Painful swollen legs in a diabetic patient

Introduction

A total of 117 cases of diabetic muscle infarction (DMI) have been described in the specialist metabolic and radiological journals. Many general clinicians are unaware of the condition.

An acutely tender swollen thigh in a patient with poorly controlled diabetes is the most common presentation. The pathogenesis is unknown although several theories will be discussed. Appearance on magnetic resonance imaging (MRI) is characteristic and specific. Treatment with rest and analgesia results in complete resolution of symptoms in a matter of weeks; however, occurrence of DMI is a poor prognostic indicator. Greater awareness of this complication should prevent unnecessary investigation and promote prompt management of the patient within a specialist environment.

Case Report

A 52-year-old man presented with a 6-week history of bilateral painful thighs and reduced mobility. Glycaemic control of his type 2 diabetes of 25 years' duration was poor and he had recently commenced on insulin. His disease was complicated by retinopathy, peripheral neuropathy and nephropathy. He denied trauma to the legs.

The thighs were swollen with pitting oedema extending from the ankles. There was no erythema or temperature disparity. The thighs were exquisitely tender on palpation of the anterior muscle compartment. Both calves were also tender to palpate. No mass was identified. The peripheral pulses were intact and the upper limbs were entirely normal.

Haematological investigations revealed erythrocyte sedimentation rate 136 mm/hr, C reactive protein 13 mg/dl, normal white cell indices and normal coagulation profile. On biochemical analysis urea and creatinine were elevated; creatine kinase was increased at 250 U/litre. Glycosylated haemoglobin was 14%. All immunological and vasculitic profiles were normal. Urinary protein excretion was 12 000 mg/24 hours.

This man was admitted for investigations, rest and rigorous control of his diabetes. He underwent ultrasound Doppler of his legs ruling out deep venous thrombosis or insufficiency of the large arteries. A computed tomography scan of the thighs revealed diffuse inflammation of the right thigh musculature. Nuclear bone scan confirmed increased uptake in the muscles but no bony abnormality. Magnetic resonance imaging was the definitive investigation showing diffuse enhancement on T2 weighted images of the anterior muscle compartment of the right thigh (vastus intermedius and vastus lateralis) with lesser changes noted in the left thigh and both calves (soleus) (*Figure 1*). A focal area of non-enhancement in the right rectus femoris following administration of gadolinium was consistent with an area of infarction (*Figure 2*).

An open biopsy specimen showed non-specific inflammation and regenerating muscle fibres. Occasional necrotic muscle fibres were remarked upon. No haemorrhage was noted and the intramuscular blood vessels were normal.

The diagnosis of diabetic muscle infarction was made. After 1 month of rest, analgesia and good glycaemic control the swelling and pain had completely resolved. A similar episode affecting the left thigh some months previously was reported. He is the only recorded patient to have had involvement of both thighs and calves bilaterally in the same episode.

Discussion

Diabetes mellitus is an increasingly common problem and is often difficult to manage effectively. Complications of the disease are commonplace and have the most serious consequences for the patient. DMI was first described in the medical literature in 1965 by Angervall and Stener. Since then only 117 cases have been reported, the majority of these in the late 1990s with the advent of MRI. It is possible that the condition is misdiagnosed as a result of unfamiliarity with the features in the general medical setting and that DMI occurs more commonly than these figures would suggest.

DMI arises in young patients (mean age 31 years, range 19–81 years) and is slightly more common in type 1 diabetes. Patients tend to have been diagnosed with diabetes for some years (median 15 years) and glycaemic control is inadequate in the majority. Of reported patients 92% had microvascular complications and 33% were dialysis dependent. Macrovascular complications of coronary artery disease and peripheral vascular disease do not seem to be associated (Umpierrez et al, 1996; Trujillo-Santos, 2003).

