MARSHALL JOURNAL OF MEDICINE
Expanding Knowledge to Improve Rural Health.

Volume 5 | Issue 4 Article 6

2019

Diabetic Muscle Infarction: A Rare End-Organ Vascular Complication of Diabetes

Callie Seaman, Michael Amos, Adam M. Franks, Asher Sexton, Kimberly McClelland, and Erika M. Harris

Author Affiliations

Callie Seaman (*Marshall University Joan C. Edwards School of Medicine, Huntington, West Virginia*)

Michael Amos (*Marshall University Joan C. Edwards School of Medicine, Huntington, West Virginia*)

Adam M. Franks (*Marshall University Joan C. Edwards School of Medicine, Huntington, West Virginia*)

Asher Sexton (*Marshall University Joan C. Edwards School of Medicine, Huntington, West Virginia*)

Kimberly McClelland (*Marshall University Joan C. Edwards School of Medicine, Huntington, West Virginia*)

Erika M. Harris (*Marshall University Joan C. Edwards School of Medicine, Huntington, West Virginia*)

Corresponding Author

Adam Franks MD

Marshall University Joan C. Edwards School of Medicine

Huntington, West Virginia

Email: franks1@marshall.edu

Recommended Citation

Seaman, Callie; Amos, Michael; Franks, Adam M.; Sexton, Asher; McClelland, Kimberly; and Harris, Erika M. (2019) "Diabetic Muscle Infarction: A Rare End-Organ Vascular Complication of Diabetes," *Marshall Journal of Medicine*: Vol. 5: Iss. 4, Article 6.

DOI: 10.33470/2379-9536.1232

Available at: https://mds.marshall.edu/mjm/vol5/iss4/6

DOI: 10.33470/2379-9536.1232

Diabetic muscle infarction: a rare end-organ vascular complication of diabetes

Abstract

Diabetic muscle infarction (DMI) is a rare microvascular complication of spontaneous ischemic necrosis of skeletal muscle in patients with poorly controlled diabetes. We herein describe the case of a 26-year-old woman with a history of type I diabetes and accompanying diabetic microvascular complications of neuropathy, nephropathy and retinopathy, who presented with sudden onset of swelling and sharp pain in her bilateral thighs. T2-weighted MRI imaging revealed subcutaneous edema and sub-fascial, hyper-intense enhancement of proximal thigh musculature. DMI has a relatively non-specific clinical presentation; therefore, physician awareness is key for early diagnosis, as aggressive management has been associated with poor patient outcomes. With poor long-term prognosis and high reoccurrence, DMI acts as an indicator of vascular end-organ damage.

Keywords

Diabetic Muscle Infarction, Diabetic Myonecrosis

Introduction

Diabetic muscle infarction (DMI) is a rare microvascular complication consisting of spontaneous ischemic necrosis of skeletal muscle in patients with poorly controlled diabetes. Though its characteristics have been defined, fewer than 200 cases[1,2] have been reported since it was first described in 1965 by Angervall and Stener.[3] Originally, it was termed “tumoriform focal muscular degeneration,” owing to the initial cases’ resemblance to tumors, which in that case were completely excised.[1,3-7] The condition has also known as diabetic, aseptic, or ischemic myonecrosis.

DMI can occur in patients with either type 1 or 2 diabetes, with type 1 representing around 70% of cases.[7-10] Affected patients have a history of long-standing (>15 years) and poorly controlled diabetes (average Hgb a1c of 9.4% with a range of 5.0% to 12.4%),[2,4,5,9-16] with a mean age of 43 years old at diagnosis[1,5-7,9,13,16,17] and mean duration between diagnosis of diabetes and DMI around 14.4 years.[5,7,10,13,17] There seems to be a slight predilection towards females.[1,5,7,11,13] Nearly 97%[9,13] of patients present with end-organ diabetic microvascular complications[7,11,14] including nephropathy (57%), retinopathy (71%) and neuropathy (55%).[4-7,16,17]

Due to the rarity of the disease and many alternative etiologies for the symptoms, DMI is often under-recognized, leading to delayed diagnosis, inappropriate treatment, and excessive lab and radiographic testing.[5,6,8,10] In this case, a 26-year-old woman with type 1 diabetes mellitus presents with DMI and affords a discussion of clinical features, diagnosis and pathogenesis of DMI.

