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## COVID-19 and dengue coinfection in Brazil

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### Abstract

The case we present here is a man who lives in a dengue-endemic area. Initially, the patient was diagnosed with dengue fever by clinical evaluation and laboratorial confirmation. Subsequently, he presented respiratory symptoms, and a concomitant severe acute respiratory syndrome coronavirus 2 infection was confirmed. He was hospitalized for 17 d and had a satisfactory recovery.

**Key Words:** COVID-19; Dengue fever; SARS-CoV-2; Dengue virus; Coinfection; Diagnosis

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**Core Tip:** Corona virus disease 2019 represents a big concern for public health. Simultaneously, many countries are also being affected by arbovirus epidemics, which overwhelms the health assistance services from those localities. That scenario calls attention to how these epidemics will affect the health of people living in those geographic areas. In this Letter to the Editor, we report a coinfection by severe acute respiratory syndrome coronavirus 2 and dengue virus that occurred in northeastern Brazil.

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## TO THE EDITOR

From the first cases reported in December 2019 in Wuhan, China, to May 13, 2020, the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has already infected 4179479 people worldwide<sup>[1,2]</sup>. Concomitant to the corona virus disease 2019 (COVID-19) pandemic, half of the world population is at increased risk of developing arbovirus infections, and 390 million individuals are infected by the dengue virus (DENV) every year, which makes the world health scenario even more worrying<sup>[3]</sup>. Here we report a coinfection by SARS-CoV-2 and DENV that occurred in a patient from northeastern Brazil.

This study was approved by the National Commission of Research Ethics, from the National Health Council, Ministry of Health of Brazil (Number 30700320.0.0000.0008), and a signed informed consent was obtained from the patient.

The case is a 59-year-old physician male with well-controlled comorbidities (hypertension and type 2 diabetes, in use of an angiotensin converting enzyme inhibitor and metformin) living in a dengue-endemic area with no history of recent travel. He requested medical home care on March 30, 2020 due to the onset of symptoms such as fever, chills, anorexia, and headache. Three days later, the patient was tested by immunochromatography assay for specific dengue immunoglobulins (94% sensitivity and 96% specificity). Positive IgM and negative IgG results along with the clinical data led to the diagnosis of dengue fever.

On the fourth day, the patient presented dyspnea and cough, and a bilateral ground-glass pattern was observed in his lungs by a thoracic computerized tomography. He was immediately hospitalized and found to be positive for SARS-CoV-2 infection by serology (positive IgM and IgG immunoglobulins) and by RT-PCR of the material obtained by a nasopharyngeal swab. The liver and kidney tests were within the reference values as well as the blood counts.

Two days later, the patient presented a hypoxemic respiratory insufficiency and was transferred to an intensive care unit. He underwent noninvasive oxygen therapy and developed a deep vein thrombosis in the right femoral vein, which was accompanied by increased D-dimer values. He received full-dose heparin therapy followed by full-dose enoxaparin prophylaxis. The patient was kept in the intensive care unit for 12 d and was subsequently transferred to conventional hospital care.

Five days later, a COVID-19 serological test was negative for IgM and positive for IgG, and he was discharged from the hospital with a rivaroxaban (30 mg/d) prescription. Three weeks after hospital discharge, he underwent a new immunochromatography assay for dengue diagnosis (94% sensitivity and 96% specificity), and IgG dengue specific immunoglobulin was positive, representing a seroconversion and confirming the concomitant diagnosis of dengue fever and COVID-19.

