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Co-infection with Dengue and COVID-19: A Case Report of Multiorgan Dysfunction in a Child

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Abstract:
Concomitant severe dengue with COVID-19 can be difficult to diagnose as both diseases have similar symptoms and laboratory findings. Bangladesh is currently facing a double burden of severe dengue and SARS-CoV-2 infection. Co-infection with these viruses can result in severe morbidity. Worldwide this co-infection is rare. However, we present a complicated case of severe dengue with SARS-CoV-2 infection. The child presented with multiorgan dysfunction with plasma leakage and positive for dengue nonstructural protein 1 antigen and reverse transcription polymerase chain reaction (RT-PCR) for SARS-CoV-2. Echocardiographic evaluation showed coronary arterial abnormalities. Patient was successfully managed according to dengue syndrome guidelines and received intravenous immunoglobulin with methyl prednisolone, aspirin for coronary arterial involvements. Through this case report, we aim to describe the severity of co-infection of dengue and SARS-CoV-2 in a child in a dengue endemic region during the COVID-19 pandemic. It can be fatal without early and appropriate management.

Key Words: *Dengue with Covid-19, MIS-C due to Covid-19, Co-infection with Dengue and COVID-19, Severe Dengue, SARS-CoV-2.*

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I. Introduction

Dengue fever is the most rapidly spreading mosquito-borne viral disease worldwide with an unpredictable clinical course. Most cases are usually mild and do not require hospitalization; however, some patients develop severe complications, including shock, bleeding manifestations, encephalopathy, hepatic failure, renal failure, cardiac arrhythmia, and myocarditis [1, 2].

Amidst the SARS-CoV-2 pandemic, Southeast Asia is also experiencing a dengue virus outbreak. Co-infection with both viruses poses a major health problem [3]. This case report aims to demonstrate simultaneous severe dengue and COVID-19 in a previously healthy child. Missing a case due to the overlapping symptoms and signs, pathological similarities can lead to a fatal outcome. To the best of our knowledge, this is the first case report from Bangladesh demonstrating concomitant severe dengue and COVID-19 in pediatric patients.

II. Case Report

A four-year-old previously healthy, well thriving, boy, weighing 17 kg from Dhaka, was admitted with a high continued fever for four days with abdominal pain, loose motions, and emesis, headache for the last two days. He had no history of flu-like symptoms, cough, or respiratory distress in the past month. There was a history of close contact with a COVID-19 patient, within one month of the illness. He had no previous history of dengue fever. He was tested positive for NS1 Ag for dengue on the second day of fever.

On examination, patient was febrile (Temp, 102°F), tachypneic, and tachycardic with unrecordable blood pressure. On auscultation of lungs revealed bilateral coarse crepitations with good air entry. Abdomen was mildly distended, flanks were full with mild, diffuse abdominal tenderness without any organomegaly. He had mucosal bleeding and petechial rashes on extremities and generalized edema with no lymphadenopathy. Oxygen saturation (SpO_2) was 94% in room air, 98% with 2L/min oxygen via nasal cannula. Initial investigations showed thrombocytopenia, positive C-reactive protein, hypocalcemia, hypoalbuminemia, altered liver functions and coagulation profiles (Table 1). His renal functions and serum electrolytes were within normal limits. The chest X-ray (CXR) initially revealed bilateral pulmonary infiltrations. Blood, urine, stool and throat swab culture were negative. Nasopharyngeal swab for RT-PCR for SARS-CoV-2 was positive. Patient was

isolated and treated for Expanded Dengue Syndrome with plasma leakage with SARS-CoV-2 infection, with intravenous (IV) broad spectrum antibiotics, inotropes, and colloids. Echocardiogram on the 4th day of fever was normal with good biventricular systolic functions (ejection fraction, EF- 70%). On the 6th and 7th day of illness, he developed cheilosis, and an erythematous rash over the trunk.

