A 51-year-old Somali man was admitted to an inpatient cardiology service at Saint Marys Hospital, a Mayo Clinic–affiliated hospital in Rochester, MN, with symptoms of fever and progressively worsening shortness of breath. Chest radiography demonstrated substantial pulmonary edema secondary to volume overload in the setting of acute worsening of chronic renal failure. Initial laboratory investigation yielded the following notable results (reference ranges provided parenthetically): leukocyte count, 30.3 × 10^9/L (3.5-10.5 × 10^9/L); blood urea nitrogen, 142 mg/dL (8-24 mg/dL); and creatinine, 12.6 mg/dL (0.9-1.4 mg/dL). Blood cultures were positive for Streptococcus pneumoniae in 4 of 6 specimens at 12.4 hours, and a nasal swab polymerase chain reaction was positive for H1N1 influenza. He underwent urgent dialysis, an intravenous antibiotic regimen of vancomycin and levofloxacin was initiated, and his clinical status was stabilized. His current presentation was complicated by a more than 10-year history of type 2 diabetes mellitus with poor control (glycated hemoglobin, 9.1% [4.0%-6.0%] at admission and 12.7% 1 year previously despite insulin therapy) and end-organ damage, including proliferative retinopathy, neuropathy, and nephropathy. His medical regimen consisted of the aforementioned antibiotics, scheduled dialysis, insulin therapy, and prophylactic heparin. The next 7 days of his hospitalization were unremarkable, with anticipated discharge on hospital day 8.

On the morning of hospital day 8, the patient reported sudden-onset right thigh swelling and severe right medial thigh pain. He endorsed upper thigh and groin pain on active and passive range of motion, and he refused to bear weight on the affected limb. The patient described the pain as sharp, at maximal intensity (10 on a 10-point scale), and with no alleviating factors. He denied any preceding trauma, and he had received no prior injections at the site of the pain. Physical examination revealed a right upper thigh that was warm to palpation, erythematous, and markedly swollen when compared with the left upper thigh. The skin over the medial thigh was taut and exquisitely tender to palpation, with a notable 8- to 10-cm-thick cordlike mass on the medial aspect of the upper thigh. No evidence of fluctuance or drainage was appreciated on the skin surface. Sensation was diminished to light touch and pinprick distally but was not changed from his baseline stocking-glove distribution. Posterior tibial and dorsalis pedis pulses were full and symmetrically palpable. Vitals signs showed that he was afebrile and hemodynamically stable: temperature, 37.2°C; heart rate, 80 beats/min; blood pressure, 128/63 mm Hg; and oxygen saturation, 98% while breathing room air. Laboratory values obtained from a routine morning blood withdrawal were notable for a mildly elevated leukocyte count of 11.2 × 10^9/L, a blood urea nitrogen level of 48 mg/dL, and a creatinine value of 4.2 mg/dL; findings were otherwise unremarkable.

1. Given the initial history and physical examination findings, which one of the following would not be in the differential diagnosis?
   a. Infection (septic joint, pyomyositis)
   b. Viral myositis
   c. Deep venous thrombosis (DVT)
   d. Heterotopic ossification and soft-tissue calcification
   e. Diabetes-associated muscle necrosis

   Given the acuity of presentation and debilitating nature of the pain, the differential diagnosis should remain broad. Most worrisome would be infection of the hip joint or in the skeletal muscle because both could require surgical intervention. He has known bacteremia with streptococci, which greatly increases his risk of bacterial invasion of the hip space or muscle tissue. Although Staphylococcus aureus is the most common pathogen, streptococcal infections are being reported with more frequency, especially in patients with diabetes (up to 16%). These 2 organisms account for most cases of septic arthritis and up to 90% of cases of pyomyositis. The patient’s recent history of infection with novel H1N1 influenza, documented by polymerase chain reaction, raises suspicion for a virus-mediated myositis. Although viral myositis typically presents as diffuse muscle pain, an intermediate form can present with only lower extremity involvement. Viral myositis should be considered because severe forms can progress to massive rhabdomyolysis with myoglobinuric renal failure, electrolyte abnormalities, and arrhythmias. Deep venous
thrombosis should always remain high in the differential diagnosis in hospitalized patients, and the fact that this patient has been hospitalized for acute sepsis increases his risk of DVT 8-fold. Myositis ossificans, which is the heterotopic calcification of soft tissue, typically presents with a palpable mass at the site of a previous trauma. Given the sudden onset of this patient’s pain and the lack of a documented history of trauma, myositis ossificans is the least likely diagnosis. Muscle infarction in a patient with diabetes, also known as diabetic myonecrosis, is a rare end-organ complication of diabetes and is often seen in patients with poorly controlled diabetes and additional end-organ damage. It most commonly presents with sudden thigh pain and swelling and should be considered in any patient with diabetes who has thigh pain and poorly controlled diabetes.

Additional studies were ordered in an effort to narrow the differential diagnosis, which remained very broad at this point.

