



ORIGINAL RESEARCH PAPER

General Medicine

DENGUE FEVER IN COVID -19 INFECTION- DOUBLE TROUBLE

KEY WORDS: Dengue , covid-19 , Co-infection

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ABSTRACT

Co infection of Covid -19 with Dengue fever is a serious concern & is an additional challenge to the treating physician especially in Dengue endemic areas. During initial phases the symptoms of both the infections are quite identical & difficult to differentiate unless thorough investigations are done. Timely diagnosis & aggressive management may lead to a fruitful outcome. Here we report two interesting cases of Covid-19 and Dengue co infection which were identified & managed successfully.

Introduction

After the first case of Covid-19 was identified in Wuhan City, China the numbers started increasing rapidly all over the world putting a huge burden on the entire health care system. Managing these cases posed a great challenge to the treating clinicians. At this juncture co infection with Dengue virus was reported from various Asian countries such as Singapore, Thailand, India and Bangladesh [1] adding a double punch to it. The burden of concomitant Dengue infection makes the situation worse. In the initial phases Dengue fever and COVID-19 are difficult to distinguish because they share the same clinical and laboratory features[2]. Some authors described cases who were initially diagnosed as Dengue but later confirmed to have COVID-19[3]. In this setting, complete history taking and meticulous physical examination is needed along with judicious laboratory examination including tests for both Dengue & Covid -19. So far, co-infection of SARS-CoV-2 and dengue virus has not been studied in detail until now. Here we report two cases of Covid-19 co infected with the Dengue virus .

Case- I

A 55 year old male got admitted with complaints of fever, dry cough & breathlessness of 4 days duration. He had mild throat irritation but no loss of smell or taste. He also complained of generalized bodyache, myalgia, arthralgia & retro-orbital pain. He had no co morbid conditions. There was no history of travel. In the emergency he was tested for SARS-CoV-2 infection by RT-PCR as per our institutional protocol (guided by ICMR) which turned out to be positive & he was put in the Covid positive ward.

On examination he was febrile , blood pressure was 112/64 mmHg, pulse was 96 beats per minute and oxygen saturation was 90% in room air which increased up to 95% with 4 litre/min of oxygen . Few nonpruritic maculopapular rashes were also observed over the trunk & lower limbs. His initial blood investigations revealed leucocytosis (TLC-18100/cmm) with neutrophilia (91%), lymphopenia (4%) & thrombocytopenia (Platelet count -88000/cmm). He had mild hyponatremia (serum Sodium -124 meq/l). Liver function tests were deranged with total bilirubin of 2.50 mg/dl ,serum aspartate aminotransferase (AST-49.3 u/l) & alanine aminotransferase (ALT-115 u/l). The markers like CRP(11.60mg/dl), LDH(536 u/i), Ferritin (1114.3 ng/ml) & IL-6 (72.29 pg/ml) were raised. D-dimer was found to be 1670ng/ml .Elisa for NS1 antigen was positive. He was negative for malarial parasite, Chikungunya IgM Antibody

and viral serology (HIV, HBsAg, anti HCV IgM antibody-by ELISA). His blood culture was sterile. Chest roentgenogram showed bilateral opacities [Fig-1]. High resolution computed tomogram of the thorax revealed multi-lobular pneumonia with CORADS-6 & CT severity index of 19/25[Fig -2]. Managing this patient is indeed challenging for us as we are aware of the severity and complexity of both diseases. He was treated with injection Remdesevir, IV Fluids , Low molecular weight Heparin and Steroids along with intravenous antibiotics & other supportive care. Though his platelet count reduced to 66000/cu mm from 88000/ cu mm there was no evidence of bleeding from any site. We continued steroid & LMWH. Initially he was on NIV support in the critical care unit. He was closely monitored . On day four of the CCU care he was off NIV support & put on HFNO . He had a stormy clinical course in the CCU. After two weeks his COVID -19 RT PCR became negative & he started improving. Repeat investigations showed improvement. He was shifted back to the Covid negative ward & discharged on the 29th day of hospitalization. He is being followed up in our Post covid OPD regularly & is doing well.

