Clinico-radiological characteristics and not laboratory markers are useful in diagnosing diabetic myonecrosis in Asian Indian patients with type 2 diabetes mellitus: A 10-year experience from South India

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ABSTRACT

Introduction: Diabetic myonecrosis or muscle infarction is an unusual complication of Type 2 Diabetes, usually associated with longstanding disease. It commonly presents as an acute non-traumatic palpable swelling of the affected muscle with predilection for the quadriceps and thigh muscles, often accompanied by retinopathy and nephropathy. Methodology: A retrospective review of the medical records of patients admitted with diabetic myonecrosis under the Department of Endocrinology, Christian Medical College Vellore over a period of ten years (2006-2015) was done. Data pertaining to clinical, biochemical and radiological characteristics were obtained and treatment modalities and outcomes were recorded. Results and Analysis: A total of \( n = 4 \) patients with diabetic myonecrosis and completed clinical data were included in the study. In our present series, the mean age at presentation was 45.5 years (±7.3 years), the mean duration of the diabetes was 9.0 years (±2.5 years) with an equal distribution of male and female subjects. The mean HbA1c (9.5 ± 0.6%) was suggestive of poor glycemic control at presentation with all (100%) the patients in our series having concomitant one or more microvascular complications. While laboratory parameters of elevated CPK or LDH were mostly normal, the findings of T1 hyperintense and T2 hypointense heterogenous lower limb lesions were present in all the subjects (\( n = 4 \)). Conservative management with bed rest, analgesics and good glycemic control were effective in good clinical improvement over a period of 1-2 months. Conclusions: Our series of diabetic myonecrosis in Indian patients with Type 2 diabetes mellitus, elucidates the varied clinical presentations, with MRI findings rather than laboratory markers being the mainstay of diagnosis.

Keywords: Antibiotics, creatinine phosphokinase, diabetic, magnetic resonance imaging, myonecrosis
typically shows large confluent areas of muscle necrosis and edema. The best imaging results are obtained with T2 weighted MRI scans, which have a fair characteristic, although nonspecific appearance showing the absence of a discrete mass and an increased signal within the affected muscle. The differential diagnosis includes a muscle tumor (sarcoma or lymphoma), localized abscess, hematoma, focal or systemic myositis, deep venous thrombosis, and osteomyelitis. The management should include bed rest, analgesia, tight metabolic control, and physiotherapy.

Our experience with diabetic myonecrosis includes four patients over a period of 10 years (2006–2015).

**Patient 1**
A 38-year-old woman with poorly controlled type 2 diabetes mellitus (T2DM) for 8 years, on a combination of oral antidiabetic drugs, presented with sudden onset, spontaneous pain in the left calf which gradually worsened over a 10-day period with associated swelling of the left calf. On examination, she had a temperature of 38.3°C (101°F) with a swelling of the left calf with a rigid and tense skin with mild warmth and tenderness. She had microvascular complications in the form of bilateral distal sensorimotor polyneuropathy, bilateral severe nonproliferative diabetic retinopathy with macular edema (post-panretinal photocoagulation), and diabetic nephropathy with an eGFR of 36 ml/min (Chronic Kidney Disease (CKD) stage 4). Laboratory investigation did not reveal any evidence of infection. He had a total leucocyte count of 8600/cu mm, HbA1c of 8.8%, serum creatinine of 3.21 mg/dl with a nephrotic range proteinuria of 7.7 g/24 h. His erythrocyte sedimentation rate (ESR) was 32 mm at the end of the first hour with a serum creatinine phosphokinase (CPK) of 117 U/l. A venous Doppler of the limb was normal. Ultrasound abdomen showed grade 2 renal parenchymal disease and mild hepatomegaly. An MRI of the left leg was done which revealed a heterogeneous ill-defined defined T2 hyperintensity in the posterior and lateral compartment muscles in the left thigh with relative sparing of the tibialis posterior and medial gastrocnemius muscle [Figure 1]. The muscle architecture was maintained with no obvious breakdown. There was associated subcutaneous thickening and edema. A contrast study could not be done due to renal dysfunction. She was managed conservatively with analgesia, adequate limb rest, and optimal glycemic control with insulin. She showed gradual recovery over a period of 6 weeks and was stable at discharge.

