

EXPANDED DENGUE SYNDROME (EDS) SYNDROME- A RARE CASE REPORT

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ABSTRACT

In this study the case of a 70-year male presented with complaints of high-grade fever, headache, myalgia, lassitude in the last 5 days with pain on swallowing food, rashes, exertional palpitation in the last 3 days. Patient also reported nausea, vomiting and altered mentation in the last 1 day before admission to hospital. Patient was referred to tertiary care centre as a case of supraventricular tachycardia (SVT) with shock with suspected viral encephalitis. ECG showed sinus arrhythmia and was hemodynamically unstable. Fever profile showed Dengue IgM seropositivity. NCCT brain had generalized cerebral oedema. USG abdomen had altered liver echotexture with mild hepatomegaly and TFT showed hyperthyroidism with anti TPO antibodies >600 IU/ml which was suggestive sub-acute thyroiditis. After detailed clinical examination, biochemical evaluation and imaging studies, a diagnosis of Expanded dengue syndrome (EDS) syndrome was made. Patient required RDPC transfusions and 3 cycles of forced alkaline diuresis in view of rhabdomyolysis. He was started on anti-thyroid, beta blocker and amiodarone. His fever rised everyday bone marrow analysis revealed hemophagocytic lymphangiohistiocytosis which subsided with intravenous steroids. Patient was discharged in good health on day 13.

KEYWORDS : EDS, SVT, AKI, HLH, TPO**INTRODUCTION**

Although most symptomatic dengue follows an uncomplicated course, but unusual manifestation are being increasingly seen due to rising disease burden. The World Health Organization (WHO) has coined 'Expanded dengue syndrome' to incorporate these multisystemic and multifaceted findings of dengue.¹

According to WHO about half of the world's population is now at risk of dengue with an estimated 100–400 million infections occurring each year.²

The dengue virus is an RNA virus from the genus *Flavivirus* transmitted via the bite of female *Aedes aegypti* mosquitoes. There are four virus serotypes, designated as DENV-1, DENV-2, DENV-3 and DENV-4. Infection with any one serotype confers lifelong immunity to that virus serotype and only partial cross immunity to other serotypes. However, secondary infection with another serotype or multiple infections with different serotypes can lead to a severe form of disease.³

The clinical presentation of dengue has varied patterns ranging from asymptomatic infection, to severe bleeding, hemodynamic instability and even death.

Expanded dengue syndrome (EDS) cases are underreported and pose a serious challenge for the treating physician. Knowledge of expanded dengue helps to clinch the diagnosis of dengue early, especially during ongoing epidemics, avoiding further battery of investigations.

CASE HISTORY

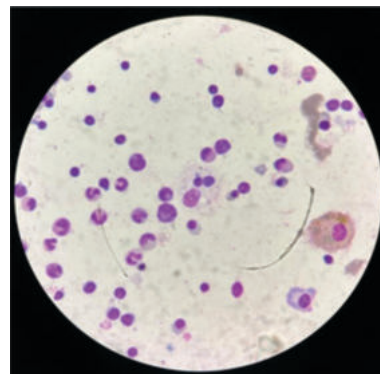
A 70-year male with no comorbidities presented with complaints of high-grade fever, headache, myalgia, lassitude in the last 5 days. Also pain on swallowing food, exertional palpitation, rash over extremities last 3 days. Patient also

reported nausea, vomiting and altered sensorium 1 day before admission to hospital.

Patient was taken to nearby private hospital and was referred to tertiary care center as a case of supraventricular tachycardia (SVT) with shock with suspected viral encephalitis.

On the initial assessment patient was disoriented, irritable, febrile (101°F) with Glasgow coma scale score of 14/15 with no neuro-deficit on examination. ECG was suggestive of supraventricular tachycardia with blood pressure of 100/50 mmHg, heart rate 164/min, respiratory rate 24/min, oxygen saturation of 96% on room air which was managed medically. There were non-palpable, non-itchy, non-scaling erythematous rashes over extremities more on lower limbs and trunk.

