Published in final edited form as:

Am J Hosp Palliat Care. 2012 September ; 29(6): 493–496. doi:10.1177/1049909111429121.

Difficult Cases of Pain and Nonpain Symptoms in Intractable Spinal Infections: A Case Series

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Abstract

In the modern age of advanced surgical techniques and pharmacologic management, bacterial spinal infections (SIs) can be managed (either eradicated or suppressed) in many hosts. However, the optimal management of SIs may be limited by patient comorbidities, which do not allow for surgical management, or limited by antimicrobial options due to side effects, toxicities, or emerging drug resistance. In these settings, frank and honest discussion regarding risks and benefits of treatment should be pursued, including that the SI may be a terminal illness. In this case series, we present 3 patients who had bacterial SIs whose treatments were limited by the above-mentioned factors. Furthermore, each case presented challenges regarding optimal medical management of somatic and neuropathic pain associated with the SI.

Keywords

neurosurgery; spinal infection; osteomyelitis; pain; palliative care; end-of-life care

Introduction

Nontuberculous bacterial spinal infections (SIs) encompass infections surrounding the spinal column, usually occupying the epidural space, with or without diskitis or vertebral osteomyelitis. Spinal infections are usually due to hematogenous or contiguous bacterial spread from another source and are caused by *Staphylococcus aureus* in two thirds of cases.¹ In some cases, SIs are caused by iatrogenic interventional techniques aimed at treating pain, such as placement of epidural catheters or vertebroplasty.

The majority of studies support a combination of both systemic antibiotic therapy and surgical drainage/debridement as the treatment of choice, though some studies report

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Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

successful management with antibiotics alone in a subset of patients.^{1,2} Spinal infections may be treated with antibiotics alone when surgery is declined by the patient or contraindicated due to high operative mortality risk or other scenarios.¹ The primary aim of surgery is to remove the septic focus, obtaining culture to guide antibiotic therapy, and to prevent neurologic sequelae (eg, spinal cord compression).

Spinal infections, while relatively rare, represent a serious etiology of back pain, and pain is a presenting symptom in roughly three quarters of cases.^{1,3} In most cases, symptoms improve with successful treatment of the infection. If not treated successfully, complications may include uncontrolled disseminated infection or permanent neurologic damage including paralysis, spasticity, or severe pain.

Despite high incidence of pain with SIs, little has been published regarding management of pain and other symptoms associated with SIs, though case reports have noted patients with severe pain requiring intravenous (IV) opioid analgesia.⁴ In this series, we present 3 patients with refractory pain due to SIs, highlighting unique challenges common to the cases, and further discuss management strategies.

Case Series

Case 1

A 56-year-old woman was admitted to our hospital for back pain and leg weakness. Her medical history was complicated including end-stage renal disease on hemodialysis, insulin-dependent diabetes mellitus, severe coronary artery disease, peripheral vascular disease with resultant below-the-knee amputation, among other issues. Two months prior to admission, she developed persistent methicillin-resistant *S aureus* (MRSA) bacteremia despite treatment with IV vancomycin, and echocardiogram demonstrated mitral valve vegetation consistent with infectious endocarditis. Antibiotics were changed to daptomycin with clearing of peripheral blood cultures; but prior to completing the planned 6-week course of antibiotic therapy, she re-presented to our hospital with back pain and left leg weakness.

Spinal imaging revealed a multilevel thoracic ventral epidural abscess with vertebral discitis/osteomyelitis. Surgical intervention was planned but eventually canceled due to profound epistaxis during intubation (later attributed to thrombocytopenia) and her care team's estimation of high perioperative mortality risk. Percutaneous drainage of the abscess was attempted but only minimal fluid was amenable to aspiration due to viscous nature and anatomical location of the fluid. The MRSA in the peripheral blood was multidrug resistant or efforts to treat with other antibiotics were limited by toxicity. Daptomycin was switched to vancomycin plus gentamicin but further testing demonstrated intermediate sensitivity to vancomycin, and the patient was switched to linezolid with ertapenem for synergy. However, the patient developed progressive thrombocytopenia and linezolid was changed to dalbapristin/quinupristin.

