

Expanded Dengue Syndrome with Multiorgan Involvement in a Woman with Twin Intrauterine Fetal Death - A Case Report

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Abstract:

Dengue is the most rapid mosquito-borne disease in the world. As per the WHO guidelines for dengue fever, a list of atypical or unusual manifestations, also termed 'Expanded Dengue Syndrome' (EDS), is mentioned. Pregnancy increases the risk of expanded dengue syndrome. A 32-year-old woman with IUID (twin) at 36 weeks gestation with H/O I C/S was reported with expanded dengue syndrome with multiorgan involvement. She was referred to a tertiary centre with H/O high fever, loose motion, less fetal movement, and dengue NS 1 antigen positive. She was eventually diagnosed as having expanded dengue syndrome with multiorgan involvement with IUID (twin) at 36 weeks. The decision of

LSCS was taken by a multidisciplinary approach. She was managed with FFP, platelet apheresis, therapeutic plasma exchange, and I/V antibiotics, in addition to liver & neurological support in the ICU unit. This case emphasised the hazards of dengue infection in pregnant women, which needs special consideration. Early recognition with careful monitoring and multidisciplinary management are the key factors in a favourable outcome for a dengue patient.

Keywords: Expanded dengue syndrome, twin IUID, Multiorgan.

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Introduction:

Dengue infection is a mosquito-borne, neglected tropical disease. Dengue is a severe health problem globally, and its incidence has been on the over recent years all over the world (1). Dengue and dengue haemorrhagic fever are caused by four antigenically distinct dengue virus subtypes. Dengue virus is transmitted by *Aedes aegypti*. (1) After incubation of 4-10 days, the mosquitoes transmit the virus, and the infection varies from self-limiting subclinical infection to lethal complications such as dengue shock syndrome and multiorgan failure. (1) There are several atypical or uncommon presentations of dengue infection, including hepatitis, encephalitis, myocarditis, arthritis, and pancreatitis. Expanded dengue syndrome incorporates a broad spectrum of uncommon presentations of common diseases. World Health Organization (WHO) established guidelines for Expanded dengue syndrome in 2012. (2)

Dengue is endemic in Bangladesh with recurrent outbreaks and is one of the significant public health

concerns in Bangladesh. Dengue virus has the potential to cause epidemics resulting in high morbidity and mortality. All four dengue serotypes have been reported in Bangladesh, predominating DEN V-1 and DEN V-2 until 2016. Since 2019, when the largest dengue outbreak was reported, DEN V-3 has been the predominant serotype. (1,3) From 1 January to 7 August 2023, the Ministry of Health & Family Welfare of Bangladesh reported 69,483 laboratory-confirmed dengue cases and 327 total deaths, with a case fatality rate (CFR) of 0.47%. Of these, 63% of cases and 62% of deaths were reported in July 2023. (4), which is higher than the previous year. On further analysis, the overall CFR is higher in females than in males (0.72% vs 0.32%), with females having four times higher CFR than males among those aged 21-40 years. (0.71% vs 0.18%) (5) As pregnancy occurs in this age group, it is crucial to have a clear understanding of physiological changes in pregnancy and the progression of dengue to appreciate the potential complications of dengue in pregnancy. There is also evidence to suggest a higher percentage of severe dengue infections happening to pregnant to nonpregnant women. Many pregnant women with dengue infection may progress to have Dengue Shock Syndrome and Expanded Dengue Syndrome, and the mortality rate triples in these

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scenarios. (6) Considering the importance of this scenario, I report a case of Expanded Dengue Syndrome of a pregnant woman with IUFD (twin) at 36 weeks gestation, with a favourable outcome of the mother with the multidisciplinary team approach.

Case presentation:

A 32-year-old lady, a known case of 2nd Gravidae, Para 1 (c/s)+0 got admitted to a tertiary care hospital through emergency at her 36⁺ weeks twin pregnancy with dengue fever on 01 September 2023. She H/O high-grade fever for 6 days, afebrile for 1 day, H/O loose motion for 1 day, less foetal movement for 1 day. She was admitted to a local hospital two days back with a high fever for 4 days, and NS-1 antigen was positive and symptomatic treatment was given there. At ER department, she was ill-looking, dehydrated, and drowsy, with BP110/70mmhg, pulse 113/min, low volume, respiratory rate 20/min, blood sugar was 2 mmol/L, Fundal height 36 weeks, FHR (*Fetal Heart Rate*) was absent. Investigation done during admission revealed -