After stabilizing his vitals and primary supportive care, NCCT brain was done which was suggestive of generalized cerebral edema with no midline shift or evidence of bleed.

**Fig.1: Bone Marrow Aspiration Slide Showing**

Hemophagocytosis Of Intact Nucleated Rbcs & Neutrophils By Macrophages

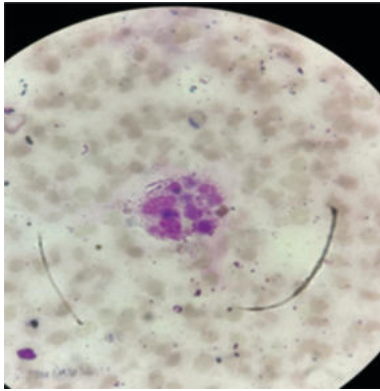


Fig.2: Bone Marrow Aspiration Slide Showing Hemophagocytosis By Macrophages

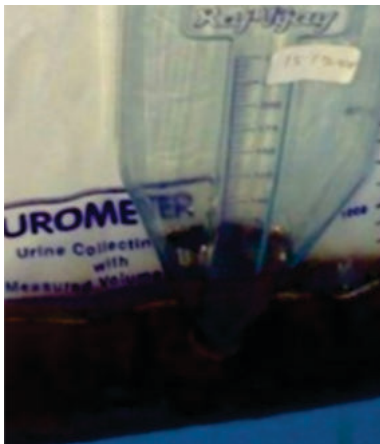


Fig.3: Dark Colored Urine Suggesting Underlying Rhabdomyolysis

Table 1: Laboratory Test Results Obtained During Hospital Admission

Lab Test	Day 2	Day 5	Day 12
Hemogram			
Hb [g/dl]	12.6	10.8	11.2
TLC [per cumm]	2400	3400	6300
Platelet [per cumm]	21,000	54,000	1,24,000
Hematocrit [%]	44	32	32
KFT			
Bld. Urea [mg/dl]	96	56	28
Creatinine [mg/dl]	2.4	1.9	1.4
LFT			
T. Bil. [mg/dl]	2.9	5	1.7
AST [U/L]	1825	1545	860
ALT [U/L]	592	636	245
Sr. Electrolyte			
Sr. Na+ [mmol/L]	156	141	136
Sr. K+ [mmol/L]	4.9	3.8	3.9
Lipid profile			
F. Tg	124	146	
T. Cholesterol	168	154	
HDL	38	40	
Coagulation Screen			
PT/INR	17/1.43		16/1.51
APTT [secs]	35		34
D-Dimer [ng/ml]		0.63	
LDH [U/L]	980	748	440
Sr. Lipase [IU/L]	23		
Urine R/M	albuminuria 1+, RBC nil/hpf, no casts/sediments.		

Fever Profile	Dengue IgM positive by ELISA, Malaria, Widal, Rickettsia Leptospirosis were Negative		
Covid RTPCR & H1N1 influenza virus	Negative		
Sr. CPK [U/L]	1800		360
Sr. Ferritin [IU/L]		1460	
HIV 1,2; Hep B, Hep C	Negative		
TSH			
f T3 [pg/dl]		480	
f T4 [ng/dl]		4.6	
TSH [mIU]		0.002	
Anti TPO Ab [IU/ml]		> 600	
ABG	Compensated metabolic acidosis with normal Anion gap		
Coomb's test	Negative		
Chest X-ray	Normal		
ECG	SVT	Atrial Flutter with 2:1, 3:1 & variable block Pattern	Normal
Qualitative Trop	Positive		
2D-Echo	45% Ejection Fraction with global hypokinesia, moderate LV systolic dysfunction		
NCCT Brain	Generalized cerebral edema		
Bone marrow study	Hemophagocytosis of cells by macrophages		

On investigation, hemogram showed bicytopenia with TLC-2400/cumm, platelet- 21,000/cumm, with deranged renal, liver functions with dyselectrolytemia. Fever profile came up to be dengue IgM [ELISA] to be positive and was negative for COVID 19, H1N1 Influenza, malaria, widal, rickettsia and leptospirosis. He was started on treatment as per protocol with CVP guided fluid therapy.

