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Epidural Steroid Injection-Induced Pancreatitis: A Case Report

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Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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Patient: Female, 73-year-old
Final Diagnosis: Pancreatitis
Symptoms: Abdominal and back pain
Medication: —
Clinical Procedure: Epidural
Specialty: Neurology

Objective: Rare co-existance of disease or pathology

Background: Degenerative disc disease of the lumbar spine can be associated with spinal canal and neuroforaminal stenosis, resulting in severe pain. Conservative approaches to treatment are generally recommended initially, especially in the elderly. Epidural corticosteroid injections can provide significant but temporary pain relief and are a commonly performed procedure in pain management. Pancreatitis caused by corticosteroids is unusual and the prognosis typically is good.

Case Report: A 73-year-old woman presented with severe intractable back pain 1 week after lumbar epidural steroid injection for symptomatic spinal stenosis. Imaging confirmed severe multi-level degenerative disc disease of the lumbar spine resulting in severe canal and bilateral neuroforaminal stenosis. Because of abdominal pain and nausea, an abdominal CT and labs were performed, revealing evidence of pancreatic inflammation.

Conclusions: Lumbar epidural steroid injection may be a risk factor for developing steroid-induced pancreatitis.

MeSH Keywords: Epidural Space • Glucocorticoids • Pancreatitis

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Background

Back pain is the fifth most common reason for all physician visits in the United States [1] and the most common musculoskeletal chief complaint in the emergency department [2,3]. Over 20% all persons over the age of 65 have radiological evidence of lumbar region spinal stenosis [4], which is a common antecedent risk factor for spinal pain and lumbosacral radiculopathy. A trial of nonsurgical conservative therapy [1] for spine pain is generally recommended initially, especially in older adults. Rest, anti-inflammatory drugs, analgesics, physical therapy, and epidural steroid injections (ESI) are all published treatment methods for symptomatic spinal stenosis [5,6]. ESI have been in use for decades and are considered safe, although the Food and Drug Administration (FDA) recently published a drug safety communication concerning new possible adverse effects of ESI, including blindness, stroke, and death [6]. Nonetheless, ESI is commonly used to treat pain in patients with radiculopathy and spinal stenosis. To date, lumbar ESI has not been reported to be associated with pancreatitis, regardless of the dose of steroids used. Systemic absorption of glucocorticoids occurs after ESI [7]. Inadvertently, systemic steroids may have an enigmatic effect on the pancreas. Acute pancreatitis is defined as clinically suspicious abdominal pain with elevated pancreatic enzymes. It occurs in approximately 30 per 100 000 population and the etiology is most often gallstones or alcohol intake. Less than 5% of cases are secondary to drug-induced adverse effects [8]. Pancreatitis has been reported to be associated with steroid medication use, even in cases in which the steroid dosages would be considered too low to suppress the HPA axis [9]. Here, we report a case of transient glucocorticoid-induced pancreatitis that occurred 1 week after lumbar epidural steroid injection.

Case Report

A 73-year-old woman presented to the emergency department (ED) with intractable lower back pain 1 week after a depot lumbar epidural steroid injection. She had been seen in the ED 2 days before with similar symptoms. The workup included a lumbar x-ray, which revealed severe multi-level spondylosis without any acute fracture. She was discharged from the ED with directions to continue rest and nonsteroidal anti-inflammatory drug (NSAID) therapy. Instead of pain relief, In the span of 1 week, her symptoms became progressive, shooting in nature, localized to the middle of the lower back with radiation down her right leg, and a severity pain scale level 9 out of 10. She denied constitutional symptoms of fever, chills, night sweats, weight loss, fecal or urinary incontinence, or sick contacts. She endorsed several days of nausea without vomiting and middle epigastric pain. Her past medical history was significant for coronary artery bypass graft (CABG) 2 years prior, hypertension on Carvedilol/Coreg 3.125 mg twice per day, dyslipidemia on Rosuvastatin/Crestor 20 mg every night, diabetes mellitus type II, with a hemoglobin A1c of 7.8% on Glargine/Lantus 10 units twice per day and Lispro/Humalog via sliding scale. Four years ago, she had an episode of acute cholecystitis and gallstone pancreatitis, which resolved with a cholecystectomy and clearing the common bile duct of stones. Her low back pain had progressed over 5 years and she had received lumbar epidural steroid injections 3 times. Her review of systems revealed no headaches, vision changes, chest pain, shortness of breath, constipation, diarrhea, or additional joint and muscle pain. Her past surgical history included splenectomy, cholecystectomy, total abdominal hysterectomy, and appendectomy. She denied any significant family history. She had a distant history of tobacco use and denied any intravenous drug or alcohol use.