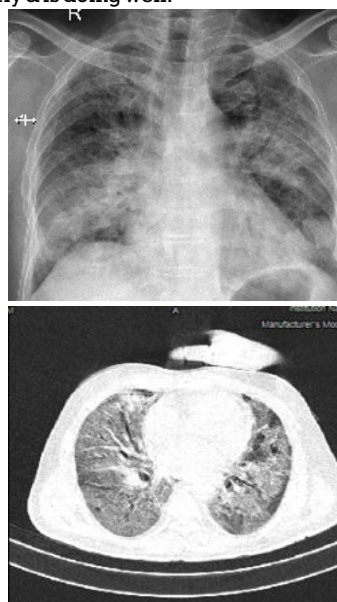


Fig -1 Chest X-Ray showing B/L Opacities
Fig -2 HRCT Thorax Showing GGOs

Case-II

A 45 year old male admitted with complaints of fever for two days followed by dry cough & breathlessness. One week prior to this he had history of multiple joint and periorbital pain. There was no history of travel .As per our protocol he was tested for Covid -19 infection by RT-PCR in emergency which was positive . On examination he was febrile , blood pressure was 140/90 mm of Hg and pulse rate was 106/min with regular rhythm. There were no rashes or ecchymotic patches noted on his body. His chest auscultation revealed extensive inspiratory crepitation. His respiratory rate was 30/min and Spo2 was 88% on room air. Examination of cardiovascular system revealed no abnormality.

Routine blood investigation showed leucocytosis (17200/cmm) with neutrophilia (88%) , lymphopenia (6%) & a marginally lower platelet count(108000/cmm). Tests for Chikungunya and malarial parasite were negative. However he was found positive for Dengue by the card test (NS1 positive) and that was confirmed by the ELISA test. His blood & urine cultures were sterile. His liver function was deranged . There was a two fold rise in liver enzymes (transaminitis). Renal function test was normal. His Inflammatory markers were raised. X-Ray chest showed bilateral non-homogenous patchy opacities[Fig -3]. His HRCT Thorax showed CORAD -5 with CT Severity score of 19/25[Fig-4]. He was treated with intravenous antibiotics , injection Remdesivir for 5 days , corticosteroids , LMWH & other supportive care. He also required HFNO. He was also on intermittent non-invasive ventilation due to type II respiratory failure. On the fourth day he had little worsening in liver function test(AST-160 U/L, ALT-122 U/L) , but PT/INR was within normal limits. Though his platelet count reduced to 87000 there were no bleeding manifestations. He also received two units of Convalescent plasma. After 10 days he turned negative for COVID-19 by RTPCR .He improved gradually & got discharged after 20 days. He is being followed up in our Post covid OPD regularly & is doing well.

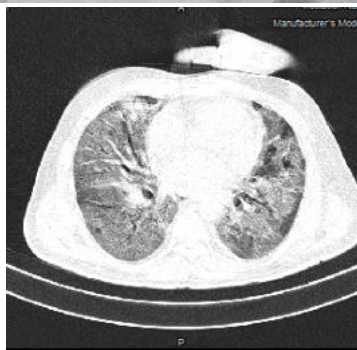


Fig-3 Chest X-Ray showing Bilateral Opacities
Fig-4 HRCT Thorax showing GGOs

Discussion

Co-infection of Covid-19 & Dengue virus has been reported recently in different dengue-endemic countries like Singapore, Thailand, India, and Bangladesh[1] causing double trouble to the already loaded health care system. Miah, M.A. and A. Husna et al described it as a serious health

concern , a dangerous combination [4] putting additional challenge on clinicians. The clinical features like fever, bodyache, rashes, thrombocytopenia, deranged liver functions etc of COVID-19 and Dengue fever almost resemble each other and may create confusion amongst the treating physicians in countries like ours where we see Dengue epidemics . Joob B et al from Thailand reported a case where a patient was initially diagnosed to have Dengue fever based on the clinical picture of petechiae & thrombocytopenia. When he developed respiratory distress there was a suspicion of Covid -19 infection & was confirmed by RT-PCR [5]. Both of our cases presented with complaints of fever , cough & breathlessness. So as per the protocol we did RT-PCR for Covid-19 which turned out to be positive. Along with that as part of the fever profile we also investigated for other conditions like , Malaria , Dengue & Chikungunya.

