

Dengue Fever with Myositis- An Uncommon Complication of a Common Disease

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ABSTRACT

Dengue has a high prevalence in tropical countries including India. Although myalgias are a common musculoskeletal manifestation in dengue but myositis is unusual. The present case series describes three cases of female patients with dengue fever (35-year-old, 30-year-old and 37-year-old), who developed severe pain and tenderness in muscles and were diagnosed with myositis. The present case series emphasises the fact that, although the condition is usually self-limiting, but it has the potential to aggravate into life threatening conditions like acute respiratory and renal failure, if left unattended.

Keywords: Creatine kinase, Dengue virus, Musculoskeletal manifestations

INTRODUCTION

Dengue is an arboviral disease caused by four closely related serotypes of dengue virus (DENV 1-DENV 4) commonly transmitted by the bite of an infected female *Aedes* species mosquito. The estimated incidence is 390 million dengue virus infections and between 50 to 100 million symptomatic cases [1,2]. Main complications of the disease include haemorrhagic fever, and shock syndrome. Although myalgias are commonly seen; but myositis is an uncommon complication of dengue virus infection [3]. In the present case series, the authors present three cases of dengue fever which developed severe myalgias along with weakness and raised Creatine Phosphokinase (CPK) enzyme levels and were eventually diagnosed as myositis. All the cases developed the symptoms after five to six days of fever onset and recovered spontaneously within a week with supportive treatment.

CASE SERIES

Case 1

A 35-year-old woman presented to the medicine emergency with complaints of high grade fever for eight days associated with generalised body ache for three days. Fever was associated with severe progressive myalgia and patient was unable to walk at the time of presentation. There was no history of bleeding from any site. The patient was non diabetic and non hypertensive and not on any long term medication prior to the illness.

On examination, patient was febrile, blood pressure was 110/70 mmHg in right arm supine position and pulse rate was 96/minute. On systemic examination, cardiovascular, respiratory and abdominal systems were within normal limits. On clinical examination for nervous system, there was decreased power of grade 4/5 along with tenderness in both lower limbs. However, higher mental functions were normal and there was no sensory impairment.

The patient was investigated thoroughly and had thrombocytopenia (platelet count, 7000 cells/cumm) at the time of presentation. Dengue serology was positive for IgM dengue antibodies. Ultrasound revealed oedema of gall bladder wall and chest X-ray was within normal limit. Considering the symptoms of myalgia, the patient was tested for CPK levels which were high, 480 units/L.

Based on the clinical evaluation and investigations, the patient was diagnosed as dengue fever with myositis and supportive treatment was offered in the form of parenteral fluids and antipyretics. The patient showed signs of recovery after two days of admission and subsequent CPK levels came out to be 300 units/L. The platelets

count also improved and finally, patient was discharged after six days of admission. The patient was doing well at two weeks of follow-up.

Case 2

A 30-year-old female presented to the medicine department with history of fever for seven days, associated with abdominal pain and body ache and difficulty in walking for past two days. There was no history of bleeding from any other site. The patient was non diabetic and non hypertensive and was not taking any long term medicine prior to fever.

On examination, patient was afebrile and vitals were normal. On systemic examination, cardiovascular, respiratory and abdominal systems were within normal limits. On clinical examination of nervous system, there was decreased power of grade 4/5 in both lower limbs without any sensory impairment and higher mental functions were preserved. On local examination, there was generalised tenderness in the bilateral lower limbs and upper limbs. The blood investigations revealed thrombocytopenia (platelet count- 20000 cells/cumm) at the time of presentation. Dengue serology was positive for IgM dengue antibodies. Ultrasound revealed mild hepatosplenomegaly and chest X-ray was normal. Serum CPK levels were high reaching up to 1000 units/L.

In view of the presenting symptoms, signs and investigation reports, a diagnosis of dengue fever with myositis was made and supportive treatment was offered with intravenous fluids. The patient started recovering and after two days of admission, CPK levels came down to 483 units/L and further declined to 320 units/L the next day. Gradually the patient started walking on her own after three days of admission. The platelet count also improved gradually and finally patient was discharged after four days of admission and the patient was doing well at one week post discharge.

Case 3

A 37-year-old female presented to the medicine department with history of fever for six days, associated with body ache for last two days. The patient was having severe limitation in walking due to severe body ache. There was no bleeding from any site. The patient was non diabetic and non hypertensive and not on any long term medication prior to fever.