On physical exam, her body mass index was 28.8 lb/in^2, heart rate of 114 beats per minute, respiratory rate of 20 breaths per minute, and systolic blood pressure of 201 mmHg/80 mmHg. She was lying in bed in the fetal position with notable pain with extension of the back. On inspection of her back, there was no erythema, edema, tenderness, or fluctuance to palpation. There was significant tenderness with flexion and relief with extension, especially in the L-2 to L-5 region. A neurological examination showed decreased sensation to light touch and deep palpation on the right lower extremity in the saphenous medial crural cutaneous distribution, patellar and ankle hyporeflexia, and 4-/5 strength on the right. There was slight guarding of her abdomen during palpation but no mass or rebound was noted. Bowel sounds were present. There was no skin rash, and bilateral extremity pulses were good. Her WBC (white blood cell count) was 12.4×10^3/µL [4.4–10.5 10^3/µL]. A peripheral blood smear was notable for leukocytosis, predominantly neutrophilia. Lipase was within normal limits on presentation to the ED.

She was admitted to the inpatient service after failing conservative therapy, with high clinical suspicion for an underlying lumbar abscess given the leukocytosis and lumbar pain following ESI. She was given oxycodone/acetaminophen 5 mg/325 mg 1–2 6 h (hours) as needed (prn), morphine 2 mg IV (intravenous) q6h prn, and ondansetron 4 mg IV push prn nausea and vomiting. She was also given baclofen 5 mg po (oral) q (every) 8 h, ibuprofen 200 mg q 8 h po, and lidocaine topical patch 5% every 4 h applied to the back. The patient received a restricted diet due to the nausea and unspecified back pain. Her vitals improved, and her diet was advanced as tolerated. A magnetic resonance imaging (MRI) of her back could not be completed because of the pain. Serum C-reactive protein (CRP) was elevated to 154.7 mg/L [≤9.9 mg/L], ESR 38 mm/h [0–30 mm/h] (erythrocyte sedimentation rate) and pro-calcitonin of 1.08 ng/mL [0.0–0.1 ng/mL]. Her WBC increased to

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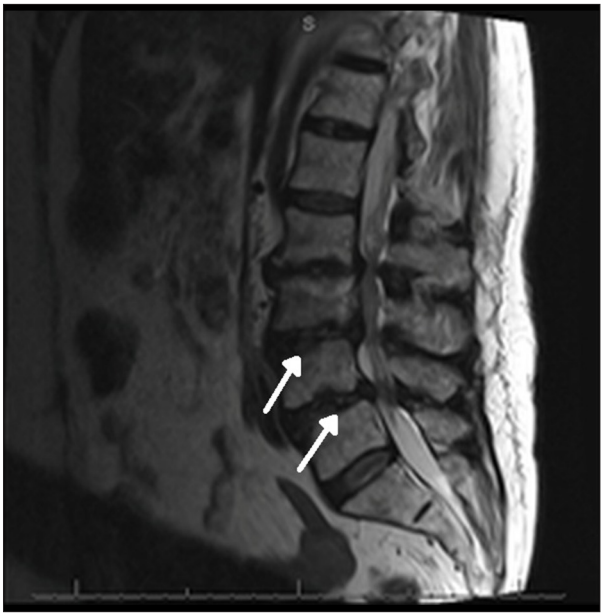

Figure 1. MRI spine, sagittal view, severe multi-level degenerative disc disease of lumbar spine, worst at L2–L3 and L3–L4 (arrows).