Case Presentation

At 26 years of age, a non-smoking type 1 diabetic patient with neuropathy, nephropathy, and retinopathy presented to her primary care physician from a local emergency room with a seven-day history of sudden swelling followed by a sharp pain in her bilateral thighs that initially occurred during a hike in the woods. The pain was constant and limited her range of motion, making ambulation difficult. No erythema, focal warmth or masses were appreciable. Her vital signs were stable, and she was afebrile. Her white blood cell count was 9.9 k/mm^3 (range: 5-10 k/mm^3) with 82.4% neutrophils. The chemistry profile demonstrated a creatinine of 3.6 mg/dL and glucose of 157 mg/dL. Hgb a1c was 10.4% (normal: < 7%). Erythrocyte sedimentation rate (ESR) was elevated at 140 mm/hr (normal: 0-20 mm/hr), as were creatine phosphokinase (CPK) and serum myoglobin at 259 U/L (normal: 30-135 U/L) and 413 ng/dL (normal: 0-110 ng/dL) respectively. D-dimer was positive at 5.1 mg/L (normal: 0.200-2.18 mg/L), but her subsequent venous ultrasound ruled out lower extremity deep venous thrombosis (DVT). A presumptive diagnosis of cellulitis was initially given, and she was treated with ciprofloxacin.

One week later, as the pain and edema increased, she was no longer ambulatory despite improving ESR (109 mm/hr), CPK (151 U/L) and myoglobin (280 ng/dL). T2-weighted MRI images showed diffuse subcutaneous edema as well as sub-fascial and hyperintense enhancement of the adductor brevis, magnus, and longus. Some involvement of the upper gracilis was also noted, and the patient was placed on bed rest. Two weeks later, she was hospitalized for acute renal failure, but her painful, edematous thighs persisted. Upon admission her ESR was 40 mm/hr, CPK was 74 U/L, and myoglobin was 214 ng/dL. Swelling and pain persisted throughout that and a second admission for acute renal failure. Because of the probable diagnosis of DMI, a muscle biopsy was not performed. With the treatment of only bed rest, pain control with non-steroidal anti-inflammatory medications (NSAIDs) and narcotics, symptoms resolved spontaneously within six weeks. Table 1 demonstrates the patient's demographic and clinical parameters compared to the accumulated ranges reported in the literature.

Diabetic Myonecrosis Trends & Comparison to Case Patient

Demographics	Range	Case Patient
Gender	54%-66% Female	Female
Age	40-49 yo	26 yo
Diabetes, type 1	41.5%-75%	Yes
Hgb a1c	5.0-12.4%	10.4
Years since Diabetes Diagnosed	14.4-17 years	17 years
Diabetes Complications	97%	Yes
Nephropathy	57%-71%	Yes
Retinopathy	57%-71%	Yes
Neuropathy	55%-75%	Yes
Symptoms		
Acute	Universal	Yes
Local Swelling	75.6%-99%	Yes
Tenderness	80%-100%	Yes
Palpable Mass	33.7%-44%	No
Lack of Fever	89%	Yes
Limited ROM	Worse with movement	Yes
Erythema	Not Common	No
Edema	Common	Yes
Unilateral	60%-91.6%	Bilateral
Proximal	66.7%-87%	Yes
Muscle Groups		
Quadriceps	60%-87%	No
Hip Adductors	13%	Yes
Hamstrings	8%	No
Hip Flexors	2%	No
Calf	13%-22.9%	No
Multiple	39%	Multiple

Diagnosis		
Erythrocyte Sedimentation Rate	increased 31.4%-88.9%	140
Creatinine Phosphokinase	increased 81.8%-90%	259
Myoglobin	increased 81.8%-90%	413
White Blood Cells	increase 8%-56.6%	9.94
Blood Culture	Negative	Negative
Ultrasound	Useful to rule out DVT	ruled out DVT
T2-Weighted MRI	Hyperintense = necrosis, edema & subfascial fluid	Hyperintense
Muscle Biopsy	Monocytic infiltration, necrosis, and fibrosis	Not Done
Prognosis		
Resolution	6 to 8 weeks	9 weeks
Recurrence	40-50%	Did not recur
Mortality	10% Mortality Rate within 2 years	Died 7.5 months later

Table 1: Denotes the consensus of demographics, signs and symptoms and diagnostic results of reported patients with diabetic muscle infarction and compares them to the case-patient.

