Case Report

Diabetic Muscle Infarction: Case Report and Review

SUNEIL KAPUR, JACQUES A. BRUNET, and ROBERT JOHN McKENDRY

ABSTRACT. We describe a 61-year-old woman with a 16-year history of type 2 diabetes mellitus with sudden and spontaneous onset of left anteromedial thigh pain and swelling. Her pain was so severe that she could not bear weight. She had no other musculoskeletal or constitutional symptoms. Her diabetes was poorly controlled. She had diabetic retinopathy and endstage nephropathy requiring dialysis. An extensive literature review of diabetic muscle infarction is provided. (J Rheumatol 2004; 31:190–4)

Key Indexing Terms:
DIABETIC MUSCLE INFARCTION

We describe a 61-year-old woman with a 16-year history of type 2 diabetes mellitus (DM) with sudden and spontaneous onset of left anteromedial thigh pain and swelling. Her pain was so severe that she could not bear weight. She had no other musculoskeletal or constitutional symptoms. Her diabetes was poorly controlled. She had diabetic retinopathy and endstage nephropathy requiring dialysis.

CASE REPORT

A 61-year-old woman with a 16-year history of type 2 diabetes mellitus (DM) presented with sudden and spontaneous onset of left anteromedial thigh pain and swelling. Her pain was so severe that she could not bear weight. She had no other musculoskeletal or constitutional symptoms. Examination revealed firm swelling of her left medial thigh consisting of a 10 × 5 cm area of induration, erythema, warmth, and tenderness. Ophthalmologic examination revealed scattered intraretinal hemorrhages without retinal neovascularization. She had decreased sensation for light touch and pinprick in a glove and stocking distribution. Peripheral pulses were palpable with no bruits. The white blood cell count (WBC) was 19 × 10^9/l (normal 4–11 × 10^9/l) with 85% neutrophils (normal 33–75%), Westergren erythrocyte sedimentation rate (ESR) was 137 mm/h (normal 0–25 mm/h), creatine kinase (CK) was 1066 U/l (normal 25–150 U/l), and glycosylated hemoglobin (HbA1C) was 6.7% (normal < 6%). Antinuclear antibodies, antineutrophil cytoplasmic antibodies, complements, and blood cultures were normal. Venous Doppler ultrasound revealed no evidence of deep vein thrombosis. Magnetic resonance imaging (MRI) revealed increased signal intensity on T2 weighted images involving the left hip adductors, with diffuse edema of the vastus medialis muscle, subcutaneous tissues, and skin, and deep fascial fluid (Figure 1).

With a working preoperative diagnosis of a left thigh abscess within infarcted muscle or necrotizing fasciitis, urgent surgery was performed. As suggested by the MRI, large fluid collections between infarcted muscles were found, but there was no abscess cavity. Cultures of the fluid, infarcted muscles, and fascia were taken and portions of her left thigh adductor brevis, longus and magnus, and gracilis, semimembranosus, semitendonosus, and biceps femoris muscles were excised. On pathological examination, there was myonecrosis with areas of edema, hemorrhage, acute and chronic inflammation, regenerating muscle, and scant fibrosis. Aerobic and anaerobic cultures were negative. She was referred to the Rheumatology Section postoperatively. The diagnosis of diabetic muscle infarction (DMI) was considered most likely, and she was treated with bed rest and analgesics. Her thigh wound healed without complications. She was discharged from hospital 2 weeks later with moderate improvement in pain and mobility, and normalization of her CK and WBC.

Three weeks after discharge, she presented with similar symptoms and signs distal to her surgical site as well as on the contralateral thigh, and then 3 months later in her right calf. Initial treatment with bed rest and analgesics was followed by prednisone 30 mg/day gradually tapered to alleviate her persistent and severe pain. MRI sections of her thighs at 8, 9, and 10 weeks from onset of her original symptoms are shown in Figure 1. By 4 months from onset, her original symptoms and signs had almost completely resolved. One month later, she died at a community hospital secondary to complications of pneumonia.

