ISSN 2456-4400

Tari et al., Int J Med Lab Res 2016, 1(2): 48-54

REVIEW ARTICLE INTERNATIONAL JOURNAL OF MEDICAL LABORATORY RESEARCH

PARVOVIRUS B19 INFECTION AND TRANSIENT APLASTIC CRISIS

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Received:14 Nov, 2016/Accepted:30 Nov, 2016

ABSTRACT: Parvovirus B19, also called erythrovirus, is a small DNA virus of parvoviridae family. It causes diseases such as erythematous infection or fifth disease, transient aplastic crisis, pure red cell aplasia, hydrops fetalis and fetal death. Disease symptoms are mainly observed in children and not in adults; however, the symptoms also appear in adults with immune deficiency. Respiratory secretions, blood and plasma derived products are the major transmission routes of Parvovirus B19.Serological methods, measurement of IgG and IgM against Parvovirus B19 as well as histopathological and immunohistochemical approaches are diagnostic methods of Parvovirus B19. In newborns, PCR as well as DNA and RNA analysis in amniotic fluid or umbilical cord blood are used for diagnosis of Parvovirus B19infection. In this review article, we reviewed the main concept of the parvovirus b19 and its disease, fifth disease, and sympthoms, finally we have discussion about its diagnosis.

KEYWORDS: Parvovirus B19, Fifth Disease, Diagnosis

INTRODUCTION:

Humanparvovirus B19 (HPV - B19)is a small virus that was discovered in 1975. Thestructure of this virus, which belongs to Parvoviridae family,consists of asingle stranded DNA surrounded by capsid. It is a human pathogen capable of causing a range of clinical symptoms fromself-limited infectious erythema in children with intact immune system to lethal cytopeniain patients with immunodeficiency and intrauterine fetal death in pregnant women infected with HIV.The virus canalsobe established and cause autoimmuneinflammatory disorder [1, 2]. Infection bythisvirusis mainlyseeninlatewinter and early spring,and is observed duringthe crisis induced by it in10%of cases in children under10 years,70% in children 5-15 years and 20% in people over15 years[3]. Parvovirus B19 is prevalent around the world, and serorpidemiological studies have shown that 40-60% of population in the worldbear specific IgG antibody against B19virus, including IgG againstVP1 capsid, which is the most common antibody[4].The main transmission routes ofthis virus includerespiration,blood products and transmissionfrom mother to child[5].

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TRANSMISSION OF VIRUS BY BLOOD AND BLOOD PRODUCTS:

As noted, blood, its products and respiratory secretions are the major transmission routes of B19. Factors such asthe level of B19 virus antigen or Anti B19 IgG in blood products as well as immune status of patients are involved in virus transmission by blood product[6]. The virusis also transmitted by plasma and plasma-derived products.Virus inactivation techniques like the use of organic solvents and detergents, filters and filtration methods as well as liquid-heat treatment are not effective upon this virus[7]. With regard to transmission of B19 Parvovirus through blood and blood products,several studies have been conducted concerning the prevalence of antibodies against B19 among blood donors around the world.The prevalence of this virus among volunteer blood donors has been reported 39.9% in India[4], 60% inGreat Britain[8],16.2% in Singapore[9] and 32.8% in Taiwan[10].The most sensitive people at risk of Parvovirus B19 infection include multitransfusion recipients particularly thalassemia major patients. In the study ofJanaket al on thalassemia major patients receiving blood,ahigh prevalence ofanti B19 IgG (81%)andanti B19 IgM (41%)was reported[11].

HEMATOLOGICAL COMPLICATIONS:

Transientaplasia of RBC progenitors is one of themost important hematological complications of Parvovirus B19.This virus directlyaffects hematopoiesis (especially erythropoiesis) and results in anemia[12, 13] In fact, infection with Parvovirus B19 can lead to erythroblastopenia and reticulocytopeniain healthy people but does not cause anemia because ofthe long lifespan ofred blood cells. However, in patients with hemolytic anemia, it can decrease hemoglobin concentration and life spanof red blood cells, which ultimately exacerbates anemiaand is known as transient aplastic crisis[14]. Transient aplastic crisis, in fact, refers to sudden self-limiting cease of erythropoies is characterized by reticulocytopenia, which leads to aggravation of anemia[5]. Two main groups of patients are at risk of severe and even life-threatening anemia: [1] fetus that can contract anemia and myocarditis through infection transmission via placenta, which can lead tohydrops fetalisand fetal death; [2] patients with accelerated blood cell destruction in whom Parvovirus B19 infection can lead to aplasticcrisis[15]. Sickle cell anemia in adults and pregnant women is among the diseases associated with transient aplastic crisis in case of infection with Parvovirus B19, which is associated with reticulocytopenia, mild neutropenia in some cases thrombocytopenia [16-19]. Anemia due to membrane defects such as elliptocytosis, erythrocyte enzyme deficiencies, thalassemia and acquired hemolytic diseases are other diseases associated with transient aplastic crisis by Parvovirus B19 [20, 21]. Chronic cases of aplastic crisis can be seen in patients with primary and secondary membrane deficiencywho are not capable of producing neutralizing antibodies against Parvovirus B19 [22, 23].

