

COVID-19 pandemic in Dengue endemic areas: A case report

Kinal Bhatt*; Maulik Lathiya; Niravkumar Godhani; Ghanshyam Motisariya; Marcos Sanchez-Gonzalez

*Corresponding Author: Kinal Bhatt

Division of Clinical & Translational Research, Larkin Health System, 7000 SW 62nd Ave, Suite 601 South Miami, FL 33143, USA

Phone: +1-928-225-0273; Email: kinalbhatt@gmail.com

Abstract

While COVID-19 caused by Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) continues to spread rapidly, raising hospitalizations and fatality rate in majority of the affected countries globally, the South and South-East Asian and Latin American countries are forced to prepare for yet another epidemic of Dengue fever. Although rare, increased risk of COVID-19 and Dengue co-infection threatens to further burden the health care system in Dengue endemic areas, which are also experiencing COVID-19 pandemic. While both Dengue and COVID-19 are largely suspected on clinical presentation, both share similar symptoms and laboratory features in the respective early manifestations. The high prevalence of many alternate viral diagnoses in addition to COVID-19 requires clinicians to be alert about alternate diagnosis and effectively mitigate spread of the diseases especially in low-income countries. With this case report, we illustrate the necessity of a systematic work-up with detailed medical history is required for clinicians to consider alternate diagnoses in addition to testing for COVID-19 during the pandemic. In-particular, this case highlights the need for clinician practicing in high Dengue endemic regions to consider possibility of common tropical diseases in all suspected patients and challenges facing the coinfections, especially in low income countries.

Keywords

COVID-19; SARS-CoV-2; coronavirus; pandemic; dengue; coinfection; tropical diseases.

Abbreviations

SARS-CoV-2: Severe Acute Respiratory Syndrome; COVID-19: Coronavirus 2019; WNL: Within normal limits; RR: Respiratory Rate; HR: Heart Rate; BP: Blood Pressure; IGG-ELISA: Immunoglobulin G Enzyme-linked immunosorbent assay; SOC: Standard of Care; RT PCR: Real time reverse transcriptase polymerase chain reaction; WHO: World Health Organization; CDC: Centers for Disease Control; CT scan: Computerized Tomography scan.

Introduction

While Coronavirus 2019 (COVID-19) caused by Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) continues to spread rapidly and raising hospitalizations and fatality rate in majority of the affected countries globally, the South and South-East Asian and Latin American countries are forced to prepare for yet another epidemic Dengue fever [1,2]. Areas with heavy rainfall and humidity are favorable for peak Dengue season. Although rare, increased risk of COVID19 and Dengue co-infection threatens to further burden the health care system in Dengue endemic areas, which are also experiencing COVID-19 pandemic [3]. While certain parts of the globe may be endemic to Dengue outbreaks, anyone traveling to high risk Dengue areas is also at high risk for contracting the infection. Just as the incidence of COVID-19 has grown dramatically, incidence of Dengue has also continued to worsen in recent decades, estimating 390 million dengue infections per year with 22,009 fatalities [4,5]. It is estimated that as much as 40% of the world's population (~ 3 billion people) happens to live in Dengue endemic areas [5].

We here present the case of a 63-year-old female with a COVID19 and Dengue co-infection. Although at first glance a COVID-19 diagnosis seemed likely, further extensive history taking allowed physicians to test the patient for Dengue viral infection. With this case report we not only aim at presenting the rare COVID19 and Dengue coinfection finding where the lack of physical manifestation of a rash might have caused not testing for Dengue. We also discuss that COVID-19 may mask and further augment other viral infections. We thus suggest how primary care doctors will continue to play a key role in early identification and containment of COVID19 and Dengue pandemic and endemic, respectively. An accurate and thorough work of a primary care doctor can further help reduce unprecedented strain on global healthcare systems.

Case Presentation

Patient

A 63-year-old female with ten year medical history of hypertension and Diabetes Mellitus type II presented to the Jeevandip Hospital emergency room, Surat, Gujarat, India on 11th July 2020, accompanied by her husband with a chief complaint of “intermittent high fever” for past 4 days. Clinical information was obtained by personal interviews and detailed medical records by trained physicians. Patient had traveled to a Dengue endemic area on 04th July 2020, where she complained of onset of fever three days later. She reports her fever was spiking in nature at night time and initially relieved with antipyretic medication within 24 hours. Patient is a housewife and lives with her husband and four adult sons. Patient confirmed none of her other family members reported similar symptoms.

Clinical, Imaging and Laboratory assessments

After initial onset of symptoms, mainly fever on 07th July 2020, the patient was seen by a primary care physician in her hometown. Initial laboratory tests were unremarkable (Table 1). The patient was neither tested for COVID-19 nor for Dengue at the outpatient clinic. Since the patient resides in Malaria and Typhoid endemic area, she was tested for both (Table 1) and discharged home as both tests were non-reactive.

