Diabetic Muscle Infarction

An underdiagnosed complication of long-standing diabetes

A. J. TRUJILLO-SANTOS, MD

OBJECTIVE — To systematically review all the reported cases of diabetic muscle infarction (DMI) and its pathogenesis, clinical features, prognostic implications, and management.

RESEARCH DESIGN AND METHODS — We searched databases (MEDLINE and EMBASE) from their inception to August 2001 and reviewed bibliographies in reports retrieved. Data were extracted in a standardized form.

RESULTS — A total of 47 references were retrieved; 115 patients and 166 episodes were included. DMI was more frequent in women (61.5%, mean age at presentation 42.6 years). Of the cases, 59% had type 1 diabetes; the mean duration of disease was 14.3 years, and multiple diabetic end-organ complications were noted. DMI affects the lower limbs with abrupt onset of pain and local swelling. Diagnosis is made by biopsy, but the characteristic features in magnetic resonance imaging are very typical. Treatment includes bed rest and administration of analgesics, but recurrence is common.

CONCLUSIONS — DMI is a very uncommon complication of long-standing diabetes; presentation is well characterized and management is simple.

Diabetes Care 26:211–215, 2003

Spontaneous aseptic diabetic muscle infarction (DMI) is a rare complication of diabetes. It has been reported as aseptic myonecrosis, ischemic myonecrosis, and tumoriform focal muscular degeneration. Clinical presentation is uniform, with acute onset of painful swelling of the affected muscle and, occasionally, a palpable mass. The differential diagnosis is extensive and DMI is frequently misdiagnosed clinically. The illness is certainly diagnosed by histological biopsy analysis, although the results of T2-weighted magnetic resonance imaging (MRI) may be sufficient to enable other clinical entities to be excluded, thus avoiding inappropriate diagnosis and treatment (1). Although DMI was first reported in 1965 by Angervall and Stener (2) and seems to be a well-characterized complication of diabetes, only a few cases have been published.

The goal of this systematic review was to identify the clinical features, pathogenesis, diagnostic aspects, therapeutic management, and prognosis of DMI.

RESEARCH DESIGN AND METHODS

Questions asked

Our review was designed to answer various questions about DMI regarding clinical features, pathogenesis, diagnosis, microscopic and macroscopic appearance, prognosis, and therapeutic aspects.

Identification and retrieval of primary studies

We searched MEDLINE (OVID Technologies and PubMed), EMBASE (OVID Technologies) using the heading "diabetic muscle infarction" and all synonyms and related terms. Databases were searched from their inception to August 2001.

Study selection and data extraction

Data were systematically extracted from all retrieved reports. Proportions were used in descriptive analysis, and the denominator corresponded to the number of cases in which the investigated characteristic was described.

RESULTS

Search results

After searching the electronic databases, we identified 47 reference sources (1–47) that included 115 patients with 166 episodes of DMI. The most frequent report was one case by reference, but two large series were retrieved, including 21 and 14 patients, respectively. In most articles, the cases were exhaustively described, but in those two large series, a lot of summary data were reported.

Data synthesis

The baseline characteristics of the DMI are shown in Table 1. In summary, DMI was more frequent in diabetic women (61.53%) and the mean age at presentation was 42.63 years (range 19–81 years). A total of 68 patients (59.1%) had type 1 diabetes and 27 patients (23.8%) had type 2 diabetes; reference to type of diabetes was not made in the remaining 20 patients (17.1%). The mean duration of diabetes, from initial diagnosis to the first episode of DMI, was 14.35 years; values ranged from 0 (diabetes not diagnosed) to 50 years. Patients with DMI usually had multiple typical end-organ diabetic complications. Vascular complications of diabetes were reported in most patients, largely in the form of nephropathy (74 of 104 patients reported, 71.1%), retinopathy (56 of 99 patients reported, 56.6%), and neuropathy (54 of 99 patients reported, 54.5%). Other complications reported peripheral arteriopathy in seven patients (7 of 92 reported, 6%), hypertension in eight patients, gastroenteropathy in four patients, and antiphospholipid antibodies in two patients.

From the Internal Medicine Service, Hospital "Costa del Sol", Marbella (Málaga), Spain.

Address correspondence and reprint requests to A. J. Trujillo-Santos, MD, C/Esperanto, 3. 1° D, 29007 Málaga, Spain. E-mail: javiertrujillo@terra.es e- trujillo@hcs.es.

