Epidural Abscess of the Central Nervous System

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An epidural abscess is a localized collection of purulent fluid between the dura mater and the overlying vertebral column (spinal epidural abscess) or skull (intracranial epidural abscess).1,2 Early diagnosis of epidural abscess is essential as without timely intervention neurologic injury with permanent sequelae can develop.3

SPINAL EPIDURAL ABSCESS

Epidemiology
Spinal epidural abscess (SEA) is more common than intracranial epidural abscess and is increasing in incidence. In 1975 the reported incidence of SEA was 0.2-2 per 10,000 hospitalized patients. Over the past four decades this has risen to 10-12 per 10,000 hospitalized patients in some referral centers.4–6 This increase is likely due to a rising number of patients with risk factors for SEA including intravenous drug use (IVDU), diabetes mellitus, advanced age, renal failure, and compromised immunity as well as degenerative spinal column disease and the growing use of therapeutic spinal interventions including instrumentation, injections, catheter placement and anesthetic procedures.7,8 The ongoing opioid epidemic in the United States has had a particular impact on the increased incidence of SEA given the risks of endovascular infection and metastatic seeding associated with intravenous drug use.9 The clinical utility of associated risk factors in the diagnosis of SEA in unclear, however, given their apparent absence in 20-50% of patients.10 Detection of SEA with the wide-spread availability of sensitive imaging modalities such as magnetic resonance imaging (MRI) has also improved diagnostic accuracy in recent decades.8

Pathophysiology
One-half of SEA infections are caused by hematogenous spread from a remote site of infection. Common sources include the skin, urinary tract, oral cavity, infection of an indwelling vascular access and endocarditis.3,5,11,12 Several regions of the spine may be involved in hematogenous infection. Hematogenous spread via the pelvic cavity’s venous drainage system which connects with those of the spine forming Batson’s plexus may facilitate infection from a urinary source.13 Contiguous extension of infection from osteomyelitis in an adjacent vertebral body or from a psoas or retropharyngeal muscle abscess or decubitus ulcer is estimated to account for up to one-third of infections.3,11 Vertebral body infection usually results from hematogenous seeding of the adjacent avascular disc space.12,14 Direct inoculation of the epidural space from spinal surgery, injection or catheter placement is another route of infection. Infection can be acquired during the procedure itself or from ascending microorganisms from the skin when a device is retained.5,15,16 Additionally, a hematoma secondary to osseous or ligamentous injury can become seeded by bacteria leading to SEA formation.5 In up to 30% of patients no source is identified.5,17,18 Neurologic impairment resulting from SEA is usually the result of spinal cord compression by the infected mass with possible contribution of vascular occlusion.19

Clinical presentation
Four stages of disease severity have been recognized in patients presenting with SEA.20 (Table 1) Presentation in stages I or II is more common, while greater residual deficit is found in those presenting in stages III or IV. Fever is present in 50–60% of patients while the classic triad of fever, back pain and neurologic deficits is seen in only a minority.21–23 Back pain, present in 95% of patients, with associated nerve root pain, radiculopathy and paresthesia may be the worst of a patient’s life, distinct from chronic back pain. Depending on

| Table 1. Symptoms of Epidural Abscess at Different Stages (adopted from (20)). |
|---------------------------------|-----------------|-----------------|-----------------|-----------------|
| Symptom                         | Stage I         | Stage II        | Stage III       | Stage IV        |
| Back or Neck Pain               | +               | +               | +               | +               |
| Radiculopathy                   | -               | +               | +               | +               |
| Weakness and/or Bladder Symptoms| -               | -               | +               | +               |
| Paralysis                       | -               | -               | -               | +               |

* Estimates from the original published data by Lee TH et al. Derivation and prospective validation of a simple index for prediction of cardiac risk of major noncardiac surgery. Circulation. 1999 Sep 7; 100(10):1043-9
# Risk estimates from Duceppe et al. Canadian Cardiovascular Society Guidelines on Perioperative Cardiac Risk Assessment and Management for Patients Who Undergo Noncardiac Surgery. These estimates were based on external validations published after the original study by Lee TH et al (1999).
sedimentation rate (ESR) are sensitive tests for the diagnosis of SEA and are usually elevated with an ESR >20 mm/h reportedly found in 95% of cases. Leukocytosis is also common, reported in 60–80% of cases. These tests are not specific for SEA. 5,10,26 Blood cultures should be obtained and may be positive in up to 60% of cases. 22,27