**Patient 2**
A 42-year-old gentleman with T2DM, managed with oral antidiabetic drugs since the last 6 years, presented with acute onset pain and swelling of the left thigh. He gave a history of rapidly worsening pain and swelling over 2 weeks. On examination, he had bilateral pedal edema with facial puffiness and pallor. He also had swelling of the left thigh with tensely thickened skin with tenderness and mild warmth. Mobility of the left lower limb was severely restricted due to pain. He had bilateral severe nonproliferative diabetic retinopathy. He also had diabetic nephropathy (CKD stage 3) with 1.1 g proteinuria and evidence of bilateral distal symmetric peripheral neuropathy. Laboratory evaluation revealed elevated plasma glucose levels of 395 mg/dl with an HbA1c of 9.9% suggesting poorly controlled diabetes. The total White Blood Cell (WBC) counts were 11,300/cu mm with an ESR of 58 at the end of first h. He also had subnephrotic range proteinuria (1.1 g/24 h) and a serum creatinine of 1.61 mg/dl without any evidence of infection. His CPK levels were 23 U/l. A venous Doppler examination was normal but showed diffuse subcutaneous edema. MRI of the left thigh showed areas of altered signal intensity and swelling of the vastus lateralis muscles with an increased heterogeneous enhancement of the vastus lateralis muscle and loss of intermuscularseptae [Figure 2] suggesting muscle infarction with mild effusion of the femoro-patellar joint though no focal abscess or collection was seen. An ultrasound of the abdomen showed mild echogenicity of the renal parenchyma. He was conservatively managed with bed rest, analgesics, insulin, and physiotherapy with gradual recovery over a period of 4 weeks.

**Patient 3**
A 49-year-old gentleman known to have T2DM since the last 12 years presented with pain and swelling of the right upper calf for last 3 weeks with acute worsening since 5 days without associated fever or systemic symptoms. The right upper calf had a localized, firm tender swelling without associated lymphadenopathy or skin changes. His fundus examination revealed a bilateral moderate nonproliferative diabetic retinopathy and grade 2 hypertensive retinopathy changes. He had diabetic nephropathy with proteinuria and bilateral distal symmetric

Figure 1: T2-weighted axial and STIR coronal images of left thigh show bulky and diffusely hyperintense vastus muscles with large areas of nonvisualized muscle fibers – suggestive of myonecrosis (arrow)

Figure 2: T2-weighted and STIR axial images of left thigh show diffuse swelling and hyperintensity of vastus muscles more in vastus lateralis muscle and there is loss of intermuscular septae (arrow)
The affected area may present with a firm tender swelling and edema. The MRI features were consistent with a muscle infarction. He was conservatively managed with bed rest, analgesics, and insulin for glycemic control. He also recovered over a period of 8 weeks and was discharged in a stable condition.

Patient 4

A 54-year-old woman with T2DM since the last 10 years presented with spontaneous onset pain and swelling of the right thigh over 7 days with progressive worsening of symptoms. On examination, she had mild bilateral pedal edema and pallor. She also had edematous swellings of the right thigh with tenderness and mild warmth. She had microvascular complications in the form of severe bilateral nonproliferative diabetic retinopathy with evidence of post-laser burn scarring, distal peripheral symmetric polyneuropathy, and diabetic nephropathy with proteinuria. A laboratory evaluation did not reveal evidence of infection. Her plasma glucose levels were 458 mg/dl with an HbA1c of 9.2%. Her CPK levels were 31 U/l. Other laboratory findings revealed a hemoglobin of 10.4 g/dl, total WBC counts of 11,000/cu mm, and ESR of 93 mm at the end of first hour. She also had proteinuria of 229 mg/24 h and a serum creatinine of 1.4 mg/dl. Venous Doppler was normal. MRI of the right lower limb demonstrated altered signal intensity involving the muscles of medial and anterior compartment of the thigh. There was predominant involvement of the adductor muscles showing heterogeneous increased enhancement without any focal abscess or collection suggestive of myonecrosis. As her imaging was done at a hospital in her hometown, the MRI images were not available for reproduction here. She was conservatively managed with bed rest, analgesics, and insulin for glycemic control. She recovered over a period of 5 weeks and was discharged in a stable condition.

The summary of the findings of the four cases is outlined in Table 1.

Discussion

Diabetes myonecrosis or muscle infarction in diabetes is a rare complication usually seen in long-standing diabetes mellitus (DM) with poor glycemic control. The first description was given by Angervall and Stener in 1965 with a report of two cases. Till date, around 200 cases have been reported with most of the available literature being in the form of case reports and retrospective smaller case series. A systemic review by Trujillo-Santos in a total of 115 patients with 166 episodes of diabetic myonecrosis found that it was more common in women (61.5%), in type 1 DM (59% of all cases) and in long-standing diabetes (mean duration of disease: 14.3 years). Further, another recent review by Horton et al. has found 108 cases that reported diabetes type at the time of diagnosis. Of those 108 cases, 54 (50%) had T2DM while 45 (41.7%) had T1DM. The mean DM duration at the time of Diabetic Muscle Infarction (DMI) diagnosis was 18.9 years for T1DM and 11.0 years for T2DM. HbA1c values were reported at the time of DMI diagnosis in 51 cases and mean value was 9.34%. The clinical presentation by large involves sudden onset pain affecting the lower limb muscles, of which the thigh muscle is the commonly involved. It has a predilection for the quadriceps (62%), hip adductors (13%), hamstrings (8%), and hip flexors (2%). Reports of upper limb involvement have been documented but are rare. Unilateral presentation is usually seen but bilateral involvement has been also reported in up to 8.4% of cases. The affected area may present with a firm tender swelling with minimal focal signs of infection or other associated constitutional symptoms. A similar clinical presentation maybe seen in diabetes with deep venous thrombosis, cellulites, soft tissue infections, acute compartment syndrome, hematoma, diabetic amyotrophy, and inflammatory myositis.