Received for publication 29 March 2002 and received in revised form 17 September 2002.

Abbreviations: CK, creatine kinase; DMI, diabetic muscle infarction; MRI, magnetic resonance imaging.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

Table 1—*Clinical features of patients with DMI*

Number of patients	Number of episodes	Episodes/ patient	Age (range) (years)	Sex (male/female)	Diabetes type	Duration of diabetes (range) (years)	Complications (*n*/reported)
115	166	1.44	42.63 (19–81)	61/54 (38.47%)/(61.53%)	Type 1: 68 (59.1%) Type 2: 27 (23.8%) Not indicated 20 (17.1%)	14.35 (0–50)	Nephropathy: 74/104 (71.1%) Retinopathy: 56/99 (56.6%) Neuropathy: 54/99 (54.5%)

Muscle involved	Weeks from onset (range)	Clinical features	CK level	Leucocytosis	ESR increased
Thigh: 139 (83.7%) Calf: 32 (19.28%) Both: 4 (2.41%) Bilateral: 14 (8.43%)	3.98 (1 day to 40 weeks)	Pain: 133 (80.12%) Swelling: 126 (75.9%) Mass: 56 (33.73%) Fever: 3 (10.71%)	High: 27/56 (48.2%) Normal: 29/56 (52.7%) Not reported: 110	7.01 (8%)	28 (52.8%)

Biopsies	Treatment	Weeks until resolution (range)	Recurrences
Fine-needle: 39 Open: 29 Total: 95 Type not reported: 27	Bed rest: 32 (19.28%) Analgesics: 48 (28.92%) Physical therapy: 23 (13.86%) Not indicated: 36 (21.69%)	4 (2–17)	Same muscle: 10 (8.69%) Another muscle: 45 (39.13%)

Clinical features

Typical clinical presentation of DMI included abrupt onset of pain in the affected muscle (133 of 166 episodes, 80% of cases), accompanied by local swelling (126 of 166 episodes, 75.9%), with subsequent partial resolution and appearance of a palpable painful mass (56 of 166 episodes, 33.7%). Fever was present in 3 of 28 episodes (10.71%) and was not present in 25 of 28 episodes (89.29%); body temperature was not indicated for the remaining 138 of 166 episodes (83.1%).

DMI most frequently affected the thigh (139 of 166 episodes, 83.7%), and the quadriceps was the most commonly affected muscle; calf involvement was reported in 32 cases (19.28%). Bilateral affection was reported in 14 cases (8.4%). The muscles more frequently affected were the vastus lateralis (40 cases of 166 episodes, 24%) and the vastus medialis (37 cases of 166 episodes, 22%). Only one case report of DMI in a muscle of the upper limb (forearm) was reported (34).

No specific marker was noted in laboratory findings. Increased plasma levels of muscle enzymes were infrequent: creatine kinase (CK) levels were elevated in 27 patients (48.2%), normal in 29 patients (52.7%), and not reported in 110 cases (66.2% of 166 episodes). Lack of correlation between muscle involvement and increased CK levels may have been a result of the delay in requesting medical advice after onset of symptoms (3,23), a reported delay of ~4 weeks (range 1 day to 40 weeks). On the other hand, leukocytosis was reported in 7 of 88 patients reported (8%; not reported in 78 episodes) and elevated erythrocyte sedimentation rate was reported in 28 of 53 patients (52.8%; not reported in 113 episodes).

Pathogenesis

The pathogenesis of DMI remains to be wholly clarified. The most likely hypothesis is that muscle infarction is caused by vascular disease such as arteriosclerosis and diabetic microangiopathy (6). Chester and Banker (25) suggest an atheroembolic phenomenon as the initial event, but in their review of six cases, no source of embolic material could be found. Instead, they observed severe distal peripheral vascular disease in the muscles of two patients, suggesting that the underlying process was arteriosclerosis obliterans. Moreover, they proposed that the initial ischemia could cause tissue swelling that, through a pressure effect, might compromise blood flow. However, some authors have shown an alteration in the coagulation-fibrinolysis system, in the form of hypercoagulability, with increased factor VII activity, impaired response of tissue plasminogen activator to venous occlusion, and increased plasma levels of both plasminogen activator inhibitor and thrombomodulin (15). The hypothesis about an alteration in the coagulation-fibrinolysis system as the cause of DMI is supported in a recent paper by Palmer and Greco (45), who described two patients with DMI and antiphospholipid syndrome. Although it is difficult to assess the relative contribution of microvascular complications of diabetes versus antiphospholipid antibodies to the DMI, the experiences of Palmer and Greco further support the assertion by Gargiulo et al. (48) that indicates the antiphospholipid antibodies as contributing factors in the progression of diabetes complications, acting as a link between the immunological and hemostatic systems in the pathogenesis of diabetic microangiopathy. Additional evidence between both systems is supported by Galtier-Dereure et al. (49), who found a high prevalence of antiphospholipid antibodies in type 1 and type 2 diabetic patients with end-organ complications but no difference between control and uncomplicated diabetic subjects. By contrast, only Umpiérrez et al. (3) found vasculitic phenomenon, characterized by fibrinoid necrosis, in patients with DMI.

