A Case of Diabetic Muscle Infarction

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While warming up for her first karate class, a 37-year-old woman with a 29-year history of type 1 diabetes mellitus developed a mild pain on the inside of her left thigh. She believed she had pulled a muscle and left the class to rest. In the ensuing days, the pain gradually worsened followed by swelling of the left thigh. Over the next few weeks, a similar pain and swelling developed over the left calf. She was seen at her local hospital emergency room approximately three weeks after onset, and was prescribed antibiotics. However, the pain and swelling continued and within eight weeks she had lost the ability to weightbear secondary to the pain.

She was admitted to hospital for further investigations. She was found to be in mild diabetic ketoacidosis. She had no history of fever, and no source of infection could be identified. Her blood work on admission was significant for a mildly elevated white cell count of 14 (N=4-11x10^9/l), erythrocyte sedimentation rate (ESR) of 84 (N=0-10 mm/hr), C - reactive protein of 151 (N=<6 mg/L), and normal lactate (0.9; N=0.5-2.2 mmol/L) and creatine kinase (100; N=35-250 U/L). She was started on antibiotics for three weeks. All of her blood, urine, and sputum cultures were negative.

She was assessed by the neurology service four months after the initial onset of symptoms. At that time, the pain in her left thigh had resolved, although the swelling remained. She continued to have severe pain and swelling of the left calf that prevented her from weightbearing on the left leg. The pain was localized to the calf and associated with calf tenderness. There was no back pain or radicular symptoms. She did not believe there was any significant weakness. Her bowel and bladder function was normal. She had no involvement of other limbs.

Her diabetes was complicated by retinopathy, peripheral neuropathy and end-stage renal disease. She had been on haemodialysis for several years prior to presentation.

Physical examination revealed mild symmetrical stocking distribution sensory impairment and absent ankle reflexes bilaterally. There was no focal muscle atrophy. Strength was normal in the right leg but difficult to test in the left leg due to pain. However, strength was at least antigravity in all muscle groups in the left leg. Reflexes were present and symmetric at the knees. The remainder of her neurological exam was unremarkable. The left calf was swollen and the medial gastrocnemius muscle was firm and tender to palpation. The medial left thigh was mildly swollen compared with the right thigh. However, the thigh muscles were soft and non-tender. She had flexion contractures at the left knee and ankle.

Doppler study of the left leg did not show any sign of venous thrombosis. A bone scan was normal without evidence of osteomyelitis. Findings on the nerve conduction studies were consistent with a mild symmetrical axonal sensorimotor polyneuropathy, presumably secondary to her diabetes.

Electromyography revealed fibrillation potentials and positive sharp waves in the left vastus medialis and medial gastrocnemius muscles, and small polyphasic motor unit potentials in the left iliopsoas and medial gastrocnemius muscles. Interference pattern was normal.

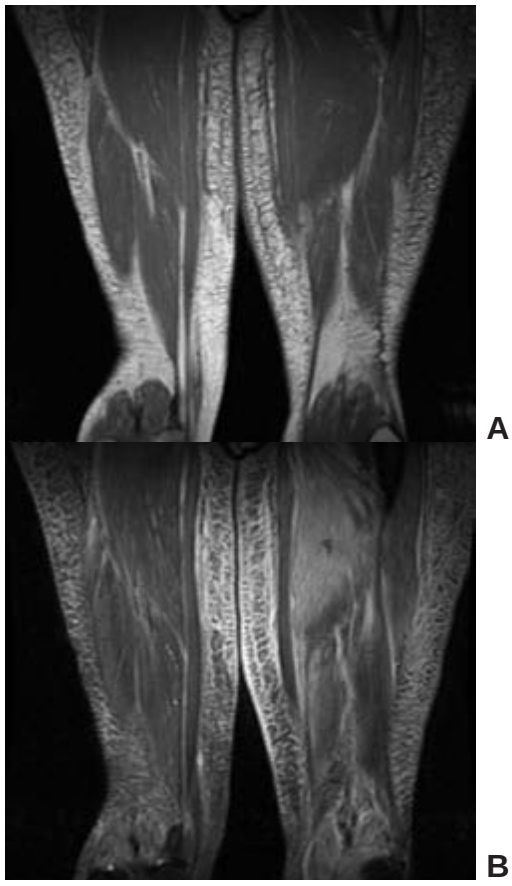

Figure 1: *Coronal MRI of left thigh demonstrating swelling of adductor magnus and partial loss of normal intermuscular septa with isointense signal on T1 (A) and hyperintense signal on FSEIR (B) sequences.*