DISCUSSION

Diabetic muscle infarction was first reported in 1965[1]. Since then, there have been more than 100 case reports[2-49]. A Medline search of the English literature from its inception to 2003 using the keywords "diabetic muscle infarction" identified previous reports of DMI[1-49]. Although this retrospective literature review has methodological shortcomings, it provides valuable information that may aid the recognition and management of patients with DMI. Most of the 116 patients reported had long-standing type 1 DM (Table 1)[1,2,4–49]. The mean age of onset was 42 years. Among 113 patients including our case, the initial episode of DMI occurred in the thigh muscles alone in 80%, the lower leg muscles alone in 17%, both the thigh and lower leg muscles concurrently in 2%, and the upper extremity muscles in 1%[1,2,4-31,33-49]. Recurrences at the same or a different site occurred in 45% of 84 patients reviewed[1,2,5-11,14-27,29-31,33–44,46-49]. Bilateral involvement occurred in one-third of

From the Division of Rheumatology, Department of Medicine, Ottawa Hospital, Ottawa, Ontario, Canada.

S. Kapur, MD, FRCPC, Rheumatology Fellow, University of Ottawa; J.A. Brunet, MD, FRCSC, Associate Professor of Surgery, Division of Orthopedic Surgery, University of Ottawa; R.J. McKendry, MD, FRCPC, Professor of Medicine, University of Ottawa, Ottawa Hospital.

Address reprint requests to Dr. S. Kapur, Bank Medical Centre, 1935 Bank Street, Ottawa, Ontario K1V 8A3, Canada. E-mail: skapur@ottawahospital.on.ca

Submitted November 25, 2002; revision accepted July 24, 2003.