On examination, patient was afebrile, vitals were maintained and on systemic examination, cardiovascular, respiratory and abdominal systems were within normal limits. On clinical examination of nervous system, higher mental functions were normal and there was

slight decrease in power of both lower limbs. However, there was no sensory impairment. The haemogram revealed thrombocytopenia (platelet count- 81,000 cells/cumm) at the time of presentation and dengue serology was positive for IgM dengue antibodies. Ultrasound revealed mild ascites and hepatomegaly and chest X-ray was normal. The CPK levels were elevated at 724 units/L.

A diagnosis of dengue fever with myositis was made and supportive treatment was offered. The patient started recovering and the next day, the patient was able to walk without support. The platelets count also improved and patient was discharged after three days of admission. The patient recovered completely and was doing well at two weeks postdischarge.

DISCUSSION

Dengue fever is caused by dengue virus belonging to the genus *Flaviviridae* and has a high prevalence worldwide and in India. Most Indian states are classified as having frequent or continuous risk of dengue transmission [4]. A meta-analysis of published studies from India estimated a dengue case-fatality ratio of 2.6% (95% CI 2.0-3.4) [5].

The disease has a wide spectrum of presentation ranging from asymptomatic infection in approximately two-third cases to mild to moderate febrile illness to severe disease with end organ impairment in some cases [6]. The common manifestations of the disease include non specific symptoms such as nausea, vomiting, rash, myalgias, arthralgias, retro-orbital pain, headache and leukopenia.

Among the neuromuscular complications of dengue, mononeuropathies, polyneuropathies, encephalitis, Guillain Barre syndrome, myositis and rhabdomyolysis have been documented. Myalgia is one of the most common presentations. Over the last decade, a decent number of studies have reported myositis as prominent presentation of dengue. One of the earliest studies was reported from Brazil in 1993, where 15 patients with dengue fever were subjected to muscle biopsy and features suggestive of myositis were found in 12 patients [7]. A study examined the neurological complications in dengue in India and principally observed two patterns of neurological involvement: one with features of encephalopathy and the other with features of pure motor weakness and myositis [8].

Garg RK et al., studied dengue related neuromuscular complications in 2015 and published a compilation of 34 studies of dengue related myositis [9]. They found the condition to be more prevalent in younger age group (mean 24.6 years) and majority of patients were males. Serum CPK levels were markedly elevated in most of the patients. The patients were reported to have symptom onset of muscle weakness ranging from 3 to 36 days (mean 9th day) of illness and recovered spontaneously in mean duration of seven days. In another study, 16 patients of dengue fever with quadriplegia were studied [10]. All of them had elevated CPK level and transaminases. Similarly, a study from India reported seven cases of dengue fever with myositis with raised CPK levels of which three had respiratory muscle involvement [11]. Although in most of the studies, myositis usually resolved after few days of onset of dengue fever, but there are instances where it has been reported to persist beyond several weeks after onset and finally, responded when the patient was administered steroid therapy [12].

Nonetheless, myositis is still an uncommon presentation of dengue and is seldom suspected. Thus, it usually remains underdiagnosed. A few studies have emphasised the early recognition of this condition, as sometimes it can progress to a state of rhabdomyolysis with ensuing acute renal failure if undetected or untreated. A study by Sargeant T et al., reported such a case, where a 25-year-old initially diagnosed with dengue fever, later developed complaints of passage of dark coloured urine and subsequently was diagnosed with myositis with rhabdomyolysis with very high values of CPK [13]. Similar studies of dengue fever with acute fulminant myositis progressing to acute renal failure have also been reported from Sri Lanka and India [14,15]. Another study from Australia reported two cases of dengue fever with rhabdomyolysis, one of which rapidly progressed to acute renal failure with multiorgan dysfunction and eventually, succumbed due to the disease [16].