As the patient's condition was critical, with evidence of multiorgan involvement, she was admitted to the ICU department. After admission, the patient was evaluated clinically through general and systematic examination and a relevant investigation was carried out. Bedside USG of the whole abdomen showed G-11 fatty liver, partially contracted gall bladder, IUFD of twin pregnancy fetus A – 35⁺ 2 weeks, fetus B – 34⁺ 2 weeks with Spalding sign. Bedside ECHO showed features likely of myocarditis, mild LV, global hypokinesia, moderate MR, severe PR, Severe Pulmonary HTN, PASP 60 mmHg, RA RV

borderline dilated, EF 55%. The patient was jointly consulted with critical care medicine, obstetrician, cardiologist and gastroenterologist diagnosed as a case of Expanded Dengue syndrome with dengue hepatic encephalopathy myocarditis, severe metabolic acidosis, with twin IUFD pregnancy, history of c/s. and was treated as per dengue protocol. As the patient has a history of IUFD of twin fetuses and features of consumption coagulopathy, termination of pregnancy by LSCS was decided. Before LSCS, therapeutic plasma exchange was done, and 1 unit of plasma apheresis and 6 unit of FFP was given to her. LSCS was done under G/A on 02 September 2023. Two macerated dead female baby was taken out. Per operative, blood loss was average, and the uterus was well contracted by uterotonic. Her post-operative P/V bleeding and drain tube collection were average. She received another two sessions of plasma exchange on D-3&D-4, and 6 unit of FFP was transfused. However, her extubation was not possible on D-3 and deteriorated on the level of Glasgow coma scale. She developed persistent high temperature (103⁰ F). MRI of the brain on 04 September 2023 revealed dengue encephalitis involving both thalamus. A neurology consultation was taken. She was carefully resuscitated with blood products, including platelet FFP, platelet apheresis and therapeutic plasma exchange. Dengue encephalitis and hepatic encephalopathy were managed accordingly. Although the urine culture was negative, the blood culture revealed growth of Klebsiella, which was treated with a sensitive broad-spectrum antibiotic. Her fever gradually settled while on I/V antibiotics, and the level of liver enzymes was also improving (Table 1).

CBC:

Hb-14.6 gm/dl

HCT-49.5%

Platelet -34k/ μ l

WBC-20.8 k/ μ l

S. Electrolytes:

Na 137mmol/

K5.5 mmol/L

Cl111mmol

CO₂ 7 mmol/l

S.Cr 0.9 mg/dl

Liver Function Tests:

ALT-3230 U/L

AST-9704 U/L

LDH-8737 U/L

S Albumin 2.7g/dl

S. bilirubin- 3.9

Ammonia-78 μ mol/l

CRP-57mg/L

Trop1 .21ng/ml

ckMB 48 U/L

Coagulation Profile:

PT 23.4 Sec

Fibrinogen-102 mg/dl

FDP-55.7 μ gm/ml

D dimer 16.14 mg/l

aPTT 54.1 Sec

INR 1.98

Table-I

<i>Indicators of gradual improvement of the patient.</i>								
Investigations	Date of	02/09/2023	03/09/2023	04/09/2023	05/09/2023	08/09/2023	09/09/2023	12/09/2023
	admission (D1)	(D2)	(D3)	(D4)	(D5)	(D8)	(D9)	(D12)
Hb	14.6	12.2	9.7	9.4	9.9	10.8	11.6	9.9
HCT	49.5	40.5	31.1	29.1	31.7	38.4	40.5	32.3
Platelet	34	29	86	65	69	87	102	113
PT	23.4	18.8	17.1	19.5	14.4		15.5	
aPTT	54.1	43	37.5				27.4	
INR	1.98	1.57	1.43	1.64	1.19		1.30	
Fibrinogen	102.3			68.4	135			
ALT	3230		827	425	202	108		
AST	9794		2493	1189	520	111		
Ammonia			78	66	54	20	23	
TCO2	7	23	28	36	33			
S. Albumin		2.7		2.9				
CRP	57.4				17.4		22.4	
PCT		0.62			0.40		0.22	

She was extubated on 09 September 2023 (D-9). After being haemodynamically stable, she was shifted to the cabin as per step-down protocol, and stitches were removed on D-12. Her overall general condition was improving gradually. However, she was mentally unstable because of the disease process and the loss of her babies. She was discharged on 17 September (on day 17 of her admission) with a follow-up schedule one week later.