Imaging Studies

MRI with gadolinium is the imaging study of choice with a high sensitivity and specificity for detection of SEA (Figure 1b). Imaging the entire spine to exclude noncontiguous SEA is recommended. 28 MRI is also the study of choice for detection of vertebral osteomyelitis and/or discitis in patients presenting with back pain. 18,29 Comparison of T1 and T2 weighted contrast enhanced images is used in anatomic localization of SEA and to define the extent of infection including assessment for multi-level involvement. 30

Computed tomography (CT) with intravenous contrast is an alternative diagnostic imaging study with lower sensitivity and specificity than MRI.18 Myelography followed by CT scan is a highly sensitive study although an invasive procedure requiring exposure to ionizing radiation with a lower specificity than MRI. Myelography is usually reserved for patients who cannot undergo MRI. Spinal puncture for myelography should be performed distant from the area of suspected infection.5,17,18 Echocardiography is indicated in all cases of epidural abscess to exclude endocarditis.

Microbiology

Pathogen identification is very important for the diagnosis of SEA and are usually elevated with an ESR >20 mm/h reportedly found in 95% of cases. Leukocytosis is also common, reported in 60–80% of cases. These tests are not specific for SEA. 5,10,26 Blood cultures should be obtained and may be positive in up to 60% of cases. 22,27

Diagnosis

The diagnosis of SEA may be delayed with up to 75% of cases misdiagnosed on first presentation. Back pain, with a wide differential diagnosis, may be attributed to arthritis or muscular pain.7,10 Patients presenting with sepsis and/or altered mental status may be unable to provide a history.25 One series looking at 63 patients found that a correct diagnosis of SEA was made after 2 emergency room visits in 51% of cases, while a further 11% were identified on a third visit. This is significant as residual motor weakness was identified in up to 45% of the cohort who experienced delays vs 13% of those who did not.22 The increased incidence of SEA has not impacted this diagnostic delay.5,21 Recognition of SEA prior to the onset of neurologic symptoms is critical in patients who present with back pain. Diagnosis should be suspected based on clinical presentation and supported with testing. Definitive diagnosis of SEA requires drainage and culture.2

Laboratory Testing

Inflammatory markers including C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) are sensitive tests for the diagnosis of SEA and are usually elevated with an ESR >20 mm/h reportedly found in 95% of cases. Leukocytosis is also common, reported in 60–80% of cases. These tests are not specific for SEA. 5,10,26 Blood cultures should be obtained and may be positive in up to 60% of cases. 22,27

Table 2. Pathogens in Spinal Epidural Abscess

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Staphylococcus aureus</td>
<td>60–90</td>
</tr>
<tr>
<td>Gram-negative bacilli</td>
<td>10–15</td>
</tr>
<tr>
<td>Streptococcus species</td>
<td>10</td>
</tr>
<tr>
<td>Coagulase-negative staphylococci</td>
<td>3–6</td>
</tr>
<tr>
<td>Enterococci</td>
<td>1–2</td>
</tr>
<tr>
<td>Fungi</td>
<td>1–2</td>
</tr>
<tr>
<td>Anaerobes</td>
<td>1–2</td>
</tr>
<tr>
<td>Mycobacteria</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Polymicrobi</td>
<td>5–10</td>
</tr>
</tbody>
</table>

Based on references 1, 3–7, 15, 17, 18, 22, 23, 25

Figure 1a.

