DOI: 10.7860/JCDR/2021/49440.15291

Case Report

Internal Medicine Section

# Co-infection of SARS-CoV-2 with Dengue Fever-A Case Report

SHREYA REDDY SINGIREDDY[1], SWAMY MIRYALA[2], SRIKRISHNA RAGHAVENDRA BODDU[3], SURESH INUGURTHI[4]



## ABSTRACT

The current pandemic circulation of Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) along with Dengue Virus (DENV) in disease endemic countries may produce unfavourable circumstances with co-infection, delays in emergency mitigation measures and management of the disease as both the viral diseases have many similar close characteristics and presentations. This is a case report of a 50-year-old diabetic and hypertensive female admitted with complaints of fever with chills for one week duration. On initial evaluation due to the ongoing pandemic as per the protocol, the patient was found negative with rapid antigen testing for SARS-CoV-2, Reverse Transcriptase-Polymerase Chain Reaction (RT-PCR) test along with negative High-Resolution Computed Tomography (HRCT) of the chest. Basic initial investigations suggested decreased platelet count and elevated acute phase proteins. Two days after admission, the patient was found to be Dengue IgM and IgG positive and the patient's symptoms were managed accordingly. Later, the patient suddenly showed decrease in oxygen saturations and warranted a ventilator immediately. The CT pulmonary angiogram was done to rule out suspected pulmonary thromboembolism, which was showing infective lesions with Coronavirus disease 2019 Reporting and Data System grade 4 (CO-RADS 4). Repeat RT-PCR for SARS-CoV-2 was positive. The Patient was immediately shifted to high isolation Intensive Care Unit (ICU) and treated according to the Standard Operating Protocol (SOP) of SARS-CoV-2 infection. The overlapping clinical presentations of SARS-CoV-2 infection and DENV in resource-constrained settings and the complexities of interpreting results make identification of SARS-CoV-2 in the dengue endemic areas difficult. Therefore, a high degree of alertness should be maintained for SARS-CoV-2 infection in DENV endemic areas.

**Keywords:** Coronavirus disease-2019, Endemic areas, High suspicion, Severe acute respiratory syndrome coronavirus-2, Viral infections

## CASE REPORT

A 50-year-old female presented to the emergency with complaints of fever and breathlessness since three days. According to her medical history, she was suffering from controlled Diabetes Mellitus Type 2 which was diagnosed a year back and was kept under control by lifestyle modification along with metformin (biguanide). She was also diagnosed with hypertension five years earlier and was on regular medication with telmisartan (Angiotensin Receptor Blocker). The patient was having an oxygen saturation of 92% at room air which increased to 96% when 2 litres oxygen/min was administered. As part of hospital emergency SOP in a patient with acute febrile illness and breathlessness, she was tested for SARS-CoV-2 by rapid antigen testing and HRCT chest to look for any radiological findings suggestive of the disease. The RT-PCR test was also done which takes considerable time for the result. However, both the Rapid antigen test card and HRCT chest were negative for viral infection with CO-RADS grading reported as 2. All routine investigations including cultures along with serologies suspecting a possible Acute Febrile Illness (AFI) were conducted. The patient was put in an observation ICU, monitoring oxygen requirement with empirical treatment.

The following day patient was found to be symptomatically better requiring minimal intermittent oxygen therapy and was also found to be RT-PCR negative for SARS-CoV-2 infection. However, routine investigations including Total leucocyte count, Platelet count and Packed Cell Volume (PCV) [Table/Fig-1] were suggesting a picture of viral disease with thrombocytopenia and blanching rash. Investigations pertaining to DENV were done. Dengue Non-Specific Antigen 1 (NS-1) was negative on the admission day and IgG and IgM Dengue serologies were reported to be positive.