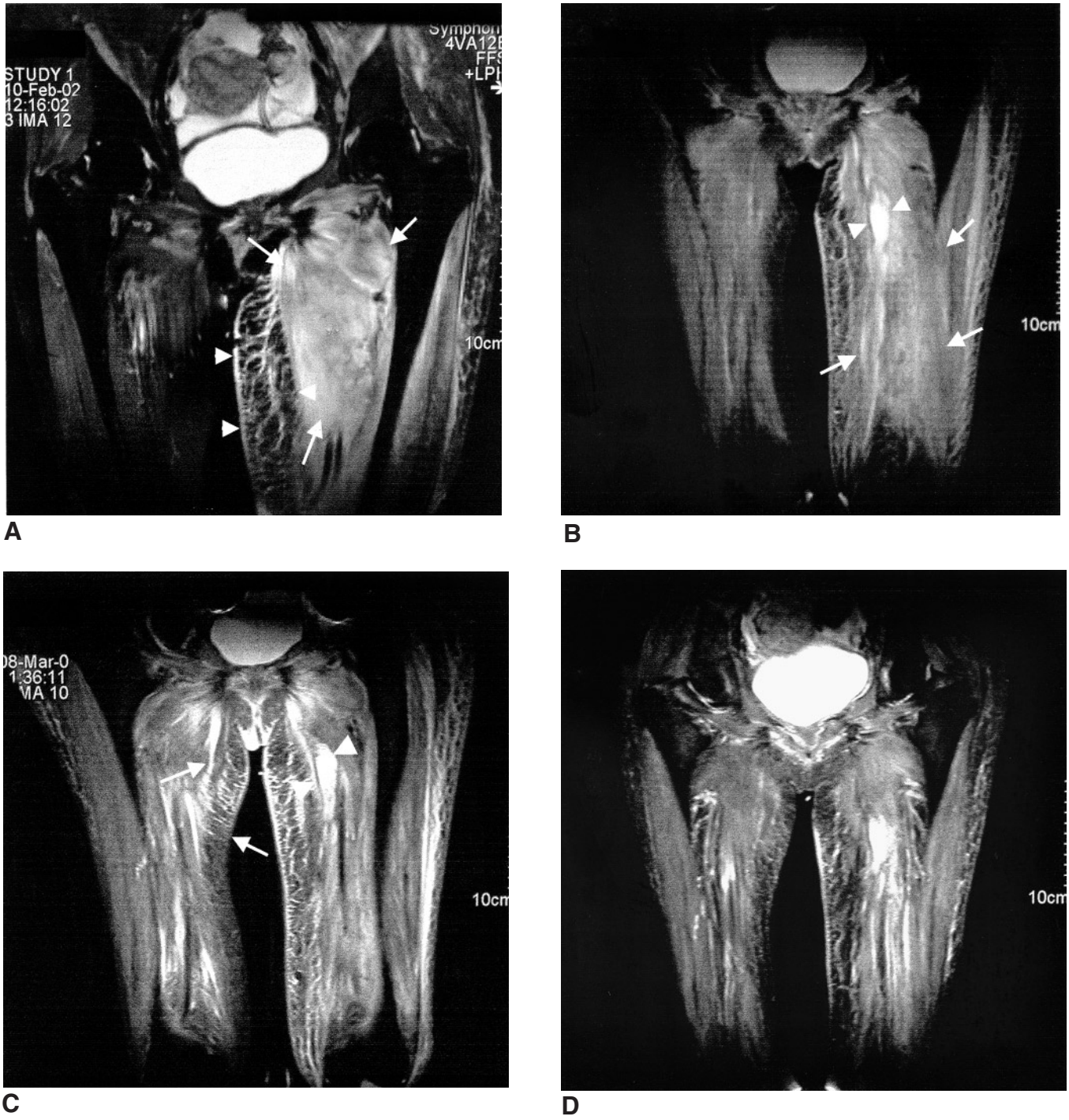

Figure 1. MRI images of the patient's thighs showing areas of ischemic muscle. A. T2 weighted coronal image through both thighs taken 5 weeks from onset of symptoms. There is high signal intensity involving mainly the adductor muscle group of the left thigh, in keeping with muscle edema (white arrow). Subcutaneous and skin edema is also shown (white arrowhead). B. Short tau inversion recovery (STIR) coronal image taken 8 weeks after symptom onset. Edema (white arrow) involving the quadriceps compartment of the left thigh. The small fluid collection (white arrowhead) is considered to be postsurgical. C. STIR coronal image taken 9 weeks after symptom onset. There is persistent edema in the left thigh involving quadriceps muscles and subcutaneous fat. The small fluid collection (white arrowhead) is considered to be postsurgical. There is new subcutaneous edema in the medial aspect of the right thigh (white arrow). D. STIR coronal image taken 10 weeks after symptom onset. There is decreased edema within the subcutaneous fat and the vastus intermedius and vastus lateralis muscles.

Table 1. Demographic, clinical, and laboratory features of diabetic muscle infarction in 116 patients and this case report.

Clinical Features	Cases Reported, n = 116 (%)	Case Report Data
Age, mean, yrs	41	61
Male/female	55/61	Female
Duration of DM, yrs	Mean 15	16
Type 1 DM, n (%)	77/104 (74)	Type 2 DM
Diabetic R, K, or N, n (%)	69/71 (97)	Yes
Retinopathy, n (%)	53/90 (60)	Yes
Nephropathy, n (%)	73/92 (80)	Yes
Neuropathy, n (%)	66/104 (64)	Yes
Acute onset of symptoms, n (%)	85/95 (90)	Yes
Painful swelling, n (%)	109/110 (99)	Yes
Palpable muscle mass, n (%)	47/108 (44)	Yes
WBC > 11 × 10^9 /l, n (%)	21/60 (35)	Yes (19 €× 10^9 units)
ESR > 50 mm/h, n (%)	26/35 (74)	Yes (137 mm/h)
CK > 150 U/l, n (%)	20/47 (45)	Yes (1066 U/l)

R: retinopathy, K: nephropathy, N: peripheral neuropathy.

Table 2. MRI and pathological findings of DMI reported in the literature compared to the case report[1, 2, 4–10, 12–27, 29–49].

Description	Cases Reported, n = 77 (%)	Case Report Data
MRI findings[2,5–10, 12, 14, 16–27, 30–4, 38, 39, 41–46], n (%)		
T2 - Hyperintense signal of infarcted muscle	77/77 (100)	Yes
T2 - Muscle enlargement	46/46 (100)	Yes
T2 - Subcutaneous edema	37/41 (90)	Yes
T2 - Subfascial edema	33/37 (90)	Yes
Pathology[1, 2, 4, 6, 7, 9, 12–17, 19–23, 26, 27, 29–32, 35–37, 39, 40, 42, 43, 45–49], n (%)		
Muscle fiber necrosis	72/74 (97)	Yes
Inflammatory cell infiltrate	47/55 (85)	Yes
Microvascular abnormality	53/64 (83)	Yes
Edema	26/54 (48)	Yes
Hemorrhage	26/55 (47)	Yes
Fibrosis/granulation	35/59 (59)	Yes
Tissue-regenerating muscle fibers	32/58 (55)	Yes

MRI results are T2 weighted.

patients. About 97% of patients had other microvascular complications including nephropathy, retinopathy or neuropathy[1,2,4-30,32,34-49]; about 60% had diabetic retinopathy, 80% had nephropathy, and 64% had neuropathy. Twenty-five percent of patients with nephropathy were dialysis-dependent.

Of all the known cases of DMI, 9 of 12 had HbA1C greater than 7%, suggesting that DMI occurred in poorly controlled diabetics[4-13]. Laboratory tests were not very informative. About one-third of patients had leukocytosis; three-quarters had ESR > 50; and half had an elevated CK[2,4–44]. These may be overestimates, as normal values may have been underreported.