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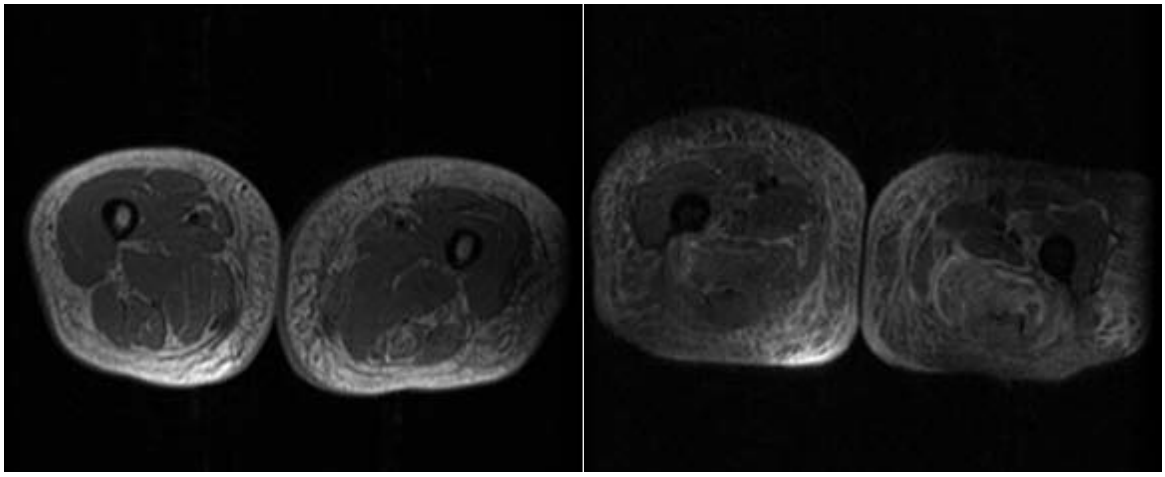

Figure 2: *Axial images of left thigh again demonstrating swelling of adductor magnus with isointense signal on T1 (left) a hyperintense signal on T2 (right) sequences.*

Magnetic resonance imaging (MRI) of the left thigh showed diffuse enlargement of the adductor magnus muscle and partial loss of normal fatty intermuscular septa. There was subfascial, and subcutaneous edema. There was no discrete fluid collection identified to suggest an abscess. The affected muscles showed iso-intense signal on T1, and hyper-intense signal on T2 and fast spin echo inversion recovery (FSEIR) sequences (Figure 1 and Figure 2). These muscles also showed enhancement with Gadolinium.

The clinical diagnosis of diabetic muscle infarction (DMI) was supported by the MRI findings. The patient was treated with supportive care only. At one year follow-up, the muscle pain and swelling had resolved and she was back to walking independently.

Discussion

Diabetic muscle infarction refers to spontaneous non-gangrenous focal muscle necrosis occurring primarily, if not exclusively, in patients with diabetes mellitus (DM). The precise cause is unknown. It was first reported by Angervall and Stener[1] in 1965. It is more common in patients with the combination of diabetes and end-stage renal disease. In DM patients on dialysis, it has an estimated incidence of 1/233 patient-year[2]. In larger series, women are affected more frequently than men by a 3:2 ratio[3].

In a review of the literature, Trujillo-Santos et al[3] found that DM was present in 83% of published cases, of which 59% involved type 1 diabetes. Diabetes mellitus status was not indicated in the remaining 17% of cases they reviewed. We did find one reported case of DMI in a patient that did not have DM[4]. In patients with DM, mean duration of disease prior to development of DMI is 14 years and most patients have diabetic microvascular complications (retinopathy 71%, nephropathy 54%, and neuropathy 51%) at the time of presentation with DMI[3]. The most frequently involved muscles are those in the anterior/medial thigh (84%) followed by the calf muscles (19%). Two percent of patients have involvement of both thigh and calf muscles, and 8% have bilateral involvement[3].

Patients with DMI present with swelling (76%) and pain (19%) of the affected muscle group. A palpable mass is present in the affected region in approximately 30% of patients. The most common laboratory abnormalities are an elevated ESR (53% of patients) and/or a mildly elevated creatine phosphokinase (CPK) (up to 700 IU/l). However, both of these measures may be normal. In a minority of patients fever and/or leukocytosis are present, adding to the difficulties of making a firm diagnosis of DMI[3].

