

Diabetic Myonecrosis: An Indian Experience

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Diabetic myonecrosis is an under-recognized and under-reported complication of longstanding diabetes. In this case series, we have attempted to report the clinical and radiological characteristics of six patients with diabetic myonecrosis along with a review of existing literature.

Case Report 1

A 53-year-old woman presented with painful swelling of the right thigh that had been present for the past 9 days. The pain was of acute onset, dull-aching, and constant and was sufficient to make her nonambulatory. There was no history of trauma or fever. She had been diagnosed with type 2 diabetes 1 year ago and hypertension 5 years ago.

On examination, her right thigh was swollen with a diffuse, indurated tender mass over the anterolateral aspect (Figure 1). The margins were not distinct, and there were no other signs of inflammation or pus formation. She was afebrile. A vibration



Figure 1. Case report 1: right thigh showing diffuse swelling (white arrow) anterolaterally.

perception test revealed moderate peripheral neuropathy. There was no evidence of nephropathy or retinopathy.

Laboratory investigations revealed poor glycemic control (fasting plasma glucose [FPG] 327 mg/dl, postprandial plasma glucose [PPG] 417 mg/dl) and dyslipidemia (total cholesterol 206 mg/dl, triglycerides 156 mg/dl, LDL cholesterol 141 mg/dl, and HDL cholesterol 34 mg/dl). Her serum creatine kinase (CK) was 311 U/l (normal < 167 U/l), and her serum lactic dehydrogenase (LDH) was 394 U/l (normal 240–480 U/l). Total leukocyte and differential counts were normal. Lupus anticoagulant and antiphospholipid antibodies were negative.

Ultrasonography showed an ill-defined hypoechoic area measuring 25 × 15 cm² over the lateral aspect of the right mid-thigh. Magnetic resonance imaging (MRI; T₂-weighted short TI inversion recovery images) showed heterogenous and hyperintense areas involving the anterior and medial group of right thigh

IN BRIEF

Diabetic myonecrosis is an uncommon muscular complication of diabetes with significant morbidity. Clinical features and radiological findings are helpful in the diagnosis of myonecrosis. Management is conservative and focused on symptomatic relief and control of diabetes.

muscles mainly in its lower half. A post-gadolinium contrast study showed mild enhancement, and there was no area of pus collection. Adjacent subcutaneous tissue was edematous. A muscle biopsy revealed infiltration of lymphocytes and plasma cells. There was evidence of degeneration and necrosis in the muscle fibers (Figure 2).

She was managed with bed rest, analgesics, and optimal glycemic control. The pain and swelling resolved completely within 4 weeks. She came to us again 2 years later with recurrence of myonecrosis on the opposite thigh (Figure 3).

Case Report 2

A 37-year-old woman with type 2 diabetes for 8 years presented to us with painful swelling of the left thigh for the past week. She was afebrile, and there was no history of local trauma. There was no weakness in the left thigh, but movement was restricted because of severe pain. She

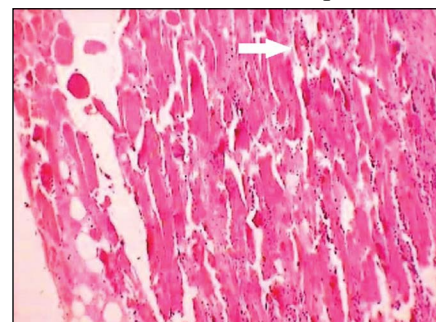


Figure 2. Case report 1: muscle biopsy of right thigh showing infiltration of inflammatory cells with muscle fiber degeneration (white arrow).



Figure 3. Case report 1: swollen left thigh (white arrow) with scar on right thigh (black arrow) from previous biopsy.

had received antibiotics, which did not relieve her symptoms.

Her glycemic control was poor (FPG 289 mg/dl, PPG 389 mg/dl, A1C 9.2%). Other laboratory findings revealed a hemoglobin level of 10.2 g/dl, erythrocyte sedimentation rate (ESR) of 32 mm/hour, serum creatinine of 2.1 mg/dl, total cholesterol of 211 mg/dl, LDL cholesterol of 112 mg/dl, and triglyceride level of 287 mg/dl. There was no evidence of systemic inflammation, and muscle enzymes (CK and LDH) were normal.