Pain and nonpain symptom management was extraordinarily challenging. Prior to admission, the patient used only oral oxycodone as needed. On this admission, she required parenteral hydromorphone via patient-controlled analgesia (PCA), but titration was limited

by adverse effects including somnolence, respiratory depression, delirium, depressed mood, anxiety, and hallucinations. Opioid rotation was attempted to minimize side effects, and given renal insufficiency oxycodone was tried. The sedation lessened, but limitations remained regarding medication titration. Nonsteroidal anti-inflammatory medications were considered but due to previous respiratory distress and bleeding concerns, these were not started. Other adjuvant therapy including pregabalin and tricyclic antidepressants were considered but limited due to sedating effects.

Her pain continued to be severe and persistent for most of her hospitalization. Anesthesia pain and palliative medicine teams were consulted. Baclofen was substituted for cyclobenzaprine to minimize anticholinergic delirium, and low-dose haloperidol was used for agitated delirium. Methadone was considered but was not used due to long QT interval, concerns for prolonged sedation, and drug–drug interaction with many antimicrobials the patient received. Selective serotonin reuptake inhibitors were considered for depression and anxiety but were unsafe due to linezolid use and risk of serotonin syndrome. Despite these multiple adjustments, the patient's suffering remained severe and she remained resolute in maximally fighting her infection with aggressive medical measures.

During family care conferences, multiple teams discussed with the patient and her family the infection's incurable nature. Initially, her family opted for palliative sedation and withdrawal of dialysis to focus on comfort cares, but due to varying opinions by family members and subspecialty consultants, full life-sustaining treatments were continued despite the patient's incurable infection and intractable suffering. Ethics consultation was requested due to moral distress experienced by some staff, centered on need for beneficence and nonmaleficence in the setting of treatment of disputed efficacy and intense patient suffering.

The patient was transferred to the intensive care unit for monitored respite palliative sedation (as patient remained “full code”) after repeated and unsuccessful attempt for drainage. After respite sedation, pain control was slightly improved and allowed the patient to be transitioned from PCA to long-acting oral oxycodone. She was dismissed to a skilled nursing facility. Requests for transfer back to our facility for treatment of the infection were made, but there were no further therapies available to provide a survival benefit in this setting. The patient died 1 month after hospital discharge at a local institution and details surrounding sedation needs at the end of life are unknown.

Case 2

A 49-year-old man was admitted to our hospital with back and leg pain. His medical history included nonalcoholic steatohepatitis with cirrhosis, coronary artery disease, insulin-dependent diabetes mellitus, obstructive sleep apnea, and morbid obesity. One month prior to admission, he had presented to outside facility with severe back pain and fever resulting in hospital admission. During that hospitalization, blood cultures demonstrated methicillin-susceptible *S aureus* (MSSA) bacteremia as well as a sacral decubitus ulcer. Prior to awareness of this bacteremia, the patient underwent lumbar vertebral kyphoplasty for control of back pain in the setting of spinal compression fracture. After the procedure, the patient developed escalating back pain without symptoms of neurologic compromise and was transferred to our institution for pain control and evaluation. At that time, imaging

demonstrated ventral lumbar and sacral epidural abscess surrounding the kyphoplasty cement. Imaging-guided biopsy and culture confirmed MSSA. Orthopedic spine surgery felt the patient was a poor surgical candidate, given his extensive comorbidities. He was treated conservatively with IV cefazolin and external back brace for spine stabilization and dismissed to a skilled facility.

Two months later, he developed progressive lower extremity weakness resulting in declining functional ability. Imaging showed progression of the epidural abscess with osteomyelitis resulting in increased central spinal canal stenosis. Surgery again was deferred, given marked concerns of high perioperative mortality risk, and the patient was switched to IV ertapenem and was followed as an outpatient. He was offered a second opinion regarding surgery, and anterior debridement of infection was offered if the patient's multiple medical comorbidities could be optimized. Shortly prior to his planned operation, the patient canceled the procedure due to his concern regarding surgical mortality risk. At his most recent follow-up 6 months after hospitalization, he continued to receive daily IV ertapenem with no plan for discontinuation.

