor of aplastic crisis in patients with hemolytic disorders.

Methods: The laboratory records of 73 patients' serum samples, which were tested for detection of specific Immunoglobulin M and Immunoglobulin G antibody by means of the recurrently available indirect enzyme linked Immunoassay during the period from March 1998 to March 2001, were reviewed retrospectively at the Armed Forces Hospital, Riyadh, Kingdom of Saudi Arabia.

Results: For all patients there were 11 (15%) who were diagnosed as acute infections while 50 (68%) had serological evidence of previous exposure. Eight out of the 11 acute patients had chronic hemolytic disorder as the underlying disease while, the 3 other patients were organ transplant and connective tissue disease patients.

Conclusion: Seventy-eight percent of our infected patients were known to have an underlying blood disorder, while 22% had immunosuppressed disorders such as organ transplant and connective tissue disorder. Parvovirus B19 can be considered as one of the predisposing factors of hemolytic crisis in patients with chronic hemolytic disease.

Keywords: Parvovirus B19, aplastic crisis, chronic hemolytic anemia, sickle cell anemia, thalassemia.

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Human parvovirus B19 is a non-enveloped, single-stranded deoxynucelic acid (DNA) virus with a predilection for infecting rapidly dividing cell lines, such as bone marrow erythroid progenitor cells.[1] It is classified as an erythrovirus as complete replication of B19 has been found only in these cells.[2] Parvovirus B19 was discovered in 1975 by Cossart and colleagues,[3] who unexpectedly found viral particles in the sera of asymptomatic patients while being screened for hepatitis B infection. Biochemical and molecular characteristics subsequently demonstrated that these particles were parvoviruses and specimen 19 of panel B contained the unexpected virus, parvovirus B19 was so designated.[4] Parvovirus B19 is the only parvovirus known to be pathogenic in humans - its effects range from asymptomatic infection and self limited illness to life threatening aplasia, fetal anemia and death in utero.[5] Human parvovirus B19 has been associated with several diseases; erythema infectiosum (5th disease), aplastic crisis in chronic hemolytic anemia, arthritis and intrauterine infection with hydrops fetalis. Human parvovirus B19 has been shown to be cytotoxic for erythroid cells and this effect can be

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neutralized by antibodies to human parvovirus B19.[6] In view of B19 tropism for erythroid progenitor cells, individuals who have a shortened red blood cells (RBCs) survival time, such as those with sickle cell disease, and other hemolytic anemias are at high risk for B19 - induced crisis due to RBCs aplasia. Individuals who are immunosuppressed are also at risk of severe life threatening anemia.[2] However, most infections with parvovirus B19 remain asymptomatic, and therefore the majority of exposed persons have no recollection of previous symptoms.[4] The specific immunoglobulin M (IgM) antibody detection has been the core of diagnosing acute parvovirus B19 infection, while the appearance of immunoglobulin G (IgG) antibodies is indicative of previous exposure to the virus.[2] In this study we describe the prevalence of the serum IgM antibody using enzyme linked immunoassay (ELISA) among 73 patients who presented either as outpatients or were admitted with clinical symptoms compatible with parvovirus B19 infection.

Methods. The laboratory records of all serum samples sent to the virus serology laboratory requesting IgM and IgG antibodies to parvovirus B19 between March 1998 through to March 2001 were reviewed retrospectively in Riyadh Al Kharj Armed Forces Hospital, Riyadh, Kingdom of Saudi Arabia (KSA). These showed 73 patients aged between 2 months and 48 years, 30 males and 43 females. The ELISA test used was Biotrin International Parvovirus B19 IgM (3rd generation) which, is a μ-capture sandwich enzyme immunoassay for the detection of IgM class antibodies to parvovirus B19 in human serum, while Biotrin parvovirus B19 IgG (3rd generation) is a sandwich enzyme immunoassay for the detection of IgG class antibodies to parvovirus B19 in human serum. The procedure as specified by the manufacturer was followed.

Results. Out of the 73 patients investigated, 11 (15%) were diagnosed with acute infection by the detection of specific IgM antibodies, 50 (68%) had only specific IgG antibodies, and 12 (16%) did not have any serological evidence of viral exposure. In the 11 patients with acute infection, their mean age was 14 years old (range one year through to 48 years), 6 were females and 5 males. Of the 3 patients who were concurrently positive for IgG and IgM, 2 were organ transplant patients and one was a thalassemic patient. Only 3 patients were followed up serologically and they seroconverted to IgG positivity with the loss of IgM within 6 weeks. Eight (73%) of these patients had blood disorder; sickle cell anemia, thalassemia and spherocytosis, while the other 3 patients were organ transplant and connective tissue disease patients. As seen in **Table 1,** fever was the most frequent presenting symptoms in all age groups, followed by arthralgia and arthritis that mainly affected adult females. Rash was seen only in young children.

Table 1 - Symptoms recorded in the 11 patients with acute infection and its relation to age and sex.

Age (Years)	Sex	Underlying disorder	Fever	Joint symptoms	Rash
1	Male	Spherocytosis	+	-	+
2	Male	SCA	+	-	+
3	Female	SCA	+	-	-
4	Male	Liver cirrhosis	+	+	-
9	Male	SCA	+	-	-
10	Female	SCA	+	+	-
14	Male	SCA	+	-	-
17	Female	Kidney transplant	-	+	-
28	Female	SCA	-	+	-
32	Female	Thalassemia	+	+	-
48	Female	Connective Tissue disorder	-	+	-

SCA - sickle cell anemia, + - positive, - - negative

Discussion. The majority of the patients in this study had an underlying blood disorder with hemolytic crisis leading to the screening for parvovirus B19 as a possible predisposing factor. Eight (74%) of our infected patients having specific IgM antibodies were known to have blood disorder. This finding was compatible with another study in KSA[7] that reported evidence of recent human parvovirus infection in 91% of the cases. Aplastic crisis was reported in our study in several types of chronic hemolytic anemia; 55% of the patients had sickle cell disease, similar to another report by Hanada et al[8] and Kelleher et al.[9] None of our patients developed skin rash typical of erythema infectiosum. Absence of this diagnostic sign may be explained by its late development following the resolution of the crisis, and relative difficulty in observing the rash among dark skin patients.[10] It has become increasingly clear over the past several years that parvovirus B19 causes arthritis and arthralgia in adults and children.[4] Although parvovirus infections in adults are most commonly asymptomatic, an estimated 60% of women with symptomatic disease manifest arthropathy while men appear to be less frequently affected.[11] In our patients arthralgia was present in 64%. The most common presentation of

parvovirus related arthropathy was acute onset of arthralgia or frank arthritis involving hand, knee, wrist and ankles. The incidence of parvovirus related arthropathy was lower in children than adults and females were more likely than males as reported by Sabella et al.[4] The observed IgG prevalence of 60% among our small number of patients was relatively higher than that reported as 19% in the general Saudi population,[12] and this maybe due to selection bias.

In conclusion, this retrospective study confirmed the correlation between parvovirus B19 infection and hemolytic crisis in patients with chronic hemolytic blood disorders. Screening for parvovirus B19 during such episodes could be a helpful diagnostic test and is recommended even in the absence of the classic symptom of the disease.

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