Diabetic Muscle Infarction

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ABSTRACT

Diabetic muscle infarction is an uncommon complication of long-standing, poorly controlled diabetes. Although awareness is increasing, it is likely that diabetic muscle infarction remains underdiagnosed and underreported. The typical presentation is acute, atraumatic, unilateral thigh pain and swelling. Magnetic resonance imaging has emerged as the diagnostic modality of choice. It is hoped that by describing typical features of diabetic muscle infarction, awareness of this potentially life-threatening complication will increase. Two illustrative cases are presented. (Adv Stud Med. 2003;3(8):464-466)

CASE 1

A 52-year-old woman was admitted for initiation of hemodialysis. She had a 33-year history of type 1 diabetes mellitus complicated by diabetic nephropathy, retinopathy, peripheral neuropathy, and gastroparesis. She developed acute right medial thigh pain and swelling, which prevented her from walking. The medial aspect of the thigh was firm, edematous, and exquisitely tender, but without warmth, erythema, or fluctuance. The distal leg was normal and neuromuscular function was intact.

Venous duplex examination did not reveal evidence of venous thrombosis. Ultrasound of the medial thigh demonstrated a hypoechoic area in the adductor compartment, but no material could be aspirated. Laboratory studies were notable for a white blood cell (WBC) count of 9800 per mL and an erythrocyte sedimentation rate (ESR) of 79 mm per hour. Magnetic resonance imaging (MRI) of the right thigh demonstrated edema of the adductor muscle group and overlying subcutaneous tissue. A focal area of brighter signal in the adductor brevis suggested a mass.

The clinical and radiographic findings were consistent with diabetic muscle infarction (DMI). Pain medication and bed rest were initiated, followed by physical therapy. The right leg pain gradually improved over the next month. Repeat MRI showed resolution of the mass-like area and decreased edema.

CASE 2

A 57-year-old man presented to the emergency department with a 3-day history of right thigh pain. His detailed medical history included poorly controlled type 2 diabetes mellitus complicated by peripheral neuropathy, retinopathy and nephropathy; congestive heart failure, and hypertension. The medial aspect of the right thigh was exquisitely tender but without warmth, erythema, or fluctuance. Neuromuscular function was intact. Venous duplex examination was without evidence of venous thrombosis. He was discharged from the hospital after 3 days of pain medication, bed rest, and physical therapy.

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DIABETIC MUSCLE INFARCTION

He returned 1 week later with persistent thigh pain. Examination results were unchanged. The patient's WBC was 13,000 per mL³, creatinine kinase level was 201 U/L (normal <195 U/L), and ESR was 77 mm per hour. MRI of the right thigh revealed edema of the vastus medialis and adjacent vastus intermedius muscles—best seen on T-2 weighted images—as well as moderate subcutaneous edema (Figure). The patient was admitted to the hospital, received analgesics, and achieved improved glycemic control. Despite these measures, the thigh pain worsened. Creatinine kinase level rose to >1000 U/L and ESR to >100 mm per hour. A repeat MRI showed extension of the previously identified signal abnormality, with a central region of low signal intensity, suggestive of muscle necrosis; however, early abscess formation could not be excluded. The patient was taken to the operating room for exploratory surgery of the right thigh. The muscle was markedly edematous with grossly hemorrhagic fluid. Cultures for bacteria, fungi, and mycobacteria were negative. Histopathology of muscle samples showed myofiber atrophy with extensive edema but normal microvasculature. The patient initially improved with continued supportive treatment, but died 1 month later of an acute pulmonary embolism.

DISCUSSION

DMI is an uncommon complication of long-standing diabetes mellitus. First described in 1965, it has recently become more widely recognized.¹ The diagnosis should be considered in patients with diabetes and extensive microvascular disease who present with acute atraumatic thigh pain and swelling.