The patient's chronic renal failure worsened, and within a month she was placed on peritoneal dialysis before having a simultaneous kidney-pancreas transplant four months later. Her postoperative course was complicated by an abdominal hematoma that needed to be evacuated. She also suffered a CVA with right-sided hemiparesis that led to seizures. Two and a half months from her transplant she succumbed to vancomycin-resistant enterococci (VRE) sepsis secondary to pneumonia and pyelonephritis.

Discussion

The findings suggestive of DMI in this patient begin with her spontaneous acute muscular pain, markedly in her thighs, with no history of trauma or indication of infection.[1,2,5,7,9-11,15,18] The severe pain, even at rest, was exacerbated by movement, which limited her mobility.[8,11,12,14,17,19,20] DMI usually presents unilaterally [4,10,18] in the proximal lower extremity (81-83%) with rare reports of distal leg involvement.[2,5,8,11,14,19,20] Muscles commonly affected include quadriceps (60%),[4,10,16,18] hip adductors (13%),[4,10,11,14,16] hamstrings (8%)[4,10,16,18] and hip flexors (2%).[4,10,16] Patients are typically afebrile, without skin discoloration,[9,11,20] and usually present with accompanying local swelling (90%- 99%),[1,2,4,5,7-13,16-20] tenderness,[1,2,4-10,12,13,15-19] and painful, palpable mass (44%).[2,6,7,9,11-14,17-20]

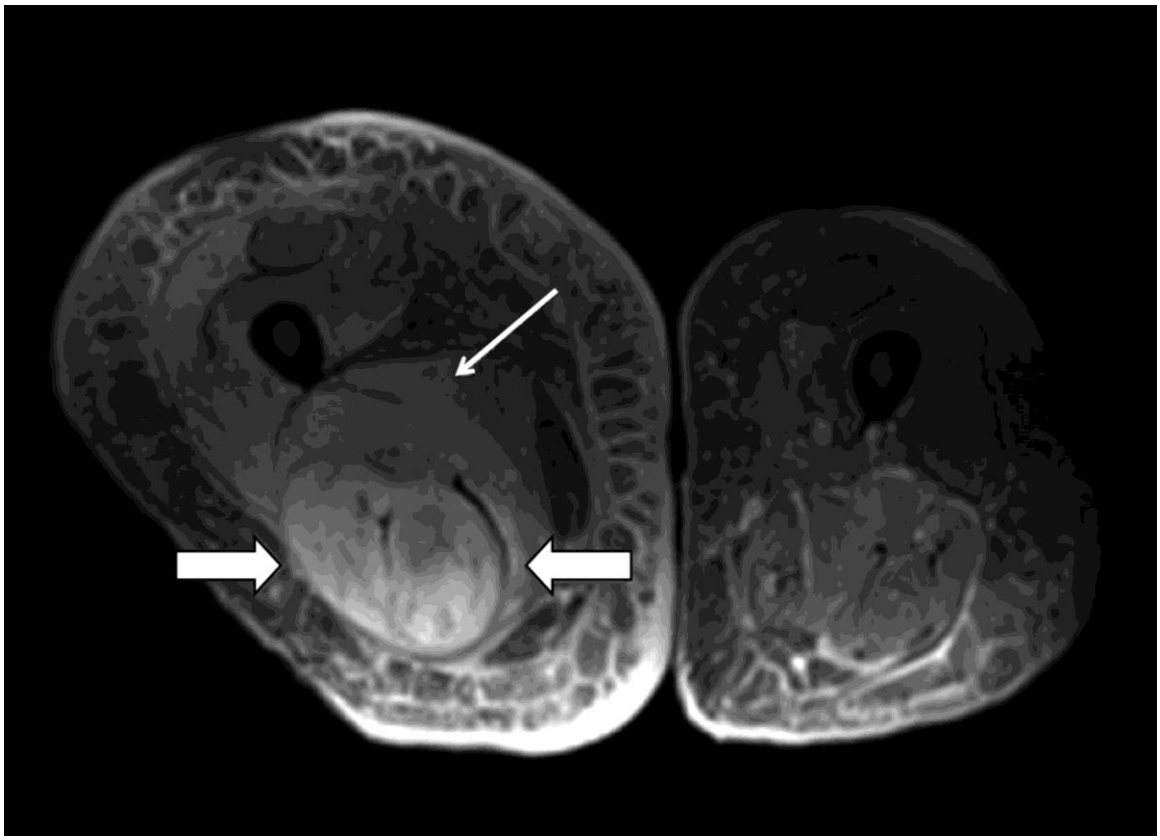
DMI is frequently misdiagnosed because of the significant overlap of its clinical features with other life- and limb-threatening etiologies, and there remains no clear consensus of diagnostic criteria.[1,6,15] Differential diagnoses considerations are extensive (Table 2). Currently, diagnosis of DMI consists of a clinical assessment and MRI.[5-7,19] Muscle biopsies, revealing some combination of monocytic inflammation, hemorrhagic necrosis, fibrosis, atrophy, and neovascularization, are the gold standard, carrying 90% sensitivity and 95% sensitivity[19], and are not recommended because of procedural complications, including delayed healing and infection.[1,2,4-7,10,15,16,19] If attempted, a minimally invasive approach is recommended, which should be reserved for patients with an atypical presentation, uncertain diagnosis, or those that do not improve with treatment.[2,7,15,19]

