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Case Study

A Complex Infectious Case of Dengue Fever with Thrombocytopenia, Acute Hepatitis A, Influenza B, URTI(Upper Respiratory Tract Infection), and Secondary HLH (Hemophagocytic Lymphohistiocytosis): A Diagnostic Challenge

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A B S T R A C T

Worldwide, dengue is the most frequent trigger for viral haemorrhagic fever. Although it is chronic in many tropical nations, instances from non-endemic areas have also been documented on a regular basis in recent years. Nonetheless, the World Health Organization's revised classification of dengue splits it into three groups: severe dengue, dengue with warning signals, and dengue without warning signs. Significant dengue is defined as those who have a significant vascular leak, hypotension, severe bleeding, or severe organ involvement. Hepatitis, the influenza virus, respiratory infections, liver failure, and Hemophagocytic lymphohistiocytosis (HLH) linked to dengue fever have all been documented; most of these cases involved children, with a small number of adult case reports. Fatal results including a 50% mortality rate have been documented in the child's research. Here we have presented a case of a 17-year-old teenager with dengue fever and co-morbidities of hepatitis, influenza, lung diseases, and HLH.

Keywords: Dengue, Hepatitis A, Influenza, Respiratory Infections, Thrombocytopenia, HLH

Introduction

Dengue fever is an arbovirus illness caused by a flavivirus.[1] There are many different clinical presentations of dengue, such as atypical forms, conventional dengue symptoms, silent dengue, and dengue haemorrhagic fever. Dengue can cause changes in the way the liver works as well as the usual signs of acute hepatitis, including jaundice, hepatomegaly, right hypochondrium discomfort, and increased transaminase levels. Within three weeks of the onset of hepatitis, the transaminase levels return to normal after peaking on the ninth day.[1] Usually, Secondary hemophagocytic lymphohistiocytosis (HLH) is an uncommon diagnosis that can be linked to a number of viral triggers, particularly Epstein-Barr virus, dengue virus, scrub typhus, autoimmune illnesses, cancer, and genetic abnormalities in the family.[2] Influenza and dengue virus epidemics have significant negative effects on the world's economy and health. Clinical observations imply that co-infections of influenza with dengue viruses may significantly worsen illness severity.[3] In our case, there is a severe combination of dengue fever, acute hepatitis A, influenza B, URTI, and secondary HLH. Given the severity of this combination, we evaluated the diagnosis, clinical challenges, and management strategies for these conditions.

Case Report

A 17-year-old teenager was admitted to a multispecialty hospital in west India with complaints of high-grade fever, cough with expectoration, central chest pain, generalised weakness, joint pain, sneezing, and loss of appetite. Before being admitted to the hospital, he was already dengue-positive. He also didn't have any travel experience; he couldn't remember ever getting bitten by a mosquito or coming into touch with infected people.

On arrival at the hospital, he was conscious; he had a high fever (103 °F) with a normal respiratory rate, pulse rate, and blood pressure. On physical examination, he had yellowish skin, mild tenderness, and swallowing of body parts.

As shown in Table 1, laboratory investigations suggest thrombocytopenia (12000 platelets/mcL) and leucopenia (1300 WBC/mcL). The iron study evaluated a high ferritin level (1233 ng/mL). Total bilirubin (11.1 mg/dL), direct bilirubin (9.6 mg/dL), indirect bilirubin (3.0 mg/dL), and SGOT (750 U/L) confirmed hepatic abnormalities.

Urine analysis evaluated the presence of bile salts and bile pigments. Blood culture indicated primary no growth detected. Gram stain was negative. Chest X-ray showed pleural effusion in the lungs. The flu panel suggested influenza B viral RNA. A bone marrow aspiration was sent, and it detected hypocellular bone marrow with hemophagocytic lymphohistiocytosis (HLH).

The patient was isolated and treated carefully with constant monitoring. A combination of antibiotics (ceftriaxone + sulbactam) 1 gm given BD, oseltamivir (75 mg) an antiviral given twice a day, ursodeoxycholic acid (300 mg) a hepatoprotective agent given twice a day, prednisolone (30 mg) a steroid given twice a day, L-glutathione (500 mg) an anti-oxidant given twice a day, tab. Heptagon was used as a nutraceutical, and a few multivitamins were used to treat the patient. After monitoring for a few days and observing improvement in the patient, the patient was discharged with the continuation of the same drug therapy.