Pain limiting mobility, swelling and a mass at the site are common findings. Peripheral pulses tend to be normal. Fever was a feature in only three of the reported episodes. The thigh is the most commonly affected site. The calf is involved less often. Bilateral findings have been described in 17 patients (Trujillo-Santos, 2003). Bilateral involvement of both the thighs and calves in one episode has not been previously reported.

Blood investigations are usually unhelpful. A raised erythrocyte sedimentation rate (ESR) is the most reproducible finding. White cell count and coagulation indices tend to be normal. Levels of muscle enzymes are inconsistent in previously reported cases – in half of the cases the creatine kinase (CK) level was entirely normal. The measurement may be dependent on time of sample from onset of symptoms; a number of cases have shown that if measured early in the course of the illness CK is elevated but falls to normal within 13 days (Trujillo-Santos, 2003).

MRI is the investigation of choice. Other radiological investigations such as radiographs, bone scans and Doppler ultrasound serve to rule out other pathology. MRI has characteristic and relatively specific appearances when evaluated in the clinical context (Umpierrez et al, 1996; Trujillo-Santos, 2003).

Clearly a number of conditions present in a similar manner and it is important to differentiate DMI from these as treatment strategies differ. These are summarized in *Table 1*.

The question of whether or not to proceed to biopsy is contentious. It should be possible to diagnose DMI on clinical suspicion and consistent MRI findings with-

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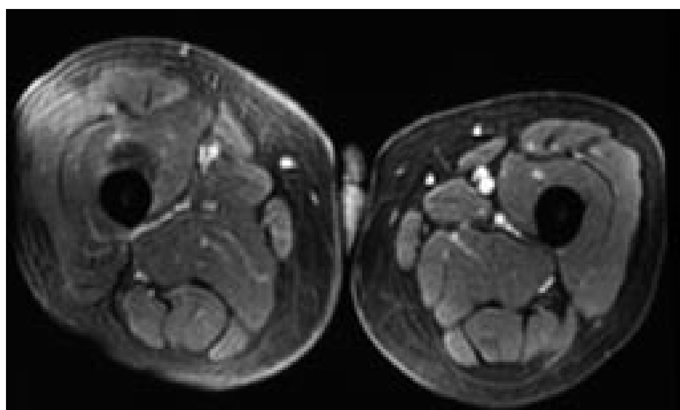

Figure 1. T2-weighted fat suppression image of left and right thigh. Notice the diffuse inflammation in the anterior compartment of the right thigh.

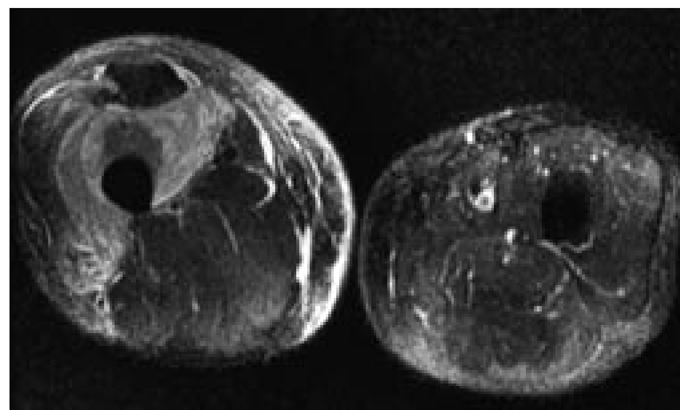

Figure 2. T1-weighted images following gadolinium administration, showing area of non-enhancement in the vastus intermedius muscle adjacent to the periosteum.

out biopsy. Biopsy in itself may not facilitate the diagnosis of DMI as findings are non-specific. In cases where the presentation is not typical and there is concern over a neoplastic process or abscess, it is reasonable to proceed to needle core biopsy given the very low complication rate with this procedure (Aboulafia et al, 1999).