Diagnosis

DMI may be diagnosed by means of a combination of clinical presentation and radiological imaging. The most valuable diagnostic technique is MRI; axial images are the best plane for diagnosis, although

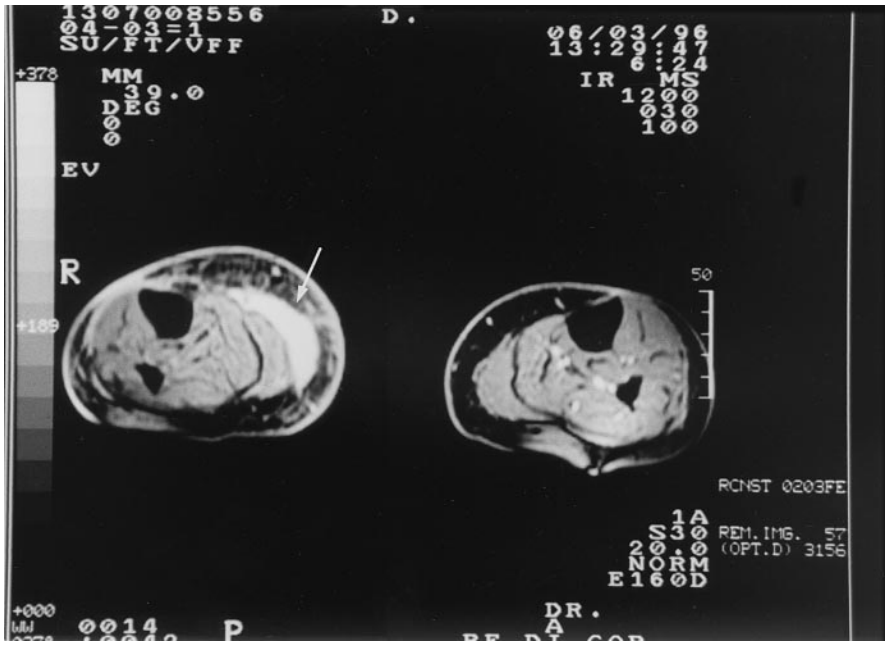

Figure 1—*T2-weighted MRI scan: increased density of the lesion in the right internal gastrocnemius, corresponding to focal muscle infarction (arrow) (47).*

coronal and sagittal images may be useful to document the extent of involvement (3). Moreover, this technique enables the exclusion of other conditions that frequently require differential diagnosis, such as deep venous thrombosis, pyomyositis, and primary or secondary muscle tumors. The characteristic feature of DMI in MRI is an increased signal from the affected muscle area (intramuscular and perimuscular tissues) in T2-weighted, inversion-recovery, and gadolinium-enhanced images and isointense or hypointense areas on T1-weighted images, secondary to increased water content from edema and inflammatory changes that accompany the infarction (4) (Fig. 1). Other features are a diffuse enlargement with ill-defined borders secondary to loss of the normal fatty intramuscular septa (more easily shown in T1-weighted images) and tiny foci of hyperintense signal consistent with foci of hemorrhage (4). After intravenously administered gadolinium, the areas of MR contrast enhancement have higher signal intensity than unaffected skeletal muscle, similar to those of the T2-weighted and inversion-recovery sequences, and small focal areas of rim enhancement that correspond to areas of high signal intensity on T2-weighted images (that represent infarction or necrosis within the areas of ischemic muscle) (4). However, in one case report, an atypical feature was found: a hyperintensity of the affected muscle on T1-weighted images, probably caused by hemorrhage within the infarcted muscle (43). Images obtained by MRI are not specific for DMI, because some inflammatory or autoimmune myopathies may prompt similar changes (3).