She had microvascular complications in the form of diabetic nephropathy (chronic kidney disease [CKD] stage 3), bilateral severe nonproliferative diabetic retinopathy (NPDR), and distal symmetrical polyneuropathy (DSPN). Ultrasonography showed a diffuse hypoechoic area covering the anterolateral aspect of the left thigh. MRI revealed features suggestive of muscle inflammation.

She was managed with bed rest, analgesics, and optimal glycemic control and recovered in a period of 6 weeks.

Case Report 3

A 53-year-old woman with type 2 diabetes for 5 years presented with pain in her right thigh of 5 days' duration. The pain was abrupt and spontane-

ous and had curtailed her day-to-day activities. The right thigh was swollen uniformly and was tender.

She had microalbuminuria, bilateral NPDR with clinically significant macular edema, and DSPN. She had a history of foot ulcer.

Laboratory investigation revealed poor glycemic control, leukocytosis, elevated ESR, and dyslipidemia. Serum CK and LDH levels were within normal limits. Serum anti-nuclear antibody, rheumatoid factor, and antiphospholipid antibodies were not detected.

Ultrasonography showed hypoechoic areas in the muscle and minimal fluid collection in the intermuscular spaces. Culture of the aspirated fluid was sterile. MRI was suggestive of diabetic myonecrosis.

The patient was managed with bed rest, analgesics, and optimal glycemic control and recovered in a period of 4 weeks.

Case Report 4

A 55-year-old man with type 2 diabetes for 12 years and poor glycemic control presented with bilateral painful thigh swelling of 4 days' duration. The swelling was asymmetrical and more prominent on the left side.

He had micro- and macrovascular complications in the form of nephropathy, DSPN, bilateral mild NPDR, and coronary heart disease.

Laboratory investigations did not reveal any evidence of inflammation. Serum CK and LDH levels were within normal limits.

Venous Doppler of the lower limbs was normal. Ultrasonography showed a diffuse hypoechoic area in the quadriceps muscles bilaterally. Because he could not afford an MRI study, a bilateral muscle biopsy was performed and revealed degeneration and necrosis of muscle fibers.

He was managed with bed rest, analgesics, and optimal glycemic

control and recovered in a period of 4 weeks.

Case Report 5

A 55-year-old man with type 2 diabetes for 10 years presented with painful swelling of the right thigh for the past 2 days. His evaluation revealed microvascular complications in the form of bilateral NPDR and DSPN. There was no evidence of nephropathy.

MRI and ultrasonography of the right thigh was suggestive of myonecrosis.

He was managed with bed rest, analgesics, and optimal glycemic control and recovered in a period of 4 weeks.

Case Report 6

A 56-year-old woman with type 2 diabetes for 25 years presented with rapid-onset spontaneous painful swelling of the right thigh and leg for 2 weeks. On examination, there was a diffuse swelling over the right thigh and leg.

She was on insulin and anti-hypertensive drugs. Her glycemic control was poor (FPG 292 mg/dl, PPG 401 mg/dl, A1C 10.2%). She had microvascular complications in the form of diabetic nephropathy (CKD stage 3) and DSPN.

Fundus examination was normal. Total leucocyte count, ESR, and muscle enzymes (CK and LDH) were normal. MRI (Figure 4) and

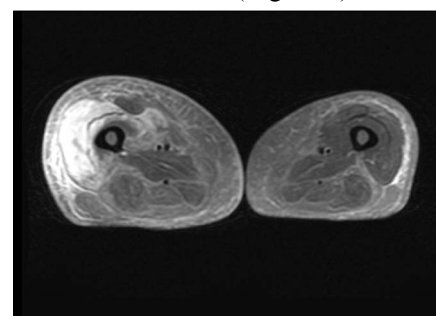


Figure 4. Case report 6: T₂ MRI (fat suppressed) of both thighs with right thigh showing increased signal intensity over quadriceps muscles.

