

Dengue Hemorrhagic Fever With Mobitz Type 2 Block And Diabetic Ketoacidosis, A Rare Presentation.

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Abstract

Dengue hemorrhagic fever (DHF) is a severe manifestation of dengue virus infection, primarily characterised by plasma leakage, hemorrhagic tendencies, and organ impairment. While cardiac complications are recognized in the spectrum of DHF, the occurrence of Mobitz Type 2 heart block as a consequence of the infection is exceedingly rare. This is a case study of a 45-year-old male, previously healthy and without any prior history of diabetes mellitus, who developed DHF along with the uncommon complications of Mobitz 2 heart block and concomitant transient diabetic ketoacidosis (DKA). Despite prompt initiation of supportive care and specific management strategies for both DHF and DK. The patient's clinical course was complicated not only by plasma leakage found in DHF but also due to the osmotic diuresis found in diabetic ketoacidosis (DKA), the management of coexisting cardiac and metabolic emergencies have made the treatment much challenging. The underlying mechanisms linking DHF, heart block, and DKA remain unclear, warranting further investigation to elucidate the intricate pathophysiological interplay between these conditions.

Keywords: Dengue Fever, Mobitz II Heart block, Diabetic Ketoacidosis

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I. Case Report

A 45 year old male, was brought to the Emergency Department with complaints of breathlessness, high grade fever associated with chills and rigour, nausea and multiple episodes of non-bilious vomiting, generalised weakness and fatigue for three days. Patient was alert and had a blood pressure of 90/60 mmHg, pulse rate of 40 bpm, respiratory rate 34/min and oxygen saturation of 95% on room air. He was febrile with a temperature of 40.5°C. Capillary blood glucose was 395 mg/dl, Glasgow Coma score was 15/15, systemic examination was unremarkable. IV line secured on the right cephalic vein with 18G cannula. In view of tachypnea and mild respiratory distress, oxygen supplementation was initiated with a non re-breathable mask at 10 litres/minute. An electrocardiogram (ECG) was taken which showed intermittent non-conducted P waves without progressive prolongation of the PR interval suggestive of AV Block: 2nd degree, Mobitz II (Hay block). While Mobitz type 1 might improve with atropine, giving atropine in the setting of Mobitz type 2 can worsen the block and increase the risk of complete heart block or asystole [2]. Isoprenaline infusion was started at 5-20 mcg/min which successfully increased the heart rate to 65 bpm. Temporary transvenous pacemaker was not the first choice since there was a life threatening thrombocytopenia without any obvious cardiovascular symptoms. The initial Arterial Blood Gas (Table 1) revealed high anion gap metabolic acidosis pH of 7.31, with elevated lactate 7.0 mmol/L, Bicarbonate 12 mmol/L. Urine ketone dipsticks showed a ketonuria of “++”. The ABG findings along with increased blood sugars (above 250 mg/dl) were diagnostic of Diabetic ketoacidosis [4-5]. Insulin infusion was initiated at 0.1 unit/kg/min and concomitant potassium correction was also started at 20 meq/hour through a central venous catheter. Bedside 2D echo was normal, cardiac biomarkers were negative. 1 litre of Intravenous 0.9% Saline was infused over one hour followed by isotonic saline and half saline continuously administered at the rate of 500 mL/hr, along with potassium supplementation. HRCT chest revealed patchy consolidations with bilateral lower and upper lobe ground glass opacities and bilateral pleural effusion which were consistent with Plasma Leakage and alveolar haemorrhages. Dengue IgM antibody and NS1Ag were positive which indicates the primary cause of fever towards dengue viral infection. The complete blood picture (table 2) showed a thrombocytopenia with leukopenia with 80% Neutrophils and 23% lymphocytes, hemoconcentration with raised hematocrit, this is consistent with dengue fever. Serum magnesium, calcium and thyroid profile were normal.

