

Spinal epidural abscess secondary to gram-negative bacteria: case report and literature review

Eric D. Van Baarsel^b, Yazeed Kesbeh^b, Huthayfa A. Kahf^b, Vandan Patel^b, Bruce Weng^a and Made Sutjita^a

^aDepartment of Internal Medicine, University of California, Riverside, CA, USA; ^bDepartment of Internal Medicine, Riverside University Health System, Riverside, CA, USA

ABSTRACT

Bacterial spinal epidural abscess (SEA) is a rare suppurative infection that commonly presents with nonspecific symptoms along with the infrequent triad of fever, back pain, and neurological deficits. Risk factors include diabetes mellitus, intravenous drug use, degenerative disc disease, infection with human immunodeficiency virus, and recent trauma or surgery. Patients with SEA often experience poor outcomes such as permanent neurological deficits, residual motor weakness, and even death. *Staphylococcus aureus* is the most predominant organism known to cause SEA; however, gram-negative bacteria are isolated in a small percentage of cases. Here we report three cases of SEA caused by gram-negative organisms. Each patient had identifiable risk factors known to increase the risk for SEA, and upon presentation had symptoms of SEA. Upon work up, the patients had positive cultures for gram-negative organisms and MRI imaging confirmed the presence of SEA. One patient made a full recovery while the other two cases resulted in permanent paraplegia. These cases stress the importance of considering SEA even in the presence of gram-negative infections, despite them being a rare cause. Furthermore, these cases emphasize the importance of broad-spectrum antibiotics that cover gram-negative bacteria in patients found to have risk factors along with symptoms of SEA.

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1. Introduction

Bacterial spinal epidural abscess (SEA) is a rare suppurative infection by which bacteria gain access to the epidural space through contiguous spread or haematogenous dissemination [1]. Diabetes mellitus (DM), intravenous drug use, alcohol abuse, infection with human immunodeficiency virus (HIV), degenerative joint disease, recent trauma or surgery, presence of spinal stimulators or catheters, and many other factors have been shown to confer risk for SEA [2–4]. Infection within the epidural space is thought to cause injury to the spinal cord by direct mechanical compression, interruption of arterial supply, thrombosis of veins, bacterial toxins, and inflammatory mediators [1,5]. The classic triad of SEA is back pain, fever, and neurologic deficits; however, this triad is rarely present and is only seen in as few as 8% of patients [2]. The combination of many potential risk factors along with many nonspecific symptoms makes it challenging to diagnose SEA, often resulting in poor clinical outcomes.

The incidence of SEA is estimated to be approximately 1.2 to 8.0 per 10,000 admissions and appears to be increasing [1–3]. *Staphylococcus aureus* is the most predominant pathogen isolated in SEA (approximately 57–65%); whereas gram-negative bacteria account for a significantly smaller portion of cases (approximately

13–16%) [6–8]. Despite the rare nature of gram-negative SEA, clinicians should still entertain the possibility of SEA in patients found to have gram-negative infections. This paper highlights the presentation and management of three different patients found to have SEA caused by gram-negative organisms.

2. Case presentation

Patient 1: A 51-year-old male with a past medical history of poorly controlled type II diabetes mellitus, hepatitis C (HCV), and osteomyelitis of the left middle finger due to *Enterobacter cloacae* requiring concurrent treatment with cefazolin and sulfamethazole-trimethoprim presented to the emergency department complaining of severe neck pain and stiffness for one day. Pain radiated to the lower back with an associated two-day history of nausea and vomiting. Patient denied headache, fever, or chills and was afebrile on presentation. Physical exam demonstrated paraspinal muscle tenderness which reproduced pain, but otherwise had a normal neurological exam. He had a normal white blood cell count (WBC) with a normal differential, but blood glucose was 355 mg/dL. Symptoms were attributed to an acute back strain and patient was discharged home.