On foleys' catheterization, he was passing high colored urine with adequate urine output. His urine analysis showed albuminuria 1+, with no RBC or casts. His total CPK was sent and came to be highly elevated. ABG analysis showed normal anion gap metabolic acidosis with no hyperlactatemia. He was given 3 cycles of forced alkaline diuresis in view of rhabdomyolysis induced acute kidney injury. His urine output was maintained adequately without fluid overload.

His sensorium improved but he continued to have intermittent arrhythmias with atrial flutter 2:1, 3:1 and variable block pattern. Thyroid function showed hyperthyroidism with anti-TPO antibodies > 600 IU/ml suggesting sub-acute thyroiditis. USG Thyroid glands had diffused gland enlargement with increased vascularity. He was started on anti-Thyroid medication, beta blockers, steroid and amiodarone.

His fever continued spiking daily despite blood cultures being sterile. A clinical suspicion of HLH was made and bone marrow was done. Bone marrow analysis revealed hemophagocytic lymphangiohistiocytosis [HLH]. After a diagnosis of secondary HLH along with other supportive investigations, he was started on intravenous steroid therapy. His clinical condition improved with lab normalization.

Patient was discharged in good health on day 14.

DISCUSSION

Dengue is enlisted by World Health Organization (WHO) as one of ten threats to global health in 2019 and it has emerged as one of the major public health concerns with rapidly evolving epidemiology throughout tropical and subtropical regions.⁴

As a result, a large number of cases with atypical

manifestations of the disease are seen. Patient described in this case report is one example and reinforces the concept of classifying these atypical presentations as separate entity called expanded dengue syndrome.

In our case report, it was found 1+ albumin in urine, with deranged KFT as non-oliguric AKI. Nathan A. et.al.⁵ stated that a wide spectrum of unusual manifestations of dengue infection affecting various organ systems including gastrointestinal, hepatic, neurological, pulmonary and renal systems has been described.

In our case study 3 cycles of forced alkaline diuresis was given in view of Rhabdomyolysis similarly Arif A. et. al.⁶ quoted that rhabdomyolysis-induced acute kidney injury is one of the renal manifestations of EDS, which is characterized by elevated serum creatine kinase and increased excretion of myoglobin in the urine along with an increase in serum creatinine.

In our patient TFT showed hyperthyroidism with anti TPO antibodies >600 IU/ml. Further USG of thyroid showed diffuse gland enlargement with increase vascularity in study by Assir MZ. et. al.⁷ Subacute thyroiditis may develop during the course of dengue fever and should be included as a manifestation of expanded dengue syndrome. It should be suspected in patients with dengue fever who develop painful thyroid swelling and clinical features of hyperthyroidism.

Sheraz et.al.⁸ stated that dengue virus is rarely known to cause subacute thyroiditis. It can present as hyperthyroid, hypothyroid or euthyroid state; and in majority of cases, there is a complete recovery from altered thyroid state when disease subsides.

Medical treatment for hyperthyroidism is often not needed for transient thyroiditis because symptoms of transient thyroiditis are short lived. However, beta blockers may prove beneficial for symptomatic relief. In present cases we used beta blockers and steroids.

Carlos Henrique et al.⁹ study showed dengue causing acute myocarditis leading to arrhythmias, cardiogenic shock due to severe left ventricular dysfunction and death. This fulminant course of myocardial damage could be due to direct action of virus on myocytes or could be due to the release of inflammatory mediators.

CONCLUSION

EDS is a well-known entity that can present with Gastrointestinal, cardiac, renal, hematological, neurological, respiratory or endocrine manifestations. tachyarrhythmias, jaundice, anemia, increased bowel movements in patients with dengue fever with or without thyroid enlargement guard us to further investigate the case for evidence of hyperthyroidism. The nature and course of this syndrome depend on the severity of the clinical presentation. There is no direct correlation between the severity of dengue and the type of organ involvement, and even without the classical features of dengue, serious complications can arise. Hence quick and aggressive management is needed to prevent complications and fatality.

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