Diabetic Muscle Infarction Differential Diagnoses

Infectious	Inflammatory	Malignancy	Musculoskeletal	Vascular
Abscess	Dermatomyositis	Benign Tumors	Acute Arthropathy	Compartment Syndrome
Cellulitis	Polymyositis	Lymphoma	Baker's Cyst Rupture	DVT
Necrotizing Fasciitis	Pyomyositis	Metastatic Tumors	Diabetic Amyotrophy	Hematoma
Osteomyelitis	Other: ▪ Focal ▪ Nodular ▪ Proliferative	Sarcoma	Muscle Rupture	Thrombophlebitis
Parasitic Infection			Statin-Induced	Vasculitis
			Trauma	

Table 2: Categorization of the diagnoses in the differential for diabetic muscle infarction. (DVT = deep venous thrombosis. Diabetic amyotrophy is also known as diabetic lumbosacral radiculoplexus neuropathy, proximal diabetic neuropathy, and diabetic polyradiculoneuropathy)

MRI with T2-weighted imaging is the most valuable diagnostic imaging method, carrying a sensitivity close to 100%,[1,2,6,8-11,13,15,17,19] with hyperintense images of subfascial fluid from edema and hemorrhage with enlargement of defined muscles (Picture 1).[2,4,5,7,10,11,13,14,20] This contrasts with T1-weighted images, which would show water content from edema and water content as hypointense.[2,7,10,13,15,20] Other radiographic techniques, such as ultrasound and CT, are not considered satisfactory to confirm the diagnosis but are useful for excluding other disorders.[7,9] In contrast to imaging, there is a lack of consistency in lab findings.[5-7,10] White blood cell counts, CPK levels, and inflammatory markers may be normal to elevated.[2,6,7,9,14,15,18] It is suggested CPK is elevated during the early presentation and falls to normal levels later in the disease course.[17] Patients' delay in seeking medical attention, approximately four weeks on average, may prevent the detection of these changes and likely account for the variation of finding in the literature.[5,7] Table 3 demonstrates the laboratory and physical exam variations in the case-patient. This trend seems to correlate with the variability of a necrosis-reperfusion process and has not yet been explored in the literature.



