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Parvovirus B19 Antibodies in Immunocompromized Children in Thailand

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SUMMARY **Parvovirus B19, a non-enveloped single stranded DNA virus is distributed worldwide. Sero-prevalence in adult populations amounts to approximately 50%. Clinical manifestations vary depending on the immune status of the infected individuals and may include mild childhood infection as well as hydrops fetalis due to intrauterine infection. To determine the prevalence of this infection among the immunocompromized individuals in Thailand, we determined, by indirect ELISA, levels of IgM and IgG antibodies to the parvovirus B19 in 106 immunocompromized children. These included 49 children who were on chemotherapy for treatment of malignancies, 18 who were receiving immunosuppressive drugs after organ transplantations, 14 who were under a regimen of corticosteroids and 25 who were positive for antibodies to HIV. The average prevalence of IgG antibodies in 106 children was 16.0%; the prevalence of antibodies was 33.3% in post-transplanted group, 16% in children positive for HIV, 12.2% in the group receiving chemotherapy for malignancies and 7.6% in the group treated with corticosteroids. All children were negative for IgM antibodies to parvovirus B19.**

Parvovirus B19 is a non-enveloped virus with a single-stranded DNA genome of 5.6 kb.[1] It was first isolated from sera of healthy blood donors as well as patients, one of whom had been diagnosed with acute hepatitis.[2] Clinical manifestations of the infected patients vary greatly and include erythema in infected children, aplastic crisis in patients with hemolytic anaemia, chronic bone marrow failure in immunocompromized hosts, and hydrops fetalis after intrauterine infection of infants.[3] Infants who survive parvovirus B19 induced hydrops fetalis frequently develop congenital hepatic dysfunction[4] while the infants with hepatitis tend to be fatal.[5]

Parvovirus B19 is ubiquitous and approximately 50% of the world's population have antibodies by the age of 15 years.[6] Infection frequently presents in the form of common childhood disease, i.e. erythema infectiosum. By the age of 70, seroprevalence ranges from 80 to 100%. Depending on the individual's immune status, the clinical manifestations induced by the virus vary in severity. Exanthematous disease and arthropathy have been reported mainly in women, whereas aplastic crisis and chronic anaemia have been observed among chronic haemolytic anaemia patients and immunocompromized hosts.

In a previous study, we examined the frequency of antibodes to parvovirus B19 in two groups of children; one with acute unrelated illness and another group comprising healthy children and in adult voluntary blood donors.[7] The present communication reports frequency of parvovirus B19 infection among immunocompromized children.

MATERIALS AND METHODS

Population study

The population investigated comprised 106 children who

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were admitted to the Pediatric Ward of Chulalongkorn Hospital, Bangkok. The subjects who met at least one of the following inclusion criteria were enrolled to the study: 1) under a chemotherapy of malignancies, e.g., leukaemia, lymphoma, neuroblastoma, hepatoblastoma or other malignancies for at least one month (49 children aged between 1 and 15 years); 2) under treatment with immunosuppressive drugs due to post-organ transplantations, i.e. liver or bone marrow, for at least one month (18 children, between 1 and 13 years of age); 3) under treatment of SLE or nephrotic syndrome with corticosteroids at a dosage above 0.5 mg/kg/day for at least one month (14 children aged between 1 and 14 years); and 4) children with asymptomatic or symptomatic infection with the human immunodeficiency virus (HIV) confirmed by ELISA (Abbott Laboratories, North Chicago, Ill, and by gel particle agglutination test (Fujirebio, Tokyo, Japan) (25 children, between 1 and 10 years of age).

Upon receiving the parents' informed consents, we collected venous blood samples individually from the children during the course of 1998 to 1999. The sera were separated from the blood by centrifugation and stored at -20°C until further analysis.

Laboratory methods

The sera were subjected to an enzyme-linked immunosorbent assay (ELISA) using the commercially available human parvovirus B19 (recombinant) ELISA kit (Genzyme Virotech GmbH, Russelsheim, Germany) for detection of anti-parvovirus B19 IgG and IgM antibodies. Samples were tested at a dilution of 1:100 with positive and negative controls provided in the kit. Absorbance at 450 nm was recorded for each sample reaction. Positive and negative results were justified using cutoff values specified by the manufacturer. Samples given equivocal results in this assay were retested to confirm the results.

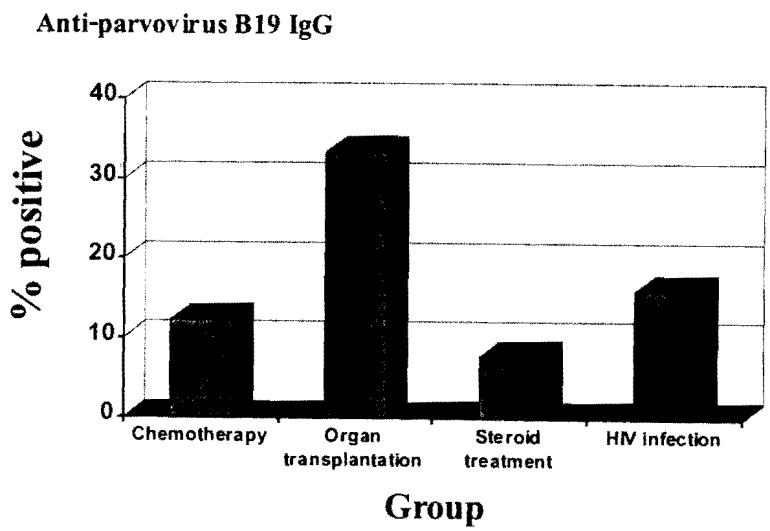

Fig. 1 Percentages of anti-parvovirus B19 IgG in immunocompromized children in relation to the underlying disorders.