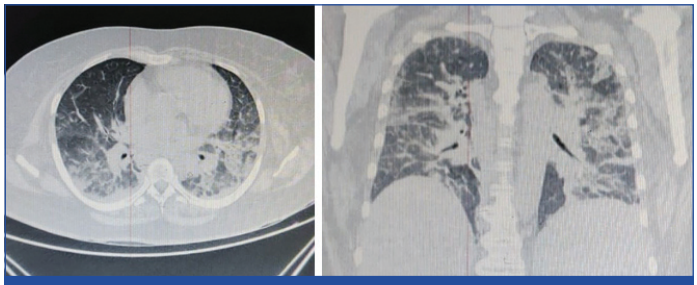
The patient was started with IV fluids as the initial management and later treated according to the laboratory parameters along with monitoring of decreased platelet count. Further investigations were done which revealed elevated D-dimer levels [Table/Fig-1] for which the patient was started on injectable anticoagulant Clexane (Enoxaparin). The patient was also started on doxycycline (antibiotic) for its property of inhibiting dengue virus serine protease thereby decreasing the replication of the virus. Lactate Dehydrogenase (601 U/L) and Alkaline Phosphatase levels (689 IU/L) are the other elevated parameters found in the initial workup, indicating the presence of an infection. The patient was treated based on the laboratory reports and was shifted to a step down ICU. Both the blood and urine cultures were sterile. On Day 5 of admission around noon patient suddenly started showing decreased oxygen saturation and was immediately warranted endotracheal intubation. Arterial blood gas analysis [Table/Fig-1] was suggesting respiratory acidosis. The patient also complained of chest heaviness at that time though the cardiac leads were showing normal sinus rhythm with a pulse rate of 97 beats per minute with a blood pressure of 140/96 mm of Hg.

Pulmonary thromboembolism (PTE) was suspected, and immediate CT pulmonary angiography was done for the patient [Table/Fig-2] which revealed the patient to be negative for PTE, but it showed pulmonary oedema and infection changes with CO-RADS staging 4. Repeat RT-PCR for SARS-CoV-2 was done which was positive on the same day. The patient was immediately shifted to a high isolation ICU and anticoagulants were continued along with the initiation of SOP for COVID-19 (SARS-CoV-2 infection). The patient was started on antiviral medication Remdesivir (200 mg IV stat on the first day followed by 100 mg IV once daily for four days) and Methyl Prednisolone (0.5 mg/kg. body weight). The patient was continued on antibiotics and supportive constitutional treatments including antitussives, analgesics, proton pump inhibitors and multivitamin supplements along with monitored hydration. After four days according to the improvement of symptoms, the patient was weaned off of the ventilator, extubated, shifted to step down ICU and

| Parameters | 1st Day of admission | 2nd Day of admission | 3rd Day of admission | 4th Day of admission | 5th Day of admission | Findings |
|---|---|---|---|---|---|---|
| Hb (g%) | 9.2 | 8.2 | 8.8 | 7.5 | 7.8 | RT-PCR-Negative |
| PCV (%) | 26.6 | 23.6 | 24 | 23.6 | 24.9 | Rapid Antigen for SARS-CoV-2-Negative- On the day of admission |
| Total leucocyte count (cells/cu.mm) | 6900 | 5780 | 7800 | 4490 | 5430 | NS1-Negative<br>IgG and IgM Dengue- Positive on 2nd Day<br>(Titres IgG-40 and IgM-15) |
| Neutrophils (%) | 60 | 58 | 60 | 64 | 77 | |
| Lymphocytes (%) | 38 | 40 | 36 | 30 | 18 | |
| Platelet count (lakhs/cu.mm) | 0.46 | 0.60 | 0.77 | 0.697 | 0.63 | Ultrasound Abdomen-Hepatomegaly<br>Splenomegaly |
| Creatinine (mg/dL) | 1.2 | 1.2 | 1.2 | 1.1 | 1.1 | |
| NLR | 1.5 | 1.45 | 1.6 | 1.7 | 4.2 | CT Pulmonary Angiogram-On 5th Day |
| Procalcitonin (ng/mL) | 2 | | | 1.8 | | - No evidence of Pulmonary thromboembolism in the study |
| D-dimer (mcg/mL FEU) | | 10,100 | | 5920 | 3170 | - Pulmonary edema with super added infection |
| Cultures-Blood and Urine | Negative | | | | Negative | CO-RADS 4 |
| Lactate Dehydrogenase (U/ L) | | | 601 | | | Repeat RT-PCR for SARS-CoV-2-Positive |
| CRP (mg/ L) | 24 | | | | | ABG on 5th Day afternoon |
| Alkaline phosphatase (IU/L) | 689 | | | | | • pH-7.34<br>• $pCO_2$-46 mmHg<br>• $pO_2$-58 mmHg<br>• $SaO_2$-88% |
| Alanine transaminase (IU/L) | 65 | | | | | |
| Aspartate transaminase (IU/L) | 86 | | | | | HbA1c-6.5 |

**[Table/Fig-1]:** Laboratory investigations during the course.

later shifted to the wards. After a total of 16 days of admission, the patient was discharged and sent home with detailed medical advice including awake prone positioning as done during the treatment, low dose prophylactic anticoagulants (Eliquis 2.5 mg once a day for 10 days), pulse oximeter monitoring at home and asked to follow-up in two weeks.