Picture 1: Proton density fat-saturated MRI showing increased signal within the semimembranosus, biceps femoris, and adductor magnus musculature that is found to be consistent with edema due to early muscle infarction.[1]

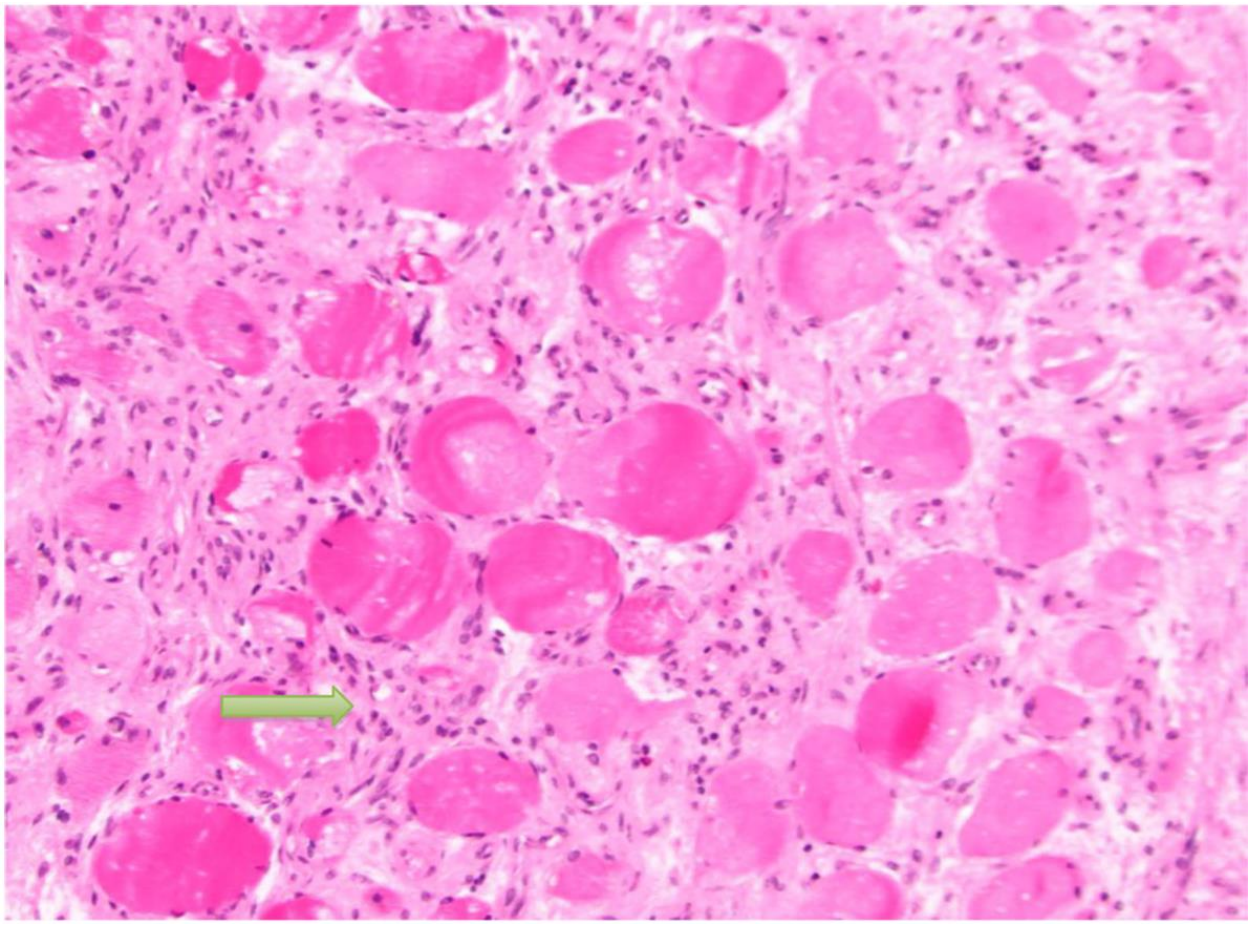
DOI: 10.33470/2379-9536.1232

Case Patient Lab Trends and Physical Exam Findings

			Onset	*Day 8*	*Day 13*	*Day 18*	*Day 68*	
Lab Test	**Normal**	**DMI Trend**	**ED**	**1st Visit**	**Follow-up**	**Hospital**	**Recovery**	**Trend**
WBC	5- 10 k/mm^3	increased 8%-56.6%	9.94	12.3		9.2	7.46	Variable
ESR	0-20 mm/hr	increased 31.4%-88.9%	140	109		40		Descending
CPK	30-135 U/L	increased 81.8%-90%	259	151	215	74	133	Variable
Myoglobin	0 - 110 ng/dL	increased 81.8%-90%	413	280	251	214	206	Descending
Physical Exam Findings			**ED**	**1st Visit**	**Follow-up**	**Hospital**	**Recovery**	
Leg Swelling			Yes	Increased	Stable	Continued	Improved	
Leg Pain			Yes	Increased	Stable	Continued	Improved	
Weakness			Yes	Increased	Stable	Continued	Improved	

Table 3: Comparison of the trend in lab work for the case patient over time in relation to symptoms. (WBC = white blood count, ESR = erythrocyte sedimentation rate, CPK = creatinine phosphokinase)

The literature predominately laments that the pathophysiology of DMI is not well understood, and more research is needed.[1,2,5,8-10,12] Patient history, clinical presentation, histological features, and radiographic imaging seem to point to a unifying theory of a microangiopathic vascular complication.[1,5,7,9-12,15,16,18,19] A cascade initiated by microvascular endothelial damage leads to tissue ischemia activating inflammatory cascade causing local tissue damage. This damage is followed by the focal replacement of the infarcted muscle with collagen (Picture 2). Reperfusion occurs, resulting in impaired endothelial-dependent dilation of arterioles, increased oxygen radicals, and decreased nitric oxide leading to further injury.[1,5,11] Increased edema creates intra-compartmental pressure, decreasing blood flow further creating ischemia from compartment syndrome.[1,5,7,17] Muscle regeneration occurs as well and may be seen histologically at time of care.[11]