Pain and symptom management were challenging throughout the illness trajectory given the patient's comorbidities (most notably, hepatic cirrhosis). From hospitalization to initial follow-up, he was treated with a combination of long- and short-acting oxycodone, transdermal fentanyl, hydromorphone, amitriptyline, and gabapentin. After hospitalization, sedation and suboptimal pain control led to outpatient palliative medicine evaluation. This resulted in greater continuity of care and consolidated decision making regarding pain and quality of life issues. Given multiple opioids being utilized, his regimen was consolidated to oral methadone for long-acting therapy with oral hydromorphone for breakthrough control. Both medications required dose titration and frequency reassessment to optimize dose, but prolonged QT interval made concerns of escalating methadone further a concern. To this end, oral keta-mine was added as an opioid-sparing adjuvant and was utilized with success. This combination resulted in less frequent bouts of uncontrolled severe pain and less somnolence.

Additionally, the patient developed myoclonus, likely related to hydromorphone (approximately 120 mg orally per day). Titration of methadone and ketamine enabled decreased reliance on hydromorphone, resulting in the resolution of myoclonus. Given his active infection, he was not deemed to be a candidate for spinal cord stimulator or implantable drug delivery system. Adjuvant infusional lidocaine was considered but had not yet been required. Previously, the patient was receiving cyclobenzaprine and occasional low-dose, ultra-short acting benzodiazepines (eg, alprazolam) for back spasms. Low-dose baclofen proved minimally effective for muscle spasms as well but control remained suboptimal. As these agents likely contributed to sedation, were ineffective, and were less safe, they were discontinued, given the patient's cirrhosis.

Case 3

A 50-year-old male presented for evaluation of severe pain. He had had long-standing Crohn disease with a diverting colostomy 28 years ago, and chronic MRSA sacral osteomyelitis due to crush injury trauma (legs/spine) approximately 8 years ago. He had previously

undergone a sacrectomy and proctectomy and then completed 6 months of IV vancomycin, followed by linezolid. Pain control remained suboptimal with transdermal fentanyl and high-dose oxycodone, so the patient was started on oral methadone, initially with benefit. He was later admitted to the hospital with concerns for methadone overuse and a prolonged QT interval.

A normal QT interval was observed on telemetry, but pain scores at “9 of 10” were reported despite methadone 30 mg orally every 8 hours and hydromorphone 12 mg orally every 3 hours. Computed tomography scans demonstrated a new fluid accumulation near the iliopsoas muscle, so the patient was taken to the operating room for debridement and cultures. He was started on vancomycin, imipenem-cilastatin, rifampin, and caspofungin empirically. Subsequent magnetic resonance imaging demonstrated that the osteomyelitis had spread to L5, sacrum, bilateral sacroiliac joints, and iliac bones despite appropriate antibiotics. Multiple surgery consultations ensued and the patient was offered a hemi-corpectomy as a way to remove the infected vertebrae and tissue. After much discussion with his family, staff psychologists, and chaplain, he decided to elect for antibiotics and comfort cares first.

The patient's pain was extremely difficult to control. On admission, he was started on an IV hydromorphone PCA at 6 mg/h basal with a 3 mg PCA dose, which brought the pain to 7/10. Despite acknowledging potential risk of infection or central nervous system seeding, an epidural catheter was placed in an attempt to optimize pain control. Epidural bupivacaine, morphine (then hydromorphone), and clonidine were used to control his pain but significant pain remained. An intrathecal (Du Pen) catheter was placed by the neurosurgery team to allow long-term neuroaxial access, to allow for addition of baclofen for spasticity, and to potentially deliver higher concentrations of medications. Near the time of death, the intrathecal pain regimen consisted of preservative-free morphine 8 mg/h, clonidine 2 mcg/h, bupivacaine 0.25% at 8 mL/h, and baclofen 1 mcg/h. His IV hydromorphone PCA was at 10 mg/h with 10 mg PCA dose every 6 minutes and 20 mg boluses every hour as needed as well as ketorolac. Methadone via PCA was tried but resulted in delirium and sedation. Ketamine and lidocaine IV infusions were tried with no effect.

