

## Clinical Problem-Solving

## A PAIN IN THE BACK

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An 80-year-old man with degenerative arthritis of the hip and spine began to have midthoracic back pain and worsening pain in his left hip. The pain began suddenly, was not preceded by trauma, did not radiate, and was not relieved in any position. The back pain persisted for two weeks despite rest and treatment with ibuprofen. The patient took no other medications.

In an 80-year-old with back pain, I would worry about osteoporosis, either primary or secondary. The midthoracic area is a common site of compression fractures. Although osteoporosis is more common in women than men, at this age the men start to catch up. Osteoporosis with a compression fracture is the most likely diagnosis in this setting, and I would obtain an imaging study. The patient could also have metastatic cancer. I would want to know whether he has pain that keeps him awake at night or any other symptoms that are red flags. Osteoarthritis of the lumbar spine can also be associated with nonspecific back pain.

The patient's medical history included a partial resection of the colon 10 years earlier for a villous adenoma and benign prostatic hypertrophy, with a serum prostate-specific antigen level of 5.6 ng per milliliter and benign findings on biopsy of the prostate 2 years earlier. He had a normal temperature, pulse, and blood pressure and normal results on cardiac, pulmonary, and abdominal examinations. The area over the spine and hips was not tender, but the paraspinal muscles at the T7 level were tender. Straight-leg raising did not worsen his pain. The patient had normal strength, sensation, and reflexes in his legs. Radiographs of the thoracic spine revealed marked degenerative changes in the T1 through T6 vertebrae, with large anterior and small posterior osteophytes.

The patient has a history of a colonic neoplasm. It is unusual for colon cancer to metastasize to the

spine, but it is possible. The radiographs are essentially negative, a finding that effectively rules out a compression fracture. Multiple myeloma is unlikely in a patient of his age. I would measure the erythrocyte sedimentation rate.

The physician prescribed acetaminophen with codeine. The patient returned three weeks later with worsening pain, which had moved from the thoracic to the lumbar region. He had to sleep sitting up because lying flat worsened the pain. He had no bowel, bladder, or radicular symptoms; no symptoms of claudication; and no fevers, chills, night sweats, weight loss, or pain elsewhere. His prostate gland was enlarged and symmetric and had no nodules. The white-cell count was 9400 per cubic millimeter, with 70 percent granulocytes, 14 percent lymphocytes, 14 percent monocytes, and 2 percent eosinophils. Other laboratory values were as follows: hemoglobin, 12.5 g per deciliter; mean corpuscular volume, 95  $\mu\text{m}^3$ ; prostate-specific antigen, 8.9 ng per milliliter; and erythrocyte sedimentation rate, 112 mm per hour. Liver aminotransferase levels were normal, as were the results of urinalysis and serum and urine protein electrophoresis; a test for fecal occult blood was negative.

The patient now has persistent, marked pain that is worse when he lies flat. I am worried about the possibility of an epidural metastasis. The prostate-specific antigen level is something of a red herring in a man of this age. Metastatic lesions from prostate cancer are usually blastic, and his radiographs were negative for metastases. The elevated erythrocyte sedimentation rate is worrisome and makes me wonder whether a chronic infection, a metastatic tumor, vasculitis, or multiple myeloma could be present. The patient does not have constitutional symptoms to suggest the presence of either infection or vasculitis. Myeloma is unlikely, given the normal results of urine and serum protein electrophoresis.

Radiographs of the hip and lumbar spine showed marked degenerative changes. A bone scan showed increased uptake of the tracer in the shoulders, the cervicothoracic junction, and the L4 and L5 vertebrae. A computed tomographic (CT) myelogram showed severe spinal stenosis at the level of L3 to L4, with short pedicles, an asymmetric bulge in the disk, and hypertrophy of the ligamentum flavum. The thecal sac was compressed and displaced posteriorly by abnormal soft tissue

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that extended from the midbody of the L4 vertebra to the midbody of the L5 vertebra. The radiologist thought that the soft tissue was most likely a herniated disk. The patient received oral morphine sulfate to control his pain.

The patient has spinal stenosis on the CT myelogram, but he does not have the clinical findings of pseudoclaudication. Abnormal findings are very common on imaging of the spine, even in patients who are asymptomatic. The physician needs to match the imaging results to the patient's symptoms. The patient has a soft-tissue mass interpreted as a herniated disk. Herniated disks are unusual at his age; they occur more commonly among those who are 30 to 55 years of age. When herniated disks do occur in older patients, they are often higher up in the lumbar spine. I am very concerned that this abnormal soft tissue may represent an epidural metastasis rather than a herniated disk.

I am not sure what to make of the bone-scanning results. The changes in the shoulders and cervicothoracic junction are probably age-related degenerative changes. The lesion at L4 to L5 probably represents a reaction to the soft-tissue lesion. The mass could be a primary lymphoma that extends into the epidural space.