Table 1. Characteristics of Our Patients With Diabetic Myonecrosis

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6
Age (years)	53	37	53	55	55	56
Sex	Female	Female	Female	Male	Male	Female
Duration of diabetes (years)	1	8	5	12	10	25
Local trauma	None	None	None	None	None	None
Fever	None	None	None	None	None	None
Neuropathy	Present	Present	Present	Present	Present	Present
Nephropathy	Absent	Present	Present	Present	Absent	Present
Retinopathy	Absent	Present	Present	Present	Present	Absent
Leucocytosis	Absent	Absent	Present	Absent	Absent	Absent
ESR	Normal	Elevated	Elevated	Normal	Normal	Normal
Muscle enzymes	Elevated	Normal	Normal	Normal	Normal	Normal
Ultrasonography of muscles	Hypoechoic	Hypoechoic	Hypoechoic	Hypoechoic	Hypoechoic	Hypoechoic
Muscles involved	Quadriceps	Quadriceps	Quadriceps	Bilateral quadriceps	Quadriceps	Quadriceps, calf muscles
Biopsy	Necrosis	Necrosis	Necrosis	Necrosis	ND	ND
Resolution time (weeks)	4	6	4	4	4	3
<i>ND, not done</i>						

ultrasonography revealed features suggestive of myonecrosis involving the right thigh and leg. She was managed with bed rest, analgesics, and optimal glycemic control and recovered in a period of 3 weeks.

Table 1 presents a summary of the patients in these six case reports.

Overview of Myonecrosis

Diabetic myonecrosis is a complication of longstanding diabetes. Since its first description by Angervall and Stener in 1965,¹ ~ 100 cases have been reported in the literature.² Diabetic myonecrosis is also known as spontaneous diabetic muscle infarction (DMI), aseptic myonecrosis, ischemic myonecrosis, and tumoriform focal muscular degeneration.

Diabetic myonecrosis is rare, and there is a relative lack of awareness

about it compared to other complications of diabetes. Hence, there is often a delay in diagnosis, which in turn increases the morbidity associated with the disease.³ Women with longstanding type 1 diabetes are the most common patients to develop this disease. In patients with type 2 diabetes, older individuals are more commonly affected.^{4,5} Diabetic myonecrosis is usually seen in patients with longstanding diabetes who are on insulin therapy and have multiple micro- and macrovascular complications.⁴⁻⁶

The diagnosis criteria for diabetic myonecrosis are summarized in Table 2 and discussed in detail below.

Clinical presentation

Clinical presentation of myonecrosis

typically includes an abrupt onset of diffuse painful swelling of involved muscles and occasionally a palpable mass without antecedent trauma or infection. Bilateral involvement is seen in 8–10% of cases.^{4,5} An increase in the dimensions of the thigh may be the initial presenting feature. Fever and other signs of inflammation are usually absent.

Thigh muscles are commonly affected, with the quadriceps being the most frequently involved muscle group.⁷ Vastus lateralis and vastus medialis are the most commonly affected muscle sites.⁸ Involvement of calf and upper-extremity muscle groups has also been documented.^{4,8,9} With time, the swelling localizes, and the predominant symptom

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Table 2. Criteria for Diagnosis of Diabetic Myonecrosis

Clinical features:

- Abrupt onset of severe pain and swelling of affected area
- Usually asymmetrical
- Absence of fever and other signs of inflammation
- History of trauma usually absent
- Diabetes with end-organ damage

Laboratory features:

- Normal leucocyte count
- Normal or mildly elevated ESR
- Normal or mildly elevated muscle enzymes

Radiological features:

- Ultrasound: well-margined, hypoechoic, intramuscular lesion with no features of abscess*

**Internal linear structures that suggest muscle fibers coursing through the lesion, lack of a predominately anechoic region, and absence of motion or swirling of fluid with transducer pressure are suggestive of myonecrosis and rule out soft-tissue abscess.*

may be pain with restriction of movement.¹⁰

Pathophysiology of myonecrosis

Possible pathological mechanisms revolve around diabetic microangiopathy, vasculitis with thrombosis, hypoxia-reperfusion injury, and atherosclerotic occlusion.^{11,12} Patients generally have end-organ complications of diabetes, suggesting the role of small vessel disease and atherosclerosis as an underlying pathology.