Table 1: Initial ABG

pH	7.31
pCO ₂	24 mmHg
pO ₂	72.3 mmHg
HCO ₃	12 mmol/L
K ⁺	3.6 mmol/L

Lactate	7.9 mmol/L
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Table 2: Complete blood picture on Day 1

Tests	Result	Units
Haemoglobin	14.3	mg/dl
Total counts WBC	3700	cells/cum
Platelet counts	25,000	Per/cum
PCV	45.2	%
Sr. Creatinine	1.0	mg/dl

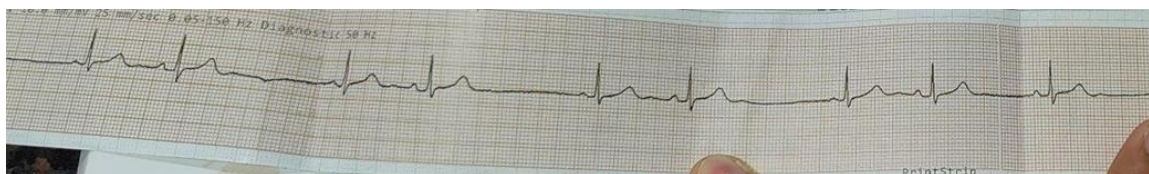
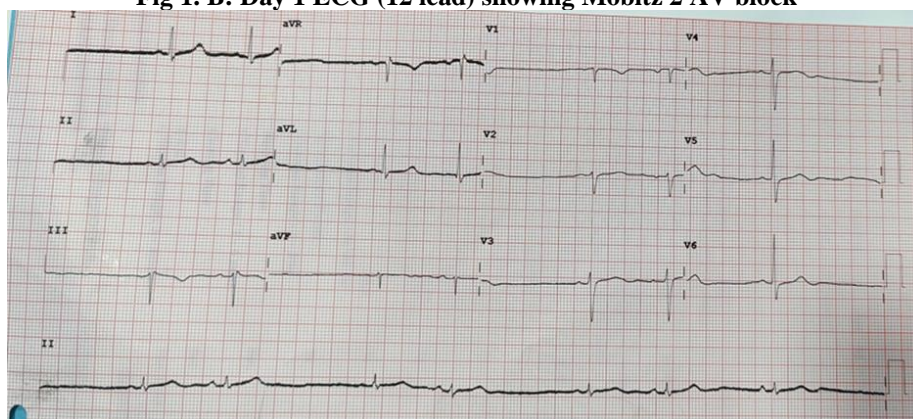


Fig 1. A: Day 1 ECG rhythm strip showing Mobitz 2 AV block

The blood sugars were 180 mg/dl, pH 7.42 and HCO₃ > 15 mmol/L after 14 hours of starting fluid and insulin therapy which were titrated and weaned off after 2 hours of administering 0.5 U/kg subcutaneous insulin and initiation of oral feed. The patient started improving symptomatically from day 2 and the fever started subsiding, however repeat Complete blood picture showed a deteriorating platelet count at 16,000/cum, PCV 43%, WBC: 6500, patient had no bleeding manifestations. 1 unit of Single donor platelets were transfused on day 2 and, the repeat platelet count started to increase with an upward trend and reached 1 lakh/cum by day 5. Isoprenaline was tapered and weaned off from day 2 onwards, later converted to oral tablet Orciprenaline 10mg once daily and on day 7 the patient was discharged with a resting heart rate of 70 bpm, Normal sinus Rhythm. Tab. Orciprenaline was continued for 1 month. On 1 month follow-up, heart rate was at a range of 65 to 85 bpm at resting and mild exertion respectively and the patient had no other complaints.

Fig 1. B: Day 1 ECG (12 lead) showing Mobitz 2 AV block



II. Discussion:

Dengue hemorrhagic fever (DHF) is one among the most deadly viral diseases Globally (1). It is a severe and life-threatening complication of dengue virus infection which is otherwise self resolving and benign. There are 4 grades of DHF based on the severity: grade I and II without shock; grade III shock and grade IV profound shock. DHF grade III and IV are also called Dengue Shock Syndrome (DSS) (1,4). The patient presentation was complicated not only by plasma leakage found in DHF but also osmotic diuresis found in diabetic ketoacidosis (DKA). DHF is characterised by **high grade fever** (up to 104°F/40°C), typically lasting for 2-7 days, Plasma Leakage causing fluid leakage from blood capillary, leading to Hypovolemia and shock. Thrombocytopenia and Endothelial dysfunction can cause bleeding, Easy bruising, Petechial rash which can be elicited by a tourniquet test. In severe cases, the above disorders contribute to organ dysfunction and cardiovascular collapse. (1,4)

