

Parvovirus infection and pregnancy

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ABSTRACT

Issues regarding parvovirus B19 infection in pregnancy continue to arouse the interest of obstetricians all over the world, the main concern focusing on maternal outcomes and fetal consequences of the intrapartum infection. Parvovirus B19 infection remains one of the main etiologies of fetal anemia and non-immune hydrops, implying a high risk of neonatal demise. This high rate of maternal and neonatal morbidity entails a special attention towards the clinical manifestations and treatment of parvovirus B19 infection during pregnancy time. A systematic literature review was obtained from over 100 articles related to the chosen subject, out of which 27 articles were chosen as relevant to the above-mentioned subject.

Keywords: parvovirus B19, infection in pregnancy, fetal anemia, fetal hydrops

INTRODUCTION

Parvovirus B19 is a solely human virus, its main characteristics residing in its small dimensions, about 25 nm, hence its name "parvo" meaning "small" in Latin and unenveloped DNA feature, with a linear and single-stranded DNA (ssDNA), while erythrocytes and erythroblasts serve as the main sites of replication, having the capacity to induce anemia in prone patients [1]. There are multiple human parvoviruses, nonpathogenic such as adeno-associated viruses (AAVs) and pathogenic such as human Parvovirus B19 (B19V) and human bocavirus 1 (HBoV1) [2]. While analyzing the serum of nine healthy blood-donors and two patients during a 1975 study, Cossart et al. discovered a different agent that could easily be mistaken for hepatitis-B antigen, later known as parvovirus B19 [3]. According to Heegaard, B19 infection clinical manifestations vary from erythema infectiosum to acute symmetric polyarthropathy, red cell aplasia and chronic anemia to fetal death in utero, hydrops fetalis and congenital anemia [4]. Diversely, HBoV1 infection

occupies a major place in the etiology of acute respiratory tract infections, implying rhinitis, pharyngitis, cough, dyspnea, wheezing, pneumonia, acute otitis media, fever, nausea, vomiting, and diarrhea, according to Jartti et al. [5].

TAXONOMY, VIROLOGY, AND CHARACTERISTICS OF PARVOVIRUS B19 INFECTION

Cotmore et al. studied the B19 taxonomy and stated that it originates in the Parvoviridae family and Parvovirinae and Densovirinae subfamilies, while Parvovirinae subfamily subsumes 8 genera: Protoparvovirus, Amdoparvovirus, Aveparvovirus, Bocaparvovirus, Dependoparvovirus, Erythroparvovirus, Copiparvovirus, and Tetraparvovirus [6]. The parvovirus capsid compile 60 copies of the capsid (VP) proteins, in an icosahedral symmetry [7]. The covering of the capsid exhibits the main characteristics that are involved in the adherence to specific receptors, intracellular signaling, nuclear passage and egress and genome encapsidation, leading

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to the immune response [8]. Parvovirus B19V infection avers a close connection to the bone marrow cells, especially the erythroid progenitor cells, including burst-forming unit-erythroid (BFU-E) and CFU-erythroid (CFU-E), the main sites of the progenitor cells being the bone marrow, umbilical or peripheral blood or fetal liver [9]. The fundamental receptor of B19V is the globoside or P antigen, which is commonly found in the human erythroid progenitors' outer layer, its main role residing in systemic dissemination, according to Bönsch et al. [10]. Via an endosomal passage, B19V is transferred to the nucleus of the cell [11] and later to the lysosomal compartment, with the mentioning that the lysosome has the capacity to demean the viruses' characteristics if it is not capable to abscond from the late endosome [12]. In a 2011 study, Chen et al. noted that, in order to achieve an adequate viral DNA replication, the signaling passage is modified, enlisting 3 phases: S-phase-dependent viral DNA replication, epo-dependent B19V DNA replication and hypoxia-facilitated B19V replication [13].