Cases of diabetic myonecrosis also have been reported with cirrhosis and antiphospholipid antibody syndrome. Diabetes is a proinflammatory state, with increased activity of factor VII, plasminogen activator inhibitor-1, and thrombomodulin. This in turn creates a hypercoagulable state.^{5,13,14} The coagulation abnormalities associated with cirrhosis may put patients at risk for hematoma formation and infection. Ischemia and associated edema may aggravate the local pressure effect, which may further compromise blood flow to the affected muscles.¹⁵ Hence, ischemia and edema may form a vicious circle leading to worsening of diabetic myonecrosis.

Galtier-Dereure et al.¹⁶ have shown a high prevalence of antiphospholipid antibodies in patients with type 1 or type 2 diabetes and end-organ complications. The coexistence of diabetes and antiphospholipid antibodies increases hypercoagulability and puts patients at high risk for thrombotic complications and diabetic myonecrosis. Vasculitis with fibrinoid necrosis, although reported in diabetic myonecrosis, is rare.¹⁷

Laboratory investigations and radiology

Laboratory evaluation shows an elevated ESR in half of the cases.⁴ Leucocytosis is generally absent. Serum levels of muscle enzymes such as CPK and LDH are usually normal or mildly elevated.⁸ Serum levels of aspartate and alanine transaminases are generally normal.

Bedside ultrasonography is the first-line imaging diagnostic modality in diabetic myonecrosis. Ultrasonography generally reveals a well-margined, hypoechoic, intramuscular lesion with the following additional features: internal linear structures that suggest muscle fibers

coursing through the lesion, lack of a predominately anechoic region, and absence of motion or swirling of fluid with transducer pressure.¹⁸ The advantages of ultrasonography include easy availability, noninvasiveness, early diagnosis, and exclusion of other causes such as soft-tissue abscess.

Imaging studies may be quite useful in the diagnosis of diabetic myonecrosis and can simultaneously exclude other differential diagnoses such as cellulitis, abscess, fracture, tropical pyomyositis, necrotizing fasciitis, diabetic lumbar plexopathy, and deep vein thrombosis.

MRI studies show increased signal intensity from the affected muscle area in T₂-weighted, inversion recovery, and gadolinium-enhanced images and isointense or hypointense areas on T₁-weighted images. The pathological basis of these findings is the presence of increased water content resulting from edema.¹⁹ Other findings include diffuse enlargement of affected muscles, ill-defined borders secondary to loss of the normal fatty intramuscular septa, and hemorrhagic foci.²⁰ The disadvantages of MRI include its high cost, lack of universal availability, and nonspecificity. Many MRI findings seen in diabetic myonecrosis can also be found in other inflammatory myopathies. Computed tomography (CT) scans show diffuse muscular enlargement with diminished attenuation of the affected muscle, increased attenuation of the subcutaneous fat, and thickening of subcutaneous fascial planes and skin.²¹

Because MRI and CT scans are nonspecific, many patients also are subjected to biopsy. Findings on muscle biopsy depend on the stage of the myonecrosis. Early on, light microscopy shows large areas of muscle necrosis and edema, phagocytosis of the necrotic muscle fibers,

and variable presence of granular tissue and collagen. At a later stage, there is a fibrous replacement of the necrotic tissue, myofiber regeneration, and mononuclear cell infiltration.²² Small vessel walls are often hyalinized and thickened with evidence of atherosclerosis. Some small vessels may be occluded with fibrin or calcium fragments.

