Epidemiological Alert
Mayaro Fever

1 May 2019

Given the recent detection of Mayaro fever cases through laboratory surveillance in areas where cases had not previously been reported, the Pan American Health Organization / World Health Organization (PAHO/WHO) encourages Member States to implement and maintain capacity to detect this disease, including laboratory diagnostic capacity and raising awareness among healthcare workers.

Situation summary in the Americas

Mayaro virus (MAYV) was isolated for the first time in Trinidad and Tobago in 1954. However, a retrospective study showed evidence of infection by MAYV in sera collected during the construction of channels in Panama and Colombia between 1904 and 1914 (1, 2). Since then, cases have been reported in Central America and South America, particularly in the regions around the Amazon basin.

Following the cases identified in Trinidad and Tobago, Mayaro fever cases were reported in Brazil (1955), Colombia (1958-1960), Bolivia (1959), Suriname (1964), Peru (1965), the United States of America (cases imported from Peru and Bolivia, 1997), Ecuador (1997), French Guiana (1998), Venezuela (2000), Mexico (2001), Panama (2010), and Haiti (2015) (3, 4).

Although some studies suggest transmission in urban areas (5, 6), outbreaks described in the last decade in the Americas were reported among residents of rural communities in the Amazon region of Brazil, Bolivia, Peru, and Venezuela. The majority of human cases occurred among persons who work or reside in tropical rainforests. For the documented outbreaks, the vector identified was the *Haemagogus* mosquito found in rural and sylvatic habitats. The reservoir for MAYV is unknown, but some studies have

Mayaro fever

Mayaro fever is a zoonosis caused by an arbovirus of the *Alphavirus* genus, *Togavirus* family. Transmission by *Haemagogus* mosquitoes has been documented. Human cases are associated with recent exposures to humid forest environments inhabited by these vectors (7).

In the first days, the disease presents as a nonspecific clinical picture similar to other arboviruses: fever, headache, myalgia, retro-ocular pain, chills, severe arthralgia, dizziness, nausea, photophobia, anorexia, often incapacitating joint edema, rash (mainly on the chest, legs, back, arms and less frequently in the face), abdominal pain, leukopenia and thrombocytopenia, and in some cases mild hemorrhagic disease symptoms have been described (5, 8-13).

The incubation period is relatively short, ranging between 1 to 12 days (4, 7). The disease is self-limiting, with a duration from 3 to 5 days, with persistence of arthralgia that can remain for weeks or months (9,11,12,14); a fatal case with encephalopathy has been documented (13).

Suggested citation: Pan American Health Organization / World Health Organization. Epidemiological Alert: Mayaro fever. 1 May 2019, Washington, D.C.: PAHO/WHO; 2019

reported virus isolation or high levels of antibodies in host vertebrates, such as nonhuman primates (8).

In 2015, one case of Mayaro fever was reported in Haiti. The case is an 8-year-old child from a rural area who was diagnosed with a coinfection of dengue and Mayaro (15).

In 2018, Peru reported 35 cases of Mayaro fever (16).

In 2019, 2 cases were confirmed in Peru in the provinces of Quispicanchis (Cusco Region) and La Mar (Ayacucho Region) (16).

Additionally, on 26 April 2019, Ecuador reported that of 34 samples that were negative for dengue, chikungunya, Zika, and leptospirosis, 5 were positive for Mayaro. The cases correspond to four different cantons: Guayaquil (2 cases), Portoviejo (1 case), Santo Domingo (1 case), and Babahoyo (1 case). These cantons are in the eastern part of the country, with a distance of up to 300 kilometers between them. The detection occurred through laboratory surveillance of MAYV which has been implemented in Ecuador since 2018.

Advice for national authorities

Given the broad distribution in the Region of the mosquito implicated in transmission and in light of the recent detection of cases in new geographic areas, PAHO/WHO encourages Member States to implement actions for detecting cases and keeping healthcare professionals informed to therefore consider Mayaro fever as part of the differential diagnosis for other arboviruses such as chikungunya, dengue, and Zika.

Below is a summary of the main recommendations.

