Two viruses in a pod: a case series of coinfection of COVID-19 with dengue

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INTRODUCTION

The diagnosis and management of Coronavirus disease 2019 (COVID-19) are associated with a unique problem in dengue-endemic countries [1]. Owing to the similarity in the presenting features of dengue and COVID-19, it is often difficult to differentiate between the two entities. It becomes all the more difficult when both the infections present simultaneously. The management of these cases of coinfections has its challenges as well. In this case series, we describe seven cases of coinfections of dengue with COVID-19 in a tertiary care centre in South India.

CASE SERIES

The records of all patients admitted to our tertiary care teaching hospital between June 2020 and April 2021 were screened for cases of coinfection of COVID-19 and dengue. The cases of coinfections were identified from the medical records of the hospital using the International Classification of Diseases codes for dengue and COVID-19. A total of seven cases of dengue coinfection were identified during this period (Table 1). All seven patients presented with fever. The duration of febrile illness ranged from 3 to 9 days. Constitutional symptoms such as myalgia (n=5) and fatigue (n=5) were also common. Abdominal pain and rash (diffuse erythematous) were seen in two patients each. None of the patients had any bleeding manifestations, jaundice or hepatosplenomegaly.

Case 1

A middle-aged hypertensive lady presented with fever and vomiting for 3 days. COVID-19 real-time polymerase chain reaction assay (PCR) on the throat swab done at admission was positive. Dengue NS1 antigen Enzymatic-linked immunosorbent assay (ELISA) test sent because of thrombocytopenia and transaminitis was also positive. She was treated symptomatically with antipyretics and intravenous (IV) fluids. She had an uneventful hospital stay and was discharged after 8 days of hospital admission.

Case 2

A middle-aged diabetic gentleman presented with fever, erythematous rash and thrombocytopenia. He was found to be positive for both COVID and dengue. In addition to antipyretics and IV fluids, he was transfused with platelets as his platelets dropped to 9000/mm³ in the hospital. The rest of the hospital stay was uneventful, and he was discharged in 7 days.

Case 3

A young pregnant lady (33 weeks’ gestation) presented with fever, cough and thrombocytopenia. She was found to be positive for both infections. She was managed with oral fluids and antipyretics. Her hospital course was uneventful, and she was discharged after 7 days of hospital stay.

Case 4

A middle-aged hypertensive male presented with fever, generalized erythematous rash, thrombocytopenia and raised inflammatory markers. He was diagnosed with both infections. During the hospital stay, platelet count dropped to 7000/mm³. He was treated with antipyretics, IV fluids and platelet transfusion. His platelet...
count improved during the hospital stay, and he was discharged after 8 days.

**Case 5**

A middle-aged gentleman presented with fever and respiratory distress. He was hypoxic on arrival and was immediately started on oxygen using a venturi mask. Chest X-ray showed bilateral peripheral opacities. In view of positive contact history and presenting features, COVID PCR was sent, which was reported as positive. In view of thrombocytopenia, dengue IgM ELISA was sent, which turned out to be positive. He was started on injection dexamethasone (6 mg IV once daily) and low molecular weight heparin (40 mg subcutaneously once daily). He was eventually weaned-off oxygen and discharged after 11 days.

**Case 6**

A young male patient presented with fever, thrombocytopenia and transaminitis. He was found to be positive for both COVID-19 and dengue. His platelet count dropped rapidly to 12,000/mm$^3$ during the hospital stay. In anticipation of a further drop in platelets, he was transfused with platelets. His rest of the hospital stay was uncomplicated, and he was discharged after 8 days.

**Case 7**

A young male presented with a history of fever for 3 days. He was referred from a primary care hospital with a diagnosis of dengue. Since the patient had fever, he was tested for COVID as per the hospital protocol. He received antipyretics and IV fluids. He improved clinically and was discharged after 9 days.

The diagnosis of dengue was made using NS1 antigen in six patients. The remaining patient was diagnosed based on IgM ELISA. Dengue was tested in any patient presenting with thrombocytopenia or rash, or both. All patients were diagnosed with COVID-19 by real-time reverse transcriptase-polymerase chain reaction assay. It was our hospital protocol during the above time period to test all patients presenting with fever for COVID-19 in view of the pandemic. Due to the similarity in the initial presentation of the two diseases, it is difficult to ascertain which disease the patient contracted first. Barring one case where dengue was diagnosed before the hospital presentation, tests for both samples were sent within 24 h of hospital admission. This period of 24 h is less than the average incubation period of both diseases. Therefore, it is unlikely that any of the infections were hospital-acquired. It is, however, possible that some of the patients acquired COVID-19 during transport to the hospital. Laboratory investigations revealed thrombocytopenia in six patients (Table 2). Four patients had leucopenia at admission, and none had leucocytosis. Transaminitis was seen in all but one patient in our series. All patients except one had mild or moderate COVID-19, according to the WHO classification [2]. None of the patients required mechanical ventilation or hemodialysis. All the patients had a complete recovery. The mean duration of hospital stay among the patients was 8.28 days. The course of hospital stay is summarized in Table 3.