Conflicting reports suggest that biopsy may be associated with hematoma formation, infection, and an extended recovery period.^{15,17,23} Cultures for bacteria and fungi are generally negative unless there is a complicated myonecrosis.⁶ However, because biopsy is invasive and noninvasive investigations such as ultrasound are easily available, biopsy should be reserved for cases in which the clinical presentation is atypical or the diagnosis uncertain or when appropriate treatment fails to elicit clinical improvement.^{15,19,24}

Differential diagnosis

Other conditions that may mimic myonecrosis include soft-tissue abscess, necrotizing fasciitis, pyomyositis, dermatomyositis, benign muscle tumors, lymphomas, sarcomas, diabetic amyotrophy, drug-induced myositis, osteomyelitis, muscle rupture, hematoma, ruptured Baker's cyst, deep-vein thrombosis, diabetic lumbosacral plexopathy, and thrombophlebitis. Clinical presentation, laboratory investigations, MRI, and sonographic features, along with the course of the disease, all help in differentiation. Soft-tissue abscesses on ultrasound are anechoic or hypoechoic, well defined, and show posterior acoustic enhancing and intrinsic motion of fluid. Patients with pyomyositis generally will have systemic symptoms with fever and leucocytosis. ESR, CPK, and LDH are generally elevated. Blood cultures and local tissue cultures may grow *Staphylococcus aureus*. Venous

Doppler studies may be required to rule out deep-vein thrombosis.

Treatment and prognosis

Treatment for diabetic myonecrosis is generally conservative and supportive. Bed rest is usually advised, although there are conflicting reports on the benefits of physical therapy.^{8,12,15} Nonsteroidal anti-inflammatory drugs and narcotics may be used for inflammation and pain control. Good glycemic control during the hospital stay is recommended. Anticoagulants may be used only if a patient has a hypercoagulable state such as antiphospholipid syndrome. In general, surgical interventions should be avoided unless there is a complicated diabetic myonecrosis with abscess formation or peripheral arterial compromise.¹⁴

Generally, the short-term prognosis is good for diabetic myonecrosis. The swelling and pain lessen, and patients become mobile in 1–2 months. However, patients usually have associated micro- and macrovascular complications that affect the long-term prognosis and elevate 5-year mortality.^{3,4} Patients are known to have recurrences, and most events occur within a period of 2 months after the initial presentation.

Experience with diabetic myonecrosis

Diabetic myonecrosis has been more frequently reported in women. Four (66.6%) of the patients in our series described above were women. The mean age at presentation was 51.5 ± 7.2 years (range 37–56 years), which is higher than noted in a previously published review.⁵ The fact that all of our patients had type 2 diabetes may have contributed to the higher mean age.

The mean duration of diabetes, from initial diagnosis to the first episode of myonecrosis, was 10.16 ± 8.23 years (range 1–25 years). Our patients had multiple end-organ

diabetes complications. All of our patients had neuropathy and diabetic dyslipidemia. Nephropathy was present in five cases, and retinopathy was present in four cases.

All of our patients presented with typical clinical features of diabetic myonecrosis such as abrupt onset of pain and swelling in the affected muscles. Fever has been reported in ~10% of patients with diabetic myonecrosis, but none of our patients had a fever.

Diabetic myonecrosis has a predilection for thigh muscles. In our series, all six patients had involvement of the quadriceps, and one patient (case report 6) had involvement of calf muscles in addition to the quadriceps. One of our patients had bilateral involvement (case report 4). In the literature, bilateral involvement was reported in 8–10% of cases.

Plasma levels of muscle enzymes were elevated in only one of our patients (case report 1). Leucocytosis and elevated ESR were reported in ~8 and 52% of patients, respectively. We noted leucocytosis in case report 3 and elevated ESR in case reports 2 and 3.

We managed our patients with bed rest and analgesics. Glycemic control was optimized. All of our patients had complete resolution of myonecrosis without any complications in 4.16 ± 0.96 weeks.

In diabetic myonecrosis, recurrence was reported in ~47% of patients. The majority (81%) of these patients have recurrences in a different muscle. In our series, one patient (case report 1) had recurrence of myonecrosis in the opposite thigh 2 years after the first presentation.

Conclusion

Diabetic myonecrosis is an uncommon complication of longstanding diabetes. Patients may present with pain and swelling of involved muscle

groups, leading to significant morbidity. Management is conservative, with good short-term prognosis. The long-term prognosis of these patients is poor, in part because many of them already have micro- and macrovascular complications of diabetes.

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