On 11th July 2020, the patient experienced another spike of fever, which persisted throughout the day. As of 11 Jul 2020, she also recorded onset of new symptoms; nonproductive cough, body ache, generalized fatigue, lethargy, non-bloody and non-bilious vomiting. Patient was brought to the Jeevandip Hospital in Surat, Gujarat, India. There was no history of rash, bowel movement, weight changes, conjunctivitis, sore throat or mouth sores. Her vitals were within normal limits (WNL); Blood Pressure (BP) 120/80 mm Hg, Respiratory Rate (RR) 24 respirations/minutes, Heart Rate (HR) 74 beats/minute and SpO₂ 99%. Her physical exam was also WNL. She has been suffering from hypertension and DM for past 10 years and confirmed she is compliant with antihypertensive and antidiabetic medication. She follows up with her primary care physician regularly and the last visit was 3 weeks ago. Patient has not reported any known history of allergies to food or medication. Her past hospitalization was 20 years ago, for a total hysterectomy.

Considering the patient's travel history to Dengue endemic area and suspicious COVID-19 symptoms during the pandemic, she was admitted to the hospital with droplet and contact precautions with provisional diagnosis of viral pneumonitis. The personal protective equipment was provided for staff caring for the patient. Upon admission, patient tested positive for COVID-19 Antibody IGG-ELISA, Dengue virus IgM and IgG serology.

Chest X-ray was obtained upon admission; prominent bronchovascular markings with patch ground-glass soft tissue opacities are seen at bilateral mid-lower zones (Figure 1). A high resolution computed tomography followed; viral pneumonitis (bilateral asymmetrical patchy peripheral pleural based ground glass opacities with early inter and intra lobular wall thickening are seen involving all lobes of both lungs, predominantly involving bilateral lower lobes (Figure 2).

The patient was treated with IV hydration and antibiotics sulbactam sodium and cefoperazone sodium. As per the hospital Standard Of Care (SOC), she was also given IV pantoprazole, granisetron, a cocktail of vitamin C, B12, niacinamide and folic acid, and oral tablets of chloroquine, vitamin C with chewable zinc and vitamin D3 (Table 3). In Surat, India, patients are admitted at the hospital when positive for COVID-19 and discharged as per India's health ministry guideline updated on 8th May 2020 based on mild, moderate and severe criteria. This patient's case was considered mild and was discharged as per the guideline: No fever for at least 3 consecutive days, no need for repeat COVID19 RT PCR prior to discharge and patient was advised to isolate at home and self-monitor her health for 7 days.

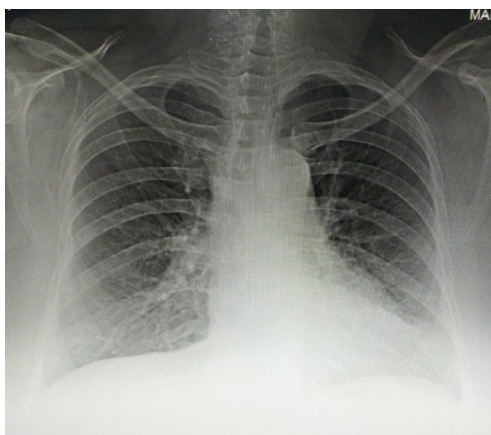


Figure 1: Chest X-ray on 11th July, 2020



Figure 2: Chest CT scan 11th July, 2020.

Table 1: Outpatient clinic laboratory results on 07 Jul 2020.

Variable	Reference Range	Date: 07 Jul 2020
Hb(g/dL)	16-Dec	10.8
Hct (%)	36-46	32.4
Platelets ($\times 10^9/L$)	150000-400000	166000
White blood cell count ($\times 10^9/L$)	4000-11000	4100
Neutrophils (%)	55-70	60
Lymphocytes (%)	20-40	36
Monocytes (%)	8-Feb	2
Eosinophils (%)	6-Jan	3
CRP (mg/L)	0-6	-
D-Dimer ng/ml	<500	-
Sr. Ferritin (ng/ml)	4.63-204	-
S.typhi "O"	Non Reactive(-ve)	Non Reactive(-ve)
S.typhi "H"	Non Reactive(-ve)	Non Reactive(-ve)
Thick and thin smear microscopy for malaria	Not Detected(-ve)	Not Detected(-ve)

Table 2: Jeevandip hospital laboratory results from 11 Jul 2020 to 16 Jul 2020.