27×10^3/μL, with the peripheral blood smear indicative of well-differentiated neutrophils without any abnormalities. No antibiotics were started as the patient remained afebrile without any particular source. An ultrasound of the lower back was performed and showed no mass or abscess. Blood and urine cultures were obtained and remained negative. The patient finally tolerated the MRI with light sedation. The lumbar MRI showed no cystic or solid mass in the lumbar spine, with severe multi-level degenerative disc disease of lumbar spine worst at L2–L3 and L3–L4 (Figure 1). Severe canal and bilateral neuroforaminal stenosis was diagnosed. Neurosurgery was consulted and recommended L2–L5 lumbar laminectomies with posterolateral instrumented fusion. Due to the recent onset of nausea, mid epigastric pain, and leukocytosis, a serum lipase was obtained, which found to be elevated at 690 U/L [11–82 U/L]. An abdominal CT (computed tomography) was performed with light sedation. The CT (Figure 2) showed severe edema containing ill-defined low-density areas in the head and uncinate process of the pancreas. The findings were consistent with pancreatitis. She was placed on maintenance intravenous fluids, kept nothing by mouth (NPO), and continued pain control. She improved and underwent the neurosurgical procedure with complete resolution of pain. The follow-up lipase result was normal. Her clinical status improved, and she eventually underwent the procedure, with improvement in mobility and pain. The patient was eventually discharged to a skilled nursing facility for rehabilitation.

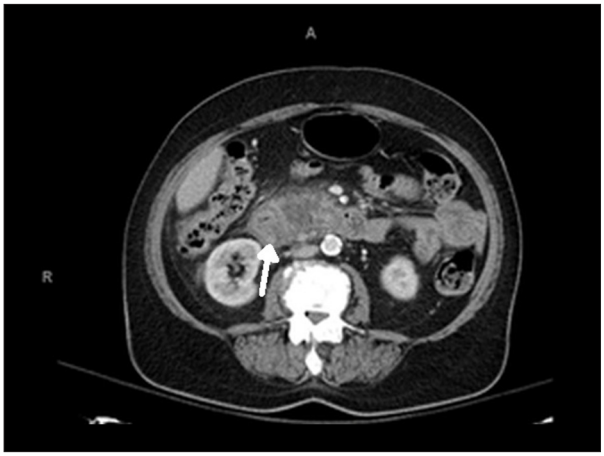

Figure 2. Severe edema containing ill-defined low-density areas in the head (arrow) and uncinate process of the pancreas.

Discussion

Acute pancreatitis is the cause of approximately 230 000 hospitalizations in the United States per year [2]. Most of the cases are mild to moderate, but severe and even fatal cases can occur. The mortality rate for severe pancreatitis can reach as high as 33–54% [2,3]. Although biliary disease/gallstones and alcohol abuse account for 80% of cases [3], the actual risk of each etiology in developing acute pancreatitis is less than 2% [3]. Once triglycerides, gallstones, and/or alcohol abuse have been excluded, other etiologic factors of pancreatitis must be considered in the setting of the patient history, laboratory studies, and imaging tests [3]. A rare cause is drug-induced pancreatitis or chemical pancreatitis; accounting for 3–5% of all cases of acute pancreatitis [4], a WHO database shows that over 500 drugs have been linked to pancreatitis [5]. Drug-induced pancreatitis is self-limited. The true epidemiology is unclear due to the lack of adequate and consistent reporting. Most cases may fall into the category termed idiopathic pancreatitis [5,6]. Most patients admitted to the hospital are already taking a medication [4], making the diagnosis difficult to establish. Evidence of a drug reaction (as rash, lymphadenopathy, or eosinophilia) in drug-induced pancreatitis is rare. There are no currently known clinical, biochemical, or radiological features to distinguish this etiology from other causes of pancreatitis [4,7].

The diagnosis of drug-induced acute pancreatitis requires a diagnosis of acute pancreatitis [2], and requires 2 of the following 3 features: characteristic abdominal pain of acute pancreatitis, elevated lipase >3 times the upper limit of normal, and characteristic CT findings of acute pancreatitis. A careful clinical evaluation to rule out more common etiologies (e.g., alcohol-induced and gallstone/biliary-induced). A review of current medications and their duration of use is needed. If there is high

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suspicion for drug-induced pancreatitis, immediate discontinuation is required to prevent ongoing pancreatic injury [2,7]. An early diagnosis can facilitate prompt cessation of the offending agent and prevent recurrence [4], thereby reducing complications and length of hospital stay [2]. Failure to identify a drug that is an offending agent can result in critical delays [2]. Further management includes making the patient NPO, giving aggressive fluid replacement, continuous oxygen saturation monitoring, and parenteral narcotic medications.

ESI inhibits the synthesis of prostaglandins that cause inflammation and ectopic discharge from a sensory nerve, decreasing the sensation of pain. The advantage of ESI is that it is minimally invasive for patients with lumbar pain. Significant complications after ESI are rare but can result from mechanical ischemia, direct needle injury, infection, or injection solution [10]. It is likely the ESI in our patient was associated with the acute pancreatitis. The pathophysiology of steroid-induced pancreatitis follows a dose-dependent mechanism [11]. This suggests steroids have a mild inhibitory effect on pancreatic secretion mediated through an increase in viscosity. With increased steroid exposure, there is decreased pancreatic enzyme secretion and enhanced local inflammation.