Three weeks later, the patient underwent a decompressive laminectomy. Preoperative laboratory studies revealed a white-cell count of 8300 per cubic millimeter, a hemoglobin level of 11.1 g per deciliter, a platelet count of 267,000 per cubic millimeter, normal serum electrolyte levels, normal renal function, and normal coagulation studies. At surgery, the surgeon found marked stenosis at the L4 level, with hypertrophy of the ligamentum flavum and central bulging of the L4–L5 disk. Routine pathological evaluation of the excised material revealed multiple fragments of normal bone and fibrous cartilage. No special studies were performed.

The patient has now undergone decompressive spinal surgery. I assume that either the surgeon or the pathologist would have recognized a tumor if one was present. Perhaps this patient had an atypical presentation of spinal stenosis, but I remain concerned that another process is being overlooked. Given the patient's presentation, I do not think that I would have operated on him; I would have performed a needle biopsy to look for underlying tumor or infection.

One month after surgery, the patient still had back pain that required oral narcotics. Shortly thereafter, he slipped and fell, worsening his back pain. His physical examination was unchanged.

He had a hemoglobin level of 10.6 g per deciliter and a persistently elevated erythrocyte sedimentation rate of 104 mm per hour.

The patient still has back pain with worsening anemia and an elevated sedimentation rate. I think the correct diagnosis has not yet been made, and I believe that he probably has a chronic infection, lymphoma, or metastatic cancer.

Radiographs showed loss of the inferior end plate of the L4 vertebral body, the superior end plate of the L5 vertebral body, and the anterior cortexes of both vertebrae, with associated collapse. In retrospect, the intraoperative films obtained a month earlier showed subtle irregularities of the end plates. A fine-needle aspiration biopsy of the L4–L5 disk space revealed blood-tinged, slightly cloudy fluid. Gram's staining showed numerous white cells but no organisms. Cytologic evaluation showed no evidence of cancer. Culture of the fluid grew *Staphylococcus epidermidis*. Two sets of blood cultures and a urine culture were negative.

The destruction of the end plates and the finding of white cells in the biopsy specimen suggest the presence of an infection of the disk space; there is no evidence of cancer. Older patients can have a chronic infection without having a fever or an elevated white-cell count. The patient did not have an epidural abscess at surgery, but the findings of nonmechanical back pain, an elevated erythrocyte sedimentation rate, and worsening anemia are all consistent with the presence of an unrecognized, smoldering infection. I am uncertain whether *S. epidermidis* is the actual pathogen or a contaminant.

The patient received six weeks of intravenous vancomycin. Over the next several months, his back pain resolved, his erythrocyte sedimentation rate normalized to 20 mm per hour, and radiographs of his spine showed gradual improvement.

The improvement in the patient's symptoms and the normalization of his erythrocyte sedimentation rate with antibiotic therapy confirm my suspicion that infection was the cause of his problems.

#### COMMENTARY

Low back pain is a common disorder, ranking second only to upper respiratory tract infection as a reason for visits to physicians in the United States. It is generally a local, musculoskeletal problem that is seldom attributable to any specific disease or pathologic lesion.<sup>1</sup> Occasionally, however, back pain is caused by a serious systemic disorder such as cancer or infection. To avoid missing the serious causes without over-

testing patients who have the typical, self-limited musculoskeletal problems, close attention should be paid to specific clues that raise the possibility of serious systemic disease. Anatomical abnormalities on imaging studies are common, even in asymptomatic persons, and any such abnormalities should be meticulously correlated with the patient's clinical presentation in order to avoid erroneous judgments.<sup>2</sup>

A probabilistic approach to clinical decision making in patients with back pain can be quite helpful. Indicators of high risk include an age of more than 50 years, history of cancer, unexplained weight loss, pain that lasts more than one month, the absence of a response to therapy, pain that is worse at rest, a history of intravenous drug use, and the presence of a urinary tract or other infection.<sup>3</sup> The presence of these so-called red flags can help the physician identify a subgroup of patients with an increased probability of having a serious underlying cause of back pain. Wipf and Deyo have estimated that patients with low back pain and one or more red flags have a pretest probability of serious systemic disease of up to 10 percent.<sup>1</sup> When the pretest probability of a disease is high, only a negative result on a very sensitive test will lower the probability enough to rule out a diagnosis of that disease.