Epidemiology and Risk Factors

The true incidence of DMI is unknown. Grigoriadis et al have noted that patients tend to be relatively young (mean age 41.5 years) without gender predilection.² The typical patient has long-standing, poorly controlled diabetes with end-organ microvascular complications. Three fourths of reported cases occur in persons with type 1 diabetes mellitus.² The mean duration of diabetes at the time of diagnosis is 15 to 17 years but cases have been reported in patients recently diagnosed.²⁴

The information available on DMI is limited to case reports and small case series. In the last decade, increasing awareness has led to publication of larger case series. For example, 14 patients referred over a 5-year period to an orthopedic oncology clinic for evaluation of a leg mass were diagnosed with DMI.³

Even with this increasing awareness, it is likely that DMI remains underdiagnosed and underreported. In a more recent case series, nearly two thirds of patients had nephropathy; more than one half had neuropathy; and one third had retinopathy.² Microvascular end-organ damage and poor glycemic control have been consistently identified as risk factors.²⁴

Clinical Presentation and Differential Diagnosis

Severe unilateral leg pain and swelling in the absence of antecedent trauma is the typical presentation. The onset of pain is acute or, less frequently, subacute. Although neuromuscular function of the leg remains intact, activity is limited by pain. The thigh muscles, especially the quadriceps and hip adductors, are most commonly affected. Calf muscle involvement occurs in 20% of patients.² One case of DMI involving the forearm has been reported.⁶ Bilateral thigh muscle infarction has also been reported.⁷

On physical examination, patients exhibit swelling and tenderness of involved muscles. Edema of the affected muscles and overlying subcutaneous tissue can be remarkable, although the site is usually not erythematous. A palpable mass or well-demarcated area of induration is relatively common. Fever is atypical and therefore should lead to consideration of alternative diagnoses, particularly infectious etiologies.

Diagnostic considerations in the patient with acute, atraumatic thigh pain and swelling include venous thrombosis, spontaneous muscle rupture or

Figure. Axial T-2 Weighted Image of the Right Thigh

Increased signal intensity is seen in the vastus medialis and adjacent vastus intermedius.
hematoma, neoplasm (sarcoma, in particular), focal myositis, and infection. Infectious etiologies such as abscess, pyomyositis, and necrotizing fasciitis should be pursued in patients with fever or cutaneous findings suggestive of skin and soft-tissue infection. Autoimmune inflammatory myopathies (eg, dermatomyositis or polymyositis) rarely begin as a focal process, however, unlike DMI these disorders progress to affect bilateral, proximal muscles.

**Diagnosis Testing**

No single test is diagnostic. The diagnosis may be made based on characteristic MRI findings in a patient with typical clinical features. The WBC count, creatinine kinase level, and ESR are inconsistently elevated. Computed tomography may reveal muscle and soft-tissue edema. Increased T-2 weighted signal is indicative of edema of the affected muscles as well as subcutaneous and subfacial fluid. Biopsy should be considered in patients with atypical clinical features or MRI findings. Early authors discouraged biopsy due to the risk of hemorrhage and clinical deterioration, but more recent series have reported few complications with core needle biopsy.

**Pathogenesis**

The pathophysiology of DMI remains unclear. Infarction of skeletal muscle is unusual because of the rich blood supply to the area. The first report of DMI described “regions of haemorrhagic necrosis surrounded by muscle tissue that showed regressive changes and signs of regeneration” and thickened vessel walls that “agreed with those recently described as diabetic microangiopathy.” Subsequent authors have also reported patchy areas of muscle necrosis and hemorrhage, with mild lymphocytic or neutrophilic infiltrate and interstitial edema. Most, although not all, biopsy specimens demonstrate thickened, periodic acid-Schiff-positive arterioles and capillaries, consistent with microangiopathy.

Silberstein et al postulated that minor trauma, such as an insulin injection, may cause a small hematoma with resultant compression of adjacent atherosclerotic small vessels. A cycle of ischemia, edema, and compression of vessels in the surrounding tissue may ultimately result in involvement of an entire muscle or muscle compartment and eventual necrosis. Recent research raises the possibility that a state of hypercoagulability is causative.

**Treatment**

Standard care includes glycemic control, analgesia, and bed rest followed by gradual return to activity. Because the diagnosis is uncommon, controlled trials of therapy for DMI are lacking. Proposed but unproven therapies include anticoagulation, pentoxifylline, and dipyridamole, all believed to improve blood flow to the affected muscles. The short-term prognosis is favorable, with gradual resolution of pain and swelling over a period of weeks to months. However, recurrence has been observed in nearly one half of patients. Unfortunately, in the few patients who have had long-term follow-up, mortality rates have been high, presumably reflecting the severity of the underlying disease.

**Summary**

As the population of patients with diabetes increases, primary care physicians must be aware of the potential complications, both common and uncommon. DMI is likely to be more common than previously recognized. Therefore, this diagnosis should be entertained in patients with long-standing diabetes who present with acute thigh pain.

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**REFERENCES**