Only a handful of case reports have documented the co-occurrence of DHF, Mobitz type 2 block, with DKA and also noted the complexity of managing such cases. Since this co-occurrence is exceptionally rare and the exact interaction between these conditions remains elusive, several potential mechanisms have been hypothesised. Dengue virus can directly damage myocardial cells, leading to conduction abnormalities (5). Additionally, the inflammatory response associated with dengue infection can further contribute to cardiac dysfunction. (6-8). Diabetic Ketoacidosis can cause hyperkalemia and hypocalcemia, both of which can affect

cardiac conduction (9). DHF can lead to plasma leakage and collection of fluid in spaces such as the pericardial sac, which causes abnormal electrophysiological changes, dehydration, leading to hypovolemia and decreased cardiac output, These can further impede coronary blood supply resulting in a cascade of ischemia. (10-12). Bradycardia is the most common electrical disturbance seen in dengue (13). All varieties of brady-arrhythmias can be seen in dengue but higher the degree of the block, more prominent is the probability of asystole, ventricular arrhythmias, hemodynamic compromise and requirement of more aggressive and invasive interventions in the form of pharmacotherapy, pacing and ICU admission. (13,14).

Type 1 diabetes mellitus is frequently linked to autoimmunity, leading to persistent activation of the immune system and evident signs of inflammation in tissues and capillaries. This heightened inflammatory state is more likely to result in the liberation of pro-inflammatory cytokines, particularly in the endothelium. This phenomenon explains the elevated risk of plasma leakage in individuals affected by dengue fever. On the other hand, Type 2 diabetes mellitus is characterised as a metabolic disorder causing a lasting inflammatory condition that alters both the anatomical and physiological integrity of the endothelium. This condition arises from the activation of T-lymphocytes, leading to the release of pro-inflammatory cytokines such as gamma interferon (IFN γ) and tumour necrosis factor alpha (TNF- α). Consequently, individuals with Type 2 diabetes mellitus face an increased susceptibility to dengue hemorrhagic fever (15-18).

The occurrence of transient hyperglycemia with ketoacidosis, as observed in our patient, was only documented in one Srilankan case report by Dalugama, C. et al. (15). Moreover the combination of DHF, Transient DKA and Mobitz 2 heart block has not been reported in the literature yet.

III. Conclusion:

Dengue fever is hyperendemic in India and Southeast Asia, this case presents a rare and complex clinical scenario involving the simultaneous occurrence of multiple challenging disorders. The patient's initial presentation with severe manifestations of dengue, including high-grade fever, plasma leakage, and thrombocytopenia, was further complicated by the development of Mobitz Type 2 heart block and DKA.

The management of this patient required a multidisciplinary approach, considering the delicate balance between addressing the infectious, cardiovascular, and metabolic components of the clinical presentation. Isoprenaline infusion proved effective in managing the heart block without resorting to a temporary transvenous pacemaker, given the patient's concurrent life-threatening thrombocytopenia.

The co-occurrence of DHF, Mobitz Type 2 block, and DKA is exceptionally rare, and the mechanisms underlying their interaction remain complex and multifaceted. The literature review revealed that only a few documented cases have reported such a triad, emphasising the unique challenges in diagnosis and management.

Potential mechanisms for the intricate interplay of these conditions include direct myocardial damage by the dengue virus, inflammatory responses contributing to cardiac dysfunction, and the impact of DKA on electrolyte imbalances affecting cardiac conduction.

This case underscores the importance of a comprehensive and individualised approach in managing complex medical conditions, necessitating careful consideration of the unique interactions between infectious, cardiovascular, and metabolic systems. Further research and additional case reports are warranted to enhance our understanding of this rare triad and to refine treatment strategies for similar complex presentations in the future.