Other radiographic techniques may help to exclude other illnesses more than make the correct diagnosis of DMI. Standard radiographic films are rarely helpful, except to exclude bony abnormalities or soft-tissue calcifications (19). Sonographic findings in DMI include a well-marginated, hypoechoic, intramuscular lesion with the following additional features: internal linear echogenic structures coursing through the lesion, an absence of internal motion or swirling of fluid transducer pressure, and a lack of a predominantly anechoic area. These findings may help differentiate DMI from a necrotic mass or abscess, although a direct sonographic comparison of these entities has not been made (38). Computed tomography examination shows diffuse muscular enlargement with diminished attenuation of the affected muscle (24 Hounsfield units; 1,000 scale), increased attenuation of the subcutaneous fat, and thickening of subcutaneous fascial planes and of the skin (33). On gallium scintigraphy, areas of DMI show no increase in uptake, differentiating these areas from tumor or inflammation. Bone scintigraphy, however, shows increased blood flow and isotope accumulation at the site of muscle infarction but not in the skeleton (14,16).

Needle electromyography of the muscle affected of DMI shows fibrillation potentials and positive sharp waves and small motor unit potentials with early recruitment in some areas and reduced interference pattern. Some areas of the muscles, however, can be electrically silent, both at rest and after voluntary contraction, thus indicating replacement of muscle fibers by fibrous tissue (14,40).

In the systematic review, we found that the diagnosis of DMI was confirmed by biopsy in 95 cases (57.2%): 39 fine-needle biopsies, 29 open biopsies, and 27 biopsies of unreported type. Currently, because of the potential complications of excisional and incisional biopsy in DMI and the possibility of diagnosing the condition using MRI, and with a good prognosis, physicians tend to eschew all invasive diagnostic methods. Biopsy should be reserved for cases in which the clinical presentation is atypical or the diagnosis uncertain or when appropriate treatment fails to elicit improvement (25).

Grossly, DMI presents as a nonhemorrhagic, pale, whitish muscle. Light microscopy shows large areas of muscle necrosis and edema, phagocytosis of necrotic muscle fibers, and appearance of granular tissue and collagen (Figs. 2 and 3). Findings at later stages include replacement of necrotic muscle fibers by fibrous tissue, myofiber regeneration, and mononuclear cell infiltration (37). There is only one report of vasculitis and small-vessel angiopathy in patients with DMI (3), the latter indeed being one factor that differentiates DMI from the small-vessel vasculitis typically found in elderly patients with type 2 diabetes.

Differential diagnosis of DMI was most frequently required with regard to deep venous thrombosis and pyomyositis, although soft-tissue abscess, necrotizing fasciitis, dermatomyositis, proliferative myositis, focal myositis, nodular myositis, primary lymphoma of muscle, benign tumors or sarcomas of the muscle, diabetic amyotrophy, osteomyelitis, exertional muscle rupture, and ruptured Baker's cyst. The clinical course, the MRI images, and obviously, the histologic specimen can confirm the correct diagnosis (4,22,25).

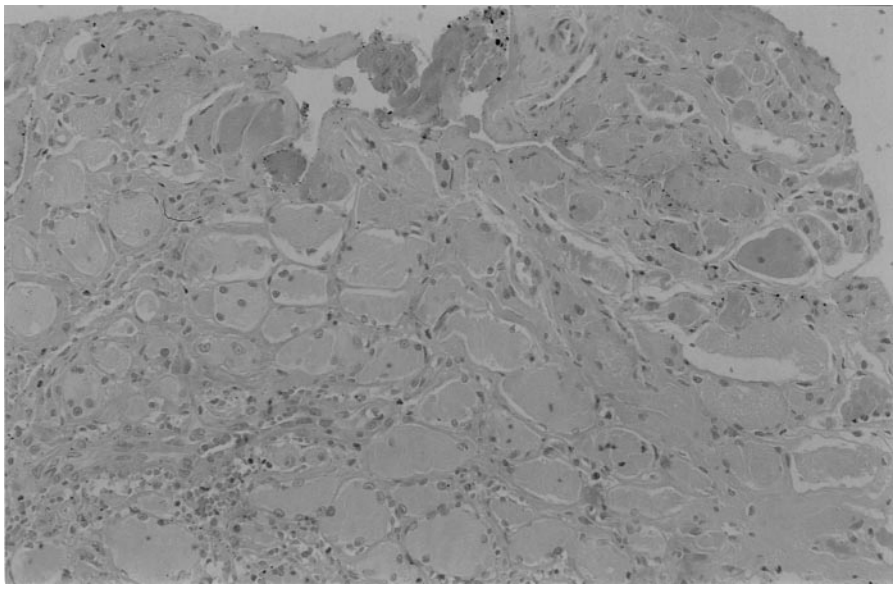

Figure 2—*Necrotic muscle fibers and extravasation of blood (hematoxylin-eosin stain, ×40) (47).*