On the 8th day of fever, the patient developed a cough and respiratory distress, still febrile and maintaining blood pressure with inotropes (nor-adrenaline, dobutamine). Oxygen saturation was 88% in room air and 96% with 5L/min oxygen through face mask. Repeat CXR revealed bilateral inflammatory lesions with pleural effusion (Figure I). The ECG was still within normal limits. Dengue IgM was also positive after seven days of fever. However, echocardiogram on 8th day revealed dilated coronary arteries [Left main coronary artery, LMCA- 5.3 mm (+2.8 standard deviation, SD), Left coronary artery, LCA- 4.0 mm (+2.5 SD)] with the loss of distal tapering (Figure II) and good left ventricular (LV) function (ejection fraction, EF, 69%) (Figure III). Serum ferritin, NT-pro-BNP, D-dimer, serum troponin I were markedly raised (Table 1). According to pediatric cardiologist, we administered one dose of intravenous immunoglobulin (IVIG) 2 g/kg, over 24 hours. Thereafter, methyl prednisolone, subsequently aspirin (3 mg/kg/day), enoxaparin (0.5mg/kg/dose, 12 hourly for 10 days) was added.

Meanwhile, the patient became afebrile, general condition improved with normal vitals without inotropes, SpO_2- 98% in room air, a gradual return of appetite. Three days after the IVIG, serum ferritin, NT-pro-BNP and serum troponin I were decreased. Hematocrit came to baseline with corrected thrombocytopenia, and coagulopathy. At this point, the patient was transferred to the ward and discharged after five days with the necessary advice and follow-up appointment.

Table no 1: Shows investigation profile of the case.

Investigations	**Reference range**	**Before management**	**After management**
Hemoglobin (g/dl)	male, 12-17; female, 11.5-15.5	13.2	12.7
Hematocrit (%)	male, 40-52; female, 36-48	38	36.9
Total WBC (10^9/L)	4-11	4.6	8.6
Neutrophils (%)	40-75	60	80
Platelet count (10^9/L)	150- 450	35	195
C-reactive protein (mg/dL)	0.01-0.30	3.5	1.04
Serum procalcitonin (ng/mL)	<2.0	0.62	1.5
Serum albumin (g/dl)	3.4-5.0	2.0	5.06
Serum calcium (mg/dl)	8.20- 10.20	6.6	8.9
Alanine transferase; ALT (U/L)	<40	303	58
Aspartate aminotransferase; AST (U/L)	<37	755	27
Prothrombin time; PT (sec)	control- 12	18	12
Activated partial thromboplastin time; APTT (sec)	control- 28	40	36
Blood urea (mg/dl)	10-40	28	35
Serum creatinine (mg/dl)	0.2-0.7	0.68	0.66
Serum ferritin (ng/ml)	7-140	>2000	580
D- dimer (mg/L)	<0.5	>5	1.35
NT- pro-B-type natriuretic peptide (pg/ml)	<125	4038	662
Serum troponin I (ng/ml)	0.00-0.056	0.398	0.011

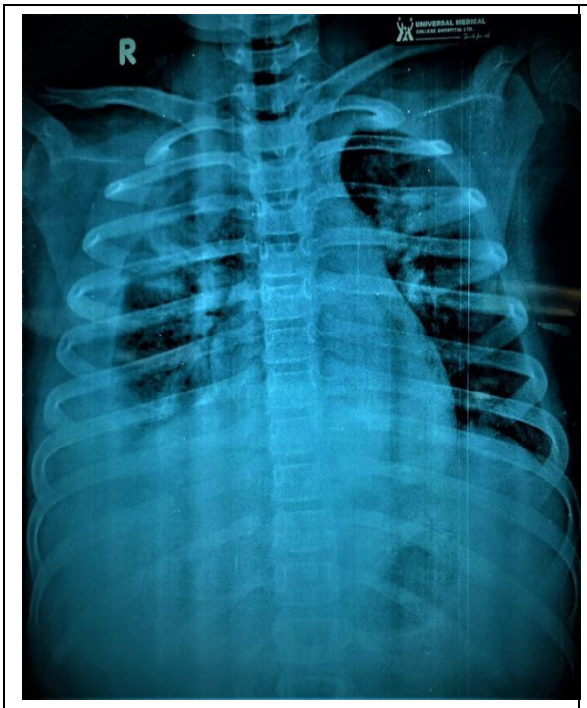

Fig. I: CXR of the case showing bilateral pneumonitis with pleural effusion.