Three days after initial encounter, he returned to the emergency department with progressive worsening of mental status for 2 days which was attributed to hepatic encephalopathy. Patient was afebrile with the following labs: WBC 10.9x10³/ul, neutrophil count 8.4x10⁹/L, glucose 430 mg/dL, lactate 2.14 U/L. A computed tomography (CT) head without contrast demonstrated no acute abnormalities. He was admitted to the hospital and started on cefepime. Initial blood cultures grew *Enterobacter cloacae* with the source thought to be from the patient's left middle finger osteomyelitis. During the hospital stay, his mental status improved and repeat blood cultures became negative after 3 days. On day seven of admission, however, the patient developed rapid onset bilateral lower extremity weakness and urinary retention. STAT magnetic resonance imaging (MRI) demonstrated a spinal epidural abscess spanning C5-C7 that was compressing the cervical cord (Figure 1). Inflammatory markers were found to be elevated with ESR 80 mm/hour and CRP 10.3 mg/L. Despite urgent laminectomy by orthopedic surgery, the patient developed permanent paraplegia and decreased hand strength bilaterally (Table 1).

Patient 2: A 77-year-old female with a past medical history of hypertension, poorly controlled type 2 diabetes mellitus, chronic kidney disease, and degenerative disc disease presented to the emergency department with a 3-day history of generalized weakness, fever, chills, and lower back pain. On presentation, she was also confused and hypotensive with a blood pressure of 90/58. Subsequent urinalysis showed leukocytes and the patient was empirically started on ceftriaxone for a complicated urinary tract infection (UTI). After cultures and sensitivity found extended spectrum B-lactamase (ESBL) *Escherichia coli* (*E. coli*), the patient was switched to ertapenem. On day three, the patient became septic and was admitted to the ICU for fluid resuscitation. The patient continued to have severe lower back pain which was attributed to her history of chronic back pain. Two days after completing the ertapenem

course, the patient developed progressive leukocytosis and repeat blood cultures returned positive for ESBL *E. coli* and she was subsequently restarted on ertapenem. Further workup and imaging by MRI revealed several small psoas abscesses that were too small to be drained. The patient's clinical condition improved upon completing 3 weeks of ertapenem and the patient was discharged home on oral ciprofloxacin.

Two months later, the patient presented with nausea, vomiting, generalized weakness, and severe constant lower back pain which radiated down the lower extremities bilaterally. The patient was afebrile and physical exam revealed tenderness to palpation over the lumbar spine. An urgent MRI revealed a ventral epidural abscess with osteomyelitis of the



Figure 1. T2 weighted sagittal MRI of the spine with gadolinium demonstrating a 4.0 × 0.3 × 1.7 cm anterior epidural fluid collection with peripheral enhancement compatible with epidural abscess spanning C5-C7. There is early suspected discitis and osteomyelitis at the C5-C6 level. The epidural collection compresses the cervical spinal cord resulting in cord edema at the affected levels.

Table 1. Summary of patient cases 1–3.

Patient no.	Age/Gender	Predisposing factors	Culture	Diagnosis	Symptoms	Antimicrobial agent	Surgery	Outcome
1	51 M	Poorly controlled type II DM, Chronic HCV, IV drug use	<i>E. cloacae</i>	Spinal epidural abscess spanning C5-C7	Neck pain, Bilateral lower extremity paralysis, Right upper extremity weakness, Left hand weakness	Cefepime	Yes	Permanent paraplegia, Decreased hand strength bilaterally
2	78 F	Poorly controlled type II DM, Degenerative disc disease, Chronic kidney disease	<i>E. coli</i>	Spinal epidural abscess spanning L2-L3 with osteomyelitis spanning L2-L4	Lumbar back pain, Fever	Ertapenem	No	Complete recovery with no neurological deficits
3	63 F	Degenerative disc disease	<i>B. fragilis</i>	Spinal epidural abscess spanning T6-T9	Bilateral lower extremity weakness and tingling, Urinary incontinence, Fecal incontinence	Ertapenem	Yes	Permanent paraplegia



