Original Research Paper

Volume-8 | Issue-2 | February-2018 | PRINT ISSN No 2249-555X

Pathology

RHABDOMYOLYSIS ASSOCIATED WITH DENGUE FEVER-FAVORABLE OUTCOME IN A BIOPSY PROVEN PATIENT.

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ABSTRACT **Background:** Dengue viral infection has varied clinical presentation and rhabdomyolysis is rare.
Case presentation: A male patient presented with acute onset of fever, headache and myalgias of one week duration. On investigation, he had mild leucopenia, thrombocytopenia, microscopic hematuria, mildly elevated serum creatinine, myoglobinuria and markedly elevated creatine kinase. Dengue antibodies IgM were positive. Muscle biopsy showed marked myofiber necrosis without inflammation. Patient made complete recovery with hydration therapy and supportive care.
Conclusion: Rhabdomyolysis is reported to be the most severe form of muscle involvement, occurring in patients with dengue fever and is associated with high morbidity and mortality. Early diagnosis and treatment can prevent complications.

KEYWORDS : Dengue fever, rhabdomyolysis, myofiber necrosis.

Background:
Dengue virus infection is endemic with outbreaks reported from various parts of India.[1] The clinical presentation is varied and includes neuromuscular manifestations that include myalgias/transient muscle dysfunction, myositis, rhabdomyolysis and hypokalemic paralysis.[1-3] Rhabdomyolysis is reported to be the most severe form of muscle involvement, occurring in 0.66-0.84% of patients with dengue fever and associated with high morbidity and mortality.[1,4] Garg et al reviewed the neuromuscular manifestations of dengue fever and noted 14 reported cases of rhabdomyolysis.[1] Twelve more patients were reported since then.[4-7] We report a patient with dengue fever with biopsy proven rhabdomyolysis, who made uneventful recovery.

Case report:
A 36 year old male presented with fever, headache and myalgias of one week duration. Fever was of high grade and associated with chills and rigors. He complained of painful limb movements, especially of lower limbs. There was no history of rash, altered sensorium or bleeding manifestations. He gave history of one episode of dark colored urine one day prior to admission. On examination, he was febrile with temperature 100 degrees F, pulse of 80/minute, blood pressure of 130/80 mm Hg. He was conscious, coherent with normal higher intellectual functions. There was no neck stiffness, no cranial nerve palsies. There was diffuse tenderness of lower limb muscles with power in the proximal muscles 3/5 and distal muscles 4/5. Deep tendon reflexes were preserved. The respiratory, cardiovascular and abdominal examination was unremarkable. Chest radiograph and ultrasound abdomen were unremarkable. Complete blood picture showed hemoglobin of 12 g/dl; total leukocyte count of 3,500/cu mm, platelet count of 80,000/cu mm. Peripheral smear was negative for malarial parasite and antigen test for *Plasmodium falciparum* was negative. Urine examination was negative for sugar and albumin; microscopic examination showed 10 RBC /high power field. Urine was positive for myoglobin. Serum creatinine was 2 mg% and serum creatine kinase (CK) was 12,000IU/L. Rest of the biochemical investigations were within normal limits. Serology for dengue antibody IgM was strongly positive and serology for leptospira, hepatitis B and C viruses was negative.

Open muscle biopsy from left vastus lateralis showed significant myofiber necrosis with myophagocytosis and vacuolation of sarcoplasm.

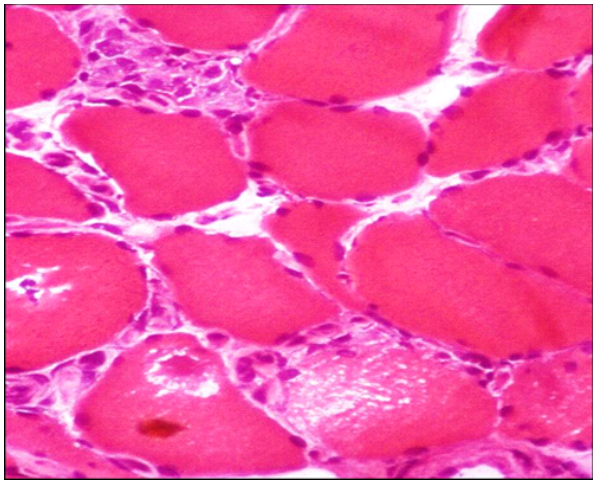

Figure: Photomicrograph shows muscle biopsy with myofiber necrosis with myophagocytosis and sarcoplasmic vacuolation. Hematoxylin and eosin x40.

There were no perivascular or endomysial inflammatory infiltrates. There were no mitochondrial abnormalities and stains for lipids were negative. A diagnosis of rhabdomyolysis associated with dengue fever was made and patient was treated with aggressive hydration therapy and supportive care. He improved symptomatically and was discharged after one week. His serum CK was 800 IU/L and serum creatinine was 0.8mg% at the time of discharge.

Discussion:
Severe myositis and rhabdomyolysis are reported in association with several viruses, but rhabdomyolysis associated with dengue virus infection is uncommonly reported.[1,4-8] Huang et al reported 9 patients with rhabdomyolysis in a review of 1076 patients with dengue fever and observed that fever and myalgias were the common manifestations of rhabdomyolysis.[4] Our patient had severe myalgias, diffuse tenderness, painful movements and mild muscle weakness associated with myoglobinuria and markedly elevated CK. Correlation was reported between severity of muscle weakness, CK and degree of myositis.[9] The muscle biopsy features include perivascular inflammatory infiltrates, myositis, myofiber necrosis, mitochondrial abnormalities, lipid accumulation, type grouping and

rhabdomyolysis.[1,5,6,10] Muscle biopsy in our patient showed myofiber necrosis with myophagocytosis and sarcoplasmic vacuolation. In most of the reported cases of rhabdomyolysis in dengue fever, diagnosis was established on clinical, serological and biochemical evidence and muscle histopathology was not sought.[4,5,8]

It is reported that rhabdomyolysis, acute renal failure and multiorgan failure are associated with high mortality in dengue fever and hypertension, myalgia and acute kidney injury were independent risk factors for rhabdomyolysis.[4,8] Though clinical evidence of bleeding manifestations and renal failure were not present in our patient, the investigations showed mild leukopenia, thrombocytopenia, microscopic hematuria and mildly elevated CK in our patient. He made an uneventful and complete recovery probably due to prompt treatment and no associated hypertension or acute kidney injury.

The pathogenesis of rhabdomyolysis in dengue fever is unknown. Immune mediated damage of muscle fibers, myotoxic cytokines including tumor necrosis factor and interferon alpha released during viral infection and elevated levels of intracellular calcium were implicated in the pathogenesis.[1,4,8]Huang et al reported elevated levels of IL-6 and TNF-alpha in patients with dengue fever and rhabdomyolysis.[4]

Serological confirmation of dengue fever is important in endemic areas like India in epidemics of fever and early recognition and prompt institution of treatment prevents potential complications like rhabdomyolysis which may be associated with high morbidity and mortality.

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