PARVOVIRUS B19 INFECTION IN CHILDREN:

Infection with Parvovirus B19, which is a virus specific to RBC precursors, is seen in children around the world. Acute infection with his virus can lead to cease of erythropoiesis for 5-7 days as well as increased apoptosis of RBC, which can eventually lead to reduced hemoglobin concentration for 1-2 weeks [24]. Studies have shown that the prevalence of infection with Parvovirus is higher in children with blood disorders, which can lead to anemia [25]. In one study, the prevalence of IgM and IgG antibodies against Parvovirus B19 in children with thalassemia major was reported 41% and 81%, respectively[11]. Furthermore, a high prevalence of this infection has been reported in children with leukemia and lymphoma undergoing chemotherapy. Children with leukemia and lymphoma under chemotherapy have been recommended to be screened for Parvovirus B19 infection before changing the chemotherapy protocol in case of developing anemia [26]. In addition, Jitschin et al showed that the prevalence of Parvovirus B19 infection in healthy children, children with benign hematologic malignancy and children with malignant lymphoma was43.6%, 38.5% and 52%, respectively [27].

PARVOVIRUS INFECTION IN PREGNANT WOMEN:

Parvovirus B19 is potentially dangerous for the fetus during pregnancy because it can infect embryonic erythroid precursor cells and tissues. It has broad complications in the fetus, including transient embryonic anemia, non-immune hydrops fetalis and abortion (intrauterine death). In addition, symptoms such as myocarditis, endothelial lesions, fetal brain damage, thrombocytopenia secondary to B19 infection, chronic anemia and congenital heart disease may be seen [28, 29]. Studies have indicated that approximately 65% of women in North America show evidence of previous infection with B19, and about 1-2% have acute B19 viral infection, which may reach up to 10%. Infection in pregnant women with a sound immune system is usually without symptoms [1]. Moreover, in 30% of pregnant women, the infection manifests as poly-arthralgia, 30-90% with skin rashes especially on face and 30-50% have no symptoms [30, 31].

FIFTH DISEASE:

As noted, varied clinical symptoms from no sign to severe infections can be seen in patients [32]. In children, infection with this virus manifests as erythematous infection or fifth disease, which is also referred to as slapcheek [33, 34]. The rashes appearing on the skin of these children can be transient or appear with higher intensity, depending on other factors, including environmental factors such as exposure to sunlight [35].

ARTHROPATHY:

Less than 10% of children infected with erythematous infection show arthralgia. In addition, 19% of children who develop arthritis show evidence of recent infection with B19 virus [36]. In adults, arthralgia and arthritis are the most common manifestations of primary B19 infection while skin symptoms are less common [16, 37, 38].

PARVOVIRUS INFECTION AND SYSTEMIC LUPUS ERYTHEMATOSUS:

Parvovirus B19 infection is associated with various types of rheumatoid diseases, including rheumatoid arthritis, systemic lupus erythematosus and vasculitis. B19 infection may showclinical and laboratory signs of SLE, which can be helpful in early diagnosis of SLE and can exacerbate the disease conditions. B19 virus infection in children can show similar clinical symptoms with SLE, including symptoms such as red rash, fatigue and arthritis [31]. Studies have also indicated that infection with B19 in both adults and children is similar with SLE in terms of signs and serological results. Therefore, B19 infection may predispose the patient to lupus [39].

PARVOVIRUS B19 DIAGNOSIS:

Parvovirus B19 cannot replicate in culture systems. Therefore, viral capsid is isolated from patients bearing high titers of virus in serum and is used for antibody tests. In addition, since the virus is difficult to grow and cannot be cultured, it is diagnosed using several approaches including serological tests and PCR as well as immunohistochemistry and histopathological methods [40]. B19 infection in pregnant women and in people with immune deficiency is diagnosed using molecular methods. Furthermore, neonatal infection diagnosis is based on PCR and detection of viral DNA in amniotic fluid or umbilical cord blood [41, 42]. Overall, we can mention different diagnostic procedures depending on their complications. For example, in conditions that cause transient aplastic crisis, presence of large and giant normoblasts can indicate B19 infection. Visualizing the virus under electron microscope, ELISA for detection of B19 antigen and even hemagglutination are among the methods to diagnose infection as well as PCR and hybridization to detect viral DNA. Hybridization is a proper approach to detect B19 in transient plastic crisis and pure red cell aplasia due to B19 infection. Patients with low viremia usually remain undiagnosed. PCR has a higher sensitivity than hybridization and detects the cases with low viremia but there is likelihood of contamination during PCR for the technician. Detection of anti B-19 IgM indicates recent infection in patients with a sound immune system.Nearly 85% of patients with erythematous infection or aplastic crisis caused by B19 bear IgM antibody that is detectable for 2-3 months.

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CONFLICT OF INTEREST: Authors declared no conflict of interest