

Myositis : Rare Presentation of Dengue, not Uncommon in Children

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Abstract:

Dengue myositis is a recently recognized category of idiopathic inflammatory myopathies manifested as symmetric proximal muscle weakness with severe limb pain and high serum creatine kinase (CK) levels, in dengue patient (NS1 positive or IgM positive).

A total 4 cases of dengue myositis were admitted at Shaheed Suhrawardy Medical College during the period from August to October, 2023. All were male & they presented mainly with severe limp pain with inability to walk they were diagnosed as dengue fever serologically. Two cases presented during febrile phase & two following fever. Their S. CPK level were high with mildly low platelet count. None of

them developed shock or hemorrhagic manifestation. They were treated supportively and all 4 cases recovered without any sequelae.

Dengue myositis in children is usually benign and is differentiated from other causes of flaccid paralysis by tenderness of calf and thigh muscles and raised CPK levels with other normal neurological findings. But sometimes it may result in serious consequences, so all children with dengue infection should be followed up carefully with S.CPK level.

Key Words: Myositis, Dengue, S. CPK

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Introduction:

Dengue, a global public health concern, is a mosquito-borne viral infection transmitted through a human-mosquito-human cycle commonly of warm and tropical regions.¹ Dengue cases reported by the World Health Organization (WHO) have increased 10-fold during the past 20 years.²

In 2023 dengue epidemic season, the country has been witnessing the deadliest outbreak of dengue fever ever since the first outbreak in Bangladesh in 2000. As of 19th October, 2023, the Directorate General of Health Services (DGHS) has reported 249,543 hospitalizations and 1,214 deaths due to the *Aedes* mosquito-borne tropical disease in the 2023 outbreak year.³

According to National Guideline for Clinical

Management of Dengue Syndrome, 4th edition, 2018 (revised) Bangladesh, the onset of DF is sudden with a sharp rise in temperature and is frequently associated with the features like headache, retro-orbital pain, photophobia, backache and pain in the muscles and joints or bones. Neurological manifestations of dengue vary from febrile seizures in young children, to encephalopathy, encephalitis /aseptic meningitis, intracranial hemorrhages/thrombosis, mononeuropathies, polyneuropathies, Guillain-Barré Syndrome or transverse myelitis. Recent observations suggest that neurological manifestations are being increasingly reported, with their incidence rates varying from 0.5% to 20%.³ Even though this is rare, neurological manifestation of DF is an increasingly recognized entity in recent years resulting in significant mortality and morbidity.⁴

Myalgias are common but myositis is an atypical neuromuscular manifestation in pediatric dengue patients.⁶ Dengue myositis is a recently recognized category of idiopathic inflammatory myopathies manifested as symmetric proximal muscle weakness with severe pain and high serum creatine kinase (CK) levels, along with specific histopathological finding in dengue patients (NS1 positive or IgM positive).⁵ The probable mechanisms of dengue myositis is because of invasion of muscle cells by virus directly as evidenced by detection of dengue virus in the Central Nervous System

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(CNS) by assessing viral proteins, ribonucleic acid (RNA) and immunoglobulins (Ig).⁷ Generation of toxins inside the muscle cells also play some role, various myotoxins has been seen like tumor necrosis factor (TNF) and interferon-(IFN)- α .⁸

Dengue myositis is considered as a diagnostic challenge as there can be atypical presentation and if the diagnosis is delayed, the risk of morbidity and mortality increases.⁹ On the other hand, Rhabdomyolysis is a potentially life-threatening condition caused by rapid breakdown of skeletal muscle with leakage of muscle contents into circulation resulting in raised muscle enzymes and acute renal failure in the setting of hypovolemia in dengue patients.¹⁶ There is a current paucity of data in our country on the clinical phenotype of dengue myositis in the pediatric population.

Here, we presented 4 cases of myositis with raised serum CPK in serologically proven dengue patients who were admitted in Shaheed Suhrawardy Medical College Hospital from August to October, 2023 and recovered. Parental consent both written and verbal was taken beforehand for publication.