Spinal infection (osteomyelitis or diskitis), which this patient had, poses a difficult diagnostic challenge. It is a rare cause of back pain, accounting for less than 0.01 percent of cases in a primary care setting.<sup>4</sup> In formulating the differential diagnosis, however, physicians should not rely on the presence of the typical features of infection to trigger the thought of a possible spinal infection. Fever and leukocytosis are specific but quite insensitive findings for vertebral osteomyelitis. Deyo<sup>4</sup> estimated that fever was present in only 52 percent of patients with pyogenic osteomyelitis and only 4 percent of patients with diskitis. The estimated specificity of fever for osteomyelitis in patients with low back pain is 98 percent.<sup>5</sup> Therefore, the presence of fever increases the odds of spinal infection by a factor of 26; more important in this afebrile patient, the absence of fever reduces the odds only by half. Similarly, leukocytosis (a white-cell count of more than 12,000 per cubic millimeter) is present in only about 43 percent of patients with spinal infection and 6 percent of patients with nonspecific mechanical low back pain who do not have a spinal infection.<sup>4,5</sup> The presence of an elevated white-cell count therefore increases the odds of spinal infection by a factor of 7, but a normal white-cell count, as the patient under discussion had, decreases the odds to 0.59 times the initial odds. Thus, although the presence of fever and leukocytosis greatly increases the odds of spinal infection, the absence of fever and leukocytosis does not substantially decrease the odds. In this patient, who had a relatively high probability that his back pain had a serious sys-

temic cause, the absence of fever and leukocytosis is scant evidence against a diagnosis of spinal infection.

Typical radiographic changes and a fine-needle aspiration of purulent material containing staphylococci eventually confirmed this patient's diagnosis. Most spinal infections are caused by *S. aureus*, and about a third are due to gram-negative aerobic bacilli and are often found in patients with a predisposing urinary tract infection.<sup>6</sup> *S. epidermidis* is more typically associated with postoperative disk infection; in one large series, however, this organism was isolated from 16 percent of patients with spontaneous spinal infections.<sup>7</sup> Furthermore, in the case under discussion, because the signs of spinal infection were present on the intraoperative radiographs, we can exclude the possibility that the infection was acquired during the surgery.

The discussant identified several clues to the presence of an underlying serious systemic cause for this patient's back pain. The persistence of pain in all positions, the fact that the pain worsened when the patient was lying flat, the patient's lack of response to conservative therapy, and the extreme elevation of the erythrocyte sedimentation rate caused the discussant to worry about the possibility of an underlying cancer or infection. His concern persisted despite the finding of spinal stenosis and disk herniation on the CT myelogram, because these diagnoses did not fit the symptoms and failed to explain important features of the case.

Sciatica occurs in the majority of patients with an intervertebral-disk herniation, with an estimated sensitivity of 95 percent and a specificity of 88 percent.<sup>8</sup> The absence of sciatica is strong evidence against a diagnosis of disk herniation. Historically, neurogenic claudication — leg pain with walking that resolves with rest, lumbar flexion or both — is the hallmark of spinal stenosis of the central canal, whereas patients with lateral recess stenosis often have radicular leg pain. Neurogenic claudication has a reported sensitivity of 60 percent for spinal stenosis, whereas leg pain has a reported sensitivity of 85 percent.<sup>8</sup> The absence of leg symptoms in the patient under discussion substantially reduced the odds that disk herniation or spinal stenosis was the cause of his symptoms, even though these anatomical abnormalities were present. A patient's characterization of the location of back pain (which in this patient moved from the thoracic to the lumbar region) tends to be imprecise and, with the exception of radiculopathy and perhaps compressive fractures, is usually not helpful in identifying the cause of the pain.

One of the most important features that was not accounted for by the diagnosis of spinal stenosis was the patient's extremely elevated erythrocyte sedimentation rate. The erythrocyte sedimentation rate can provide an important clue to the presence of serious underlying disease,<sup>9</sup> but it appears to have been

ignored in this case. The erythrocyte sedimentation rate is often thought to be too nonspecific to be useful diagnostically, but it is actually quite helpful in the case of patients with an increased pretest probability of tumor or vertebral osteomyelitis. As compared with a lower rate, an erythrocyte sedimentation rate of more than 100 per hour is associated with a likelihood ratio of 55 for a serious underlying cause of back pain.<sup>5</sup> In this elderly man whose unremitting pain worsened when he was supine, the pretest probability of serious systemic disease was estimated to be about 10 percent (pretest odds, 1:9).<sup>1</sup> His extremely elevated erythrocyte sedimentation rate raised the odds of systemic disease by a factor of 55, to about 6:1, or a post-test probability of 85 percent. Given such a high probability, the discussant was correct in continuing to worry that the patient had some underlying problem even after the myelogram showed severe spinal stenosis.

In conclusion, several important points are raised by this case. First, in evaluating patients with the common symptom of back pain, physicians need to be alert for red flags that indicate rare, serious causes. Second, although the erythrocyte sedimentation rate is generally a nonspecific test, extreme values are extremely valuable, since a rate of more than 100 per hour in a patient with atypical back pain substantially raises the odds of cancer or osteomyelitis. Finally, the choice of a diagnostic test and the interpretation of the results must reflect clinical thinking. CT myelography is a very useful test in evaluating patients

whose symptoms are strongly suggestive of disk herniation or spinal stenosis. However, both CT and magnetic resonance imaging have a false positive rate of approximately 20 percent in patients with spinal stenosis.<sup>10</sup> To avoid clinical errors, abnormalities on images of the spine should be correlated with the patient's symptoms.

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