Picture 2: Histologic Slide of a Diabetic Muscle Infarction biopsy under H&E stain. Macrocytic invasion is seen along with the collagenous replacement of infarcted tissue.[4]

Early recognition of DMI is important to avoid inappropriate treatment.[2,5,10,11,17] Current recommendations are based on limited evidence[1,19] and consist mainly of supportive care,[4,5,8-10,13-16,18,20] including bed rest combined with aspirin and NSAIDS.[1,2,4,6-11,13-18,20] Perhaps the most important intervention, however, is rigorous glycemic control. Hyperglycemia may contribute to DMI by affecting the remodeling of vasculature, platelet function, and coagulation factors.[6] Surgical intervention is not recommended and has shown poor outcomes with increased recovery time, risk of infection, hematoma, nerve palsy, sepsis, and compartment syndrome.[1,4,8,10,15,17,20] Physical therapy should be avoided in the acute phase as muscle stretching can increase pain and swelling, ultimately prolonging recovery, but may have a place in care following the acute injury.[1,5-8,14,17]

One should view the prognosis rates as similar to a patient with a myocardial infarction.[2] Short-term prognosis of the patients is good, and a majority make a full recovery with spontaneous resolution of symptoms within weeks to months.[2,5,9,10,17] However, patients are at high risk of reoccurrence (~50%),[1,12] within the original muscle (8.7%)[7,9] or a different muscle group (40%).[8,10,16] Unfortunately, the long-term prognosis is poor, as most patients die within 2-5 years

of diagnosis.[2,6,7,9,10] The presence of DMI acts as an indicator suggestive of end-organ vasculopathy, and patients should undergo evaluation for other vascular damage.[9]

Conclusion

The overall literature on DMI is small and the publications have a significant overlap in findings. While the prevailing principles for presentation, diagnosis, and management are in general agreement, the small individual cohorts lend themselves to wide variability in specific percentages. Making sense of proper diagnostic and management principles is important, as more aggressive options have deleterious effects. Clearly, overall, DMI is a harbinger of vascular end-organ damage and should be treated as such.