Table 1.Laboratory Findings

Investigations	Findings	Normal Range
Haemoglobin	12.9 g/dL	13.8–17.2 g/dL
WBC	1300 /mcL	4000–11000 /mcL
Platelets	12000 lacs/mcL	1.5–4.1 lacs/mcL
CRP	29.2 mg/L	0.0–5.0 mg/L
S. Na^+	132 mmol//L	135–145 mmol/L
S. K^+	4.3 mmol/L	3.5–5.1 mmol/L
SGOT/ AST	750 U/L	6–28 U/L
Total bilirubin	11.1mg/dL	0.1–1.2 mg/dL
Direct bilirubin	9.6 mg/dL	0.1–9.3 mg/dL
Indirect bilirubin	3.0 mg/dL	0.2–0.8 mg/dL
PT	22.9 sec	11.0–13.5 sec
INR	1.72	0.8–1.1
Ferritin	1233 ng/mL	30–400 ng/mL
Triglyceride	255 mg/dL	< 150 mg/dL

SGOT/AST: Serum glutamic-oxaloacetic transaminase/ Aspartate aminotransferase
PT: Prothrombin time
CRP: C reactive protein
INR: International Normalized Ratio

Discussion

The clinical characteristics of dengue fever, influenza, malaria, respiratory illnesses, and viral hepatitis can all overlap, leading to significant misdiagnosis. Jaundice and fever are symptoms of viral hepatitis and dengue fever. Certain viral strains or genotypes may produce tissue tropism, circulatory impairment brought on by hypotension or localised vascular leakage within the liver capsule, or direct effects of the infection or host immune reaction on liver cells.[4]

While dengue fever frequently causes hepatic involvement, serious hepatic derangement is uncommon. Hepatitis A infection presents similarly, with a few exceptions; jaundice typically appears after a fever has subsided, and there is typically a one-to-seven-day interval between the two.[5] While the ratio of AST/LDH is significantly more than 4 in viral hepatitis, SGOT values are significantly higher during

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influenza-related hepatitis (8–10 times normal) than in dengue fever (2–3 times normal).[6] It has been discovered that in the case of dengue, SGOT rises faster than SGPT, peaks at a greater level, and returns to normal sooner.[5,6]

Thrombocytopenia, haemo-concentration, and third-space loss of fluid are other distinguishing characteristics of dengue fever. In our case, the patient suffered from severe thrombocytopenia. The coagulation profile is typically normal in dengue fever patients; therefore, elevated blood coagulation levels may indicate an underlying condition such as hepatotropic influenza or disseminated intravascular coagulation, potentially leading to sepsis.. Our patient had also elevated prothrombin time, which directly indicates a malfunction in liver functions. This pattern differs from that typically observed when acute hepatitis results from hepatitis viruses.[7]

It is well recognised that co-infections between influenza and bacteria can result in serious illness; however, less is known about infectious diseases with other severe viruses. Dengue and seasonal influenza viruses frequently co-circulate in tropical areas.[8] The influenza virus A belongs to the Orthomyxoviridae family, has a segmented genome of (-)-sense RNA, and is divided into subtypes based on the proteins neuraminidase (N) and hemagglutinin (H). Following airborne infection, influenza A virus that infects the respiratory tract's epithelial cells results in respiratory illness, which is typified by high fever, coughing, headaches, muscular soreness, and extreme malaise that appears suddenly.[9] Lung pathology can occur in both influenza and dengue patients. Pleural effusion in lung tissue might result from vascular leakage in dengue shock episodes. Although intravenous fluid delivery is a useful treatment for compensating for plasma leaks, pleural effusion can also result from administering too much fluid too quickly. Less often, other lung abnormalities in dengue occur in conjunction with co-morbidities.[10]

Pleural effusion, non-cardiogenic pulmonary oedema, acute respiratory distress syndrome, asthma, and pulmonary haemorrhage are some of the respiratory symptoms of dengue.[11] Although the exact pathophysiology behind dengue lung problems is yet unknown, it seems to be related to thrombocytopenia and capillary leak syndrome. Lung injury and inflammatory alterations have been observed in severe dengue infections.[12] Physicians may have difficulties in diagnosing dengue patients who mostly exhibit respiratory symptoms, underscoring the significance of careful diagnosis. According to studies, lung problems are present in most patients who have deadly infections, which may raise death rates.[13]

Secondary HLH is associated with immunologic stimulation resulting from cancer and bacterial or congenital infections. Secondary HLH is most commonly caused by viral infections, including those caused by HIV, CMV, EBV, Dengue and ProB19.[14] Few case reports of dengue-associated HLH have been found in adults, despite the fact that it has been extensively documented in children. The most prevalent viral disease in humans that is spread by arthropods is dengue. Asymptomatic illness to haemorrhagic fever caused by dengue (DHF) with dengue shock disorder (DSS) is among the clinical symptoms of dengue.[15]

There are important therapeutic drug classes used to treat this complex, severe case: cephalosporin antibiotics, hepatoprotective agents, anti-virals, nutritional supplements, corticosteroids, antioxidants, and multivitamins.