We performed a MEDLINE search of the English language literature via PubMed from January 1, 1946 to present, using the MeSH terms and keywords 'pancreatitis', 'epidural', 'steroid', and 'injection'. We found 1 previous article that described a case of pancreatitis 4 days after receiving an intra-articular injection of cortisone to the right knee [12]. Whether the present case or the intra-articular injection case share a cause-and-effect relationship between the steroids and the pancreatitis is only speculative, but some elements are clear. First, glucocorticoids, even in small doses, are a commonly known risk factor for pancreatitis [9,13]. Second, the literature shows the risk for development of pancreatitis after taking oral steroids is highest 4–14 days after the medication is taken [13]. In each case, the pancreatitis occurred within this time frame. Third, the acuity of pancreatitis secondary to medication is generally less malignant [14] than with other more common causes. Therefore, the recovery is rapid and without severe consequences, assuming the offending substance is identified and eliminated. Again, each case recovered rapidly. Fourth, the patient lacked hypertriglyceridemia and alcohol use, and the gallbladder was removed years earlier. Acetaminophen was the only other known medication she was taking intermittently that was associated with pancreatitis [15,16]. Fifth, the patient had 2 risk factors for drug-induced pancreatitis: being elderly and a female. Epidemiological data suggest that individuals are at higher risk for drug-induced pancreatitis if they are pediatric or elderly, female, and have advanced HIV infection and/or inflammatory bowel disease [5].

However, there are other elements that suggest no cause-and-effect relationship. ESI is frequently used to treat spinal pain, and no other case has been reported to date [11]. Also, it is possible our patient had chronic non-drug-mediated pancreatitis and coincidentally had a relapse. This is unlikely considering she was asymptomatic with a normal lipase result on admission. Unfortunately, we do not have an abdominal CT showing a normal pancreas in the interval from her cholecystectomy until her admission. In hindsight, there was no clinical suspicion she had chronic pancreatitis. Possibly, the patient had recurrent mild pancreatitis, but the abdominal pain was masked by the intermittent analgesic or even the ESI. In addition, she could simply have had recurrent pancreatitis from her previous ESI, but the implications are the same. The duration of effect of the ESI is 4 weeks and the analgesics were clustered sporadically, medically supervised, and coincided with episodes of severe back pain. Consequently, determining a temporal connection with any medication other than the ESI is difficult. Finally, it is possible she did not have pancreatitis at all. However, her nausea, abdominal pain, CT scan results, and lab work are diagnostic, even if her initial presentation was latent. An elevated WBC in the setting of prior steroid injection, elevated pro-calcitonin/CRP, and slightly elevated ESR pointed to an acute inflammatory change. Infectious etiologies were ruled out with normal sputum, blood, and urine cultures. She admitted to non-radiating epigastric abdominal pain, which was worse with intake of food. Her pain improved with narcotics per protocol, ruling out narcotic-induced pancreatitis. With a high suspicion for an intra-abdominal process, a CT was obtained, showing signs of pancreatitis. Testing revealed that lipase was elevated, confirming pancreatic involvement. The elevation of lipase was a sharp increase from the initial lipase result, which was within normal limits.

Conclusions

In conclusion, ESI appears to have a rare association with pancreatitis. The symptoms of pancreatitis may be mild and the disorder difficult to diagnose, especially in patients already dealing with the comorbidity of severe back pain. Patients who receive ESI should be informed to contact their health care provider if they develop characteristic symptoms of pancreatitis. Although benign, back pain is a long-term condition that may require repetitive ESI. As this patient was exposed to ESI 3 times, there may be a cause-and-effect relationship as the frequency of injections increases. For the physician, it is imperative to correlate clinical findings with the temporal relationship of ESI to avoid complications of pancreatitis. In addition, the health care provider can identify a high-risk group that may prone to ESI-related pancreatitis. Patients with previous pancreatitis, heavy alcohol users, and those having repeated ESI may be at risk and should be counseled accordingly.

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The relationship of ESI with drug-induced pancreatitis may be multifactorial and requires more thorough investigation than a case report.

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Conflict of interest

None.

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