The largest series review to date on the frequencies of MRI and pathological abnormalities in DMI is presented in Table 2[1,2,4-10,12-27,29-49]. Although MRI findings are not pathognomonic for DMI, characteristic features include extensive edema within the muscle, muscle enlargement, subcutaneous edema, and interfascial edema. Even more characteristic is multifocal areas of involvement in a "patchwork" pattern that is unusual in pyomyositis.

The pathogenesis of DMI is uncertain. One plausible theory is that diabetic microangiopathy and/or arteriosclerosis lead to ischemia of muscle and this results in an intense inflammatory response, edema, hyperemia, and reperfusion[1,3-5,7,20,29,34-37,44]. These events create further ischemia by generation of reactive oxygen radicals and from pressure within the fascial compartment. This cycle of hypoxia–reperfusion injury eventually culminates in infarction. In addition, the presence of a hypercoagulable state in diabetics, including elevated concentrations of factor VII, fibrinogen, thrombomodulin, and antiphospholipid antibodies, and decreased levels of prostacyclin, antithrombin, and tissue plasminogen activator, may contribute to a thrombogenic state[3,16,22,48].

The differential diagnosis of DMI includes infection (pyomyositis, necrotizing fasciitis), focal inflammatory myositis, vascular events, trauma, tumor, and diabetic amyotrophy[7,15-23,45]; MRI often cannot distinguish these entities, with the exception of diabetic amyotrophy, which would have a normal appearance. Cases of pyomyositis typically have a subacute presentation with pain, swelling, constitutional symptoms, as well as increasing muscle tenderness. In typical pyomyositis investigations reveal an elevated WBC and ESR, normal CK, pus on aspiration, positive cultures and areas of contiguous involvement on MRI[21,45]. Differentiating features of focal myositis include lack of pain, involvement of facial and tongue muscles along with limb muscles, absence of CK elevation, absence of recurrences, and occasional progression to polymyositis[15,45]. Patients with local nodular myositis present insidiously; they can develop constitutional symptoms, pain, recurrences, and diffuse wasting with involvement of facial and bulbar muscles[15,16,45]. Myositis ossificans evolves over months to years and reveals ossification on radiography by 6 weeks from onset[15,22]; elevated WBC, ESR, and CK are unusual. Primary lymphoma of the muscle is insidious in onset, progressive, and unilateral[45]. Soft tissue sarcomas of the leg are usually painless and cause little leg dysfunction with normal cell counts and ESR[22]; if pain develops it may be insidious if tumor necrosis occurs or sudden if tumor hemorrhage occurs. Patients typically have a nontender firm mass on examination.

In a patient with long-standing diabetes and microvascular complications, DMI can be diagnosed with confidence

when the characteristic clinical features and MRI findings are present[3,8,9,24-29]. If other diagnoses are considered, then a computer tomography guided core needle aspiration and biopsy for gram stain, culture, and pathology may be helpful. Unless compartment syndrome or abscess is suspected, open biopsy and excision may be inadvisable, as this may be associated with postoperative complications including seroma, hematoma, infection, poor wound healing, delayed recovery, and recurrences[24,25,27-29].

A review of the literature revealed a trend toward faster recovery in patients treated with antiplatelet and/or antiinflammatory drugs compared to rest and analgesics or surgical excision[1,2,4,5,7,8,10,11,15-18,20,21,23-26,28-41,47-49]. The average recovery times from treatment onset were 5.5 weeks for patients treated with antiplatelet and/or antiinflammatory drugs, 8 weeks for those treated with bed rest and analgesics, and 13 weeks for those treated with surgical resection. Among the 49 patients in all 3 treatment groups, baseline characteristics, including age of patient, duration of diabetes, microvascular complications, and extent of muscle infarction as determined by MRI, were similar. The recurrence rates and mortality rates were highest in the surgically treated group. The mean recurrence rate in all treatment groups was 40%; the mean mortality rate was 10% within 2 years from DMI onset[1-3,7-10,12,15,16,18,20,21,23,24,26-28,30-32,34-39,45-49]. The causes of death were mainly due to macrovascular events such as myocardial infarction, stroke, or gangrene. Although a surgical approach was chosen in this case due to a strong suspicion of necrotizing fasciitis or pyomyositis, we do not advocate surgical resection as primary management of this condition.

