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Molecular detection of human Parvovirus B19 in serum samples collected from 1998–2011 in Manaus, Amazonas State, Brazil

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Abstract

Parvovirus B19 (B19V) belongs to the *Parvoviridae* family and *Erythrovirus* genus and is predominantly transmitted by respiratory secretions. It is responsible for many diseases, such as infectious erythema, acute or chronic arthropathy in adults, transient aplastic crisis, anemia in immunodeficient or immunocompromised patients, and fetal hydrops in pregnant women. However, most infections are asymptomatic or manifest only nonspecific symptoms, such as fever, headache, arthralgia, rash and coryza and can therefore be easily confused with other viral infections. The first case of laboratory-proven B19V infection in Amazonas was reported in 2005. IgM antibodies against B19V were detected in serum samples collected from 1999 to 2003 from pediatric patients suspected of suffering from dengue fever. This study presents the first molecular detection of B19V in samples collected from 1998 to 2011 from Manaus, Amazonas. 177 serum samples collected during the acute phase (0–6 days) negative for dengue and stored at -80 °C were subjected to viral DNA extraction and nested PCR according to the protocol for B19V DNA detection. 92 samples (51.9%) tested positive for B19V, with the highest positivity in those from 2002. The youngest patient was 2 months old and the oldest was 76 years old, and the largest number of samples belonged to the 20–59 age group. Both genders were equally infected, with symptoms being similar to those of dengue. These results confirm the presence of autochthone of B19V in DENV samples since 1998 and the underreporting in Manaus, highlighting the importance of differential diagnosis during epidemics.

Keywords: Parvovirus B19; Manaus; Amazonas; Brazil

1. Introduction

Parvovirus B19 (B19V) belongs to the *Parvoviridae* family, *Erythrovirus* genus, and is predominantly transmitted by respiratory secretions; however, it can be transmitted vertically from mother to fetus, through blood transfusion, bone marrow transplantation, and organ transplantation [1,2,3]. B19V is responsible for many diseases, such as infectious erythema, acute or chronic arthropathy in adults, transient aplastic crisis, anemia in immunodeficient or immunocompromised patients, and fetal hydrops in pregnant women [1,4]. The association between B19V infection and human diseases was first documented in 1981 and later confirmed in several experiments and seroepidemiological studies [5,6]. However, most infections are asymptomatic or manifest only nonspecific symptoms, such as fever, headache, arthralgia, rash, coryza, nausea, and occasional diarrhea, and can therefore be easily confused with other viral infections [2].

In Amazonas, the first report of laboratory-proven B19V infection was described in 2005, where IgM antibodies to B19V were detected in serum samples collected in the period 1999–2003 from pediatric patients suspected of suffering from

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dengue fever [7]. This study presents the first molecular detection of B19V in samples collected in the period 1998–2011 in Manaus, Amazonas. 1998, 1999, 2001, 2008, and 2011 were the dengue epidemic years in Amazonas.

2. Material and methods

The study was approved by the ethics committee of the Tropical Medicine Foundation Doctor Heitor Vieira Dourado (FMT-HVD), under registration number 0004.0.114.000-05.

2.1. Sample Collection

In the years 1998, 1999, 2001, 2008, and 2011, 177 patients sought medical attention at FMT-HVD, the reference hospital for infectious diseases in Manaus, Amazonas. As per the inclusion criteria, malaria negative and dengue negative (DENV) samples from patients with undifferentiated febrile syndrome and at least three of the following signs and symptoms: fever, headache, eyeball pain, myalgia, arthralgia, prostration, and exanthema, collected during the acute phase (0–6 days), and stored at -80 °C, were selected for molecular testing for B19V. Samples that were positive for malaria, collected more than six days after the onset of symptoms, or were not DENV, were not considered for analysis.

