

## 73-Year-Old Woman With Anterior Thigh Pain

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A 73-year-old woman presented to the Saint Marys Hospital emergency department for anterior thigh pain. This pain began 2 weeks before presentation when she noticed difficulty lifting her right leg into her car. She noticed progressive worsening of these symptoms such that she could not put on her socks and shoes. On the day of presentation, while attempting to raise her right leg into bed, she developed severe burning pain in the anterior aspect of her thigh. The severity of the pain, 10 on a 10-point scale, prompted her to seek evaluation in the emergency department. She denied trauma, change in activity level, back pain, bladder or bowel dysfunction, and saddle anesthesia. Her medical history was notable for coronary artery disease with placement of a drug-eluting stent in the distal circumflex coronary artery 6 months previously via the right radial artery, paroxysmal atrial fibrillation, diabetes mellitus with a recent glycated hemoglobin concentration of 6.0%, and chronic lower extremity lymphedema. Her medications included aspirin, clopidogrel, diltiazem, lisinopril, simvastatin, metoprolol, warfarin, and glyburide. She had no recent changes in medications, was receiving a stable warfarin dose, and her international normalized ratio (INR) was within normal limits. She denied tobacco, ethanol, and intravenous drug use. In the emergency department, radiography of the femur and lumbar spine were performed, showing no evidence of fracture.

On admission, her vital signs were as follows: temperature, normal; pulse, 72 beats/min; and blood pressure, 126/68 mm Hg. Findings on cardiac and pulmonary examinations were within normal limits. Her abdomen was soft, obese, and nontender; no masses were palpable. Both lower extremities were warm and well perfused; dorsalis pedis and posterior tibial pulses were palpable. Musculoskeletal examination revealed intact internal and external rotation of her right hip. She was unable to do a straight leg raise or flexion/extension of both the hip and knee because of the severe pain. The spine and sacroiliac joints

were not tender to palpation, but she did have tenderness to palpation over the greater trochanter of the right leg. She was able to perform transfers, but her ability to do so was limited by severe pain. During sensory testing, the patient noted a subjective difference in fine touch of the right vs the left anterior thigh.

**1. On the basis of this patient's description of her sensory deficit, which one of the following nerves is most likely involved?**

- a. Obturator nerve
- b. Femoral nerve
- c. Saphenous nerve
- d. Medial sural nerve
- e. Ilioinguinal nerve

The obturator nerve provides cutaneous innervation to the medial aspect of the thigh. Injury to the obturator nerve can result in paresthesias of the medial aspect of the thigh and weakness of adduction that results in gait instability. This patient's fine touch sensation alteration does not correspond with this distribution. In contrast, injury to the femoral nerve will result in weakness of the quadriceps, with associated knee extension weakness and paresthesias of the anterior aspect of the thigh. Given the patient's physical examination findings, the femoral nerve is the most likely to be involved. Damage to the saphenous nerve, a branch of the femoral nerve that can be injured during procedures such as knee arthroscopy, knee arthrocentesis, and cut-down of the saphenous vein, results in paresthesias of the medial aspect of the leg distal to the knee. This patient described no distal leg involvement. The sural nerve innervates the posterior leg distal to the knee and lateral foot. The patient's description of anterior thigh pain does not correlate with the sural nerve innervation pattern. Originating from the lumbar plexus, the ilioinguinal nerve innervates the skin overlying the medial femoral triangle, which is bounded by the inguinal ligament, the adductor longus, and the sartorius.<sup>1</sup> Injury to this nerve would not explain the large area of involvement experienced by this patient. Her description of pain and paresthesias and her denial of any history of trauma were consistent with spontaneous femoral neuropathy.

Because of the substantial tenderness over the greater trochanter of the right leg, a trochanteric bursa injection was performed. The area of maximal tenderness was identified and injected with methylprednisolone and lidocaine.

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See end of article for correct answers to questions.

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After 15 minutes, the local tenderness had resolved, but her anterior thigh pain remained unchanged. On evaluation of her gait, an important finding was made.

**2. Given this patient's presentation, which one of the following would be her expected gait?**

- a. Trendelenburg gait
- b. Steppage gait
- c. Festinating gait
- d. Scissor gait
- e. Knee "buckling"

