

Diabetic myonecrosis: four-year experience of managing a rare disease in a tertiary care hospital in Bangladesh

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ABSTRACT

Background: Diabetic myonecrosis is an under-reported complication of long-standing, poorly controlled diabetes mellitus. It is usually a self-limiting condition and responds well to conservative management. Patients with diabetic myonecrosis frequently have other microvascular complications. Although the short-term prognosis is good, the long-term prognosis is poor. Less than 200 cases have been reported in the literature since it was first described 46 years ago. There is no clear 'standard of care' for managing these patients. Due to a lack of awareness, the diagnosis is often missed, resulting in unnecessary and deleterious interventions such as antibiotics, muscle biopsies and surgery which can complicate the recovery. We report six cases of diabetic myonecrosis admitted in a tertiary care hospital; all of them recovered well by conservative measures like analgesics and bed rest. Our report aims to emphasize the importance of early diagnosis of diabetic myonecrosis and to find out the pattern of clinical, biochemical and radiological profiles among the myonecrosis cases.

Methods: Patient's socio-demographic, clinical, laboratory data were recorded systematically in case-record forms after obtaining informed written consent from patients or attendants over four years from 2018 to 2021.

Result: We report six cases of diabetic myonecrosis managed in a tertiary care hospital over four years. Five of the cases were female and all had type 2 diabetes mellitus, with a mean duration of diabetes was 14.5 years. The presentation was acute in four patients and sub-acute in another two patients. All these patients had poorly controlled diabetes mellitus; the average HbA1c was 10.8%. Microvascular complications of diabetes mellitus were found in all the cases.

Conclusion: Diabetic myonecrosis is an underdiagnosed complication of diabetes mellitus. It should be considered in the differential diagnosis for diabetic patients who present with painful swollen muscles. A high index of suspicion requires for the diagnosis, which avoids unnecessary intervention.

Key words: Diabetes Mellitus, myonecrosis, magnetic resonance imaging

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INTRODUCTION

Diabetic myonecrosis is a rare and under-diagnosed complication of diabetes mellitus. Clinically, it presents with acute to subacute onset of swelling, pain and tenderness of muscle(s) without systemic manifestations.¹ Magnetic resonance imaging (MRI) is helpful in diagnosis, exclusion of other causes and localisation of affected muscle for biopsy in atypical cases. Muscles of the thighs are commonly affected in diabetic myonecrosis.² Here, we present the summary of six cases diagnosed in the last four years in a tertiary care hospital. All these patients had a long duration of diabetes with microvascular complications and poor glycemic control. Our cases were treated conservatively with rest and analgesics. This study aims to emphasize the importance of early diagnosis of diabetic myonecrosis and to find out the pattern of clinical, biochemical and radiological profiles among the myonecrosis cases.

METHODS

This case series included six patients (including one published case)² who were diagnosed as a case of

diabetic myonecrosis at Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorders (BIRDEM) General Hospital, Dhaka, Bangladesh from 2018 to 2021. Diabetic myonecrosis was confirmed by histopathological/radiological evidences of muscle necrosis at the affected sites. MRI was done in five patients and one patient was diagnosed by muscle biopsy. Patients' selected demographic, clinical and laboratory data were recorded in the case record forms after getting informed written consent. Patients were followed up clinically and over the phone, as appropriate, for six months since the first diagnosis of myonecrosis.

RESULTS

In this small series, we report on six patients of diabetic myonecrosis managed in a tertiary care hospital over a period of four years (Table I, Table II and Table III). Three patients had thigh muscle involvement (Figure 1 A,C,D), two developed myonecrosis in the calf muscle group (Figure 1,B) and entire leg involvement was found in one patient (Figure 1, E). All were type 2 diabetes