### DISCUSSION

Coinfection of COVID-19 with dengue poses a diagnostic and therapeutic dilemma to primary care physicians practising in tropical countries [3]. This dilemma is especially important during the monsoons as dengue is a vector-borne disease associated with waterlogging and mosquito breeding. Although fever, myalgia and fatigue can be commonly seen in both COVID-19 and dengue, erythematous rashes are more commonly attributed to dengue fever when compared with COVID-19 [4–6]. In this series, the erythematous rash was seen in two patients of coinfections. Thrombocytopenia is another important differentiating factor between these two infections. Although it is uniformly seen in dengue, thrombocytopenia is uncommon with COVID-19. In this series, thrombocytopenia was seen in six patients. Thrombocytopenia was observed in dengue–COVID-19 coinfections in other case series as well [7, 8].

All but one patient in our case series was diagnosed with dengue using NS1 antigen. IgM anti-dengue ELISA was used to diagnose dengue in one patient who presented with >5 days of fever. It must be emphasized here that although antigen testing is highly specific, it might be negative after the first 5 days of illness. IgM ELISA for dengue is done in such cases, which can be falsely positive [9]. This false positivity can be either due to high prevalence and background positivity or cross-reactivity.

Management of patients with coinfection poses some unique challenges, such as fluid resuscitation, management of coagulopathy and steroids. The pathogenesis of dengue involves increased vascular permeability that leads to a decrease in intravascular volume. Fluid resuscitation, therefore, forms the cornerstone of therapy in patients with dengue. In absence of a diagnosis of dengue coinfection in a patient with COVID-19, fluid therapy may get neglected leading to poor outcomes. Also, since COVID-19 creates a pro-thrombotic state, patients with severe COVID-19 are prescribed anticoagulation. Dengue, however, is associated with thrombocytopenia, which precludes the use of anticoagulation. Although none of our patients had bleeding manifestations, three were given platelet transfusions. Although recent evidence suggests the futility of such transfusions in the absence of bleeding, the national guidelines recommend prophylactic platelet transfusion may be considered in patients with a platelet count of <10,000/mm$^3$ in the absence of...
bleeding manifestations [10]. In our series, only one patient had severe COVID-19. Fortunately, the patient did not have severe thrombocytopenia, and anticoagulation could be prescribed. A study from Bangladesh suggested that in cases of coinfection, anticoagulation can be administered when platelets are above 75,000/mm³ [11]. More research is required to establish the appropriate strategy for managing coagulopathy in coinfections. Perhaps, diagnostic tests such as thromboelastography may find an application in such situations. The choice and dose of anticoagulation in COVID-19 have been studied in various trials. We used the standard prophylactic dose of low molecular weight heparin (40 mg subcutaneously once daily) for one patient (Case 5). This was per the hospital protocol at that time, which recommended prophylactic heparin to patients with COVID-19 requiring oxygen and therapeutic anticoagulation with low molecular weight heparin (40 mg subcutaneously twice daily) for those patients who required non-invasive ventilation and mechanical ventilation. All the patients in our case series had a complete recovery. The pregnant patient with coinfection also had an uneventful recovery. The cases series from Brazil and Argentina also reported no ICU admission or mortality suggesting that coinfection might not necessarily increase fatality rates [4, 7].

We report this case series to highlight the importance of suspecting dengue coinfection in patients with COVID-19. Although COVID-19 should be suspected in any patient presenting with fever, additional coinfection with dengue should be suspected in those with fever accompanied by a rash, thrombocytopenia or both. It is important to identify dengue in patients with COVID-19 as dengue patients require meticulous fluid therapy guided by the hydration status. Also, steroids and anticoagulation for severe COVID-19 must be judiciously used in dengue patients, especially those with severe thrombocytopenia. The coinfection with the two viruses may not necessarily lead to worse outcomes.

**CONFLICT OF INTEREST STATEMENT**

No conflicts of interest.

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**ETHICS APPROVAL**

Kasturba Medical College and Kasturba Hospital Institutional Ethics Committee approval was taken (IEC no. 546/2021).

**CONSENT**

Consent was taken by the patients for including their data in the study.

**GUARANTOR**

Dr Nitin Gupta and Dr Prithvishree Ravindra are nominated as guarantors of the manuscript.

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