

Parvovirus B19 Testing in Transfusion

Mona Papari, MD, Associate Medical Director, LifeSource Blood Center
Ram Kakaiya, MD, Medical Director, LifeSource Blood Center

CHARACTERISTICS: Parvovirus B19

Human parvovirus B19, discovered in 1975, is a non-enveloped, single stranded DNA virus that belongs to the Parvoviridae family, genus Erythrovirus. The virus is usually transmitted by the respiratory route.

CLINICAL MANIFESTATIONS

In children, infection with parvovirus B19 manifests as erythema infectiosum (also known as the fifth disease), a mild illness where the main symptom is an erythematous cutaneous eruption that may be accompanied by fever, joint pain and mild anemia. In adults, the infection generally manifests as an acute polyarthropathy. Disease complications include transient aplastic crises which can cause acute anemia in patients with sickle cell disease or other hemolytic anemias. In immunocompromised patients, infection can be complicated by chronic bone marrow failure. Fetal infection occurring between weeks 9 and 20 of gestation can lead to severe complications, such as severe anemia, congestive heart failure, hydrops fetalis and even intrauterine fetal death (3-10% of infected mothers).

EPIDEMIOLOGY

Acute infection with parvovirus B19 manifests as a transient viremia, with the virus circulating at very high titers for one to two weeks, followed by the appearance of IgM antibodies and then IgG antibodies, with long persistence. The virus has tropism for the erythroid cells and replicates in the erythroid progenitor cells of the bone marrow resulting in inhibition of erythropoiesis. Even in healthy individuals, the virus can be present at very low levels for long periods of time, even years. Recent data suggests that the virus has the potential to reactivate in immunodeficient individuals.

Worldwide epidemics are known to occur, especially in late winter or early spring, with cyclical peaks every 3 to 6 years. Seropositivity in the adult population is approximately 60% by age 20 and can reach 90% in older adults. There are three genotypes identified by sequence homology of the parvovirus B19 DNA, with genotypes 1 and 2 circulating in North America and Europe, genotype 1 being the most prevalent.

Recently, genotype 3 was reported as being detected in a plasma donor in the United States. This specific genotype is prevalent in Ghana, but has also been observed sporadically in France and Brazil.

TRANSFUSION TRANSMISSION

Transmission by blood components and other plasma derivatives is also known to occur. Organ transplantation constitutes another mode of transmission. Parvovirus transmission due to administration of clotting factor concentrates and following infusion of solvent/detergent-treated plasma has been reported, being especially common before introduction of DNA testing. Transmission from IVIG, although rare, has also been documented. Transmission through transfused blood components is very rare with only 4 clinical cases having been documented in the literature. The actual frequency of transmission has not yet been determined. Of particular concern for parvovirus infection acquired through transfusion are patients with hemolytic anemias, immunocompromised patients and pregnant women, where the complications can cause significant morbidity.

TESTING FOR PARVOVIRUS B19

PLASMA FOR DERIVATIVE MANUFACTURE

Due to the very small size of the virus, filtration methods are ineffective for removal of parvovirus B19. The virus is also resistant to common inactivation methods employed during plasma derivative production. Therefore, in July 2009, the FDA issued guidance for nucleic acid testing (NAT) of all plasma from which derivatives, such as intravenous immunoglobulin (IVIG), coagulation factor concentrates etc., are manufactured in order to reduce the risk of transmission of parvovirus B19. According to the FDA and based on the known risk of transmission from plasma derivatives, the recommended upper limit for viral load of parvovirus B19 in plasma should not exceed 10^4 IU/ml. The NAT assays used for screening of plasma donations are recommended to target those viral genome regions that are common to all three genotypes. Current testing of plasma intended for manufacturing of plasma derivatives is performed by

NAT of plasma mini-pools. It is well-documented that a viral load higher than 10^3 IU/ml is required for transmission by transfusion of plasma derivatives. One hypothesis is that low viral titers from pooled plasma products may be neutralized by antibodies against parvovirus B19 present in other units from the same pool.

BLOOD COMPONENTS

At this time, there is no recommendation for routine testing of blood components, such as red blood cells, platelets and fresh frozen plasma (FFP). The logical question that arises is whether the same low viral titers seen to be noninfectious in plasma derivatives are also noninfectious when present in transfused blood components. The answer to this question is yet to be established, but the risk appears to be low despite the high prevalence of persistent parvovirus infection. Because low level viremia and the presence of antibodies are relatively common, differentiating between transmission through transfusion and viral reactivation in previously infected recipients can be a very difficult task. In a linked donor-recipient study recently published, Kleinman and colleagues found no evidence of parvovirus transmission from transfusion of components where the DNA concentration was less than 10^6 IU/ml.

PREVALENCE IN BLOOD DONORS

Lefrere and colleagues report the rate of persistent parvovirus infection to be as high as 7.9% in immunocompetent blood donors, despite the presence of IgG antibodies. Data from a Japanese study done by Matsukura and colleagues shows that viral loads in healthy individuals decline below 10^4 IU/ml approximately one year after the acute infection and to 10^3 IU/ml after two years. The Retrovirus Epidemiology Donor Study (REDS-II) data suggests that the prevalence of parvovirus B19 DNA among US blood donors is approximately 1% (detection limit for DNA concentration of 20 IU /ml). IgG antibodies against parvovirus B19 were detected in all of the DNA-positive donations and in 73% of the DNA-negative donations. IgM seropositivity occurred only in 23% of the DNA-positive donations and in none of the DNA-negative donations being associated with increasing DNA levels. By contrast, the prevalence was found to be much lower in studies performed by plasma manufacturers (ranges from 0.008 to 0.04%), but the sensitivity of the PCR assays was also lower (detection limit for DNA concentration of more than 10^5 or 10^6 IU/ml).

CONCLUSION

It is not yet clear what viral load is required for transmission of infection to a recipient of a simple blood component transfusion vs. a plasma derivative. .

Currently, there are no FDA-approved screening tests for detection and prevention of transmission through transfusion of blood products and the general consensus is that the risk is low enough so that testing may not be of benefit. Nonetheless, parvovirus B19 infection should be considered in any recipient of a plasma derivative or blood component who develops aplastic anemia, unexplained anemia after transfusion or other clinical syndrome consistent with parvovirus B19 infection.

RESOURCES

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Editor: Donald L. Kelley, MD, MBA: dkelley@itxm.org.

For questions about this TMU, please contact:

Ram Kakaiya, MD at: rkakaiya@itxm.org 847-803-7825.

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