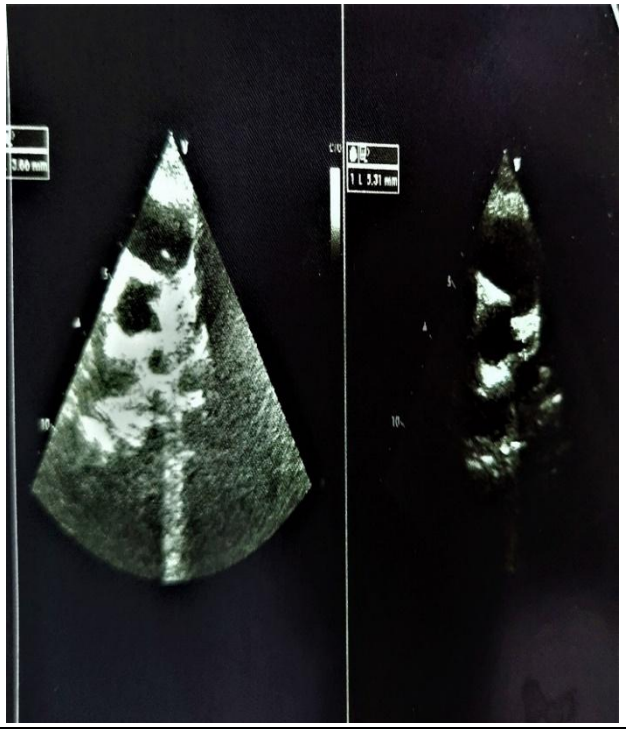

Fig. II: Echocardiograph showing dilated LMCA and LCA.

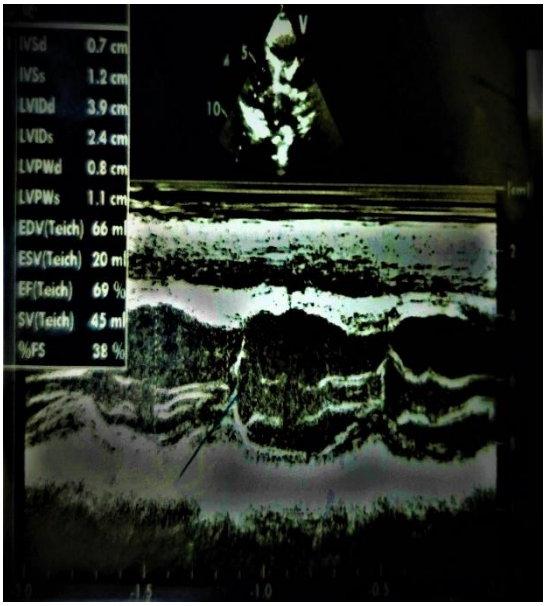

Fig. III: Echocardiograph showing fair biventricular systolic functions (ejection fraction, EF- 69%).

III. Discussion

Bangladesh experienced its deadliest outbreak of dengue in 2019, with 101,354 reported cases [3]. Meanwhile, the worldwide burden of severe COVID-19 and MIS-C due to COVID-19 in the pediatric age group is increasing according to several cohort studies [4, 5]. In pediatric age group, SARS-CoV-2 infection thought to cause less severe disease, but hyperinflammatory state leading to multiorgan dysfunction (MIS-C) and intensive care admission is a concern [4]. Feldstein et al has shown that 73 (39%) of pediatric MIS-C due to COVID-19 was RT-PCR positive [5]. Signs and symptoms of these two entities can overlap significantly and can be difficult to distinguish.