The Trendelenburg gait describes the result of weakness of the gluteal muscles often associated with muscular dystrophy, L5 radiculopathy, and myopathies. The pelvis drops on the opposite side, making the opposite leg "too long," resulting in leaning toward the affected side to clear the opposite foot. This gait is not associated with femoral neuropathy because the femoral nerve does not innervate the gluteal muscles. The steppage gait is associated with foot drop that requires flexion at the hip to raise the leg higher than with a normal gait in order to "clear" the foot. This is classically associated with L5 radiculopathy or peroneal nerve damage. In the case of injury to the L5 root, this gait can occur in conjunction with a Trendelenburg gait. A festinating gait (ie, a Parkinsonian gait) is usually characterized by short, shuffling steps and increasing step acceleration, resulting in a high risk of falls. The scissor gait refers to thigh adduction during leg swing that can result in legs crossing each other. The increased tone leads to decreased motion of the hip and knee joints during the gait cycle, resulting in a stiff gait. Such a gait can be seen in association with upper motor neuron lesions in patients with cerebral palsy and multiple sclerosis.<sup>2</sup> Femoral neuropathy can result in quadriceps muscle weakness and the sensation of the knee buckling during the load-response, making knee buckling the correct response.<sup>3</sup>

During ambulation, the patient required the support of a walker and described feeling "unsteady" while walking with the feeling that her knee would "give out." Physical therapy was consulted for assistance with her ambulation, and pain control was attempted with oral oxycodone. She continued to have difficulty with her gait and had ongoing pain despite physical therapy and oral narcotics. Because of the unknown etiology of her femoral neuropathy, further investigation was necessary.

**3. At this stage, which one of the following laboratory investigations would be most helpful?**

- a. Serum glucose levels
- b. Ionized calcium levels
- c. INR
- d. Thyroid-stimulating hormone levels
- e. Vitamin B<sub>12</sub>

Hypoglycemia can result in a sensation of generalized weakness; however, this patient's most prominent symptom was pain. Although diabetes mellitus is most commonly associated with a distal symmetric neuropathy affecting sensory and autonomic fibers in the classic stocking/glove distribution, it can also cause mononeuropathies, including the femoral nerve and diabetic lumbosacral radiculoplexus neuropathy (DLRPN).<sup>4,5</sup> Initially, DLRPN can present as an asymmetric lower extremity pain that is often followed by weakness and often occurs in the setting of weight loss. Although DLRPN may explain her symptoms, a single glucose measurement would provide little insight into the etiology of pain, particularly when DLRPN can occur in patients with well-controlled diabetes.<sup>5</sup> Hypocalcemia can cause generalized paresthesias, classically in a perioral distribution; a femoral nerve distribution would be less likely. Hypercalcemia can result in weakness but does not explain the patient's predominant symptoms of pain and paresthesias. Because the patient was taking warfarin for paroxysmal atrial fibrillation, checking an INR would be appropriate. One adverse event that can be associated with anticoagulation is spontaneous bleeding, which includes bleeding in the retroperitoneal space that results in the sudden onset of femoral neuropathy.<sup>6</sup> On rare occasion, hypothyroidism results in meralgia paresthetica, causing pain and paresthesias in the anterolateral thigh.<sup>7</sup> However, this patient did not describe any of the other symptoms associated with hypothyroidism. Vitamin B<sub>12</sub> deficiency can result in paresthesias and varied neurologic symptoms in addition to hematologic effects; however, it would classically present over a longer time course than did this patient's symptoms and would not explain her pain.<sup>8</sup>

On the morning of the patient's admission, her INR was 3.0, and her hemoglobin concentration was 13.3 g/dL (reference ranges provide parenthetically) (13.5-17.5 g/dL). However, approximately 24 hours later her hemoglobin concentration decreased to 10.2 g/dL. She remained hemodynamically stable without orthostatic hypotension. Her platelet count remained within normal limits at  $139 \times 10^9/L$  ( $150-450 \times 10^9/L$ ). She denied melena, hematochezia, epistaxis, and hemoptysis.

**4. Which one of the following imaging studies would be least helpful in identifying the etiology of this patient's symptoms and laboratory findings?**

- a. Indium In 111-labeled white blood cell scan
- b. Plain radiography
- c. Ultrasonography
- d. Computed tomography
- e. Magnetic resonance imaging

An indium In 111–labeled white blood cell scan would be the least helpful. Although it can provide information about infection and inflammation, it is unlikely to reveal the cause of her pain and paresthesias. Also, this test has the disadvantage of taking up to 24 hours to complete. Plain radiography can provide diverse information about underlying pathology, including fractures. Further, asymmetry of the psoas muscle can be present in the setting of retroperitoneal hemorrhage; however, this can also occur in other pathologies as well as normal variants.<sup>6</sup> Ultrasonography can be used to evaluate the abdomen, including retroperitoneal structures, and to rapidly visualize retroperitoneal hemorrhage with little risk to the patient. However, success can be limited by the patient's particular anatomy, including body habitus.<sup>6,9</sup> Computed tomography is an excellent imaging modality for evaluating retroperitoneal hemorrhage, which can be recognized by increased density areas that are typically asymmetric. Magnetic resonance imaging also provides very exact anatomic information about the extent of involvement of retroperitoneal hemorrhage. Further, it can provide information about nerve compression.<sup>6,9</sup>

Magnetic resonance imaging showed rounded foci of slightly increased T1 and T2 signals within the right iliacus and inferior psoas muscle consistent with intramuscular hematomas.