Figure 2. T2 weighted sagittal MRI of the spine with gadolinium demonstrating 0.55 cm ventral epidural abscess at the level of L2-L3 with discitis osteomyelitis at L2-L3 and loss of height at the L2 and L3 vertebral bodies. Additionally, there is osteomyelitis of the posterior aspect of the L4 vertebral body.

posterior aspect of the L4 vertebral body (Figure 2). Labs demonstrated ESR 119 mm/hour and CRP 3.25 mg/L. The patient was started on ertapenem and had gradual clinical improvement over the next 7 days and had no neurologic deficits. After further evaluation by orthopedic surgery and infectious disease, the decision was made to defer surgical intervention due to the location of the abscess and her marked improvement of weakness and pain. The patient was discharged without any residual neurological deficits and was prescribed oral ciprofloxacin with close follow up with infectious disease (Table 1).

Patient 3: A 63-year-old female with past medical history of morbid obesity and degenerative disc disease presented with complaints of bilateral leg weakness and tingling beginning after standing up from a seated position that led to a fall at home. She reported new onset low back pain after falling along with urinary and fecal incontinence. On exam, the patient had positive Babinski reflex and negative anal wink. Lab work included urinalysis demonstrating 2–5 WBCs with positive nitrites. Vital signs, complete blood count with differential, and complete metabolic panel were all within normal limits. CT of the spine without contrast demonstrated multilevel degenerative disc disease without osseous abnormalities. A computed tomography myelogram of the spine showed poor visualization but no obvious cord compression lesion, but MRI was recommended to rule out a potential mass. The patient had to be

transferred to an outside facility for MRI secondary to morbid obesity.

Due to the requirement for outside facility MRI, it was not completed until 3 days after the initial presentation. MRI spine revealed spinal epidural abscess spanning from T6–T9. She was started on IV vancomycin, metronidazole, and ceftazidime. Additionally, labs were significant for ESR 101 mm/hour and CRP 12 mg/L. Neurosurgery immediately performed a T6–T9 laminectomy and decompression. Abscess fluid culture grew *Bacteroides fragilis* and she was treated with a 6-week course of intravenous ertapenem. Unfortunately, the patient's neurological deficits in the bilateral lower extremities did not improve and she was left with permanent paraplegia (Table 1).

3. Clinical symptoms and workup

It has been reported that clinical symptoms may progress in a stepwise fashion. Four distinct stages have been identified. The first stage typically includes back pain at the affected level of the spinal cord, fever, and spine tenderness. As the abscess grows in size and inflammation increases, symptoms progress to the second stage, which include radicular pain along the dermatomal distribution, nuchal rigidity, and hyperreflexia. The third stage occurs with continued growth of the abscess and prolonged damage to the spinal cord and includes hypoesthesia, bowel and bladder dysfunction, and weakness. The final stage takes place when irreversible damage has occurred to the spinal cord due to various pathologic mechanisms and leads to paralysis [9]. As such, it is crucial to have a high index of suspicion when patients complain of new-onset back pain.

As mentioned above, the classic triad of fever, back pain, and neurological symptoms can appear in as little as 8% of patients [2]. Back pain, however, has been reported in 70–100% of patients. Fever and neurological deficits are not as reliable as they are typically seen in approximately 50% of patients [4]. Atypical symptoms such as new-onset headache, malaise, and mental status change have also been noted [10].

Initial evaluation should include CBC, blood cultures, and inflammatory markers [2]. Elevated ESR has shown to be a sensitive marker for SEA. One study showed that 100% of patients had an ESR >20 mm/h [11]. When the index of suspicion is high for SEA, the gold standard for diagnosis is MRI. However, in situations where MRI cannot be performed due to patient factors or unavailability, CT scan with IV contrast may be used, though it is less sensitive [2,4].

Once imaging studies are done, it is necessary to get an aspirate of the abscess for further evaluation and culture. Lumbar punctures are not routinely

done for SEA, as they typically have a low diagnostic yield and can in fact be clinically detrimental when an SEA is present. Positive cultures in abscess aspirate, blood cultures, and lumbar puncture are 90%, 62%, and 19%, respectively [2].

