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B19 Virus Infection and Blood Safety

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Abstract

Human parvovirus B19 (B19) belongs to the family of parvoviridae and viral particle measures 23 nm in diameter. B19 virus has single-stranded DNA genome and is n non-enveloped virus. It is widespread in the world. The virus can be transmitted via respiratory route and blood-derived products in addition to be transmitted vertically from mother to fetus. B19 infection can cause a lot of symptoms, such as fever, headache, erythema infectiosum, ystemic lupus erythematosus, hydrops fetalis. Because B19 virus is resistant to heat inactivation and solvent detergents, the risk of B19 virus transmission through transfusion still exists.

Keywords: Human parvovirus B19; Transfusion; Transmission

Description

Human parvovirus B19 (B19) belongs to the family of parvoviridae and measures 23 nm in diameter. It was first discovered in 1974 [1]. B19 was named after the coding of a serum sample that was used to test for hepatitis B virus surface antigen. In panel B, the number 19 serum sample is discovered anomalous results by counter-immunoelectrophoresis and radioimmunoassay [1]. Electron microscopy (EM) found that there exist 23 nm diameter particles resembling animal parvoviruses.

Because the genomic stability and without lipid envelope, B19 virus is resistant to heat inactivation and solvent detergents normally used to inactivate viral concomitants in blood products [2]. The risk of B19 virus transmission through transfusion still exists.

Genome Structure

B19 virus has single-stranded DNA genome without envelope. There are two large open reading frames (ORFs) in the B19 genome, one encoding the single nonstructural protein (NS1) and the other encoding two capsid proteins (VP1 and VP2) [3]. The transcription of B19 genome is all initiating from the P6 promoter at the extreme left side [4]. The nonstructural protein NS1 and the two structural proteins VP1 and VP2 are the most important viral proteins [4].

Nonstructural protein (NS1)

The nonstructural protein (NS1) has a molecular mass of 77 kDa [5] and is encoded by the gene (2016 bp in length) on the left side of the genome. NS1 is involved in the apoptosis pathway. The apoptosis may involve caspase 3 but Bcl-2 proto-oncogene can protect cell death from NS1 induction of apoptosis [6]. It has been shown that NS1 covalently binds to cellular DNA to cause DNA damage in the cells, which may lead to cell apoptosis [7]. In addition to promote host cell apoptosis, NS1 plays an important role in inflammation. Previous study indicated that NS1 increases the expression and secretion of interleukin-6 after it is transfected into cells [8] and induces STAT3/PIAS3 activation to modulate the inflammatory signaling [9]. In monocytic cells, TNF-α transcription can be up-regulated by NS1 through the activation of AP-1 and AP-2 motifs [10].

Capsid proteins (VP1, VP2)

The gene fragment of VP1 has 2346 base pairs which encodes VP1 protein with a molecular mass of 84 kDa. VP1 accounts for 4% of the total capsid proteins [11]. The gene fragment of VP2 has 1665 base pairs and the molecular mass of VP2 is 58 kDa [11]. VP2 protein accounts for 96% of total capsid proteins [11]. The difference between VP1 and VP2 protein is that VP1 has an additional 227 amino acids (VP1 unique region, VP1u) [12]. Anti-B19-VP1u antibodies can decrease the platelet count and prolong the thrombocytopenia time [13]. B19-specific IFN-γ responses were stronger than IL-10 responses in general [14]. N-terminal region of VP1u can interact with the receptor and plays pivotal role in the internalization of the virus [15]. VP1 protein can also inhibit K^+ channels [16] and Na^+/K^+ ATPase activity [17].

Viral life cycle

B19 is a non-enveloped DNA virus. Its life cycle consists of the following steps: virus attaching to the receptors of the host, penetration, uncoating, DNA replication, RNA transcription, protein translation, assembly of virions and cell lysis [18].

Epidemiology

B19 virus is widespread in the world year round [19]. Following infection, patients will develop IgM and IgG antibody. At the early stage, IgM is the main antibody, and with the progression of infection, IgG becomes dominant. About 71% pregnant women whose IgM is positive have increased risk of fetal loss [20] and fetal deaths may occur if infection was acquired before 20 weeks of gestation [21]. In epidemic seasons, high titers of B19 virus was detected in the blood donor blood without concurrent antibodies [22]. Younger females are more likely to be infected by B19 [23]. Anti-human parvovirus B19 antibody or deoxyribonucleic acid levels can be used to distinguish B19 infection from other infections [23].

Transmission

B19 can be transmitted via respiratory route and blood-derived products. In addition, it can also be transmitted vertically from mother

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to fetus. The infection can be found both in children and adults and after transplantation [24].

Symptoms

The prodromal symptoms may include fever, coryza, headache, and nausea. Among children, prevalent manifestation is erythema infectiosum [25]. B19 is also associated with arthritis and it is believed to be caused by the B19-specific antibody among healthy adults [26]. Apart from arthritis, B19 infection can cause numerous autoimmune disorders such as systemic lupus erythematosus (SLE) [26]. The autoimmune disorders may occur when the anti-B19 antibody is lacking in the patients who are immunocompromised or using the immunosuppressive drugs [26].

In pregnant women, B19 infection is more significant. Vertical transmission is reported to occur in the first or second trimester [27]. Hydrops fetalis can be developed by such infection [28]. Except for the hydrops fetalis, B19 infection can also cause congenital anemia, hypoalbuminaemia, inflammation of the liver, myocarditis [29] and severe fetal thrombocytopenia [30].

B19 Infection and Blood Safety

There are a lot of patients requiring blood transfusion, so under such condition it is necessary to ensure a safe and sufficient supply of blood and blood products.

B19 can be present in blood and in plasma products, circulating at extraordinarily high titers, and thus recipients may be infected [31]. Due to the fact that B19 virus is lacking lipid envelopes, it can't be inactivated by solvents and detergents (SD) [32]. In addition, very high temperature can't inactivate B19 virus in plasma either [33]. It has been reported that robust virucidal [33] and pasteurization of human serum albumin [34] can successfully inactivate B19 virus. Apart from above methods, photochemical treatment (PCT) combined with amotosalen and ultraviolet A (UVA) can inactivate B19 virus efficiently [35].

Conclusion

B19 virus belongs to the family of Parvoviridae. It can be present in blood and plasma and circulate in human body, but B19 is not included in the blood screening strategy for blood donors now. Under such condition, there is still some threatens in blood safety caused by B19 virus and further investigation on how B19 virus interacts with the host is necessary.

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