

Case Series

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Dengue and SARS-CoV-2 co-infection: A case series from Sri Lanka and literature review

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Abstract

Background: The spreading of COVID 19 pandemic in Dengue endemic tropical countries such as Sri Lanka has increased the risk of dual outbreaks as well as the risk of Dengue and COVID 19 coinfection. Such coinfections are clinically challenging as Dengue and COVID 19 show similarities in symptoms and laboratory findings.

Case presentation: This is a case series of four patients presented to a COVID 19 treatment hospital, Sri Lanka. All four patients were diagnosed to have Dengue and COVID 19 coinfection, while two of them were complicated with Dengue Hemorrhagic Fever. Fluid resuscitation according to the dengue management guideline and supportive treatments improved their clinical symptoms and all recovered fully.

Conclusion: Here, we emphasize the similar clinical symptoms and laboratory findings in COVID 19 and Dengue infections and the importance of extensive diagnostic workup and timely management. Raising awareness among health care providers as well as the public is necessary to face upcoming challenges during the COVID 19 pandemic especially in dengue-endemic countries.

Keywords: COVID 19; dengue; SARS-CoV-2; covid -19; co-infection.

Abbreviations: SARS-CoV-2: Severe Acute Respiratory Syndrome Coronavirus-2; rRT-PCR- Real time Reverse Transcription Polymerase Chain Reaction; ELISA: Enzyme Linked Immunosorbent Assay; ALT: Alanine Transaminase; AST: Aspartate Transaminase.

Introduction

COVID 19 pandemic caused by Severe Acute Respiratory Syndrome Coronavirus- 2 (SARS-CoV-2) has spread worldwide including Sri Lanka [1]. Being a Dengue endemic country Sri Lanka is also facing dengue outbreaks during the rainy seasons [2]. Dengue is considered the commonest arboviral infection

in Southeast Asia [3,4]. According to the Epidemiological Unit, Ministry of Health, Sri Lanka; a total of 31,162 suspected Dengue cases were reported for the year 2020 and 6389 suspected Dengue cases from January 2021 until the time of writing this report. To date, Sri Lanka has 101,379 confirmed COVID 19 cases with 642 deaths [5].

Both Dengue virus and SAR-CoV-2 infections have similar clinical and laboratory features as well as the disease course making the differentiation between the two diseases difficult and there is always the possibility of coinfection [6,7]. Whether such coinfection may lead to greater severity is not yet known [7]. Cases were also reported with serological cross-reactivity between Dengue and COVID 19 causing false positive detection of SARS-CoV-2 infection in dengue patients [1,8]. Reports about Dengue and SAR-CoV-2 coinfection are scarce [9]. Coinfection of these viruses has been reported in Dengue endemic countries such as Singapore, Thailand, India, and Bangladesh [10].

Herein, we present four cases of patients who presented to a COVID 19 treatment hospital, Sri Lanka with possible Dengue and COVID 19 coinfection with two of them having Dengue haemorrhagic fever.

Cases

Case 1

A 56-year-old male with comorbid hypertension and dyslipidemia presented with fever for 6 days associated with headache, stuffy nose, arthralgia, and myalgia. On admission, he had a temperature of 36.7°C, a pulse rate of 102 beats per minute, blood pressure of 142/107 mmHg, and Oxygen saturation of 96% on room air. His Real-Time Reverse Transcription Polymerase Chain Reaction (rRT-PCR) test for SARS-CoV-2 and Dengue NS-1 antigen test which were done on day 01 of fever were positive. However, his Dengue ELISA serology of anti-dengue IgM and IgG done on day ten was negative. Other laboratory findings are tabulated in Table 01. During the hospital stay, he developed anosmia and diarrhea. He did not develop other complications of dengue infection such as plasma leakage or shock. He was treated for Dengue fever and COVID 19 coinfection of mild severity. He received supportive treatment and became asymptomatic gradually. He was discharged after 14 days as per Sri Lankan guidelines at the time.

Table 1: Indicating laboratory profile of case 1.