**5. Which one of the following interventions would be most appropriate?**

- a. Continue warfarin at a lower dose
- b. Discontinue warfarin until the INR has normalized
- c. Discontinue warfarin and give oral vitamin K
- d. Discontinue warfarin and give intravenous vitamin K and fresh-frozen plasma (FFP)
- e. Discontinue warfarin and start low-molecular-weight heparin therapy

In the setting of severe bleeding, continuing warfarin even at a lower dose would place the patient at severe risk of adverse outcomes from bleeding. Although withholding warfarin without giving vitamin K is recommended in the setting of a minimally elevated INR without substantial bleeding, this patient has signs of substantial bleeding and should be treated more aggressively. Per American College of Chest Physicians recommendations, withholding warfarin and giving oral vitamin K would be sufficient for substantially elevated INR without evidence of bleeding.<sup>10</sup> For substantial or life-threatening bleeding, regardless of INR level, the recommendation is to use intravenous vitamin K for INR reversal along with FFP or recombinant vitamin factor VIIa. The clinical status of the patient is what dictates whether FFP or recombinant factor VIIa is necessary. Low-molecular-weight heparin would not be recommended in the setting of active bleeding. Further,

low-molecular-weight heparin is not readily reversible and thus poses an additional risk in the setting of bleeding.<sup>10</sup>

Careful risk-benefit analysis was considered for this patient with “triple” anticoagulant therapy, including warfarin, aspirin, and clopidogrel in the setting of atrial fibrillation and a drug-eluting stent. Warfarin and aspirin were discontinued. Fresh-frozen plasma and 10 mg of vitamin K were given intravenously. Clopidogrel was continued because guidelines recommend clopidogrel continuation for 1 year to prevent in-stent thrombosis.<sup>11</sup> The patient's pain was controlled with opioid therapy. Physical therapy assisted throughout the hospitalization, and at dismissal she was able to ambulate with the aid of a walker. She was discharged to a skilled nursing facility for further work with physical therapy; 2 weeks later, she returned home with no requirement for pain medications.

## DISCUSSION

Retroperitoneal hematomas can result in femoral neuropathy at 2 different locations along the femoral nerve's course. The first is the iliopsoas gutter due to the rigid surrounding fascia. The second is at the inguinal ligament overlying the femoral canal, which contains the femoral nerve.<sup>6,12</sup>

The causes of retroperitoneal hemorrhage are diverse. Combination therapy with multiple anticoagulant and antiplatelet agents is becoming more common. In a cohort study of elderly patients receiving different combination treatments, bleeding rates were increased in patients taking warfarin alone, aspirin plus warfarin, aspirin plus ticlopidine or clopidogrel, or aspirin plus warfarin plus ticlopidine or clopidogrel compared with patients taking aspirin alone. Despite the reported elevation of bleeding risk, the cohort taking aspirin, warfarin, and ticlopidine or clopidogrel experienced only 1 bleeding event per 11.8 patient-years, making it impossible to calculate an odds ratio.<sup>13</sup> More experience is required to define bleeding risk for patients receiving “triple therapy.”

Retrospective studies have attempted to define characteristics that can differentiate the prognosis of patients with retroperitoneal bleeding in the setting of anticoagulation. Combined use of anticoagulant and antiplatelet agents resulted in increased admissions to the intensive care unit along with more days spent in the intensive care unit but no difference in mortality when compared with the use of an anticoagulant or antiplatelet agent alone.<sup>14</sup> Higher rates of intensive care unit admission also occurred in patients with coronary artery disease.<sup>14</sup> Discussion among patients, their primary care physicians, and cardiologists is necessary to determine which anticoagulant agents are needed on a case by case basis, particularly in the setting of a history of substantial bleeding.

Surgical options may also play a role in the management of retroperitoneal hemorrhage. Successful management using surgical decompression<sup>6</sup> and endovascular embolization<sup>15</sup> has been reported. However, most of the evidence in the literature derives from case series of patients and involves treatments that were implemented only when conservative measures failed. Thus, it is difficult to extrapolate the success of an intervention in an individual patient to a more general population. This patient's continued hemodynamic stability, continued requirement of clopidogrel, and lack of progressive neurologic dysfunction led to nonsurgical options being pursued.

Retroperitoneal hemorrhage requires a high index of clinical suspicion, particularly among patients receiving anticoagulant or antiplatelet therapy. The risk of bleeding must be weighed against the serious medical conditions that prompt the use of these agents. In the aftermath of retroperitoneal bleeding, individualized decisions must be made to optimize future health benefit.

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