Management and prognosis

In the review, DMI was managed with bed rest (32 cases of 166 episodes, 19.28%) and analgesics (48 cases of 166 episodes, 28.9%), although resolution of the illness has been complication-free in most cases and treatment was generally symptomatic. Careful metabolic control of diabetes is usually recommended, although perhaps, because the rare nature of the condition hinders the drawing of valid conclusions, this control has not been shown to influence results in a current episode. It may be of value in limiting a possible recurrence of the illness. Other therapeutic measures include nonsteroidal anti-inflammatory drugs, glucocorticoids, aspirin, and pentoxyphylline; some of these are useful in diabetic vasculitis and potentially valid in DMI. Bjornskov et al. (15) administered anticoagulant agents to two patients with hypercoagulability; no recurrence or complications were observed in these patients. Similarly, Palmer and Greco (45) treated one of their two patients with antiphospholipid antibodies with corticosteroid and anticoagulant agents (which were contraindicated in the second patient because of concerns of retinal hemorrhages), but recurrences of the DMI occurred. Other authors have not reported blood-flow alterations and, thus, have not recommended anticoagulant treatment. Some authors recommend avoidance of physical therapy (reported in 23 cases, 13.86%) because recovery is prolonged (25), but other authors have not observed this in their patients (23).

The short-term prognosis of DMI is good, although recurrence has been reported in a total of 55 cases (47.82%): 10 cases (8.69%) involving the originally affected muscle and 45 cases (39.13%) involving another muscle. Generally speaking, patient prognosis is poor, given that patients usually have end-organ microvascular complications when DMI is diagnosed.

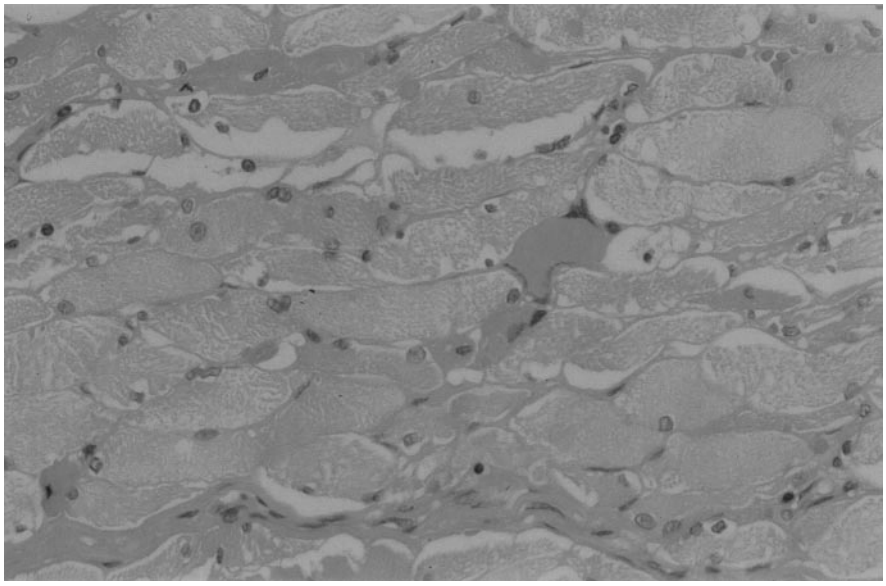

Figure 3—*Muscle fibers showing signs of regeneration (nucleolus present) (hematoxylin-eosin stain, ×400) (47).*

CONCLUSIONS — DMI is a very rare complication of diabetes, with atherothrombotic or coagulopathic cause, presenting clinically with pain, swelling, and occasionally, a palpable mass, with normal or elevated plasma CK levels. Increased signal intensity in T2-weighted MRI images is common, and the condition usually resolves spontaneously or after immobilization and administration of analgesics. Muscle biopsy is only indicated in cases of atypical presentation or progression of the condition.