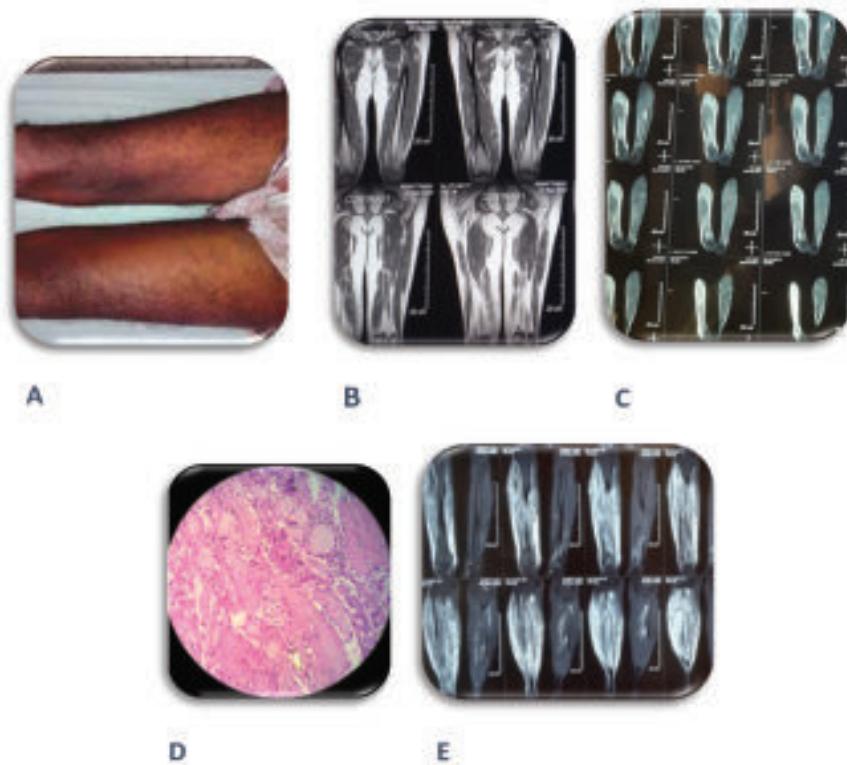


Figure 1 Selected imaging of our case series patients. A, Patient 1: Swelling of the left thigh. B, Patient 2: T2WI showing hyperintensity in the calf muscle of right leg. C, Patient 3: post-contrast view showing non-enhanced infarcted area in the right thigh. D, Patient 4: Medium power photomicrograph of muscle biopsy showing degenerated muscle fibres. E, Patient 6: T2WI showing hyperintensity in all muscles of right leg.

Table I Demographic and clinical parameters of patients of diabetic myonecrosis (N=6)

Parameter	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6
Demographic						
Age (years)	50	60	57	35	56	50
Sex	male	female	female	female	female	female
Occupation	service holder	house wife	house wife	teacher	house wife	house wife
Clinical presentation::						
Clinical features: (pain and swelling of the affected area)	+	+	+	+	+	+
Onset of symptoms	acute	acute	acute	sub-acute	acute	sub-acute
Recurrence of symptoms	no	no	no	yes	yes	no
Site of involvement	left thigh	right calf	right thigh	left thigh	both calf	right leg
Duration of Diabetes mellitus (years)	15	20	15	15	10	12
Presence of other microvascular complication:						
Nephropathy	+	+	+	+	+	+
Retinopathy	+	+	+	+	+	+
Neuropathy	-	+	+	+	+	+
Other Comorbidities:						
Hypertension	+	+	+	+	+	+
Hypothyroidism	-	-	-	+	+	-

Table II Investigation profile of patients of diabetic myonecrosis (N=6)

Parameter	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6
Biochemical:						
HbA1C (%)	9.9	15.4	11.2	11.8	8.7	7.1
Hb (gm/dl)	5	10.5	11.4	7.9	8.8	7.5
Total WBC (/cmm)	12090	10710	10600	4400	11400	13180
ESR (mm/hr)	41	69	35	60	74	58
CRP (mg/L)	136	30	3.65	3.44	33.6	23
CPK (U/L)	270	170	310	192	234	180
Serum creatinine (mg/dl)	4.7	2.8	1.6	1.8	2.7	6.0
Radiological:						
MRI	features of myonecrosis	features of myonecrosis	features of myonecrosis	Not done	features of myonecrosis	features of myonecrosis
Muscle biopsy	Not done	Not done	Not done	features of myonecrosis	Not done	Not done

Table III Treatment profile of patients of diabetic myonecrosis (N=6)

Parameter	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6
Treatment of myonecrosis	Bed rest, opioid analgesic	Bed rest, opioid analgesic, aspirin	Bed rest, opioid analgesic, aspirin	Bed rest, opioid analgesic	Bed rest, opioid analgesic	Bed rest, opioid analgesic
Duration of treatment	4 weeks	3 weeks	2 weeks	2 weeks	3 weeks	4 weeks

DISCUSSION

Angervall and Stener first described diabetes myonecrosis in 1965.¹ The exact pathogenesis is unknown but different hypotheses have been proposed; it may result from a hypoxia-reperfusion injury, atherosclerotic occlusion, vasculitis with thrombosis, small vessel atheroembolism or a state of hypercoagulability. However, the most accepted hypothesis is thromboembolic events resulting from tissue ischemia leading to oxidative stress and finally, tissue necrosis. Reperfusion injury causes further damage associated with endothelial dysfunction, manifested as impaired endothelium-dependent dilation in arterioles along with increased oxygen radicals, with less nitric oxide following reperfusion.³ Following imbalance between superoxide and nitric oxide in endothelial cells leads to the production and release of inflammatory mediators (tissue necrosis factor, platelet aggravating factor) and increased biosynthesis of adhesion molecules. The inflammatory cascade increases intra-compartmental necrosis and ischemia.²

It occurs in patients with long-standing diabetes (>15 years) along with microvascular complications including retinopathy (71%), nephropathy (57%) and/or neuropathy (55%).² Patients usually present at a mean age of 40 years with acute or subacute onset pain, tenderness and oedema of muscles.³ Muscles of thigh and hip are more commonly involved, with the most common muscle being quadriceps (60–65%), followed by hip adductors (13%), hamstrings (8%) and hip flexors (2%). Further, calf muscles may also be affected in myonecrosis.^{2,3} In our series, thigh muscles are involved in three patients.