2.2. Molecular Tests

Viral DNA was extracted from 177 samples using the QIAamp Viral DNA Mini-Kit (Qiagen, Hilden, Germany), followed by nested PCR for the detection of B19V DNA, using primers that amplify the genomic region encoding the VP1 and VP2 capsid proteins [8]. The genomic region was amplified using a Veriti thermocycler (Applied Biosystems, Foster City, CA, USA) under the following conditions: denaturation at 94 °C/5 min; followed by 36 cycles of 94 °C/1 min, 60 °C/1 min, and 72 °C/1 min; and final extension at 72 °C/7 min. The second round of amplification was conducted with 5 µL of the product of the first PCR using the PVP2/PVP3 primers [8], under identical cycling conditions. The products generated in the second round of amplification were subjected to electrophoresis on 1.5% agarose gel with ethidium bromide and analyzed under ultraviolet light.

3. Results

A total of 92 samples (51.9%) were found to be positive for B19V, with the highest positivity observed in the samples from 2002 (Figure 1). The youngest patient was 2 months old, the oldest was 76 years old, and the 20–59 age group was predominant (Figure 2); both sexes were equally infected and fever, headache, myalgia, ocular pain, arthralgia, bone pain, vomiting, exanthema, and stiff neck were the most frequent clinical manifestations (Figure 2). Among the positive patients, 6 patients lived outside Manaus (transit), and 10 had a travel history (Table 1). In Manaus, where the highest number of positive cases was concentrated, the central-west region and southern region were identified as the residential and work areas with the most positive cases, respectively.

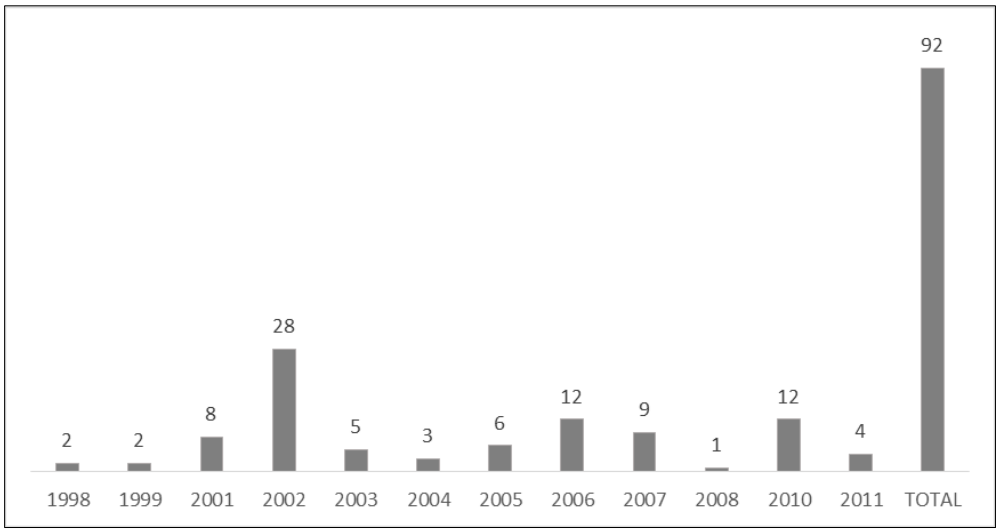

Figure 1 Distribution of B19V cases by the year of collection

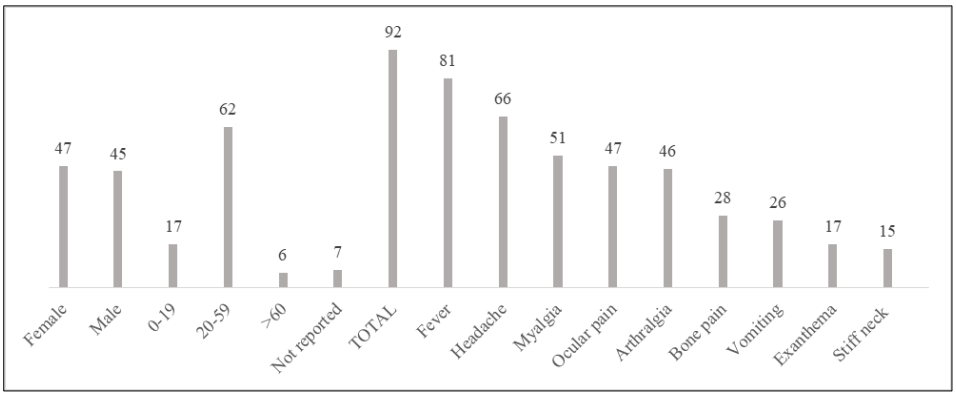

Figure 2 Distribution of B19V cases by gender, age group, and symptoms

Table 1 Patients positive for B19V who reported traveling 15 days before the onset of symptoms or who resided outside Manaus