Clinical laboratory results							
Variable	Reference range	07/11/2020	07/12/2020	07/13/2020	07/14/2020	07/15/2020	07/16/2020
Sodium (mmol/L)	136-145		141	145	140	137	140
Potassium (mmol/L)	3.5-5.0		4.6	4.2	4.0	4.6	4.0
Chloride (mmol/L)	95-105		110	90	95	98	100
Creatine (mg/dL)	0.6-1.2	1.3	1.1	1.5	1.2	1.0	1.2
ESR (mm/hour)	1-20		85	35	20	15	12
Total protein (g/dL)	6.0-7.8		6.5	6.2	5.5	6.0	5.8
Albumin (g/dL)	3.5-5.5		4.5	4.0	4.2	5.0	4.8
Aspartat aminostransferase (U/L)	8-20	25	20	16	18	12	15
Alanine aminostransferase (U/L)	8-20	30	25	20	16	14	15
Alkaline phosphatase (U/L)	20-140		78	75	65	78	80
Lactate dehydrogenase (U/L)	45-90		65	60	55	52	60
Total bilirubin (mg/dL)	0.1-1.0		0.9	0.6	0.8	0.8	0.6
Hb(g/dL)	12-16	11.30	11.30	10.8	10.6	11.0	10.5

Hct (%)	36-46	34	34	32.4	31.9	33.0	31.5
Platelets ($\times 10^9/L$)	150000-400000	309000	315000	325000	380000	395000	419000
White blood cell count ($\times 10^9/L$)	4000-11000	5700	11000	10500	7400	8500	7333
Neutrophils (%)	55-70	62	58	50	56	54	51
Lymphocytes (%)	20-40	32	37	45	38	40	41
Monocytes (%)	2-8	4	3	2	4	4	4
Eosinophils (%)	1-6	2	2	3	2	2	4
CRP	0-6	7.5	7.2	6	4	3	3
D-Dimer	<500 ng/ml				607.01		770.00
Sr. Ferritin	4.63-204				94.63		
COVID-19 Antibody IGG-ELISA	Negative: <1.0 Borderline: 1.0-1.10 Positive: >1.00	1.04					
Dengue virus IgM	Negative	Positive					
Dengue NS1 antigen	Negative	Negative					
Dengue virus IgG	Negative	Positive					

ESR: Erythrocytes Sedimentation Rate; INR: International Normalized Ratio.

Table 3: Jeevandip hospital, Surat, Gujarat, India treatment.

Drug	Dose	Route	Freq.
Inj 1.5gm contains a combination of two antibiotics sulbactam sodium and cefoperazone sodium as an active ingredient.	2 injection + Inj 100 ml NS	I.V	BD
Inj Pantoprazole	40 mg	I.V	BD
Inj Granisetron	3mg/3ml	I.V	BD
Tab.Chloroquine	250 mg	Oral	BD
Tab. Vitamin C With Zinc Chewable	Tab 1 tab	Oral	BD
Cap. Vitamin D3	60000 IU	Oral	OD

Discussion

This case illustrates need for clinicians in Dengue endemic areas to consider possibility of coinfection with COVID-19 in suspected patients and highlights importance of thorough history and physical in patients at initial presentation. While both Dengue and COVID-19 are largely suspected on clinical presentation, both share similar symptoms and laboratory features in the respective early manifestations [6]. The symptoms of Dengue last 2-7 days with 4-10 days of incubation period. COVID-19 symptoms may appear 2-14 days after exposure to the virus, with currently an estimated 5 days of incubation period. Since Dengue has at least four known viral strains (DENV-1, 2, 3 and 4), a person is at a risk of contracting the viral infection multiple times during their lifetime. Immune response to arbovirus like Dengue is considered different to bacterial and fungal infections, as it requires RNA interference evasion or suppression without

causing pathogenesis in the vector [20]. It is thought that if RNA interference response is enhanced through genetic manipulation in mosquitoes, arbovirus infection and could be interrupted. However, there is no such treatment or vaccine available as of now [20]. It is also unclear whether COVID-19 antibodies provide protection against re-infection [7,8]. In our case, since the patient developed initial symptom of fever within 3 to 4 days of potential exposure, the incubation period alone does not help differentiate between COVID-19 and Dengue fever.

Viral interference, a phenomenon explained by scientists suggests that a cell infected with a virus releases interferon, which gets released and uptake by surrounding cells making them resistant to a different viral infection [15]. It is likely that initially our patient was only infected with Dengue fever as she traveled to an endemic area. However, it is also possible that the patient's COVID-19 and Dengue coinfection may be attributed to being infected by multiple agents like virus, bacteria, protozoa etc. ("mixed infection") or a simultaneous infection of a cell or organism by multiple viruses ("coinfection"), later also termed as "superinfection" [18], both of which play a major role in further suppressing immune system. Kumar et al. (2020) has explained concept of heterologous immunity, where immunity to initial infection generates memory that may influence quality and quantity of how immune system may respond to subsequent infection [18].