A 2015 systematic review of all cases published in the English language since the initial description of the condition in 1965 identified reports of 170 episodes of diabetic muscle infarction, including 126 initial episodes and 44 episodes of recurrence, with a mean age at

presentation of 45 years (range 20 to 67 years).⁴ The number of patients with type 1 and type 2 diabetes identified in this review was similar. However, the mean age at presentation with muscle infarction was lower for type 1 diabetics than for type 2 diabetics (36 years [20 to 65 years] versus 52 years [34 to 67 years]). The mean duration of diabetes at the time of presentation with muscle infarction was longer for those with type 1 diabetes (19 years [5 to 33 years] versus 11 years [1 to 25 years]). Other complications of diabetes were present in the majority of patients, with the most common microvascular complication, nephropathy, present in 75 percent of the patients. Of the 126 cases reviewed, 47 percent had concurrent retinopathy, nephropathy and neuropathy and 66 percent had at least two diabetic complications.⁵

Diabetic myonecrosis usually presents in a middle-aged patient complaining of an acute/sudden onset of pain in the hip, thigh or calf.² Patients may experience localised oedema, swelling and tenderness secondary to internal muscle necrosis from spontaneous infarction. Diabetic myonecrosis usually presents unilaterally but 8.4% of cases are reported as bilateral.^{4,5} Similar clinical features may be found in pyomyositis, necrotising fasciitis, deep vein thrombosis, soft tissue abscess, cellulitis, hematoma acute compartment syndrome.²

Laboratory findings are nonspecific and are normal in many patients.⁶ However, patients often exhibit elevated levels of creatine kinase (CK) and elevated acute phase responses, as well as leukocytosis.⁶ MRI and ultrasonography have each been used to assess patients with possible diabetic muscle infarction. MRI with intravenous contrast enhancement appears to be the most useful diagnostic imaging technique and is the diagnostic imaging tool of choice.^{5,6} MRI may show high intensity in the involved muscle on T2-weighted sequences as well as subcutaneous oedema and sub-fascial fluid.^{3,4} The loss of the normal fatty

intramuscular septa, a relatively common finding, is optimally observed with T1-weighted images, where the affected muscles appear hypointense or isointense.⁷

The addition of gadolinium can distinguish non-enhancing infarcted muscle from surrounding inflammation or oedema.⁸ On post-gadolinium scans, there is diffuse heterogeneous enhancement with low-signal, non-enhancing foci that may represent areas of necrosis. Rim enhancement can be seen around these areas of necrosis within the areas of ischemic muscle.^{7,8} Muscle biopsy is not required to diagnose muscle infarction and is only necessary when the diagnosis remains in doubt despite careful clinical assessment, laboratory tests and appropriate imaging.⁸

Treatment of diabetic muscle infarction involves symptomatic management with rest, optimal glycemic control, analgesia and low-dose aspirin, although the optimal treatment approach is uncertain.⁹ There are very limited data suggesting that nonsteroidal anti-inflammatory drug (NSAID) treatment may improve outcome but convincing evidence is lacking.¹⁰ Diabetic muscle infarction resolves spontaneously over a few weeks to months in most patients. An analysis of previously published patient outcomes by the type of treatment received noted the following mean times to recovery: rest and analgesics – 8 weeks, antiplatelet agents and/or anti-inflammatory drugs – 5.5 weeks, surgical excision – 13 weeks.^{7,8} In our small series average treatment duration was 3 weeks.

Conclusion

Myonecrosis is a rare complication of diabetes and requires a high index of suspicion for the diagnosis, which avoids unnecessary intervention. It should be considered in patients with diabetes mellitus with a long duration of the disease and accompanying microvascular complications who present with acute–subacute onset severe focal muscle pain in the absence of systemic symptoms. MRI is the most sensitive test for diagnosis. Muscle biopsy should be reserved for atypical cases only. Tight glycemic control, bed rest and analgesia are the cornerstones of treatment.

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Conflicts of interest: Nothing to declare.

Consent: Informed written consent was taken from the patients regarding the publication of this case series and any accompanying images.

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