	Day 06	Day 07	Day 09	Day 10	Normal Range
Leucocytes $\times 10^9/L$	4.95	4.76	4.85	6.20	4.00-10.00
Neutrophils $\times 10^9/L$	2.30	2.21	2.61	4.27	2.00-7.00
Lymphocytes $\times 10^9/L$	2.17	2.17	1.78	1.49	0.80-4.00
Hemoglobin g/dl	14.2	14.5	13.4	13.6	12.0-16.0
Hematocrit %	43.3	44.1	40.9	41.4	40.0-54.0
Platelets $\times 10^9/L$	106	155	146	164	150-450
ALT U/L	56	70	51		9-50
AST U/L	29	37	23		15-40
Albumin g/L	46	48.7	44.5		40-55

Case 2

A previously healthy 33-year-old male presented with fever and dry cough for one day. He also had a headache, diarrhea, arthralgia, and myalgia. On examination, he was hemodynamically stable with a temperature of 36.9°C, respiratory rate of 16 breaths per minute, pulse rate of 58 beats per minute, blood pressure of 103/70 mmHg, and Oxygen saturation of 100% on room air. His important laboratory parameters are summarized in Table 02 which shows leucopenia and thrombocytopenia. Rapid antigen test for COVID 19 was positive on the first day of illness. Dengue NS-1 antigen test was also positive on the same day. Hence, he was treated as Dengue and COVID 19 coinfection. Dengue IgM and IgG antibodies were done on day 10 and were negative. He received supportive treatment with fluid management. He completely recovered and did not develop any complications. He was discharged after 10 days of inward treatment.

Table 2: Indicating laboratory profile of case 2.

	Day 01	Day 02	Day 04	Day 05	Normal Range
Leucocytes $\times 10^9/L$	3.40	3.08	4.61	4.47	4.00-10.00
Neutrophils $\times 10^9/L$	0.87	1.03	1.91	1.61	2.00-7.00
Lymphocytes $\times 10^9/L$	2.08	1.67	2.22	2.28	0.80-4.00
Hemoglobin g/dl	14.2	14.0	14.1	13.2	12.0-16.0
Hematocrit %	41.6	40.2	40.5	38.4	40.0-54.0
Platelets $\times 10^9/L$	86	64	106	115	150-450
ALT U/L	31.9				9-50
AST U/L	15.9				15-40
Albumin g/dl	3.45				3.50-5.20

Case 3

A previously healthy 34-year-old male presented with fever and diarrhea for the past 4 days associated with a sore throat, nausea, headache, arthralgia, and myalgia. He had a temperature of 36.6°C, respiratory rate of 20 breaths per minute, pulse rate of 72 beats per minute, blood pressure of 118/70 mmHg, and Oxygen saturation of 100% on room air on admission. His rapid antigen test for COVID 19 was positive on day 2 of fever and had leucopenia and thrombocytopenia on admission to the COVID 19 treatment center. On suspicion of Dengue, Dengue NS-1 antigen was done and it was positive. His laboratory profile is tabulated in Table 03. Later, he developed right hypochondrial tenderness with normal liver span and had a significant drop in postural blood pressure. Ultrasound scan of the abdomen showed evidence of plasma leakage with pericholecystic and hepatorenal pouch fluid collection. Urine output was normal. Dengue Hemorrhagic Fever was diagnosed and the patient was managed according to the DHF management guidelines with active monitoring and fluid resuscitation and recovered from DHF without further complication. Further, he developed a productive cough which was treated with Azithromycin for 3 days. His chest x-ray was normal and dengue IgM and IgG antibodies were positive. He improved gradually and was discharged after completion of the mandatory isolation period.

Table 3: Indicating laboratory profile of case 3.

	Day 04	Day 05	Day 07	Day 10	Normal Range
Leucocytes $\times 10^9/L$	2.84	2.81	4.34	5.64	4.00-10.00
Neutrophils $\times 10^9/L$	1.73	1.18	1.85	2.46	2.00-7.00
Lymphocytes $\times 10^9/L$	0.82	1.03	1.78	1.85	0.80-4.00
Hemoglobin g/dl	16.2	14.4	15.9	16.2	12.0-16.0
Hematocrit %	49.9	43.2	46.9	47.6	40.0-54.0
Platelets $\times 10^9/L$	41	15	36	150	150-450
ALT U/L	138.9	149.8	131.9	147.8	9-50
AST U/L	141.9	166.3	150.5	91.7	15-40
Albumin g/dl	4.05	3.43		4.07	3.50-5.20