2. Which one of the following is the most appropriate initial diagnostic test in this patient?
   a. Right hip aspiration
   b. Right thigh compartment pressures
   c. Follow-up blood cultures
   d. Electromyography and nerve conduction studies
   e. Lower extremity duplex ultrasonography

   Right hip joint aspiration could be considered given the history of bacteremia and the physical examination notable for groin pain. However, given the lack of fever, sudden onset of pain with particular focus on the medial thigh, and the fact that he has been taking broad-spectrum antibiotics, a less invasive imaging modality would be preferred as the initial diagnostic test. Right thigh compartment pressures would be the test of choice to assess for compartment syndrome. Compartment syndrome typically occurs in the setting of trauma or reperfusion after acute arterial occlusion, neither of which occurred in our patient. Also, although not necessarily reassuring because pulselessness is often a late manifestation of compartment syndrome, he had palpable pulses distally. Follow-up blood cultures would have no role in assisting with the diagnosis of his right thigh pain. Electromyography and nerve conduction studies would be indicated if the pain was thought to be neuropathic in origin. Although he has evidence of diabetic neuropathy, the sudden onset, severity, and distribution of his pain would make a neuropathic cause less likely. Lower extremity duplex ultrasonography would be the most appropriate initial diagnostic test in this patient who is chronically ill (diabetes, hemodialysis), has become acutely septic, and has been hospitalized for a period of 7 days. Given that the in-hospital case fatality rate of venous thromboembolism is 12%, it is important to diagnose it early and commence appropriate treatment immediately. If clinically suspected, a DVT should remain in the differential diagnosis and should be investigated appropriately because studies have shown development of clinically relevant DVT (0.5%-10.1%) in hospitalized patients despite heparin prophylaxis.

   Ultrasoundography demonstrated widely patent common femoral, upper deep femoral, femoral, and popliteal veins without evidence of thrombus. The posterior tibial veins, peroneal veins, and great saphenous vein were also patent and negative for thrombus. However, incidentally noted on ultrasonography was substantial subcutaneous edema in the right medial thigh with a few mildly prominent lymph nodes in the right groin. Radiography of the right hip and thigh showed no fractures, dislocations, masses, or foreign bodies. The patient continued to be in exquisite pain. His previously scheduled discharge was postponed pending further investigation and pain control.

3. Given the history, physical examination findings, and aforementioned radiological studies, which one of the following test(s) would be most helpful in obtaining a diagnosis in this patient?
   a. Magnetic resonance imaging (MRI)
   b. Inflammatory markers (erythrocyte sedimentation rate, C-reactive protein)
   c. Muscle enzymes (creatine kinase, aldolase, lactate dehydrogenase, aminotransferases)
   d. Paraneoplastic panel
   e. Joint aspiration

   Given the acuity of presentation, severity of pain, and breadth of the differential diagnosis to include infection (bone and soft tissue), inflammatory processes (diffuse and focal), and ischemia or infarction of soft tissue, efficient selection of a relatively specific noninvasive modality is preferable. An MRI is the diagnostic test of choice in this patient because it offers a noninvasive means of identifying and excluding processes in the differential diagnosis and is the most specific test when evaluating musculoskeletal symptoms. Inflammatory markers are nonspecific, especially so in this patient with recent bacteremia who is receiving hemodialysis. Elevated levels of inflammatory markers would be expected in this patient and would not greatly support one diagnosis over the other. Muscle enzymes are more specific for muscle inflammation and would be part of the work-up. However, given the broad differential diagnosis and variable presentation with regard to patterns of muscle enzyme elevation, they would not definitively confirm the underlying diagnosis. A paraneoplastic panel would not be indicated in the evaluation of this patient. Biopsy of one of the lymph nodes...
Diabetic myonecrosis is a rare complication of diabetes (type 1 or 2) first described by Angervall and Stener in 1965. Although the exact pathophysiology has yet to be clarified, it is hypothesized to result from muscle infarction secondary to atherosclerotic and diabetic microangiopathy. The most common presentation is acute, nontraumatic, painful swelling of the affected muscle with palpable mass on physical examination. The average age at presentation is 46.4 years, with disputed claims on sex predominance. The quadriceps is the most common site of presentation (62%), followed by the hip adductor (13%), hamstrings (8%), and hip flexors (1%-2%). Most commonly, diabetic myonecrosis presents in patients with other diabetic complications, such as diabetic neu-

5. Which one of the following statements regarding this patient’s prognosis would be most appropriate when counseling him about his diagnosis?

a. Most cases of diabetic myonecrosis resolve within 1 month and without long-term disability
b. Surgical management reduces short-term recovery time
c. Strict metabolic control reduces short-term recovery time
d. Diabetic myonecrosis is unlikely to recur
e. Long-term prognosis is excellent because most patients fully recover with no change in overall mortality

Muscle infarction in patients with diabetes manifests as severe debilitating pain requiring strict bed rest during the acute phase. The patient can be reassured that most cases of diabetic myonecrosis resolve in 2 to 31 days with no long-term impairment. One analysis of case reports showed patients who were managed conservatively had a recovery period of 5.5 weeks vs 13 weeks for patients who underwent surgical intervention. Patients who develop diabetic myonecrosis should certainly be educated on diet, glucose control, and insulin management because muscle infarction is thought to be due to microvascular and macrovascular complications of poorly controlled diabetes. However, it should be noted that tight control has not been shown to reduce the duration of an acute episode. Once a patient with diabetes develops diabetic myonecrosis, the likelihood of recurrence in the same muscle or contralateral limb is greater than 50%, with as many as 1 to 2 episodes per year after the initial event. As to long-term prognosis, a recent review found that most patients die of diabetic complications within 5 years of diagnosis because diabetic myonecrosis indicates substantial vascular compromise.