Figure 1b.
Sagittal T2 weighted MR image of the thoracic spine showing a mid-thoracic dorsal epidural abscess.
sample of the infected fluid should be obtained and sent for culture. Cultures for mycobacteria and fungi and serology for Brucella should be sent if epidemiologic or host risk factors are suggestive of atypical infection.\(^2,3\) As noted, blood cultures should be obtained and may be positive in up to 60% of cases.\(^{10,17,27}\)

Management

Prompt surgical decompression and abscess drainage is indicated in most cases of SEA to minimize neurologic injury and for control of sepsis. If there are focal neurologic changes, surgical debridement should be performed urgently.\(^5,7,10,33\) Over the past decade,
conservative management with antibiotics alone has become more common in patients without neurologic deficits who have an established causative pathogen confirmed either with an image-guided aspiration culture or a blood culture growing a virulent pathogen such as *Staphylococcus aureus*. The rate of failure with this conservative approach, however, is estimated to be 30–40% therefore necessitating close monitoring. Of note, while paraspinal and psoas abscesses and intradiscal spaces are routinely aspirated for microbiologic diagnosis, aspiration and/or drainage of SEA under CT guidance is a technical challenge and only dorsally located SEA without advanced bone destruction on MRI qualify for percutaneous drainage attempt.

As noted in the 2015 Infectious Diseases Society of America guidelines for Native Vertebral Osteomyelitis, empiric antimicrobial therapy should be withheld until after cultures from blood and other possible sources of infection have been obtained except in cases of sepsis or neurologic deficit. Empiric antimicrobial therapy should include coverage of staphylococci (including MRSA), streptococci and gram-negative pathogens. While the majority of cases of SEA are caused by gram-positive bacteria and therefore empiric coverage for gram-negative organisms may not be necessary in all cases, it is recommended and often implemented. VANCOMYCIN plus an third or fourth generation cephalosporin or carbapenem (Ceftazidime, Cefepime or Meropenem) is considered first line therapy with alternative coverage for gram-positive organisms including Daptomycin or Linezolid, and alternative coverage for gram-negative organisms includingAzactam or Ciprofloxacin.

Once a pathogen is identified, a course of targeted parental or highly bioavailable oral antibiotic therapy is recommended. (Table 3) While parenteral antibiotic therapy is typically preferred, especially in treating staphylococcal infection, a recently published randomized, non-inferiority trial found no difference in the treatment of a variety of bone infections including 39 cases of spinal infection some of whom had SEA, between standard parenteral therapy and an early switch (within 7 days) to oral antibiotic therapy. Any patient in whom there is a concern for meningitis should be treated with parenteral therapy dosed for CNS penetration for at least 2 weeks.

Recommendations for the duration of therapy for SEA range from 4 weeks to 3–6 months depending on many factors including the concurrent presence of endocarditis, vertebral osteomyelitis and/or retained spinal hardware. Vertebral osteomyelitis commonly occurs with SEA and is usually treated with at least 6 weeks of antibiotic therapy. Few randomized controlled trials (RCT) specifically focusing on the duration of antimicrobial therapy for SEA and/or vertebral osteomyelitis are available. An open-label, non-inferiority, RCT of 359 patients compared 6 weeks of antibiotic therapy to 12 weeks in patients with pyogenic vertebral osteomyelitis finding no difference in cure rate at 1 year. Information on outcomes with different antimicrobial regimens and durations is often derived from observational studies.

Some patients may be at higher risk for relapsed SEA and/or vertebral osteomyelitis including those with undrained paravertebral or psoas abscess, concomitant endocarditis, MRSA infection, IVDU, end-stage renal disease, or those with local spinal wound infection. In cases of infection in patients at risk for relapse or related to retained spinal implants extension of antimicrobial therapy (>8 weeks) can be considered. The optimal duration of sequential oral antibiotic suppression in spinal implant infection has not been established but has been shown to decrease the risk of relapse especially in early-onset infections (<1 month from fusion surgery). In delayed onset SEA infections associated with vertebral osteomyelitis, removal of hardware is associated with improved outcomes.

Patients with SEA should be followed to ensure response to therapy. A 25% improvement in ESR and CRP at 4 weeks of therapy in combination with improved clinical assessment should be anticipated. A failure of CRP levels to decline can be a poor prognostic marker. End of treatment imaging is not routinely recommended although a poor clinical response to therapy merits repeat MRI imaging and surgical evaluation.

**Outcome**

The most important predicting factor for neurologic outcome in SEA is the patient’s neurologic condition prior to surgical decompression. Patients presenting with stage III or IV infection show the worst recovery rate. An outcome of stable or improved neurologic function in comparison to the preoperative status is anticipated. Patients presenting with paralysis for up to 24–36 hours are expected to regain some neurologic function after surgery and this has been correlated with the rapidity of surgical intervention (within 24 hours). Patients may continue to regain neurologic function and will benefit from rehabilitation through the first year after treatment.