It has to be emphasized that there was an increase of about 70% in the number of dengue cases in Brazil in the period from December 30, 2019 to March 12, 2020 (390684 cases reported) compared to the same period in 2018-2019 (229064 cases reported)<sup>[4,5]</sup>. In addition, according to the Pan American Health Organization, Brazil registered 2226865 dengue cases in 2019, 70% of the total in the Americas<sup>[6]</sup>. Not only Brazil, but also all of the dengue-endemic world regions are at risk of suffering the consequences of the threatening cocirculation of those viruses<sup>[7,8]</sup>. As an example, a prior publication called attention to Colombia, which registered 52679 dengue notifications and 14943 COVID-19 cases during the first five months of 2020<sup>[9]</sup>. Interestingly, a study demonstrated a considerable drop in the number of dengue cases notified during the COVID-19 epidemic in the State of São Paulo, Brazil<sup>[10]</sup>. This study hypothesized that there might be an under notification of dengue cases due to the impairments in health system functioning because of the COVID-19 epidemic. The authors also theorized that the restriction of the social interactions aiming to limit the SARS-CoV-2 dissemination resulted in a lower circulation of people and could have reduced the propagation of arboviruses, decreasing the risk of dengue outbreaks in various geographic areas.

The case reported here joins some previously published descriptions of dengue and

COVID-19 coinfections. The first reported DENV and SARS-CoV-2 coinfection dates from March 11, 2020 and affected a 44-year-old male living at Mayotte in the Indian Ocean, who traveled to Switzerland and France, where his symptoms started<sup>[11]</sup>. Verduyn *et al*<sup>[12]</sup> reported another coinfection in an 18-year-old male who traveled from France to Reunion Island, also located in the Indian ocean. We have just also published a similar coinfection in a Brazilian man aged 39 years, who lived in a small county with no prior register of COVID-19 circulation and had the onset of symptoms three days after a day trip to another city<sup>[13]</sup>. Interestingly, all of the above mentioned case reports refer to travelers who potentially acquired each of the infections in different geographic areas.

In contrast, the present report describes a coinfection in a patient who had not traveled before falling ill. Such data alerts to the occurrence of a local circulation of both viruses, which can lead to serious impacts in the regional public health. Moreover, all of the previously reported cases are young adults who did not experience severe respiratory symptoms unlike the patient reported here, who also had type 2 diabetes and hypertension, two well-known risk factors for unfavorable COVID-19 outcomes.

Although the patient underwent intensive medical care and supplementary oxygen, he had a satisfactory recovery with no necessity for intubation. Some authors believe that metformin may play a protective role in diabetic COVID-19 patients because this medication has promising results when used in other lung diseases such as asthma and pneumonia<sup>[14]</sup>. Moreover, a retrospective cohort study analyzing 223 diabetic individuals who had dengue fever found a lower risk of developing severe dengue among metformin users<sup>[15]</sup>. In addition, we hypothesize that the interplay between those infections may influence the immune response in an idiosyncratic way. However, deeper analysis on that issue could not be performed in the present case, and further studies should be conducted in order to better understand this relationship.

The existence of clinical similarities between COVID-19 and dengue fever can lead to misdiagnoses, which may delay important clinical measures for the management of patients. Waterman *et al*<sup>[16]</sup> drew attention to the need for physicians in dengue-endemic areas to be alert for recognizing clinical characteristics associated with severe dengue fever in individuals with a suspected SARS-CoV-2 infection. On the other hand, the report of a 35-year-old nurse who likely got COVID-19 while sampling blood of a man who was presumed to have dengue fever highlights the risks of covert SARS-CoV-2 infections in dual viral circulation settings<sup>[17]</sup>. Complementarily, the occurrence of false-positive serology for dengue in SARS-CoV-2-infected individuals in Singapore reinforce the necessity of careful management of patients with nonspecific clinical presentations in coepidemic scenarios<sup>[18]</sup>. The discussion above gains even more importance when considering that laboratory parameters such as thrombocytopenia can be observed in both infections<sup>[19]</sup>. Taken together, health systems of dengue-endemic regions should consider social isolation procedures for patients without a clear etiologic diagnosis aiming to avoid the SARS-CoV-2 dissemination.

In view of the potential risks of a coinfection by SARS-CoV-2 and DENV, we highlight the importance of this Letter to the Editor as a way to alert health professionals to consider both diagnoses in countries simultaneously affected by these epidemics.

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