The pathogenesis of diabetic myonecrosis remains unclear. Several hypotheses have been postulated, of which atherosclerosis, diabetic microangiopathy, vasculitis with thrombosis, and ischemic reperfusion injury are primary. Thromboembolic events secondary to microvascular endothelial damage causing tissue ischemia triggers an inflammatory cascade which...
perpetuates the local tissue damage and ischemic necrosis. Alterations in the coagulation–fibrinolysis system in the form of hypercoagulability and vascular endothelial damage have also been implicated by some authors in DMI.\(^6\) Presence of antiphospholipid antibodies in T1DM patients has further pointed to a possible role of these antibodies in patients with DMI. It has also been suggested that vasculitis could be a factor as patients with diabetes are known to be susceptible to inflammatory vasculopathy.\(^7\)

Laboratory evaluation including total leucocyte count, ESR, and LDH are usually normal or mildly elevated and do not contribute to the diagnosis. CPK has been reported to be normal in most cases and do not have a correlation with the degree of muscle injury.\(^8\) Though bedside ultrasonography is the first-line imaging modality in diabetic myonecrosis, MRI remains the best imaging tool. The characteristic findings include an 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. In 103 MRI reported in patients with DMI, edema with T2 hyperintensity was noted in 76.8% of cases while T1 isointensity or hypointensity was reported in 14.6% of cases. The most commonly affected muscle was the vastus medialis, which was identified in 25 cases (17.9%). Other common locations included the vastus lateralis (15%), the vastus intermedius (7.1%), the rectus femoris (6.4%), the soleus (5.7%), and the gastrocnemius (5%).\(^5\) The pathological basis of these findings is the presence of increased water content resulting from edema. Other findings include diffuse enlargement of affected muscles, ill-defined borders secondary to loss of the normal fatty intramuscular septa, and hemorrhagic foci.\(^6\) High cost, lack of universal availability, and nonspecificity are some of the disadvantages of an MRI study. 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. Because MRI and CT scans are nonspecific, many patients also are subjected to biopsy. Though muscle biopsy has been used for confirming the diagnosis in many cases, the risks of hematoma formation, infection, and an extended recovery period have now made biopsy untenable in cases of diabetic myonecrosis. Cultures for bacteria and fungi are generally negative unless there is a complicated myonecrosis.

The 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. 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 an underlying antiphospholipid syndrome. In general, surgical interventions should be avoided unless there is a complicated diabetic myonecrosis with abscess formation or peripheral arterial compromise.\(^4\) 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. Patients are known to have recurrences, and most events occur within a period of 2 months after the initial presentation.\(^10\) The recovery period was shorter in conservative management when compared to surgical management as shown by Kapur and McKendry.\(^11\)

### Summary

Our experience with diabetic myonecrosis: Our experience with diabetic myonecrosis over a period of 10 years involves four...
cases as outlined above. In our present series, the mean age at presentation was 45.5 years (±7.3 years). The mean duration of the diabetes was 9.0 years (±2.5 years). There was an equal distribution of male and female subjects. The mean HbA1c (9.5 ± 0.6%) was suggestive of poor glycemic control at presentation with all (100%) the patients in our series having concomitant one or more microvascular complications. Similar findings have been suggested in a recent review where 46.6% had concurrent retinopathy, nephropathy, and neuropathy while 65.8% had at least two complications, indicating that DMI is often seen in patients with advanced diabetes. The most common microvascular complication associated with DMI is nephropathy, present in 75% of DMI cases. While pain was a presenting symptom in all four patients, fever was present in only 2 (50%), though evidence of systemic infection was absent in all of them. One patient (case no. 1) had a recurrence within a span of 2 years with involvement of the contralateral lower limb in the current episode. Mild leucocytosis and an ESR elevation were seen in only half of the patients while laboratory markers like LDH and CPK were normal in the majority (3 out 4, 75%). MRI of the lower limbs was done in all and showed the typical features of T2 hyperintense and T1 hypointense heterogenous lesions suggestive of muscle infarction. The involvement of the right and left lower limbs was equally distributed. Management consisted of analgesics, bed rest, and strict glycemic control in all four cases. The mean duration for recovery was 5.75 weeks (±1.7 weeks). Surgical intervention was not required in any of the cases.

Conclusions

Diabetes myonecrosis or diabetes muscle infarction is a rare and uncommon complication seen in patients with long-standing poorly controlled DM. Our series, in keeping with the literature, shows an abrupt clinical presentation with pain as the predominating symptom. The association with microvascular complications and poor correlation with laboratory markers of muscle involvement are important clinical pointers. MRI is usually the mainstay of diagnosis. Conservative management with good glycemic control, bed rest, and analgesia usually provides good short-term improvement within 1–2 months. However, the long-term prognosis in these patients is poor with recurrences reported in almost up to 47.8%, thus making it clinically challenging, albeit an uncommon complication of long-standing uncontrolled diabetes.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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