Sample	Year of collection	Travel +/- 15 days before the onset of symptoms
191;209;214;225	2002	Countryside
133;224	2002	State Highways
212	2002	Municipality of Amazonas
194;199	2002	Brazilian states
22303	2010	Municipality of Amazonas
Sample	Year of collection	Residents outside of Manaus (Transit)
10338	1998	Indian Reserve (BR-174)
73	2001	Municipality of Amazonas
160;170;171	2002	Countryside
251	2002	Municipality of Amazonas

4. Discussion

IgM antibodies to B19V were identified in Manaus for the first time in 2005 in DENV samples from 1999, 2000, and 2001 [7], and B19V DNA was recently identified in samples from 2001 and 2002 [9]; however, our findings show that B19V was already present in samples collected in 1998, when the first dengue cases were recorded in Manaus [10].

These results corroborate those of studies in other municipalities in Amazonas and other regions, which indicate that B19V is the agent responsible for febrile syndrome in children and adults of both genders [11,12,13] and is facilitated by air transmission and greater exposure of young adults who commute daily from their homes to other areas of the city (personnel). In Manaus, the midwest and southern zones had the highest number of positive cases. The midwest zone includes the neighborhoods closest to FMT-HVD, which makes it easy for their inhabitants to seek medical care. And the southern zone includes the commercial center and neighborhoods close to it, making up the industrial district that includes the industrial pole of Manaus, as we have observed since the first dengue epidemic in Manaus [10]. B19V was also detected in a resident of the Indian reservation. B19V is predominantly transmitted by respiratory secretions, which makes its transmission easy [14]. In addition, there are many asymptomatic cases or cases with nonspecific manifestations that are easily confused with dengue and other agents [15], resulting in underreporting. These clinical findings are similar to those observed in our patients, as well as those in other studies carried out in Amazonas and other regions [16, 17, 18].

In this study, the year 2002 had the highest number of B19V positive cases, corroborating the findings of Silva et al., (2020). It should be noted that most of the analyzed samples were collected this year; unfortunately, the same number of samples was not available for other years; for example, we did not have stored samples from the year 2000. It is

expected that in the years of the DENV epidemic, the occurrence of other viruses is lower; however, other etiological agents similar to dengue may be underreported as observed in Amazonas and other regions [12, 17, 18]. Despite a significant number of infected people having a travel history or living outside Manaus, it is evident that since 1998, there have been autochthonous cases of B19V. Two patients from this period were infected with B19V, out of which only one lived outside the urban perimeter, in the indigenous reserve located along BR-174, confirming the distribution of B19V both inside and outside the urban perimeter of Manaus and other municipalities in Amazonas, facilitated by its ability to transmit through air and by the increasing population movement [18].

These results confirm the presence of B19V in DENV samples since 1998 and the underreporting in Manaus, owing to their high clinical similarity with dengue and other agents common in the Amazon region; its dispersion through air and the occurrence of asymptomatic manifestations are other factors that must be considered in the inclusion of B19V in the differential diagnosis, independent of the occurrence of epidemics that show DENV cases and infections of other arboviruses.

5. Conclusion

This work highlights the underreporting of B19V, which since 1998 has been underreported in Manaus and in other Brazilian locations, the importance of the differential diagnosis that provide quick detection of emerging and reemerging diseases allowing adequate treatment of patients and early control measures against different pathogens, preventing new outbreaks.

Compliance with ethical standards

Acknowledgments

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Disclosure of conflict of interest

The author declares that there are no conflicts of interest.

Statement of ethical approval

The study was approved by the ethics committee of FMT-HVD under number 0004.0.114.000-05.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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