**[Table/Fig-2]:** HRCT (thin) Axial and Coronal on Day 5.

Follow-up was remarkably fair with no new symptoms and the patient was instructed to continue taking safety precautions and also get vaccinated.

## DISCUSSION

According to WHO, globally, as of 7th June 2021, there have been 172,956,039 confirmed cases of COVID-19 (SARS-CoV-2) infection which includes 3,726,466 deaths and the numbers were still on the rise. As of 4th June 2021, a total of 1,900,955,505 vaccine doses had been administered [1]. The global burden of COVID-19 infection has been presumed to be the worst of all the pandemics to date. Most patients experience mild to moderate respiratory illness and recover without any specific treatment. The severe disease forms have been seen with significant risk factors that include advanced age and co-morbidities. The presentation and clinical history are similar in almost all viral diseases. Dengue is one of the most common vector-borne endemic disease and it continues to be a difficult disease to manage, especially during the COVID-19 pandemic. A similar case was reported wherein the patient presented with symptoms concerning an AFI with seven days history admitted in an isolation and found to be having mild positivity on rapid antigen tests for dengue virus which was later confirmed through polymerase chain reaction to being DENV Serotype 2. Also, the patient was found to be positive for RT-PCR for SARS-CoV-2 at the same time and supportively treated according to the symptoms of the disease [2].

On the contrary, the patient in this case report was found to be negative for all the possible parameters indicative for SARS-CoV-2 infection initially along with positive serologies for dengue virus infection accompanied by early findings of thrombocytopenia and mild leucopenia or lymphopenia. The patient was treated according to the symptoms and was even considered for platelet transfusions in case she starts to bleed, or the platelet count drops further below 46,000/cu.mm noted at the time of admission [Table/Fig-1]. The patient was given all possible care in a different isolation ICU (Non COVID-19) from the start after triaging removing the scope of infectivity from other patients or fomites transfer. Patient laboratory parameters suddenly changed on the 5th day of admission, overwhelming the management with respiratory acidosis, changing the neutrophil-lymphocyte ratio indicating the severity of infection with lymphopenia [Table/Fig-1].

The risk of dengue infection exists in 129 countries, and it is endemic in more than 100 countries. Around 70% of the actual burden of disease is in Asia [3]. One modelling estimate indicates 390 million global dengue virus infections per year (95% CI 284 to 528 million), of which 96 million manifests clinically [4,5]. The COVID-19 pandemic continues to spread worldwide, and it is likely to overlap with the dengue epidemics in tropical countries. Due to overlapping clinical and laboratory features, it may be difficult to distinguish dengue from COVID-19 [3].

Laboratory diagnosis of COVID-19 with underlying infection by DENV is a greater challenge. Some reports have revealed false positive dengue antibodies in COVID-19 patients who were misdiagnosed as dengue [6-8]. Also, serological cross-reactivity is very commonly seen between viral diseases and it has been reported [9,10]. The role of special serological tests such as the Plaque Reduction Neutralisation Test (PRNT) for dengue should be considered for accurate and better diagnosis though it may serve a different purpose in testing. It is considered to be the “gold standard” to characterise and

quantify circulating levels of anti-DENV Neutralising Antibody (NAb) thereby can indirectly give a better perspective of the diagnosis in the situation [11]. Also, testing for both dengue and COVID-19 with standard principles and proper isolation of suspected cases after triaging looks promising and ideal which is already being practised in institutes and universities in other countries. Though it is a tedious process, it is the ideal procedure, taking into consideration the time and space constraints.