With the increasing prevalence of diabetes in our aging population, we should expect the prevalence of DMI to increase. MRI is an important tool for early diagnosis, and nonsurgical therapy appears to provide the most favorable outcome.

REFERENCES

1. Angervall L, Stener B. Tumoriform focal muscular degeneration in two diabetic patients. Diabetologia 1965;1:39-42.
2. Madhan KK, Symmans P, Te Strake L, van der Merwe W. Diabetic muscle infarction in patients on dialysis. Am J Kidney Dis 2000;35:1212-6.
3. Trujillo-Santos AJ. Diabetic muscle infarction. An underdiagnosed complication of long-standing diabetes. Diabetes Care 2003;26:211-5.
4. MacIsaac RJ, Jerums G, Scurrah L. Diabetic muscle infarction. Med J Aust 2002;177:323-4.
5. Toh V, Winocour P. Bilateral lower limb pain and swelling in a young girl with type 1 diabetes mellitus. Hosp Med 2001;62:783-5.
6. Bingham C, Hilton DA, Nicholls AJ. Diabetic muscle infarction: an unusual cause of leg swelling in a diabetic on continuous ambulatory peritoneal dialysis. Nephrol Dial Transplant 1998;13:2377-9.
7. Taira M, Komiya I, Taira T, et al. A case of diabetic muscle infarction in Japan. Diabet Med 1998;15:1065-7.
8. Lafforgue P, Janand-Delenne B, Lassman-Vague V, Daumen-Legre V, Pham T, Vague P. Painful swelling of the thigh in a diabetic patient: diabetic muscle infarction. Diabetes Metab 1999;25:255-60.
9. Umpierrez GE, Stiles RG, Kleinbart J, Krendel DA, Watts NB. Diabetic muscle infarction. Am J Med 1996;101:245-50.
10. Yoo WH, Kim CH, Park JH, et al. Case report: diabetic muscle infarction presenting as knee arthralgia. Rheumatol Int 2001;21:36-9.
11. Boluda B, Mesa J, Obiols G, Simo R. Focal muscle infarction in a diabetic [letter]. Diabet Metab 1989;15:269-70.
12. Heureux F, Nisolle JF, Delgrange E, Donckier J. Diabetic muscle infarction: a difficult diagnosis suggested by magnetic resonance imaging [letter]. Diabet Med 1998;15:621-2.
13. Becker BN, Otley CC, McNeill DB, Weintraub ID, Harrelson JM. Microangiopathic ischemic myopathy of semimembranosus muscle in patient with diabetes mellitus [letter]. Diabetes Care 1992;15:586-7.
14. Silberstein L, Britton KE, Marsh FP, Raftery MJ, D'Cruz D. An unexpected cause of muscle pain in diabetes. Ann Rheum Dis 2001;60:310-2.
15. Rocca PV, Alloway JA, Nashel DJ. Diabetic muscular infarction. Semin Arthritis Rheum 1993;22:280-7.
16. Palmer GW, Greco TP. Diabetic muscle infarction in association with antiphospholipid antibodies. Semin Arthritis Rheum 2001;30:272-80.
17. Pedicelli A, Belli P, Fratino M, Cina A, Di Gregorio F, Rollo M. Diabetic muscle infarction [letter]. Am J Med 2001;111:671-2.
18. Pamoukian VN, Rubino F, Iraci JC. Review and case report of idiopathic lower extremity compartment syndrome and its treatment in diabetic patients. Diabetes Metab 2000;26:489-92.
19. Morcuende JA, Dobbs MB, Crawford H, Buckwalter JA. Diabetic muscle infarction. Iowa Orthop J 2000;20:65-74.
20. Grigoriadis E, Fam AG, Starok M, Ang L-C. Skeletal muscle infarction in diabetes mellitus. J Rheumatol 2000;27:1063-8.
21. Khoury NJ, El-Khoury GY, Kathol MH. MRI diagnosis of diabetic muscle infarction: report of two cases. Skeletal Radiol 1997;26:122-7.
22. Scully RE, Mark EJ, McNeely WE, Ebeling SH, Phillips LD. Case 29-1997: case records of the Massachusetts General Hospital. N Eng J Med 1997;337:839-45.
23. Van Slyke MA, Ostrov BE. MRI evaluation of diabetic muscle infarction. Magn Reson Imaging 1995;13:325-9.
24. Keller DR, Erpelding M, Grist T. Diabetic muscular infarction. Preventing morbidity by avoiding excisional biopsy. Arch Intern Med 1997;157:1611-2.
25. Kiers L. Diabetic muscle infarction: magnetic resonance imaging (MRI) avoids the need for biopsy [letter]. Muscle Nerve 1995;18:129-30.
26. Damron TA, Levinsohn EM, McQuail TM, Cohen H, Stadnick M, Rooney M. Idiopathic necrosis of skeletal muscle in patients who have diabetes. Report of four cases and review of the literature. J Bone Joint Surg Am 1998;80:262-7.
27. Nunez-Hoyo M, Gardner CL, Motta AO, Ashmead JW. Skeletal muscle infarction in diabetes: MR findings. J Comput Assist Tomogr 1993;17:986-8.
28. Weissman A. Image interpretation session: 1996 diabetic muscle infarction. Radiographics 1997;17:246-8.
29. Chester CS, Banker BQ. Focal infarction of muscle in diabetics. Diabetes Care 1986;9:623-30.
30. Jan W, Beggs I. Painful swelling of the thigh. Br J Radiol 2001;74:773-4.
31. Sharma P, Mangwana S, Kapoor RK. Diabetic muscle infarction: atypical MR appearance. Skeletal Radiol 2000;29:477-80.
32. Anglada M, Vidaller A, Bolao F, Ferrer I, Olive M. Diabetic muscle infarction [letter]. Muscle Nerve 2000;23:825-6.