Case description:

Case 1: A 9-year-old boy weighing 30 kg was admitted with the complaints of high-grade fever for 3 days with occasional vomiting, severe limb pain with limping for 2 days. On examination patient was found febrile, toxic & irritable. His vital parameters were within normal limits, but liver was palpable & tender. Lower Limb examination revealed mildly swollen calf muscles with tenderness grading $\frac{3}{4}$, deep tendon reflexes were normal with bilateral plantar flexor. Investigations showed dengue NS1 positive and his serial blood picture showed lowest leucocyte count -4000/ K/ μ L, lowest platelet count was-168 K/ μ L, highest S.CPK - 4156 U/L and S. electrolytes, S. creatinine, urine RE showed normal report. He was treated conservatively with IV fluid, paracetamol & monitored intensively. On day 3 of admission, S. CPK came down to 2310, U/L, SGPT became 230 U/L, Patient was gradually improving & he was discharged on day 7 after admission and after 6 days of discharge, S.CPK came down to 88 U/L.

Case 2: An 8-year-old boy presented with the complaints of high-grade fever associated with headache & occasional vomiting for 5 days, severe pain in both

limbs with limping for 2 days. On examination he was found febrile, conscious & oriented, temperature was 101 F, other vital parameters were within normal limit. Lower limb examination revealed muscle bulk normal, calf muscles tenderness grading $\frac{3}{4}$ on both limbs. Deep tendon reflexes were normal with bilateral plantar flexor. Serial blood count showed lowest total count was 4,300/ K/ μ L, lowest platelet count was 133 K/ μ L. IgM antibody for dengue was found positive & his S. CPK was 4035 U/L done on the 6th day of illness. The patient was treated with oral paracetamol. After 3 days, he improved significantly & started walking without support & S. CPK level came down to 1800 U/L & he was discharged on the 5th day of admission and CPK became normal on day 11.

Case 3: A 9-year-old boy was admitted with the complaints of high grade continued fever for 3 days, severe lower limb pain for 1 day with difficulty in walking. On examination, temp was 100 F, pulse 120/ min, BP was 90/60 mm of hg, patient was irritable but conscious & oriented, calf muscles were tender with grading $\frac{3}{4}$, jerks and muscle power were normal with bilateral plantar flexor. Investigations revealed dengue NS1 was positive and serial blood picture showed lowest leucocyte count 4,600 K/ μ L, lowest platelet count 137 K/ μ L, CPK 3250 U/L on admission. After 2 days pain decreased and patient could walk spontaneously. After 5 days of follow up CPK showed 1100 U/L and he was discharged, after 7 days CPK came back to normal

Case 4: A 5-year-old boy presented with the complaints of high-grade fever for 3 days followed by afebrile period for 1 day with severe limb pain and inability to walk aq for 1 day. On examination, he was found afebrile but irritable and vital signs were within normal limit. His lower limb examination showed symmetrically swollen calf muscles, tenderness grade $\frac{3}{4}$, muscle power and jerks were normal with bilateral plantar flexor. Investigations revealed dengue NS1 was positive, serial CBC showed lowest TC count and lowest platelet count were 5800 & 120 K/ μ L respectively, S.CPK-4080 U/L, SGPT- 31 U/L, S. electrolytes & S. creatinine were within normal limits. He was treated conservatively with oral Paracetamol & oral saline. After 3 days patient was gradually improving & S.CPK on day 5 showed 1488 U/ L, ultimately the patient was discharged & follow-up CPK after 10 days showed normal level.