Follow-up a month later revealed no specific complications and adequate control of his pain. He has reported no recurrence since discharge from the hospital.

DISCUSSION

Diabetic myonecrosis is a rare complication of diabetes (type 1 or 2) first described by Angervall and Stener in 1965. Although the exact pathophysiology has yet to be clarified, it is hypothesized to result from muscle infarction secondary to atherosclerotic and diabetic microangiopathy. The most common presentation is acute, nontraumatic, painful swelling of the affected muscle with palpable mass on physical examination. The average age at presentation is 46.4 years, with disputed claims on sex predominance. The quadriceps is the most common site of presentation (62%), followed by the hip adductor (13%), hamstrings (8%), and hip flexors (1%-2%). Most commonly, diabetic myonecrosis presents in patients with other diabetic complications, such as diabetic neu-

noted on ultrasonography would likely show nonspecific inflammatory changes and would not yield information to assist with diagnosis.

The patient underwent an MRI, which showed marked muscular edema and masslike enlargement involving the adductor magnus at the level of the mid thigh with diffuse muscular edema and perifascial fluid in the surrounding thigh. No abscess or localized fluid collection was evident. On the basis of history, physical examination, MRI findings, and a high degree of clinical suspicion, the presumptive diagnosis of diabetic myonecrosis was made.

4. On the basis of the presumed diagnosis, which one of the following would be the most appropriate next step in evaluation and management?

a. Physical therapy with early range of motion of affected limb
b. Supportive care including limb elevation, analgesia, and bed rest with non-weight-bearing status
c. Muscle biopsy to confirm diagnosis
d. Surgical consultation for irrigation and debridement of necrotic tissue
e. Discharge to home with scheduled acetaminophen and ibuprofen

Although no guidelines have been established for treatment of diabetic myonecrosis and few randomized controlled trials have evaluated treatment modalities in this rare condition, a recent study showed that early mobilization and physical therapy may aggravate necrotic muscle, increasing hemorrhage and actually prolonging recovery. Patients are advised to maintain bed rest with limb elevation and non-weight-bearing status for at least 3 to 7 days. Given the severity of pain, most require the initiation of opioid medications and some require parenteral administration in the acute phase. Muscle biopsy is actually the criterion standard for the diagnosis of diabetic myonecrosis. However, given the high morbidity and prolonged recovery after biopsy, it is not recommended and should only be pursued if the diagnosis remains uncertain after noninvasive options have been exhausted. For the same reasons, surgery is not indicated in diabetic myonecrosis because irrigation and debridement are associated with serious complications, such as delayed healing and superimposed infection. As already noted, most patients require initiation of opioid therapy. Furthermore, given the considerable debility and care requirements, discharge to home might not be appropriate for all patients, some requiring temporary placement with 24-hour supervision.

The patient was treated with prescribed bed rest, opiates for short-term pain relief, and education and assistance with insulin and blood glucose management for better long-term control. He was discharged to home in the care of his large, extended family on hospital day 11 with persistent but substantially improved leg pain.
ropathy (54%), retinopathy (56.6%), and nephropathy (71.1%).

This case illustrates the difficulty of diagnosing this condition. By all accounts, it is a rare complication, with only approximately 100 cases in the literature, most of them isolated case studies. A 2002 study reviewed 25 years of Mayo Clinic records and showed only 5 documented cases of diabetic myonecrosis. It is unknown whether diabetic myonecrosis is in fact that rare or just grossly underrecognized given its similarities to more common disease processes. Our case was typical, with sudden onset of thigh pain and clinical suspicion for DVT.

A large proportion of reported cases documented no evidence of thrombosis on initial ultrasonography followed by unnecessary, potentially harmful procedures and/or prolonged hospitalizations.

This article is intended to raise awareness of this poorly understood diabetic complication. Although exceedingly low, the incidence of myonecrosis will likely increase given the overall trend of diabetes development. Myonecrosis should be suspected in all patients with diabetes who develop a painful swollen muscle. It is our hope that increased awareness among physicians will increase the recognition of this complication and lead to prompt evaluation with the appropriate diagnostic modalities. Prompt diagnosis and reassurance can lead to shortened hospitalizations and/or avoidance of unnecessary and invasive procedures.

REFERENCES

Correct answers: 1. d, 2. e, 3. a, 4. b, 5. a