33. Aboulafia AJ, Monson DK, Kennon RE. Clinical and radiological aspects of idiopathic diabetic muscle infarction. Rational approach to diagnosis and treatment. J Bone Joint Surg Br 1999;81:323-6.
34. Penglis PS, Scott G, Cleland LG. Diabetic muscle infarction presenting as a knee effusion. Semin Arthritis Rheum 1999;28:421-2.
35. Bodner RA, Younger DS, Rosoklija G. Diabetic muscle infarction. Muscle Nerve 1994;17:949-50.
36. Barton KL, Palmer BF. Bilateral infarction of the vastus lateralis muscle in a diabetic patient: a case report and review of the literature. J Diabetes Complications 1993;7:221-3.
37. Hinton A, Heinrich SD, Craver R. Idiopathic diabetic muscular infarction: the role of ultrasound, CT, MRI, and biopsy. Orthopaedics 1993;16:623-5.
38. Barohn RJ, Bazan C, Timmons JH, Tegeler C. Bilateral diabetic thigh muscle infarction. J Neuroimaging 1994;4:43-4.
39. Barohn RJ, Kissel T. Painful thigh mass in a young woman: diabetic muscle infarction. Muscle Nerve 1992;15:850-5.
40. Lauro GR, Kissel JT, Simon SR. Idiopathic muscular infarction in a diabetic patient. J Bone Joint Surg Am 1991;73:301-4.
41. Reich S, Wiener SN, Chester S, Ruff R. Clinical and radiologic features of spontaneous muscle infarction in the diabetic. Clin Nucl Med 1985;10:876-9.
42. Eady JL, Cobbs KF. Diabetic muscle infarction. J South Orthop Assoc 1997;6:250-5.
43. Chason DP, Fleckenstein JL, Burns DK, Rojas G. Diabetic muscle infarction: radiologic evaluation. Skeletal Radiol 1996;25:127-32.
44. Spengos K, Worhle JC, Binder J, Schwartz A, Hennerici M. Bilateral diabetic infarction of the anterior tibial muscle. Diabetes Care 2000;23:699-701.
45. Jelinek JS, Murphey MD, Aboulafia AJ, Dussault RG, Kaplan PA, Snearly WN. Muscle infarction in patients with diabetes mellitus: MR imaging findings. Radiology 1999;211:241-7.
46. Delaney-Sathy LO, Fessell DP, Jacobson JA, Hayes CW. Sonography of diabetic muscle infarction with MR imaging, CT, and pathologic correlation. AJR Am J Roentgenol 2000;174:165-9.
47. Ratliff JL, Matthews J, Blalock JC, Kasin JV. Infarction of the quadriceps muscle: a complication of diabetic vasculopathy. South Med J 1986;79:1595.
48. Bjornskov EK, Carry MR, Katz FH, Lefkowitz J, Ringel SP. Diabetic muscle infarction: a new perspective on pathogenesis and management. Neuromusc Disord 1995;5:39-45.
49. Vande Berg B, Malghem J, Puttemans T, Vandeleene B, Lagneau G, Maldague B. Idiopathic muscular infarction in a diabetic patient. Skeletal Radiol 1996;25:183-5.