Additionally, despite maximum antimicrobial therapy directed by infectious disease specialists, the patient clinically declined and developed sepsis characterized by extreme delirium, myoclonus, and refractory pain. This only partially responded to IV midazolam and phenobarbital. After much discussion about goals of care with the family, the patient was started IV propofol for palliative sedation. He died 96 hours later in our palliative care unit.

Autopsy confirmed dense connective tissue surrounding the cauda equina, inflammation around the lower cord, neurogenic bladder, splenomegaly due to sepsis, and an extensive abscess from the iliopsoas muscle to the prostate bed. The cause of death was ruled uncontrolled sepsis from MRSA osteomyelitis resistant to debridement and antibiotics.

Discussion

This case series highlights the unique challenges in the treatment of SIs and associated symptomatology. Each case demonstrates challenges with long-term antimicrobial management (eg, emergence of multi-drug resistant pathogens) as well as difficulty in achieving infection control without successful surgical debridement.

All 3 patients discussed had multiple medical comorbidities that limited their surgical candidacy and compromised their functional status, essentially rendering their infections as terminal conditions. Similar cases are likely to arise given the increasingly aged, debilitated population and growing prevalence of obesity-related diseases (eg, diabetes). These cases require multidisciplinary case management and can prove costly and burdensome to patients and the health care system. We emphasize the need to tailor care in similar cases to the patient's goals, with particular attention to effective communication of prognosis, goals of care discussions, and reasonable expectation setting.

In the era of modern medicine, bacterial infections are rarely publicly considered as terminal illnesses, and expectation for cure is the norm for most patients. Communication of the terminal nature of incurable SI with both patients and consulting services is essential but potentially difficult. In case 1, differing opinions were held by involved consulting services regarding estimated prognosis and treatment options, which created some distress for the patient, her surrogates, and some care providers. Although these cases represent extreme examples, they emphasize the basic importance of palliative medicine experts to help guide patients and primary services through these discussions to find mutually agreeable care plans. Understanding viable treatment options aids with prognostication, goal setting, and formulation of care plans that are acceptable and realistic for the patient and care teams.

In navigating goals of care discussions in intractable infections, it is important to consider that each individual patient and his or her surrogate decision makers must weigh the perceived burdens and benefits of care options including lifelong antibiotics, surgical drainage/debridement (if available), the withdrawing or withholding of life-sustaining measures, and palliative therapy alone, with palliative sedation representing the extreme on this care spectrum.⁵ Goals of care may shift over time through disease progression, and the burdens of comorbid conditions may also alter patient goals.

In these cases, pain management was challenging, consistent with somatic and neuropathic pain with a spinal source. Efficacy of opioids in neuropathic pain varies and adjuvants should be considered with each case. While ketamine proved to be a useful adjuvant in case 2, it was not beneficial in case 3. This approach can be considered for similar cases, if consistent with patient goals. Regardless, palliative sedation with IV benzodiazepines, barbiturates, or sedative hypnotics (like propofol) may be necessary for refractory pain at the end of life.

Conclusions

Despite major advances in surgical and pharmacologic management of SIs, medical comorbidities, poor functional status, and inability to tolerate antimicrobials due to toxicity

or acquired drug resistance may limit treatment options. Regardless of potential treatment options, the need for appropriate prognostication, ongoing iterative goals of care discussion, and clear expectation setting can promote optimal outcomes in otherwise difficult situations.

Acknowledgments

Funding

The authors received no financial support for the research, authorship, and/or publication of this article.

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