This example highlights how crucial it is for doctors to be aware of multiple illnesses in endemic areas since they can present challenges for diagnosis, cause complications, and have a protracted course.

Conclusion

In our complex case reports, clinical profiles proved that there are rare but possible connections of all these severities in one individual After contracting dengue, the patient developed more severe symptoms. Each abnormality was evaluated and confirmed through specific tests: hepatitis via liver function tests, influenza via a flu panel, HLH via bone marrow aspiration and examination, respiratory infections via chest X-ray, and other infections via blood cell analysis..

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References

1. Torres EM. Dengue. InDengue 2005 (pp. 344-344)..
2. Simon AC, Kumar CG, Basu D, Kumar RR. Hemophagocytic lymphohistiocytosis in children: clinical profile and outcome. J Pediatr Hematol Oncol. 2020 Jul;42(5):e281-5. [PubMed] [Google Scholar]
3. Schmid MA, González KN, Shah S, Peña J, Mack M, Talarico LB, Polack FP, Harris E. Influenza and dengue virus co-infection impairs monocyte recruitment to the lung, increases dengue virus titers, and exacerbates

pneumonia. Eur J Immunol. 2017 Mar;47(3):527-39. [PubMed] [Google Scholar]
4. Trung DT, Thao LT, Hien TT, Hung NT, Vinh NN, Hien PT, Chinh NT, Simmons C, Wills B. Liver involvement associated with dengue infection in adults in Vietnam. Am J Trop Med Hyg. 2010 Oct;83(4):774. [PubMed] [Google Scholar]
5. Zaki SA, Lad V. Concurrent infection of dengue fever and hepatitis A infection: a case report. Indian J Crit Care Med. 2011 Oct 1;15(4):238. [PubMed] [Google Scholar]
6. Mishra D, Chaturvedi D, Mantan M. Typhoid fever and viral hepatitis. Indian J Pediatr. 2008 May;75(5):509-10. [PubMed] [Google Scholar]
7. Hien PT, Chinh NT, Simmons C, Wills B. Liver Involvement Associated with Dengue Infection in Adults in Vietnam. Am. J. Trop. Med. Hyg. 2010;83(4):774-80.
8. Webster RG, Bean WJ, Gorman OT, Chambers TM, Kawaoka Y. Evolution and ecology of influenza A viruses. Microbiol Rev. 1992 Mar;56(1):152-79. [PubMed] [Google Scholar]
9. Weinheimer VK, Becher A, Tönnies M, Holland G, Knepper J, Bauer TT, Schneider P, Neudecker J, Rückert JC, Szymanski K, Temmesfeld-Wollbrueck B, Gruber AD, Bannert N, Suttorp N, Hippenstiel S, Wolff T, Hocke AC. Influenza A viruses target type II pneumocytes in the human lung. J Infect Dis. 2012 Dec 1;206(11):1685-94. [PubMed] [Google Scholar]
10. Guerrant RL, Walker DH, Weller PF. Tropical Infectious Diseases: Principles, Pathogens and Practice E-Book: Tropical Infectious Diseases: Principles, Pathogens and Practice E-Book. Elsevier Health Sciences; 2011 May 27.
11. Marchiori E, Hochhegger B, Zanetti G. Manifestações pulmonares da dengue. J Bras Pneumol. 2020 Mar 2;46(1):e20190246. Portugese. [Google Scholar]
12. Joob B, Wiwanitkit V. Concurrent dengue infection in a patient with pulmonary tuberculosis: the first world report. J Thorac Dis. 2013 Jun;5(3):E118. [PubMed] [Google Scholar]
13. Rodrigues RS, Brum AL, Paes MV, Póvoa TF, Basilio-de-Oliveira CA, Marchiori E, Borghi DP, Ramos GV, Bozza FA. Lung in dengue: computed tomography findings. PloS One. 2014 May 16;9(5):e96313. [PubMed] [Google Scholar]
14. Munshi A, Alsuraihi A, Balubaid M, Althobaiti M, Althaqafi A. Dengue-induced hemophagocytic lymphohistiocytosis: a case report and literature review. Cureus. 2021 Dec;13(12):e20172. [PubMed] [Google Scholar]
15. Gadhiya HP, Radhanpura YV, Sanja SA, Parekh K, Jani BR. A case study on Epstein-Barr virus infection induced haemophagocytic lymphohistiocytosis. Chettinad Health City Med J. 2024 Mar 30;13(1):99-101. [Google Scholar]

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