References

1. Kiers L: Diabetic muscle infarction: magnetic resonance imaging (MRI) avoids the need for biopsy. *Muscle Nerve* 18:129–130, 1995
2. Angervall L, Stener B: Tumoriform focal muscular degeneration in two diabetic patients. *Diabetologia* 1:39–42, 1965
3. Umpiérrez GE, Stiles RG, Kleinbart J, Krendel DA, Watts NB: Diabetic muscle infarction. *Am J Med* 101:245–250, 1996
4. Jelinek JS, Murphey MD, Aboulafia AJ, Dussault RG, Kaplan PA, Snearly WN: Muscle infarction in patients with diabetes mellitus: MR imaging findings. *Radiology* 211:241–247, 1999
5. 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)* 81:323–326, 1999
6. Scully RE, Mark EJ, McNelly WF, Ebeling

SH, Phillips LD: Case 29–1997: case records of the Massachusetts General Hospital. *N Engl J Med* 337:839–845, 1997
7. Chason DP, Fleckenstein JL, Burns DK, Rojas G: Diabetic muscle infarction: radiologic evaluation. *Skeletal Radiol* 25: 127–132, 1996
8. Van Slyke MA, Ostrov BE: MRI evaluation of diabetic muscle infarction. *Magn Reson Imaging* 13:325–329, 1995
9. Grau A, Ricart W, Solá P: Infarto muscular espontáneo en la diabetes mellitus (Letter). *Med Clin* 91:37, 1988
10. Khoury NJ, El-Khoury GY, Kathol MH: MRI diagnosis of diabetic muscle infarction: report of two cases. *Skeletal Radiol* 26:122–127, 1997
11. 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* 7:221–223, 1993
12. Ratliff JL, Matthews J, Blalock JC, Kasin JV: Infarction of the quadriceps muscle: a complication of diabetic vasculopathy. *South Med J* 79:1595, 1986
13. Boluda B, Mesa J, Obiols G, Simó R: Focal muscle infarction in a diabetic. *Diabete Metab* 15:269–270, 1989
14. Barohn RJ, Bazan C III, Timmons JH, Tegeler C: Bilateral diabetic high muscle infarction. *J Neuroimaging* 4:43–44, 1994
15. Bjornskov EK, Carry MR, Katz FH, Leflowitz J, Ringel SP: Diabetic muscle infarction: a new perspective on pathogenesis an management. *Neuromusc Disord* 5:39–45, 1995
16. Weissman A: Image interpretation session: 1996 diabetic muscle infarction (DMI). *Radiographics* 17:246–248, 1997
17. Keller DR, Erpelding M, Grist T: Diabetic muscular infarction: preventing morbidity by avoiding excisional biopsy. *Arch Intern Med* 157:1611–1612, 1997
18. Hinton A, Heinrich SD, Craver R: Idiopathic diabetic muscular infarction: the role of ultrasound, CT, MRI, and biopsy. *Orthopedics* 16:623–625, 1993
19. Reich S, Wiener SN, Chester S, Ruff R: Clinical and radiologic features of spontaneous muscle infarction in the diabetic. *Clin Nucl Med* 10:876–879, 1985
20. Lauro GR, Kissel JT, Simon SR: Idiopathic muscular infarction in a diabetic patient: report of a case. *J Bone Joint Surg Am* 73: 301–304, 1991
21. Van de Berg B, Malghem J, Puttemans T, Vandeleene B, Lagneau G, Maldague B: Idiopathic muscular infarction in a diabetic patient. *Skeletal Radiol* 25:183–185, 1996
22. Rocca PV, Alloway JA, Nashel DJ: Diabetic muscular infarction. *Semin Arthritis Rheum* 22:280–287, 1993
23. Barohn RJ, Kissel JT: Case of the month: painful thigh mass in a young woman: diabetic muscle infarction. *Muscle Nerve* 15: 850–855, 1992
24. Núñez-Hoyo M, Gardner CL, Motta AO, Wyatt-Ashmead J: Skeletal muscle infarction in diabetes: MR findings. *J Comput Assist Tomogr* 17:986–988, 1993
25. Chester CS, Banker BQ: Focal infarction of muscle in diabetics. *Diabetes Care* 9: 623–630, 1986