Electrophysiological studies reveal normal sensory and motor nerve conduction studies[3], or, as in our patient, evidence of neuropathy secondary to diabetes. Electromyography commonly demonstrates muscle membrane irritability (fibrillation potentials and positive sharp waves) in affected muscles. Motor units may be small and polyphasic (myopathic) or normal in appearance. Some insertional points can be electrically silent even with active contraction, indicating areas of fibrosis.

Although not specific, the abnormalities seen on MRI can be diagnostic in the appropriate clinical setting. The characteristic findings are increased signal from the affected muscle (intramuscular and perimysial tissues) on T2 and FLAIR (fluid attenuation inversion recovery) sequences[5]. T1 sequence usually shows isointense or hypointense signal in the affected region, secondary to increased water content from edema and inflammation accompanying the infarction. Gadolinium enhancement on T1 suggests an area of necrosis within the inflamed muscle. The affected muscle is usually diffusely enlarged with ill-defined borders due to loss of fatty intramuscular septa. Tiny foci of haemorrhage can also be present and are seen as an increased signal on T1 sequence.

Findings on muscle biopsy are non-specific and depend on the time line between symptom onset and biopsy. Gross specimens show non-hemorrhagic, pale, whitish muscle[2,6]. On

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light microscopy, large areas of muscle necrosis, phagocytosis of necrotic muscle fibres, and the presence of granulation tissue and collagen are early findings. Late in the disease course, there will be replacement of necrotic muscle fibers by fibrous tissue, myofiber regeneration, and mononuclear cellular infiltration. There is one case report of a diabetic patient with muscle biopsy findings suggestive of vasculitis[7]. Despite this, the patient reportedly recovered without specific treatment of vasculitis.

The etiology of DMI is unknown although a number of theories have been proposed, all based on the hypothesis that underlying ischemia plays a primary role[8-12]. Banker and Chester speculated that hypoperfusion and resultant anoxia produces a mild compartment syndrome that worsens the ischaemia resulting from atheroembolism[8]. Anderson and Richards hypothesized that a change of the circulatory pattern of muscle renders it particularly vulnerable to injury, promoting intra-compartmental ischaemia sufficient to cause myonecrosis[9]. Another hypothesis is that of acquired nephrosis-related hypercoagulability. This is supported by the abnormalities of coagulation and fibrinolytic pathways seen by Bjornskov et al[10] in patients with DMI, and also by the detection of prothrombotic antiphospholipid antibodies in two cases reported by Palmer and Greco[11]. Yet another hypothesis is that of hypoxia-reperfusion injury. This is based on findings of muscle hyperaemia by Tc-sestamibi scanning in an affected patient by Silberstein et al (2001)[12]. However, it should be noted that there is very little data to support any of these hypotheses and the exact cause of DMI remains unknown at the present time.

Patients with DMI are generally treated with supportive measures only, primarily bed rest and analgesia to control their pain. It is not clear whether glycemic control influences the natural history of the attack. Some clinicians have advocated treatment with anti-platelet therapy or anticoagulation[10,11,13]. Others have advocated treatment with corticosteroids[11,13]. However, again it is not clear that either of these interventions influences the natural history[13]. Kapur and McKendry found that patients treated medically (with antiplatelet agents and/or steroids) had shorter recovery times, although not statistically significant when compared with supportive therapy[13]. Both groups had similar recurrence rates of approximately 30%.

Recurrence of DMI was found in 55 (48%) cases in the literature[3]. Interestingly, patients who underwent muscle biopsy had a recurrence rate of about 70%. Mortality rate is estimated to be around 10%, most of it occurring 6-12 months from diagnosis[13].

In summary, DMI is a rare and possibly underrecognized complication of “endstage” diabetes. Its presentation can be confused with multiple more common entities, such as cellulitis, deep venous thrombosis, muscle abscess, diabetic amyotrophy and occasionally even “focal” myositis[13]. Diagnosis can be made based on clinical presentation and characteristic magnetic resonance imaging findings. Muscle biopsy should be avoided in characteristic cases, as it may be associated with an increased risk of recurrence. In the absence of any evidence of the benefit of specific treatment modalities, treatment should be supportive, directed at pain control and physical therapy to prevent joint contractures. Although the pain can be extremely debilitating, most patients appear to recover uneventfully so the key is to make an accurate diagnosis and avoid iatrogenic complications.

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