References

1. Horton WB, Taylor JS, Ragland TJ, Subauste AR. Diabetic muscle infarction: a systematic review. BMJ Open Diabetes Research & Care. 2015;3(1).
2. Chebbi W, Jerbi S, Klii R, et al. Multifocal diabetic muscle infarction: a rare complication of poorly controlled diabetes mellitus. Internal Medicine. 2014;53(18):2091-2094.
3. Angervall L, Stener B. Tumoriform focal muscular degeneration in two diabetic patients. Diabetologia. 1965;1(1):39-42.
4. Bhasin R, Ghobrial I. Diabetic myonecrosis: a diagnostic challenge in patients with long-standing diabetes. Journal of Community Hospital Internal Medicine Perspectives. 2013;3(1):20494.
5. Yong TY, Khow KSF. Diabetic muscle infarction in end-stage renal disease: A scoping review on epidemiology, diagnosis and treatment. World Journal of Nephrology. 2018;7(2):58-64.
6. Cumberledge J, Kumar B, Rudy D. Risking life and limb: a case of spontaneous diabetic muscle infarction (diabetic myonecrosis). Journal of General Internal Medicine. 2015;31(6):696-698.
7. Trujillo-Santos AJ. Diabetic muscle infarction: an underdiagnosed complication of long-standing diabetes. Diabetes Care. 2003;26(1):211-215.
8. Parmar MS. Diabetic muscle infarction. BMJ. 2009;338:b2271.
9. Mathew A, Reddy S, Archibald C. Diabetic muscle infarction. Case Reports. 2009.
10. Khanna HK, Stevens AC. Diabetic Myonecrosis: A rare complication of diabetes mellitus mimicking deep vein thrombosis. American Journal of Case Reports. 2017;18:38-41.
11. Umpierrez GE, Stiles RG, Kleinbart J, Krendel DA, Watts NB. Diabetic muscle infarction. The American Journal of Medicine. 1996;101(3):245-250.
12. Delaney-Sathy LO, Fessell DP, Jacobson JA, Hayes CW. Sonography of diabetic muscle infarction with MR Imaging, CT, and pathologic correlation. American Journal of Roentgenology. 2000;174(1):165-169.
13. Saikia U, Saikia M, Bhuyan D, Choudhury B, Sarma D, Choudhury S. Diabetic myonecrosis: an underreported complication of diabetes mellitus. Indian Journal of Endocrinology and Metabolism. 2011;15(5):58.
14. Bunch MTJ, Birskovich MLM, Eiken MPW. Diabetic myonecrosis in a previously healthy woman and review of a 25-Year Mayo Clinic experience. Endocrine Practice. 2002;8(5):343-346.
15. Janga KC, Sinha A, Wengrofsky P, et al. Diabetic muscle infarction masquerading as necrotizing fasciitis. Case Reports in Nephrology. 2017;2017:1-3.
16. Mukherjee S, Aggarwal A, Rastogi A, et al. Spontaneous diabetic myonecrosis: report of four cases from a tertiary care institute. Endocrinology, Diabetes & Metabolism Case Reports. 2015;2015.
17. Vlieger GD, Bammens B, Claus F, Vos R, Claes K. Diabetic muscle infarction: a rare cause of acute limb pain in dialysis patients. Case Reports in Nephrology. 2013;2013:1-6.
18. MacGregor JL, Chan PC, Schneiderman, Grossman ME. Diabetic muscle infarction. Archives of Dermatology. 2007;143(11):1456-7.
19. Shenavandeh S, Anushiravani A, Nazarinia M. Diabetic muscle infarction and diabetic dermopathy two manifestations of uncontrolled prolong diabetes mellitus presenting with severe leg pain and leg skin lesions. Journal of Diabetes & Metabolic Disorders. 2014;13(1):38.
20. Uçan H, Alemdaroğlu E, Yoldaş TK, Özdamar SE, Akyüz M, Hatipoğlu C. Diabetic muscular infarct: an unusual cause of extremity pain and dysfunction. Rheumatology International. 2011;32(2):525-528.