26. Bodner RA, Younger DS, Rosoklija G: Diabetic muscle infarction. *Muscle Nerve* 17: 949–950, 1994
27. Banker BQ, Chester CS: Infarction of thigh muscle in the diabetic patient. *Neurology* 23:667–677, 1973
28. García-Rubiales MA, Gallar P, Ortega O, Rodríguez I: Infarto muscular diabético: una rara complicación en diabetes mellitus de larga evolución. *Nefrología* XVIII: 173–174, 1998
29. 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* 13:2377–2379, 1998
30. Penglis PS, Scott G, Cleland LG: Diabetic muscle infarction presenting as a knee effusion. *Semin Arthritis Rheum* 6:421–422, 1999
31. Heureux F, Nisolle JF, Delgrange E, Donckier J: Diabetic muscle infarction: a difficult diagnosis suggested by magnetic resonance imaging. *Diabet Med* 15:621–622, 1998
32. Taira M, Komiya I, Taira T, Arakawa T, Hokama S, Nagasawa Y, Takasu N: A case of diabetic muscle infarction in Japan. *Diabet Med* 15:1065–1067, 1998
33. Levinsohn EM, Bryan PJ: Computed tomography in unilateral extremity swelling of unusual cause. *J Comp Assist Tomogr* 3:67–70, 1979
34. Eady JL, Cobbs KF: Diabetic muscle infarction. *J South Orthop Assoc* 6:250–255, 1997
35. Sagar M, Bowerfind WM, Wigley FM: A man with diabetes and a swollen leg. *Lancet* 353:116, 1999
36. Willenberg HS, Hauner H, Scherbaum WA: A man with diabetes and a swollen leg. *Lancet* 353:1527–1528, 1999
37. Grigoriadis E, Fam AG, Starok M, Ang LC: Skeletal muscle infarction in diabetes mellitus. *J Rheumatol* 27:1063–1068, 2000
38. Delaney-Sathy L, Fessell DP, Jacobson JA, Hayes CW: Sonography of diabetic muscle infarction with MR imaging, CT, and pathologic correlation. *AJR* 174:165–169, 2000
39. Morcuende JA, Dobbs MB, Crawford H, Buckwalter JA: Diabetic muscle infarction. *Iowa Orthop J* 20:65–84, 2000
40. Anglada M, Vidaller A, Bolao F, Ferrer I, Olivé M: Diabetic muscle infarction. *Muscle Nerve* 23:825–826, 2000
41. Spengos K, Wöhrle JC, Binder J, Schwartz A, Hennerici M: Bilateral diabetic infarction of the anterior tibial muscle. *Diabetes Care* 23:699–701, 2000
42. Madhan KK, Symmans P, Strake LT, van der Merwe W: Diabetic muscle infarction in patients on dialysis. *Am J Kid Dis* 35: 1212–1216, 1999
43. Sharma P, Mangwana S, Kapoor RK: Diabetic muscle infarction: atypical MR appearance. *Skeletal Radiol* 29:477–480, 2000
44. Silberstein I, Britton KE, Marsh FP, Raftery MJ, D'Cruz D: An unexpected cause of muscle pain in diabetes. *Ann Rheum Dis* 60:310–312, 2001
45. Palmer GW, Greco TP: Diabetic thigh muscle infarction in association with antiphospholipid antibodies. *Semin Arthritis Rheum* 30:272–280, 2001
46. Allali F, El Idrissi Lamghari A, El Hamani Z, El Hassani MR, Benaissa K, Hajjaj-Hassouni N: Calf muscular infarction in a diabetic patient (Letter). *Clin Exp Rheumatol* 18:540, 2000
47. Trujillo-Santos AJ, Alcalá-Pedrajas JN, Moreno-García MM, García de Lucas MD, García-Sánchez JE: Mujer de 70 años con dolor e inflamación en pantorrilla derecha. *Rev Clin Esp* 201:153–154, 2001
48. Gargiulo P, Schiaffini R, Bosco D, Ciampalini P, Pantaleo A, Romani B, Arcieri P, Andreani D: Diabetic microangiopathy: lupus anticoagulant dependent thrombotic tendency in type 1 (insulin-dependent) diabetes mellitus. *Diabet Med* 14: 132–137, 1997
49. Galtier-Dereure F, Biron C, Vies M, Bourgeois V, Schved JF, Bringer J: Vascular complications of diabetes mellitus: what role for phospholipid-binding antibodies? *Lupus* 7:469–470, 1998