Mortality associated with SEA has declined significantly with the availability of advanced cross-sectional imaging, expanded surgical techniques and effective antibiotic therapy. Death usually results from severe sepsis. Approximately 5–7% of patients with SEA do not survive in the hospital and 90-day mortality is estimated at 135. The best outcomes in the management of SEA are achieved with multidisciplinary care.

**INTRACRANIAL EPIDURAL ABSCESS**

**Epidemiology**

The incidence of intracranial epidural abscess (ICEA) and its related mortality have decreased since the introduction of antimicrobial therapy. As ICEA can cross the dura via the emissary veins an accompanying subdural empyema is often present.

**Pathophysiology**

Intracranial epidural abscess (ICEA) can occur following trauma or after neurosurgery including craniotomy, transnasal or transmastoid procedures. Subdural empyema can also result from direct infection of the subdural space during these procedures. ICEA may also develop as a complication of sinusitis, otitis media or mastoiditis and this route of infection is more common in children and young adults. Valveless, bidirectional blood flow
between the frontal sinus mucosa and dural venous drainage is more common in children given their highly vascular diploic bone. Drainage empties into the superior sagittal sinus, increasing the risk of subdural extension.49,50 While longitudinal spread is common in SEA, ICEA without subdural empyema is usually a localized, slowly expanding lesion that rarely extends into the spinal column given the tight adherence of the dura around the foramen magnum.50

Clinical Presentation
Presentation includes fever and headache with variation in time to presentation. Concern for sinusitis and otitis media at presentation may distract from the appropriate diagnosis of ICEA. Periorbital cellulitis and frontal edema are commonly seen.2,3,51 ICEA without subdural empyema may present with insidious onset as the space between the dura and cranium is contained, limiting abscess expansion and delaying the development of focal neurologic changes.2 If a cranial subdural empyema is also present, however, deeper extension of the infection may lead to more rapid neurologic findings. Epidural abscess after neurosurgery can present with rapid progression given the risk of subdural involvement.3,52 With or without a subdural empyema, ICEA will eventually lead to neurologic changes without a subdural empyema, ICEA will

Microbiology
Common causative pathogens in ICEA arising after neurosurgery include Staphylococcus aureus, coagulase-negative staphylococci and gram-negative bacilli. Infection arising from the paranasal sinuses or ear is typically caused by aerobic and anaerobic Streptococcus spp., anaerobic gram-negative bacilli including Bacteroides spp., and S. aureus. While no one organism predominates in this setting, Streptococcus anginosus is common. Infection may be polymicrobial. Pseudomonas aeruginosa infection can arise from otitis media and fungal infection can arise from chronic sinusitis.3,50

Management
Given the risk of progression and neurologic deterioration in ICEA, surgical intervention should be undertaken at the earliest sign of worsened neurologic status. Combined neurosurgical and otolaryngologic approaches may be needed. Open or minimally invasive craniotomy for drainage of ICEA are options depending on the location and degree of bone involvement. Single burr hole drainage may be associated with recurrence. Craniolysis of the frontal sinus may be indicated in patients with ICEA secondary to frontal sinusitis.3,56

Patients presenting with a small ICEA can be treated with antimicrobial therapy with close observation and serial imaging to monitor response. Empiric antimicrobial therapy should target the anticipated pathogens causing ICEA including aerobic and anaerobic cocci and bacilli with adequate central nervous system penetration.3,50,51 Anti-microbial therapy should be tailored based on available microbiologic testing of abscess fluid with confirmation of antibiotic susceptibilities (Table 3).

Treatment duration for ICEA has not been established. Extended duration is typically preferred and can be extrapolated from the treatment of brain abscess with courses of 4–6 weeks often used including at least 2 weeks of parenteral therapy.43,50,57

Outcome
The availability of antimicrobial therapy and advances in neuroimaging have decreased morbidity and mortality from ICEA. Poor prognosis is associated with diagnostic delay in patients presenting with vague symptoms as well as brain herniation.2,3 The absence of severe neurologic deficits on presentation, minimal co-morbid conditions and young age are associated with improved outcomes.

REFERENCES