Case 4

A 16-year-old adolescent male presented with fever for the past 5 days. He also had a headache, diarrhea, anosmia, arthralgia, and myalgia. He also complained of abdominal pain on admission. He did not have significant past medical history including dengue fever. On examination, he had a temperature of 36.6°C, respiratory rate of 22 breaths per minute, pulse rate of 72 beats per minute, blood pressure of 95/68 mmHg with no postural drop in blood pressure, normal capillary refilling time, and Oxygen saturation of 98% on room air. His rRt-PCR which was done on day 3 of fever became positive for COVID 19. On admission, he had positive Dengue NS-1 antigen, positive anti-dengue IgG, and negative anti-dengue IgM with a Platelet count of $67 \times 10^9/L$ and Packed Cell Volume (PCV) of 38. Bedside ultrasound scan of the abdomen was normal on admission and Chest X-ray was normal. He was managed accordingly as coinfection with dengue fever and Covid-19 infection. However, his condition deteriorated later on the same day and he became hemodynamically unstable with low blood pressure (88/53mmhg), tachycardia (119 beats per minute), prolonged capillary refilling time, and tachypnea. Repeat bedside ultrasound scan of the abdomen was evident of plasma leakage with fluid in the hepatorenal pouch and pericholecystic edema. His venous blood gas showed a pH of 7.34, HCO_3^- of 24.7 mmol/L, and lactate of 3.3 mmol/L with a low ionized calcium level and at the time PCV was 47. Other investigations are tabulated in Table 04. The diagnosis of dengue shock was made and was managed in the High Dependency Unit. He was resuscitated with two boluses of 0.9% saline (10 ml/kg) and calcium was corrected with 10% calcium gluconate. He required an intravenous Dextran bolus as well and became stable after Dextran bolus and then intravenous 0.9% saline was given accordingly and managed as per Sri Lankan DHF management guideline. Chest x-ray (PA) done during the recovery phase of DHF (Figure 1) showed mildly increased / serially enlarging cardiothoracic ratio and sharp cardiac borders and small left pleural effusion with no pulmonary nodules or consolidation. Pericardial effusion was suspected and this was confirmed by a 2D echocardiogram and there was no evidence of cardiac tamponade. His ECG was normal. Repeat 2D echocardiogram prior to discharge showed mild pericardial effusion. His condition improved over the next few days and was discharged after 14 days of hospitalization.

Table 4: Indicating laboratory profile of case 4.

	Day 05	Day 06	Day 07	Day 11	Normal Range
Leucocytes $\times 10^9/L$	3.66	7.01	6.75	5.72	4.00-10.00
Neutrophils $\times 10^9/L$	2.94	5.23	3.77	2.46	2.00-7.00
Lymphocytes $\times 10^9/L$	0.42	1.11	2.15	2.72	0.80-4.00
Hemoglobin g/dl	13.0	13.4	13.3	13.6	12.0-16.0
Hematocrit %	37.4	39.3	39.4	41.3	40.0-54.0
Platelets $\times 10^9/L$	27	47	60	316	150-450
ALT U/L	52	74	67	98	9-50
AST U/L	104	233	241	120	15-40
Albumin g/L	40.4	34.1	33.2	47.2	40-55

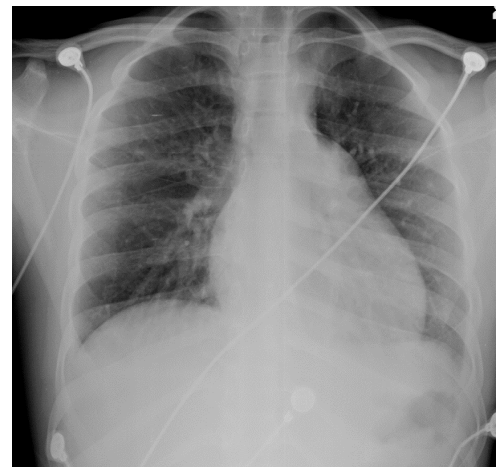


Figure 1: Chest X-ray (PA) of case 4 showing mildly increased / serially enlarging cardiothoracic ratio and sharp cardiac borders and small left pleural effusion with no pulmonary nodules or consolidation.