Table-I*Clinical features & investigation findings of four (4) cases in tabulated form*

Sl. no	Age	Sex	Onset of myositis	Duration of Myositis	Mean duration of Myositis	Bleeding manifestation	Development of shock	Lowest Total count K/ μ L	Lowest Plateletcount K/ μ L	Peak CPK level U/L	Urine routine test	S.Creatinine	ALT U/L	Outcome
1	9 year	Male	Day 4	9 days	8.75 days	Absent	Absent	4	168	4156	Normal	Normal	230	Complete recovery
2	8 year	Male	Day 3	7 days		Absent	Absent	4.3	133	4035	Normal	Normal	60	Complete recovery
3	9 year	Male	Day 2	8 days		Absent	Absent	4.6	137	3250	Normal	Normal	28	Complete recovery
4	5 year	Male	Day 3	11 days		Absent	Absent	5.8	120	4080	Normal	Normal	37	Complete recovery

Discussion:

The musculoskeletal manifestations of dengue fever include polyarthritides, rhabdomyolysis, and myositis with elevated CPK¹⁰ and the various neurological manifestations reported include encephalitis, myelitis, Guillain-Barré associated with DENV-2 and DENV-3 infections.¹¹ It is remarkable that, DENV-2 became a predominant serotype (51%) along with DENV-3 (44%) in Bangladesh in 2023.¹²

With recent epidemic of dengue fever this year, there was an increase in reported cases of unusual and rare manifestation of dengue fever, one of which is myositis.

In our series, all are male with age varying from 5- 9 years. Garg RK compiled a total of 34 studies of dengue-associated myositis where he reported that it is common in younger age group (mean: 24.6 years) with predilection for male (male: female = 26:8)¹¹. Onset of weakness varies from 3 days to 36 days (mean: 9.4 days) which is similar to our series who recovered within 7-14 days (mean 9 days).¹¹ Mekmangkonthong et al found a 9-year-old boy presented with acute proximal muscle weakness after 5 days of recovery from dengue fever.¹³ But in our series 2 cases presented during febrile period and another 2 patients presented after subsidence of fever.

In our series it is remarkable that none of our patients experienced shock or hemorrhagic manifestation. All of our patients were hemodynamically stable and none of them showed features of plasma leakage like pleural effusion or ascites or renal involvement like oliguria or hematuria platelet count was above 100K/ μ L. Davis JS et al showed 2 patients of dengue myositis who

developed rhabdomyolysis due to dengue virus infection. Among them the first patient recovered with no sequelae, but the second developed multiple organ failure and died. Rhabdomyolysis is not well described as a complication of dengue virus infection and is probably underrecognized.¹⁴ Wijesinghe et al described the case of a 42-year-old, previously healthy Sri Lankan Sinhalese man who developed acute renal failure due to rhabdomyolysis following dengue virus infection whose highest CPK was 6240 U/L & recovered after hemodialysis.¹⁵ It should be kept in mind that the threshold for suspecting rhabdomyolysis is very low in dengue fever & that's why Creatinine phosphokinase(CPK) levels should routinely be measured in all patients with dengue fever with suspected myositis for early detection of rhabdomyolysis to prevent acute renal failure.

Misra *et al.*¹⁰ observed that out of 24 patients with dengue fever aged 5–65 years, 8 had pure motor quadriplegia having muscle weakness in all four limbs who had normal NCS, myopathic EMG, and raised serum CPK suggesting myositis.

Our 4 patients recovered spontaneously without any immunosuppressive therapy (mean duration of weakness: 7 days). Misra *et al* showed all patients of his study had complete recovery by 2 weeks.¹⁰ On the other hand, Mekmangkonthong et al showed that a patient of dengue myositis, initially responding to oral steroids, experienced persistent weakness with markedly raised muscle enzymes (CPK :30,833 mg/dL) who was ultimately treated with IVIG monotherapy for 3 months

with complete recovery¹³, but all our cases showed CPK level below 5000IU.

Conclusion:

The current trend of dengue infection among children in Bangladesh shows an increased frequency of myositis. As dengue myositis is benign but may have the potentiality to give rise to serious consequences and such patients should be evaluated for rhabdomyolysis and acute renal failure which are potentially preventable complication. So all patients presented with fever, pain, and tenderness of muscles and associated raised CPK enzyme should be screened for dengue.

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