Surveillance

Considering the similar clinical presentation for Mayaro fever with that of other arboviruses, such as dengue, chikungunya, and Zika, surveillance for Mayaro fever could be integrated with existing arbovirus surveillance.

Surveillance should focus on:

- Detecting MAYV circulation in a timely manner
- Monitoring the geographical spread of MAYV once detected
- Contributing to the knowledge regarding the clinical characteristics of the disease
- Monitoring the circulating viral lineages

Laboratory diagnosis

The diagnosis of Mayaro fever is performed through virologic methods (i.e., detection of the viral genome or isolation of the virus) and/or serological methods (ELISA, PRNT). As with any other laboratory test, results need to be considered within the epidemiological and clinical context.

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Laboratory testing for Mayaro fever should be considered as a differential diagnosis for chikungunya virus (CHIKV) and should be attempted after a sample from a suspected case is negative for CHIKV (notably if negative using polymerase chain reaction (PCR) during the acute phase of infection). Dengue and Zika should also be ruled out based on the clinical and epidemiological background.

Laboratory surveillance for Mayaro fever can also be performed by analyzing a proportion of samples from patients with clinically compatible presentations and who have tested negative for dengue, chikungunya, Zika, and other prevalent arboviruses.

Virological Methods

The replication dynamics of MAYV are not well defined. In contrast to CHIKV which has high and relatively long viremia, MAYV appears to have low levels of viremia lasting up to 5 days following the onset of symptom. Therefore, samples collected during this period should be analyzed using molecular methods or viral isolation.

- *Molecular diagnostics:* Viral RNA can be detected in serum samples up to 5 days following the onset of symptoms (viremic phase) by molecular methods such as conventional or real-time reverse transcription PCR (RT-PCR). A positive result by molecular testing (when using the appropriate controls and interpretation) confirms the diagnosis of MAYV infection.

  Due to the low viremia of MAYV, high cut-off point (Ct) values can be observed with well-defined amplification curves in real time RT-PCR assays. Results should be carefully evaluated in the light of the clinical and epidemiological background.

- *Viral isolation:* Viral isolation can be performed in cell culture (using Vero or C6/36 cells). Due to its complexity, this methodology is rarely used as a first-line diagnostic tool. However, as MAYV viremia may be very low, viral isolation might increase the viral concentration for subsequent detection by molecular assays.

Serological Methods

IgM for both CHIKV and MAYV viruses can be detected as of day 6 following symptom onset, so samples collected after day 6 should be analyzed by serological methods. Serological techniques often have cross-reactions with other alphavirus infections. Therefore, the use of RT-PCR is preferred for MAYV detection and diagnosis.

- *IgM detection:* Anti-MAYV IgM antibodies can be detected by ELISA (mainly capture of IgM antibodies, MAC-ELISA) or any other immunoassay (e.g., indirect immunofluorescence). To date, there are no validated, commercially available serology kits for MAYV. Therefore, in-house protocols with purified antigens are used. Cross-reactivity of MAYV IgM assays with other alphaviruses has been described. Thus, in areas where other alphaviruses co-circulate (especially CHIKV), the probability of cross-reactivity is high. As with any IgM test, a positive result in a single sample is only presumptive of a recent infection. Laboratory confirmation requires demonstration of seroconversion in paired serum samples (acute and convalescent with at least one week apart) and no seroconversion to other relevant alphaviruses.

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Clinical management

Symptomatic management with nonsteroidal anti-inflammatory drugs (NSAIDS), rest, hydration, and supportive treatment of possible complications is recommended, following the exclusion of more severe diseases such as malaria, dengue, or bacterial infections.

There is no specific antiviral treatment for Mayaro virus infection.

Prevention measures

Public health measures to minimize exposure of persons to mosquitoes are imperative to prevent the spread of the virus and therefore, the disease.

Currently, the only preventive protective measure is to avoid exposure to MAYV vectors (*Haemagogus* species mosquitoes), which is also the vector for yellow fever virus and is present in wild or rural habitats.

The community must be informed on the risk of transmission and ways to minimize the risk of exposure to vectors, whether in a rural area or within a home in peri-urban areas or those bordering rural areas.

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