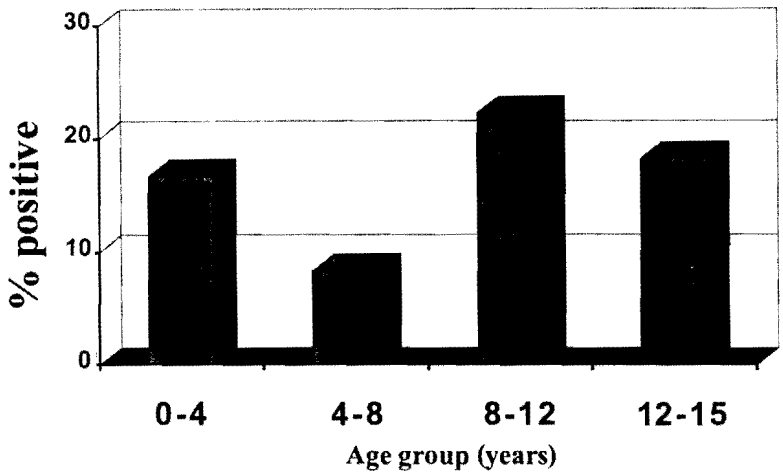

Fig. 2 Percentages of anti-parvovirus B19 in immunocompromized children in relation to the respective age groups.

RESULTS

Seroprevalence of anti-parvovirus B19 IgG was 16.0% (17/106) among the immunocompromized children. Of these, 12.2% (6/49) were in the group with chem-

otherapy (group 1), 33.3% (6/18) in the post-organ transplanted group (group 2), 7.6% (1/14) in the corticosteroid treated group (group 3), and 16% (4/25) in the HIV infected group (group 4). (Fig. 1). Seropreva lences in relation to ages are shown in Fig. 2. The prevalence was 16.7% (7/42) among the 0-to-4-years old, 8.3% (2/24) within the 4-to-8-years age group, 22.2% (4/18) among those between 8 and 12 years of age, and 18.2% (4/22) in the group of 12-to-15-years old (Fig. 2). IgM antibodies to the virus were negative in all subjects.

DISCUSSION

Among the 106 immunocompromized children whose ages ranged from 1 to 15 years, it was shown that the overall prevalence of specific IgG antibodies to parvovirus B19 was 16.0%. In a previous study performed by our center, we found the overall prevalence of the antibodies to be 20.2% in children with unrelated illness, healthy children and adult blood donors.[7] Thus, the frequency of infection in the Thai population is similar to that of other countries in the Far East.[8-9] Our previous study also found that the prevalence of IgG antibodies increases in an age-dependent manner, from 11.9% in children aged 0-6 years old to 30.3% in adults aged 20-51 years old. In this study, however, the prevalence of antibodies did not correlate with age, but rather with the conditions of immunosuppression. The highest percentage of anti-parvovirus B19 antibodies (33.3%) was evident among the transplant recipients who received immunosuppressive drugs. In addition, these subjects received multiple transfusions of blood originating from multiple donors, before, during and after surgery. This finding is in agreement with the observations of a Dutch group who found that parvovirus B19 was frequently transmitted via blood products, a process not preventable by any virus-inactivating methods currently available.[10]

Among the children with HIV infection, the sero-prevalence of anti-parvovirus B19 antibodies was 16.0%. Although all of these children contracted HIV *in utero,* they were still able to mount a humoral immune response to parvovirus B19. It has been shown that in HIV positive adults, humoral antibodies gradually deteriorate over the course of approximately one decade.[11] Thus, the data gathered in this study for HIV positive children may be interpreted in various ways. It is possible that the children could have been infected with parvovirus B19 within their first year of life, while their immune system was still capable of mounting a specific antibody response. Alternatively, they may have acquired parvovirus B19 infection when their immune system was partially impaired, but still enabled them to produce parvovirus B19 specific IgG, although not at protective levels. It has been shown previously that there was a defect in anti-parvovirus B19 antibodies taken from AIDS patients, making them incapable of neutralizing the virus and thus leading to viral persistance.[12] In addition, there has been report of AIDS patients with chronic anaemia who had parvovirus B19 viremia but in which parvovirus B19 specific IgG, and IgM, were undetectable.[13] Therefore, in cases of persistent or latent parvovirus infection, serological diagnosis alone may lead to false negative results, necessitating the screening of at-risk patients by the more sensitive method such as PCR.

Of the children receiving chemotherapy for treatment of malignancies, 12.2% showed evidence of previous exposure to parvovirus B19. It has been known that chronic infection with this agent resulted in red cell aplasia and anaemia and thereby necessitating transfusion, in children with congenital severe combined immunodeficiency,[14] children undergoing therapy for acute lymphocytic leukemia,[15] as well as in bone marrow recipients.[16] Therefore, it may imply in this particular patient group that clinical symptoms of anemia seen, among them were from parvovirus B19 infections.

Parvovirus B19 infections. has been reported to clinically mimic SLE, e.g. causing malar rash, pancytopenia, as well as prolonged arthralgia and fatigue.[17] Thus, the virus might be the causative agent of the SLE symptoms found in 7.6% parvovirus B19 IgG positive children in the corticosteroid treated group.

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