References

- [1] World Health Organization. Dengue Haemorrhagic Fever: Diagnosis, Treatment, Prevention And Control. Vol. 1. Geneva; 1997:24–30.
- [2] Kashou AH, Goyal A, Nguyen T, Ahmed I, Chhabra L. Atrioventricular Block. In Statpearls. Statpearls Publishing; 2023.
- [3] Khan AA, Khan FU, Akhtar SA, Ghaffar R. Dengue Beyond Fever-Fatal Dengue Myocarditis And Complete Heart Block: A Case Report And Brief Overview Of Cardiac Manifestations Of Dengue Fever. SAGE Open Medical Case Reports. 2023;11. Doi:10.1177/2050313X231193983.
- [4] Guzman MG, Harris E. Dengue. Lancet. 2015;385(9966):453-465. Doi:10.1016/S0140-6736(14)60572-9.
- [5] Poornima H, John J. Cardiac Manifestations In Dengue Patients In A Rural Tertiary Care Centre In Coastal Kerala. Int J Innov Res Med Sci. 2019;4(4). Doi:10.23958/ijirms/Vol04-I04/628.
- [6] Chen RF, Yang KD, Wang L, Liu JW, Chiu CC, Cheng JT. Different Clinical And Laboratory Manifestations Between Dengue Haemorrhagic Fever And Dengue Fever With Bleeding Tendency. Trans R Soc Trop Med Hyg. 2007;101(11):1106–1113. Doi:10.1016/J.Trstmh.2007.06.019.
- [7] Restrepo BN, Isaza DM, Salazar CL, Ramírez R, Ospina M, Alvarez LG. Serum Levels Of Interleukin-6, Tumor Necrosis Factor-Alpha And Interferon-Gamma In Infants With And Without Dengue. Revista Da Sociedade Brasileira De Medicina Tropical. 2008;41(1):6–10. Doi:10.1590/S0037-86822008000100002.
- [8] Kurane I. Dengue Hemorrhagic Fever With Special Emphasis On Immunopathogenesis. Comparative Immunology, Microbiology And Infectious Diseases. 2007;30(5-6):329–340. Doi:10.1016/J.Cimid.2007.05.010.
- [9] Lertdetkajorn K, Sriphrapradang C. Management Of Diabetic Ketoacidosis With Dengue Hemorrhagic Fever. Cureus. 2018;10(9):E3336. Doi:10.7759/Cureus.3336.
- [10] Chen RF, Yang KD, Wang L, Liu JW, Chiu CC, Cheng JT. Different Clinical And Laboratory Manifestations Between Dengue Haemorrhagic Fever And Dengue Fever With Bleeding Tendency. Transactions Of The Royal Society Of Tropical Medicine And Hygiene. 2007;101(11):1106–1113. Doi:10.1016/J.Trstmh.2007.06.019.

- [11] Restrepo BN, Isaza DM, Salazar CL, Ramírez R, Ospina M, Alvarez LG. Serum Levels Of Interleukin-6, Tumor Necrosis Factor-Alpha And Interferon-Gamma In Infants With And Without Dengue. *Revista Da Sociedade Brasileira De Medicina Tropical*. 2008;41(1):6–10. Doi:10.1590/S0037-86822008000100002.
- [12] Singhi S, Kissoon N, Bansal A. Dengue And Dengue Hemorrhagic Fever: Management Issues In An Intensive Care Unit. *Jornal De Pediatria*. 2007;83(2 Suppl):S22–S35. Doi:10.2223/JPED.1622.
- [13] Parchani A, Krishnan VS, Kumar VKS. Electrocardiographic Changes In Dengue Fever: A Review Of Literature. *International Journal Of General Medicine*. 2021;14:5607–5614. Doi:10.2147/IJGM.S328755.
- [14] Dhariwal AK, Sanzgiri PS, Nagvekar V. High Degree Atrioventricular Block With Ventricular Asystole In A Case Of Dengue Fever. *Indian Heart Journal*. 2016;68 Suppl 2(Suppl 2):S194–S197. Doi:10.1016/J.ihj.2016.03.023.
- [15] Dalugama C, Gawarammana IB. Dengue Hemorrhagic Fever Complicated With Transient Diabetic Ketoacidosis: A Case Report. *J Med Case Reports*. 2017;11:302. Doi:10.1186/S13256-017-1476-Z.
- [16] Supradish PO, Rienmanee N, Fuengfoo A, Kalayanaroj S. Dengue Hemorrhagic Fever Grade III With Diabetic Ketoacidosis: A Case Report. *Journal Of The Medical Association Of Thailand = Chotmaihet Thangphaet*. 2011;94 Suppl 3:S233–S240.
- [17] Brown JM, Wilson TM, Metcalfe DD. The Mast Cell And Allergic Diseases: Role In Pathogenesis And Implications For Therapy. *Clinical And Experimental Allergy : Journal Of The British Society For Allergy And Clinical Immunology*. 2008;38(1):4–18. Doi:10.1111/J.1365-2222.2007.02886.X.
- [18] Hsueh WA, Lyon CJ, Quiñones MJ. Insulin Resistance And The Endothelium. *The American Journal Of Medicine*. 2004;117(2):109–117. Doi:10.1016/J.Amjjmed.2004.02.042.