The pathogenesis of DMI is not entirely understood. Early studies concluded that the infarction occurred as a result of an embolus from an aortic plaque. Post mortem specimens often showed no such evidence (Chester and Banker, 1986). It is more likely that there is dysfunction of the smaller intramuscular arterioles consistent with the microvascular complications so often manifest in these patients. A number of factors may contribute to the development of the muscle infarction. Microangiopathy may cause varying amounts of ischaemia within the muscle in turn simulating an inflammatory response, swelling and pressure within a particular compartment. Compartment syndrome contributes to further ischaemia and eventual infarction of the muscle group (Trujillo-Santos, 2003). The background hypercoagulability of patients with diabetes may also play a role (Palmer and Greco, 2001).

Conservative treatment with rest and analgesics is successful in the majority of cases. Treatment with antibiotics, steroids, immunosuppressants or anticoagulants has not been shown to be effective (Aboulafia et al, 1999; Trujillo-Santos, 2003). Recurrence is common – a quarter of the reported cases had at least one further episode. Overall prognosis in these patients is poor; most are deceased or requiring dialysis within 5 years (Trujillo-Santos, 2003). **BJHM**

Aboulafia AJ, Monson DK, Kennon RE (1999) Clinical and radiological aspects of idiopathic diabetic muscle infarction. Rational approach to diagnosis and treatment. *J Bone Joint Surg (Br)* **81B**(2): 323–5

Angervall L, Stener B (1965) Tumoriform focal muscular degeneration in two diabetic patients. *Diabetologia* **1:** 39–42

Chester S, Banker BQ (1986) Focal infarction of muscle in diabetics. *Diabetes Care* **9**(6): 623–30

Palmer GW, Greco TP (2001) Diabetic thigh muscle infarction in association with antiphospholipid antibodies. *Semin Arthritis Rheum* **30**(4): 272–80

Trujillo-Santos AJ (2003) Diabetic muscle infarction: an underdiagnosed complication of long-standing diabetes. *Diabetes Care* **26**(1): 211–15

Umpierrez GE, Stiles RG, Kleinbart J et al (1996) Diabetic muscle infarction. *Am J Med* **101**(3): 245–50

Table 1. Differential diagnosis of diabetic muscle infarction (DMI)

	History	Examination	Full blood picture	ESR/CRP	CK	Other investigations	MRI
Diabetic muscle infarction	Complicated diabetic, excruciating pain, acute onset	Swelling, tenderness, possible mass	Usually normal	↑	⇔/↑		Characteristic
DVT	Risk factors	Swelling and erythema	Normal	Normal	Normal	Doppler or venogram	Unnecessary
Rupture or haemorrhage	Trauma, pain	Swelling, tenderness and mass	? ↓ haemoglobin ? ↑ WCC	⇔/↑	⇔/↑	Computed tomography	Characteristic
Pyomyositis	Gradual onset, fever, weakness, risk factors	Swelling, erythema, ↑temperature	↑↑ WCC	↑↑	⇔/↑	Computed tomography	Characteristic
Abscess	Gradual onset, fever	Swelling, mass, ↑temperature	↑↑ WCC	↑↑	Normal	Computed tomography	Characteristic
Osteomyelitis	Gradual onset, pain and fever	Tenderness, minimal swelling	↑↑ WCC	↑↑	Normal	Computed tomography Nuclear bone scan	Unnecessary
Polymyositis	Gradual onset, pain and weakness in arms and legs	Minimal swelling, marked weakness, abnormal muscle antibodies	⇔/↑ WCC	⇔/↑	↑↑↑	EMG characteristic	Similar to DMI
Focal myositis	Gradual onset, pain	Mass	⇔/↑ WCC	⇔/↑	↑↑		Similar to DMI
Bony/muscular neoplasm	Gradual onset, pain and mass	Mass, tenderness	⇔/↑ WCC	Normal	⇔/↑	Computed tomography	Usually unnecessary

DVT = deep vein thrombosis; ESR = erythrocyte sedimentation rate, CRP = C reactive protein, CK = creatine kinase, MRI = magnetic resonance imaging; EMG = electromyelogram; WCC = white cell count