Some of the early common symptoms experienced by Dengue and COVID19 are fever, fatigue, nausea, aches and pains and rash. The overlapping symptoms of COVID-19 and Dengue must be differentiated. Dengue patients may experience unique symptoms like headache with pain around or behind the eyeballs and some abdominal pain, while COVID-19 is notorious for more respiratory related symptoms like dry cough, nasal congestion and difficulty breathing [7,8]. In our case, distinction between dengue fever and COVID-19 clinical features were difficult, as the patient's symptoms were more consistent with COVID-19, including fever, shortness of breath, body ache, generalized fatigue, nausea and vomiting. The more common Dengue symptoms of skin erythema, retro-orbital-eye pain, photophobia, rubeoliform exanthema and headache were missing [16,17].

A group of dermatologists in China and Italy reported how cutaneous manifestations of COVID-19 and Dengue may contribute to missed diagnosis without other confirmatory tests like specific laboratory or imaging. When a patient presents with a rash, it is important for health care provider to rule out drug reactions from viral rashes, for which a thorough history and physical exam of the patient should be obtained and our patient had declined any known food or drug allergies [9-11]. Nearly all published cases we reviewed during our literature review; cutaneous manifestation of erythematous rash was almost always the leading reason for why patient was tested for Dengue. In our case, the patient did not present with a rash. Recently, skin rash has also been described in COVID-19, but it is not specific for the diagnosis [1]. During the COVID-19 pandemic, if it was not for the physician's thorough travel history leading to suspicion of Dengue fever, the patient might not have been tested for Dengue. Although infrequent, Dengue and COVID-19 may also have common laboratory findings; low platelets and high D-dimers, where high D-dimers is associated with severity of both the infections [18,19]. This further adds to possibility of misdiagnosis. In our case, the patient maintained normal platelet counts; however D-Dimer was seen to rise on Days 4 and

6 of the hospitalization, treated with subcutaneous heparin (Table 2) to prevent coagulation.

Regardless whether the patient presents with Dengue or COVID19 or co-infection, a misdiagnosed patient in the late presentation of either infection may face a fatal outcome. For Dengue suspected patients, CDC recommends Dengue virus antigen detection, serologic tests or tissue test if symptom onset recorded ≤ 7 days before. Serologic tests and tissue tests are recommended if >7 days have passed since the onset of symptoms [12]. In addition to virus antigen detection, WHO recommends chest X-ray and CT scan for COVID-19 patients to guide the care pathway from hospital admission to discharge [13,14]. Both the diseases share epidemiological characteristics such as increasing incidence and difficulty to control viral transmission when the diagnosis is delayed.

The healthcare management faces real challenge to mitigate COVID19 and Dengue impact, especially amongst low income populations. Several new coinfection cases are being reported across the globe, making it difficult for health care workers to determine diagnosis and provide timely treatment. Special measures should be taken in endemic countries to avoid burdening healthcare system on the verge of collapsing during the COVID-19 pandemic. The incidence of Dengue largely relies on climate of a geographical region [3], therefore control measures may be put in place regionally for early prevention and intervention to minimize impact.

There are a few limitations in our study. We included a patient who presented to hospital within 4 days of symptom onset, allowing early detection and treatment. Therefore, the findings may not be applicable to patients presenting late for medical care. Currently only a few cases of Dengue and COVID-19 cases are reported across the globe. This has been the only Dengue and COVID-19 coinfection case at the Jeevan-dip Hospital. There may be difference in clinical and laboratory parameters among early vs. late Dengue and COVID-19 coinfection patients. There is a need for more studies to assess these cases to evaluate and further validate challenges and gaps in knowledge of COVID-19 and Dengue coinfections.

Conclusion

In conclusion, we have shown that clinical features of Dengue and COVID-19 may overlap, and therefore laboratory markers and imaging may help differentiate the two viral infections. With this case report, we illustrate the necessity of a systematic work-up with detailed medical history is required for clinicians to consider alternate diagnoses in addition to testing for COVID-19 during the pandemic. We propose that this case highlights the need for clinician practicing in high Dengue endemic regions to consider possibility of common tropical diseases in all suspected patients and challenges facing the coinfections, especially in low income countries. There is a need for more studies to assess these cases to evaluate and further validate challenges and gaps in knowledge of COVID-19 and Dengue coinfections.

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Authors Information: Kinal Bhatt^{1*}; Maulik Lathiya²; Niravkumar Godhani³; Ghanshyam Motisariya⁴; Marcos Sanchez-Gonzalez⁵

¹Division of Clinical & Translational Research, Larkin Health System, South Miami, FL, USA.

²Jeevandip Hospital, Surat, Gujarat, India.

³Malavia Advanced Imaging Center, Surat, Gujarat, India.

⁴Jeevandip Hospital, Surat, Gujarat, India.

⁵Division of Clinical & Translational Research, Larkin Health System, South Miami, FL, USA.

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