4. Discussion

Due to the nonspecificity of symptoms associated with SEAs, clinical suspicion is often initially low, especially in the absence of neurological symptoms. In patients who present with septicemia as the source of the SEA, neurological symptoms often go unnoticed especially if the patient has altered mental status or is confined to bed during their hospital course. Increased duration of time between onset of symptoms and treatment has a significant impact on patient outcome by increasing the risk of developing permanent neurological deficits [12]. Irreversible paraplegia can occur in up to 22% of patients, residual motor weakness in up to 37% of patients, and 5% of cases result in patient death [1,8,13]. Therefore, SEA is both a surgical and medical emergency and prompt treatment is required to prevent significant morbidity and mortality.

The classic triad for SEA is back pain, fever, and neurologic deficits [2]. While the patients described herein did not have all three classical characteristics, they each had risk factors in their medical history, physical exam, and laboratory findings for SEA (Table 1). Diabetes mellitus has been cited as the most common risk factor associated with SEA which two of the three patients carried as a diagnosis in addition to other predisposing factors [2]. Additionally, all three of the patients had elevated CRP and ESR. One study demonstrated that 83 out of 83 patients with SEA had an elevated ESR > 20 mm/hour which is consistent with each patient described [11].

As seen in all three cases, CT was unable to visualize the abscesses; therefore, MRI with contrast (using gadolinium) is the diagnostic imaging of choice due to its sensitivity early in the course of the disease and its ability to provide the best visualization of inflammatory changes [14,15]. Despite these data and poor outcomes associated with SEA, clinicians should avoid over extensive screening for SEA with MRI. Interestingly, one study showed that MRI screening in ED patients suspected of having SEA actually yielded a diagnosis of SEA in less than 7% of patients [16]. This evidence along with the costs associated with MRI imaging demonstrates that widespread screening in patients with low suspicion of SEA is unfavorable.

After imaging, collection of abscess contents or blood cultures should be obtained as they are positive in 90% and 62% of cases, respectively. Clinicians should

be aware of the importance of covering gram-negative microbes when there is a high level of suspicion for SEA, despite gram negative bugs accounting for less than 16% of cases [5,6,17]. While blood cultures should be drawn prior to initiating antibiotic therapy, guidelines recommend initiation of empiric treatment prior to culture results or surgical intervention to avoid severe consequences [18]. The empiric regimen should treat staphylococci (including methicillin-resistant *S. aureus*), streptococci, and gram-negative bacteria. An appropriate empiric parenteral therapy can include vancomycin with either piperacillin-tazobactam or a third- or fourth-generation cephalosporin (e.g., cefotaxime or cefepime). If the causative pathogen is isolated, it is advised to deescalate the therapy according to culture sensitivities [4]. Although the duration of antibiotic therapy can vary on many factors, it should typically not be less than 6 weeks [19, 22]. A recent review concluded that a majority of studies advocated for early surgery because of the significant risk of morbidity and mortality associated with non-operative therapy, although some studies have also reported good outcomes with medical-only therapy [4,20]. Since there is dispute over the most appropriate treatment for patients with SEA, it is important for clinicians to tailor antibiotic regimen to culture results, be in communication with neurological or orthopedic surgery, and closely follow the patient's clinical course to help drive appropriate treatment.

The majority of SEAs are most often associated with *S. aureus*, yet blood cultures were positive for gram-negative bacteria in all three patients. Despite being a rare cause of SEA, patients with gram-negative infections, elevated inflammatory markers, and red flag symptoms including back pain, fever, and neurological deficits should warrant a high level of suspicion for SEA prompting immediate evaluation with MRI [2–4]. These cases highlight the importance of a prompt diagnosis, culture, and appropriate antimicrobial coverage to avoid catastrophic consequence in patients that suffer from SEA.

Disclosure statement

No potential conflict of interest was reported by the authors.

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