The salient features of present case series are tabulated in [Table/Fig-1], while the comparative features of some important studies reporting myositis in dengue fever are summarised in [Table/Fig-2] [3,10,11,13-16]. The studies discussed, so far amply demonstrate the importance of creatine kinase as a diagnostic tool for dengue myositis. The present case series similarly emphasises the

Case no.	Onset of myositis	Platelet count at admission	Peak CPK level (U/L)	Gender	Age	Radiology findings	Outcome	Co-morbid conditions
Case 1	6 th day of fever	7,000 cells/cumm	480	Female	35 years	Oedematous gall bladder on ultrasound, Chest X-ray normal	Complete recovery with supportive care within one week	None
Case 2	6 th day of fever	20,000 cells/cumm	1000	Female	30 years	Liver and spleen mildly enlarged on ultrasound, Chest X-ray normal	Complete recovery with supportive care within one week	None
Case 3	5 th day of fever	81,000 cells/cumm	724	Female	37 years	Mild ascites and enlarged liver on ultrasound, Chest X-ray normal	Complete recovery with supportive care within one week	None

[Table/Fig-1]: Clinical characteristics of cases in present study.

S. No.	Authors	Year	No. of cases	Gender	Age	Peak CPK level	Outcome
1.	Gunasekera HH et al., [14]	2000	1	Female	28 years	5000 U/L	Developed renal failure followed by full recovery with supportive care
2.	Davis JS and Bourke P [16]	2004	2	2 Males	33 years	17548 to 51555 U/L	One case recovered while other progressed to rhabdomyolysis with acute renal failure and multiorgan dysfunction and finally succumbed to disease
3.	Kalita J et al., [10]	2005	7	5 Males 2 Females	9-42 years	260 to 3050 U/L	All seven had quadriplegia with complete recovery in six patients, one needed ventilatory support
4.	Acharya S et al., [15]	2010	1	Male	40 years	29,000 U/L	Developed quadriplegia and respiratory failure requiring ventilatory support
5.	Paliwal V et al., [11]	2011	7	5 Males 2 Females	3-40 years	16,590 to 117,200 U/L	Complete recovery with supportive care in five patients, two succumbed to respiratory failure
6.	Sargeant T et al., [13]	2013	1	Male	25 years	3,25,600 U/L	Full recovery with supportive care
7.	Gulati K et al., [3]	2020	1	Male	14 years	3908 U/L	Full recovery with supportive care
8.	Present study	2022	3	3 Females	30-37 years	480 to 1000 U/L	Full recovery with supportive care

[Table/Fig-2]: Comparative features of dengue myositis reported in some studies [3,10,11,13-16].

presence of this condition in dengue. As evident from [Table/Fig-1], patients in the present case series were in young age group and had onset of symptoms after the fifth day of fever. This is in agreement with most of the previous studies in which myositis occurred after few days of fever, which is the time at which body's immune response to the virus is thought to get activated leading to release of inflammatory cytokines which then causes muscle damage. Another important aspect observed in the present study similar to the previous reported ones is that, the condition is self-resolving in most cases, with recovery within few days. However, the present case series stands apart from the previous ones in that all cases in present case series belong to female gender, whereas in most of previous studies, a slight male preponderance is observed.

The mechanisms involved in the development of myositis in patients with dengue fever are largely unknown. Usually, the muscle involvement in dengue is believed to be not due to direct invasion of muscle by the virus. Instead, some studies have suggested that the most likely cause may be due to release of proinflammatory myotoxic cytokines, like Tumour Necrosis Factor (TNF) and Interferon Alpha (IFN- α) released by human body in response to dengue virus [17]. The muscle biopsy in such cases usually reveals mild lymphocytic infiltrate with areas of myonecrosis [7, 18].

CONCLUSION(S)

Dengue myositis as an entity should be suspected in patients presenting with dengue fever associated with myalgias and muscles weakness. In such cases, CPK level should be assessed promptly to establish the diagnosis. Although most cases are self-limiting and recover within few days, the condition should be monitored closely with serial estimation of creatine kinase enzyme levels as some cases can progress to rhabdomyolysis and acute renal failure with unfavourable outcomes, if left undiagnosed and unattended.

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PLAGIARISM CHECKING METHODS: [Jain H et al.]

- Plagiarism X-checker: Dec 31, 2022
- Manual Googling: Feb 04, 2023
- iThenticate Software: Mar 09, 2023 (6%)

ETYMOLOGY: Author Origin

AUTHOR DECLARATION:

- Financial or Other Competing Interests: None
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Dec 30, 2022**
Date of Peer Review: **Jan 27, 2023**
Date of Acceptance: **Mar 11, 2023**
Date of Publishing: **Apr 01, 2023**