Diabetic Muscle Infarction

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Diabetic muscle infarction is a rare complication that should be suspected in patients with poorly controlled diabetes mellitus and localized muscle pain and swelling. The diagnosis is established by suggestive medical history and clinical findings, relevant imaging and muscle histology. The differential diagnosis includes malignant and infectious conditions, myositis, deep vein thrombosis and local bleeding. Pain management, activity restriction followed by gentle mobilization, and aggressive metabolic control are the main therapeutic goals. We report two illustrative cases and discuss the clinical, diagnostic and therapeutic features of this condition.

Patient Descriptions

Patient 1

A 40 year old Ashkenazi (East European origin) Jewish man with a 17 year history of type I diabetes complicated by nephropathy, retinopathy, peripheral and autonomic neuropathy was admitted for acute onset of pain and swelling in his left thigh. Past history included hypertension and anemia. One year previously he suffered from pain and swelling in his right thigh. Deep venous thrombosis and Baker's cyst were excluded by Doppler ultrasound. Rest and analgesic treatment were followed by complete clinical recovery 3 months later.

At this admission he presented with painful, well-defined swelling of the left thigh of 3 weeks duration. On examination, the left thigh was larger than the right and excruciatingly tender to palpation. Lesser tenderness was found on the medial area of the right thigh. Besides signs of peripheral neuropathy the rest of the physical examination was not contributory. Laboratory tests showed hemoglobin 9 g/dl, hematocrit 23%, white blood cells 21,100/mm³ (normal differential count), and platelets 726,000/mm³. Serum creatinine was 1.5 mg/dl. Serum creatine phosphokinase and aldolase levels were normal and there was no myoglobinuria. Serum and urine electrophoresis were normal. Autoantibodies including antinuclear antibodies, anti-DNA, rheumatoid factor, and antinuclearin were negative. Serum complement level was normal.

A plain X-ray examination of the pelvis was normal. Doppler ultrasound showed no evidence of localized abscess or deep vein thrombosis. A computed tomography scan of the abdomen and pelvis revealed signs of atherosclerosis and arteriosclerosis with calcification of the abdominal aorta, its branches and small vessels. It also included the proximal thighs with swelling of the quadriceps and adductor muscles, inter-muscular edema on the left and subcutaneous edema on both sides, more prominent on the left. Magnetic resonance imaging of the thighs showed swelling of the adductor magnus muscle on both sides and all the vastus muscles in the left thigh. The signal of the involved muscles was isointense and low compared to unaffected muscles on T1-weighted images and high on T2-weighted images (Figure A). After gadolinium injection there was enhancement of the involved muscles except for central areas compatible with ischemia with central areas of necrosis (Figure B). There were signs of bilateral intermuscular, perifascial and subcuta-
neous edema, more prominent on the left. Gastrointestinal endoscopy and abdominal CT scan did not reveal malignancy. The marked anemia was explained by erosive gastritis and chronic renal failure. Bed-rest and analgesic treatment slightly improved the patient's condition. Treatment with high pressure oxygen was not helpful.

**Patient 2**
A 53 year old Arab woman with a long history of type II diabetes complicated by diabetic retinopathy, neuropathy, and nephropathy and requiring hemodialysis was admitted for recurrent painful swelling of her left thigh during the preceding 3 months. She reported two previous episodes of muscle pain and swelling involving the left calf and the right thigh. These conditions resolved spontaneously within 3 and 4 months respectively.

On physical examination there was tender swelling of her left thigh. Laboratory tests showed hemoglobin 8.7 g/dl, white blood cell count 11,800/mm$^3$, platelets 570,000/mm$^3$. Serum CPK levels were normal and there was no myoglobinuria. Immunologic investigations were negative, except for lupus anticoagulant which was positive.

Deep venous thrombosis and neoplasm were excluded by Doppler ultrasound and total body CT scan. MRI showed muscle edema in the left thigh. Muscle biopsy was denied by the patient. Bed-rest and analgesic treatment improved her condition. She was lost to follow-up.

**Comment**
Diabetic muscle infarction is a rare complication of diabetes mellitus. It was first reported in 1965 by Angerall and Stener [1] as a "tumorform focal muscular degeneration." It tends to occur mainly in young patients (mean age 40 years) with poorly controlled and long-standing diabetes (mean 15 years). Most patients have end-organ complications due to diabetic microangiopathy. Males and females are equally involved [2].

The etiology of DMI is still unknown. Premature atherosclerosis and a procoagulant state in diabetics appear to be the main factors. It seems that an initial ischemic event, superimposed on severe diabetic microvascular disease, causes muscle edema, increased pressure within the fascial compartment, further ischemia and, finally, muscle infarction [3]. Atraumatic swelling and exquisite tenderness of the involved limb are the main clinical features. The quadriceps, hip adductor and leg muscles are affected in decreasing frequency. The upper limb muscles are rarely involved. The symptoms appear within a period of a few weeks and resolve spontaneously over several months. Erythrocyte sedimentation rate, white blood cell count and serum CPK level are elevated in some cases. The diagnosis is suggested by the characteristic clinical picture, strongly supported by imaging (ultrasound, CT scan, MRI) and established by muscle biopsy (showing confluent areas of muscle edema, necrosis and reparative tissue) [4]. MRI is a valuable non-invasive diagnostic study (abnormal in 100% of cases). This investigation excludes the need for muscle biopsy, which is considered to be harmful [2,4].

The differential diagnosis includes muscle tumors, infectious conditions, focal and systemic myositis, granulomatous lesions, deep venous thrombosis, acute compartment syndrome, etc. [5]. The differential diagnosis of pyomyositis, diabetic amyotrophy and DMI deserves special attention. Pyomyositis is a rare infection. Caused mainly by gram-positive cocci in immune-compromised patients and in poorly controlled diabetes, it may mimic DMI. Extensive investigation must rule out the presence of a septic focus, bacteremia and muscle infection. In our patient there was no evidence of infection and the clinical outcome (spontaneous previous remissions and present improvement without antibiotic treatment) did not support the diagnosis of pyomyositis.

Diabetic amyotrophy is a proximal neuropathy that typically occurs in patients with adult-onset type II diabetes and has a peak incidence during the sixth decade of life. Pain and weakness in the proximal muscles, especially in the lower limbs (unilateral, yet followed by similar signs in the opposite limb within several months), and spontaneous remission over a period of 6–18 months are common features of diabetic amyotrophy and DMI. However, unlike the poorly controlled severe diabetes in patients with DMI, most of the patients with diabetic amyotrophy are only mildly diabetic at diagnosis. Moreover, despite histologic changes compatible with myopathy and muscle fiber atrophy, clinical features (pain, weakness, sensory symptoms, absence or reduction of knee jerks), electromyographic evidence (nerve conduction disturbances) and nerve biopsy specimens (showing features of demyelination) strongly suggest that diabetic amyotrophy is a form of diabetic neuropathy with a predilection for proximal nerves.

Management of DMI includes bed-rest, analgesia and immobilization of the affected limb followed by gentle physical therapy. Aggressive metabolic control is needed. Anticoagulant therapy was used in only a few cases. The short-term prognosis is excellent and symptoms resolve spontaneously over several weeks or months. However, the long-term outcome is poor, since many patients die from the severe complications of diabetes [5].

In conclusion, DMI is a rare condition that should be suspected in patients with long-standing diabetes mellitus and painful and swollen muscles. MRI is the investigation of choice. Conservative treatment is beneficial.

**References**

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