TRANSMISSION

Customarily, more than half of the adult population is seropositive to B19 parvovirus, with rates that reach up to 40-80%, the mean age of the acquired infection being 5 to 15 years, permanent protection being attained through IgG [14]. According to Anderson et al., in a 1985 study, nasal inoculation induced pyrexia, malaise, myalgia, itching after one week, lymphopenia and neutropenia after two weeks and rash and arthralgia up to 18 days after the infection [15]. The leading pathway in the transmission of the virus is the respiratory tract, followed by blood products [16].

Erythema infectiosum known as the fifth disease is the main clinical manifestation of B19V infection in children, leading to rash and arthralgia, prevailing in the winter and spring [17]. In patients suffering from a hematological disease, anemia, pure red blood cell aplasia (PRCA) or pancytopenia are frequently mentioned, Satake et al. noting that the viral load was not correlated to the hematological manifestations [18]. The immune response is the main feature of the parvovirus B19 infection: IgM antibody are traced 8 to 12 days after the infection, while IgG antibodies emerge a few days later [18].

MATERNAL FEATURES IN PARVOVIRUS B19 INFECTION

Stillbirth or intrauterine fetal demise are among the main complications of parvovirus B19 infection during pregnancy. Maternal exposure to B19V during pregnancy, especially in the first trimester, implies serious consequences such as spontaneous

abortion [19]. More than half of the fertile adult females are seronegative for B19V antibodies, the rate of vertical transmission reaching up to 30%, while the rate of fetal demise when infection is acquired before 20 weeks of gestation reaches up to 11% as it is shown by a prospective evaluation of 1018 cases [20]. According to Lassen et al., the risk of fetal demise is higher when the infection is acquired during the first trimester [21].

An overall oedema of the fetus or newborn characterizes the fetal hydrops, frequently being associated with visceral organomegaly and with anemia as the main hematological trait. Usually, fetal thrombocytopenia, leukoerythroblastic reactions or liver inflammation are often identified [22]. The presence of the hydrops is confirmed via ultrasound, but cardiac failure is often identified. Amniocentesis and cordocentesis identify the virus, eosinophilic intranuclear inclusions and "balloon" cells being typically found [23]. Most of the times, the uterine exposure to parvovirus B19 does not imply clinical sequelae, as it is shown by a study conducted in a major diagnostic laboratory in Denmark, on a cohort of 113,228 children from parvovirus B19 seropositive mothers during pregnancy, from 1994 to 2009 [24]. Nonetheless, pure red cell aplasia remains the main complication of parvovirus B19 infection during pregnancy, with immunoglobulin infusions as a good treatment option for declining viremia and inducing remission [25]. Developmental restrictions, seizures or hydrocephalus, are a part of neurological impairment caused either by intrauterine anemia or viral load, while corneal opacification, ascites and bone injuries are a part of the generalized clinical manifestations [25]. According to Beigi et al., maternal symptoms include non-specific respiratory tract infection manifestations [26].

TREATMENT

As fetal hydrops remains one of the main complications of parvovirus infection during pregnancy, the treatment requires a materno-fetal medicine specialist to determine Doppler assessment of umbilical venous and middle cerebral artery flow velocities and the referral to a tertiary care center. According to Markenson and Yancey study, when the fetus is before term, percutaneous umbilical blood sampling is needed in order to determine fetal hemoglobin and reticulocyte values, with or without intrauterine transfusion, while delivery should be taken into consideration for a near or at term fetus, without neglecting the important role of lung maturity which could be assessed through amniocentesis or obtained with the help of corticosteroid therapy [27].

CONCLUSIONS

Parvovirus B19 infection is a serious condition that leads to a high rate of morbidity or fetal mortality during pregnancy time. Parvovirus B19 seropositivity is found in more than half of the fertile adult women, the infection having the biggest incidence in the 5-15 years age group. Infection during pregnancy implies serious fetal outcomes such as still-

birth and fetal demise, the rate of vertical transmission reaching up to 30%. The current review article emphasizes the importance of the recognition of the parvovirus B19 infection, especially in women with a child at home with symptoms of infection, but also the importance of the general measures that could lead to limitation of the viral transmission.

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