Discussion

A major challenge faced by health care providers in Dengue endemic countries during the COVID 19 pandemic situation is the differentiation between Dengue and COVID 19 infection because they have similar clinical and laboratory findings [1]. Fever, headache, arthralgia, myalgia, anorexia, diarrhea, nausea, and vomiting are common symptoms in both Dengue and COVID 19 and they were the prominent clinical features of all four cases we have reported [7,11]. Though not been identified in these cases, skin manifestations such as rashes/petechiae which are commonly found in dengue have also been reported in COVID 19 [12]. Respiratory symptoms such as cough, rhinopharyngitis, dyspnea, and anosmia are more discriminating features of COVID 19 [7]. Hemoconcentration and plasma leakage are unique manifestations of Dengue [13]. In coinfections, one virus can suppress or augment the other leading to varying clinical manifestations [9].

Dengue and COVID 19 also share similar laboratory findings such as leucopenia, thrombocytopenia, and raised ALT/AST which is evident in the above cases as well [1,14]. Confirmation of COVID 19 was by positive rRt-PCR in 2 patients and the other two patients had positive rapid antigen tests for COVID 19. Dengue was confirmed by detection of NS-1 antigen, though the gold standard for diagnosis of dengue is either by virus isolation or rRT-PCR [9]. Out of the 4 cases, 2 had negative anti-IgM

and IgG despite dengue NS-1 antigen been positive. Two cases had positive dengue serology. However, previous reports have stated not to use dengue virus antibody assay results as clinical decision-making tools in a coinfection as serological cross-reactivity between Dengue and COVID 19 has been documented [6,8]. The antigenic similarity between the two viruses has been identified as the potential cause for the cross-reactivity [1,6]. Hence, the production of anti-Dengue virus antibodies during SARS-CoV-2 infection can result in a false positive dengue IgM in confirmed COVID 19 cases[1]. Similarly, false-positive COVID 19 serology can occur in confirmed Dengue patients[8]. Positive Dengue serology in our cases can also be attributed to serological cross-reactivity.

At the current state, health care providers are more focused on the detection of COVID 19. Further investigations are performed mostly after receiving the results of rRT-PCR which might lead to potentially dangerous diagnostic delays [7]. In dengue, the critical phase occurs between 3-8 days of illness and lasts for 48 hours, and a 48-hour delay in diagnosis can be potentially lethal [4,7]. Hence, rapid antigen detection tests were used for the initial screening of patients with non-specific presentations. In addition, the possibility of Dengue and COVID 19 coinfection was considered as well. Incorrect or delayed diagnosis can lead to serious consequences as each disease has different clinical management such as fluid resuscitation, use of anticoagulants, corticosteroids, and early mechanical ventilation [11,15].

The risk of coinfection has increased as COVID 19 pandemic is spreading across tropical countries[16]. Health care providers in Dengue endemic tropical countries need to be aware of the possibility of coinfection and suspected cases need to be investigated for both Dengue and COVID 19 and isolated while awaiting the results [13,17]. However, this can overburden the public health system in a resource-limited tropical hospital setting such as in Sri Lanka [13]. On this ground, raising public awareness regarding infection by both COVID 19 and Dengue is necessary [7]. Continuing Dengue prevention methods such as destroying vector breeding places are equally important along with COVID 19 prevention measures [7,8]. Both Dengue and COVID 19 patients present initially with similar clinical symptoms and laboratory findings as evidenced by the above cases. Hence, extensive diagnostic workup with specific investigations needs to be carried out. Though coinfections are rare, health care providers need to be aware of COVID 19 and Dengue coinfection, especially in Dengue endemic countries such as Sri Lanka. Dengue prevention strategies must be continued during this pandemic situation in order to prevent co-epidemics.

Declarations

Ethics approval and consent to participate: Not applicable

Consent for publication: Written informed consent was obtained from the patients and written informed consent was obtained from the father for the patient who is 16 years old for publication of this case reports and any accompanying images. A copy of the written consents are available for review by the Editor-in-Chief of this journal.

Availability of data and materials: Not applicable

Competing interests: The authors declare that they have no competing interests.

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