This case report describes co-existing severe dengue with COVID-19 in a previously healthy child with high continued fever, with bleeding manifestations, diffuse abdominal pain, emesis, diarrhea, headache, extremity edema. He was initially in profound shock with pleural effusion and pneumonitis. Both dengue and severe COVID-19 can give these features, but the CXR findings of pneumonic infiltrations are consistent with COVID-19 infections. In dengue, pleural effusions are commonly observed. Abdominal pain and vomiting are common with dengue, but diarrhea is more commonly observed in COVID-19 infection [6]. Along with petechial and purpuric rashes, he developed erythematous polymorphous rash over extremities and cheilosis on 6th to 7th day of presenting complaints, which was difficult to differentiate dengue from the COVID-19 rashes. Similar types of rashes are observed in both viral infections due to the pathophysiological similarities. He didn't have any palpable lymph nodes, strawberry tongue or conjunctival congestion, commonly seen in Kawasaki disease. Profound shock and capillary leakage are common in severe dengue and severe SARS-CoV-2 infection or MIS-C due to SARS- CoV-2 [6, 7].

The patient had necessary laboratory workups during admission. Raised hematocrit (>20%), thrombocytopenia, and leucopenia were observed; these abnormalities settled with timely management. Dengue and SARS-CoV-2 share some pathological features such as capillary leakage, thrombocytopenia, and coagulopathies. Severe thrombocytopenia is not commonly observed in COVID-19 [4, 6]. However, it is common during the critical phase of dengue Shock Syndrome. Inflammatory markers were high, with raised D-dimer, altered liver function tests, and coagulopathy. Coagulopathy is one of the main pathologies associated with dengue infection but is also seen in SARS-CoV-2 infection [1, 6, 7]. In severe dengue and severe COVID-19, D-dimer levels seem to be increased. Evidence suggests a hypercoagulable state in COVID-19 patients, leading to pulmonary embolism, venous thromboembolism, myocardial infarction, stroke, and microvascular thrombosis [6, 7]. Though ECG was normal, cardiac enzymes were significantly high (Table 1). During admission, echocardiogram of the patient was normal but subsequently he developed coronary arterial dilatations. In Severe dengue, cardiac involvements are not uncommon including raised cardiac enzymes, sinus bradycardia, ST and T changes in ECG, global hypokinesia and reduced ventricular functions evident in echocardiogram. Cardiac involvement in dengue leads to poor prognosis [6-8]. Coronary arterial involvement is commonly seen in MIS-C due to COVID-19 or Kawasaki disease, but no case report till date demonstrated coronary arterial abnormalities due to dengue [1, 2]. Several studies have shown an association of raised troponin I and NT-pro-BNP with ventricular dysfunction and coronary artery abnormalities in severe COVID-19 infection or pediatric MIS-C with poor prognosis [4, 5].

IV. Conclusion

Overlapping outbreaks of SARS-CoV-2 infection and dengue are occurring in some Asia countries. In dengue endemic countries like Bangladesh, co-infection with COVID-19 can pose a serious diagnostic challenge and requires timely intervention. Cross-reactivity can occur between the antibodies of both viruses, and the similar signs, symptoms, and laboratory findings make the diagnosis harder. In conclusion, the unusual course of severe dengue complicated with COVID-19, required IV immunoglobulin and steroids, aspirin enoxaparin. Due to pathological cross reactivity the chances of missing appropriate diagnosis are more with delaying the start of appropriate management. Though one case report does not reveal the actual picture, but complicated cases like this one may help the physicians to keep in mind that rather than focusing on a single disease, there is the possibility of dual infection of dengue and COVID-19, especially in dengue endemic areas.

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We want to give our gratitude to the doctors and nurses who worked hard to save the life of the critically ill patient and thankful to the parents for the confidence they lay upon us.

Conflict of Interest:

None.

Consent:

Informed written consent was taken from the guardians of the patient.

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