## CONCLUSION(S)

The COVID-19 should be included in the differential diagnosis of AFI even if another infection has already been found. A strategy for precise diagnosis including many direct and indirect tests for the identification of the infection will help in minimising the time taken for management. Precautionary and prophylactic isolation of patients with AFI should be considered to prevent the spread of infection. Multi-sector differential strategies in proper prevention for both diseases should be integrated to solve this problem.

## REFERENCES

[1] World Health Organization. Coronavirus disease (COVID-19) outbreak situation. Available: Https://www. who. int/ emergencies/ diseases/ novel- coronavirus-2019 [Accessed 7 June 2021].
[2] Nasomsong W, Luvira V, Phiboonbanakit D. Case report: Dengue and COVID-19 co-infection in Thailand. Am J Trop Med Hyg. 2021;104(2):487.
[3] Wee LE, Cherng BPZ, Conceicao EP, Goh KCM, Wan WY, Ko KKK, et al. Experience of a tertiary hospital in Singapore with management of a dual outbreak of COVID-19 and dengue. Am J Trop Med Hyg. 2020;103(5):2005-11.
[4] World Health Organization. Dengue and severe dengue, 2020. Available: Https:// www. who. int/ news- room/ fact- sheets/ detail/ dengue- and- severe- dengue [Accessed 23 Aug 2020].
[5] Bhatt S, Gething PW, Brady OJ, Messina JP, Farlow AW, Moyes CL, et al. The global distribution and burden of dengue. Nature. 2013;496(7446):504-07.
[6] Chen N, Zhou M, Dong X. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: A descriptive study. Lancet. 2020;395:507-13.
[7] Ratnarathon AC, Pongpirul K, Pongpirul WA, Charoenpong L, Prasithsirikul W. Potential dual dengue and SARS-CoV-2 infection in Thailand: A case study. 2020;6(6):e04175.
[8] Tiwari L, Shekhar S, Bansal A, Kumar P. COVID-19 with dengue shock syndrome in a child: Coinfection or cross-reactivity? BMJ Case Reports CP. 2020;13(12):e239315.
[9] Brady OJ, Gething PW, Bhatt S, Messina JP, Brownstein JS, Hoen AG, et al. Refining the global spatial limits of dengue virus transmission by evidence-based consensus. PLoSNegl Trop Dis. 2012;6:e1760.
[10] Lustig Y, Keler S, Kolodny R, Ben-Tal N, Atias-Varon D, Shlush E, et al. Potential antigenic cross-reactivity between severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and dengue viruses. Clin Infect Dis. 2020;2:01-06.
[11] Thomas SJ, Nisalak A, Anderson KB, Libraty DH, Kalayanarooj S, Vaughn DW, et al. Dengue plaque reduction neutralization test (PRNT) in primary and secondary dengue virus infections: How alterations in assay conditions impact performance. Am J Trop Med Hyg. 2009;81(5):825-33. Doi: 10.4269/ajtmh.2009.08-0625. PMID: 19861618; PMCID: PMC2835862.

**PARTICULARS OF CONTRIBUTORS:**
1. Junior Resident, Department of General Medicine, Kamineni Academy of Medical Sciences and Research Centre, Hyderabad, Telangana, India.
2. Professor, Department of General Medicine, Kamineni Academy of Medical Sciences and Research Centre, Hyderabad, Telangana, India.
3. Assistant Professor, Department of General Medicine, Kamineni Academy of Medical Sciences and Research Centre, Hyderabad, Telangana, India.
4. Associate Professor, Department of General Medicine, Kamineni Academy of Medical Sciences and Research Centre, Hyderabad, Telangana, India.

**NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:**
Dr. Srikrishna Raghavendra Boddu,
1-2-234/11, HarshaKrishna Villa, New SBH Colony, Gaganmahal Domalguda,
Hyderabad-500029, Telangana, India.
E-mail: krishna030@gmail.com

**PLAGIARISM CHECKING METHODS:** [Jain H et al.]
- Plagiarism X-checker: Jun 25, 2021
- Manual Googling: Apr 30, 2021
- iThenticate Software: Jul 31, 2021 (9%)

**ETYMOLOGY:** Author Origin

**AUTHOR DECLARATION:**
- Financial or Other Competing Interests: None
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. Yes

Date of Submission: **Mar 15, 2021**
Date of Peer Review: **May 03, 2021**
Date of Acceptance: **Jul 14, 2021**
Date of Publishing: **Aug 01, 2021**