Discussion:

Dengue is one disease entity with different clinical presentations and often with unpredictable clinical evolution and outcome. Expanded Dengue Syndrome is terminology developed in WHO guideline 2012 to include unusual manifestations of patient with severe organ involvement such as liver, kidney, heart or brain, associated with dengue infection. These unusual manifestations may be associated with coinfections, comorbidities or complications of prolonged shock and can be clubbed as expanded dengue syndrome. Impacts of dengue on pregnancy are early abortion, embryopathy, APH due to placental abruption, preterm birth (3-33%), LBW (9-16%), IUGR, Foetal distress, IUFD or stillbirth (4.7-13%), increased incidence of cesarean section and postpartum haemorrhage. (7). Pregnancy is a hypercoagulable state and multiple pregnancies

impose additional physiological changes to a mother than a singleton pregnancy. Pregnancy complications like anemia, preeclampsia, gestational hypertension, polyhydramnios, and PPH are more in multiple pregnancy. In the case of IUFD, retention of the dead fetus can precipitate abnormal maternal bleeding. DIC can occur due to the gradual absorption of tissue thromboplastin (liberated from the dead placenta and decidua) into the maternal circulation and possible intrauterine consumption of fibrinogen and coagulation factors. Although the risk of DIC in IUFD is higher if the dead fetus remains more than 4 weeks in utero, in a decompensated state of expanded dengue syndrome, this feature can occur earlier (8). Acute hepatitis & hepatic failure, myocarditis, encephalitis were reported in this pregnant lady from part of the spectrum of Expanded dengue syndrome. Overall management of this pregnant patient was challenging from the onset of dengue fever. The disease followed an unusual path with several atypical manifestations like acute liver failure, myocarditis, and severe metabolic acidosis. DIC, & dengue encephalitis. The management was further complicated by the presence of twin intrauterine dead fetuses. So, she was jointly managed by critical medicine, cardiologist, obstetrician, gastroenterologist & neurologist. As she had features DIC, termination was urgent. Mode of termination in case DIC, through

vaginal root is safest because any surgical procedure may lead to profuse haemorrhage. But as she was not in labour, trial of labour by giving induction would be risky as she had twin pregnancy with H/O LSCS, which increased the risk of rupture of the previous cesarean scar. Moreover, time interval between induction-labour was uncertain, making delivery through vaginal root more complicated. So, the decision of termination by LSCS was taken by multidisciplinary approach. Before the procedure, adequate precaution was taken to prevent blood loss by giving blood products like FFP, Apheresis, small platelet, therapeutic plasma exchange. General anaesthesia was preferable to avoid epidural haematoma, as DIC increased the tendency of haemorrhage & epidural hematoma. (9) During surgery, caution was taken to minimise blood loss & and uterotonic drugs were used to control the postpartum haemorrhage. A drain tube was kept intraabdominally for monitoring. Hepatic encephalopathy, myocarditis, & encephalitis was managed along with supportive care & fluid management. Although neutrophilic predominance leukocytosis together with high fever can be observed in dengue shock, positive blood culture also supported klebsiella septicemia, necessitating management of both severe dengue & klebsiella septicemia in this patient with broad-spectrum antibiotic.

The case highlights the importance of a multidisciplinary team approach, early intervention, careful fluid management during a critical phase, and early administration of blood product in the presence of shock & coagulopathy and requires early diagnosis and management to avoid maternal mortality. High-risk pregnancy like multiple pregnancies with dengue fever should be judiciously treated. Early referral to a tertiary centre is recommended for proper management. Although we have saved the life of the mother for her living child, she has lost her two babies in utero. She also required mental health support.

Conclusion:

Dengue is a challenging disease with multisystemic, varied, atypical and sometimes life-threatening

presentation. Awareness of these rare manifestations goes a long way in early recognition, correct diagnosis, prompt intervention and treatment. Every aspect of dengue infection remains a clinical challenge. Dengue in pregnancy requires early diagnosis and treatment. Healthcare providers need to maintain a high index of suspicion when dealing with pregnant women who present with febrile illness in dengue-endemic areas. It is crucial that the onset of the critical phase is detected accurately and in a timely fashion by meticulous monitoring. It is also essential to look for unusual complications actively to improve outcomes.

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