Though, cutaneous involvement can facilitate a clinical diagnosis of Dengue it is not present in all patients. Our first case had skin manifestations in the form of non pruritic rashes & the second case did not have any cutaneous manifestations. Studies confirmed that Dengue fever may present with or without skin rash & there is no statistically significant difference in complications and mortality amongst them[6]. Skin manifestations also been described in COVID-19. In Italy few cases were reported with erythematous & widespread urticarial lesions in Covid-19 patients[7]. In Thailand, dermatologists also reported a case of fever with an exanthematous rash initially diagnosed as Dengue & later as COVID-19 [8]. Verduyn M et al published a case report of Co-infection of Dengue and COVID-19 [9] who presented with classical features of dengue like persistent fever , arthromyalgia, dyspnea and an itchy maculopapular rash. Thrombocytopenia is an important hematological abnormality in Dengue fever diagnosis but cases are reported without thrombocytopenia too[10,11,12]. Joob, B et al described a case of Dengue fever with normal platelet count. Normal platelet count is also common among early & mild dengue patients. In our cases the platelet count were marginally low but there were no haemorrhagic manifestations. Thrombocytopenia and cytolysis were also reported, respectively, in 36.2% and 21.3% of the patients with COVID-19 [13] also. Deranged liver function in Covid-19 may be either due to direct cytotoxicity by viral replication or related to hypoxic hepatitis[14]. Coinfection with other endemic virus like Dengue is likely to complicate the clinical presentation and outcome that needs to be addressed seriously and judiciously[15]. There are case reports from many Asian countries where Dengue is an endemic issue & there is probability that the combination of these two may turn it to a co-epidemic[16]. These were the first two cases of co-infection of COVID-19 with Dengue infection in our region.

Management is equally challenging in the absence of definite strategic protocol needing enhanced understanding of potential COVID-19 and dengue coinfection. Anticoagulation therapy with LMWH & Steroids are the cornerstone of therapy in Covid -19 along with drugs approved under EUA(Emergency use under authorization) . Steroids are feared to increase bleeding risk in dengue. Naira Bicudo et al reported a case of co-infection of SARS-CoV-2 and dengue virus in a 56 year old woman [17]. They have stopped anticoagulation & treated symptomatically .She improved & got discharged on 26th day of hospital stay. Bandara et al concluded that significant adverse effects are unlikely due to use of corticosteroids in patients with dengue[18]. Infact use of Methylprednisolone has been reported to be beneficial in cases of reactive haemophagocytosis in dengue[19]. The effect may be attributed to uncontrolled inflammatory response in dengue, similar to cytokine storm in COVID-19. We were in dilemma initially because anticoagulation is required in moderate to severe COVID -19 cases as per the ICMR guidelines but should be avoided in Dengue in view of

coagulopathy and thrombocytopenia. While treating dengue and COVID-19 coinfection, one has to carefully weigh the benefits of corticosteroid use and LMWH against the risk of bleeding on a case-to-case basis. Both of our patients received anticoagulation therapy under close monitoring of clinical & laboratory parameters. Our patients tolerated steroids & anticoagulation therapy well. There were no bleeding manifestations in spite of reduction in platelet count. They improved & were discharged after a long hospital stay.

Conclusion

These two cases reported here represent the tip of the iceberg. There may be many cases which remain undiagnosed. In the initial phases it is difficult to differentiate COVID-19 and Dengue fever on clinical grounds only. Therefore a high degree of clinical suspicion along with appropriate laboratory investigations should be done to rule out co-infection specially in Dengue endemic zones. The clinicians need to be vigilant in order to enable early identification of co-infections of Dengue with COVID-19. These patients should be managed with Steroids & LMWH after evaluating risk benefit ratio which needs to be decided on a case-to-case basis along with other drugs approved under EUA till definite management strategies on COVID-19 coinfection with Dengue are evolved.

Limitations

Larger randomised control trials are needed to evaluate increased morbidity & the effectiveness of corticosteroids and/or LMWH in patients with dengue and COVID-19 coinfection to guide the management.

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