

State-of-the-Art Review: Diagnosis and Management of Spinal Implant Infections

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Spinal implant infections are a serious complications of instrumented spinal fusion surgeries, carrying high morbidity and complex management challenges. Early postoperative infections may manifest with wound-healing issues, back pain, and fevers. Magnetic resonance imaging (MRI) is the preferred imaging modality, but can be limited by metal artifacts. For cases with stable implants, surgical debridement with implant retention combined with at least 12 weeks of antibiotics is currently considered appropriate treatment. Staphylococcal infections are ideally treated with biofilm-active antibiotics. Suppressing antibiotic therapy can be considered when surgical debridement has been delayed or is incomplete, and for those who are poor surgical candidates for another surgery. Chronic infections may present insidiously with implant failure or pseudarthrosis; implant removal or revision is generally pursued. As current guidance is heavily based on the periprosthetic joint infection literature and low-level studies on spinal implant infections, further research on optimizing diagnostic and treatment approaches is needed.

Keywords. spinal fusion; surgical site infection; biofilm; antimicrobial therapy; implant retention.

Instrumented spinal fusion surgeries are frequently used to treat various spinal disorders, ranging from degenerative diseases to fractures secondary to trauma and malignancy. While these procedures improve quality of life, they are not without complications. Infection associated with spinal implants is particularly concerning due to the potential for severe morbidity and complex management. These infections pose significant health risks to patients and burden healthcare systems due to extended hospital stays, the need for additional surgeries, and the long-term antibiotic treatment they often necessitate [1, 2].

This review focuses on peri-implant infections associated with instrumented spinal fusion surgeries. It does not cover superficial surgical site infections (ie, above the fascia). It also does not cover infections related to spinal stimulators, devices typically implanted to manage chronic pain. Two illustrative cases of spinal implant infections (SIIs) that infectious diseases clinicians might encounter in their practice are presented to highlight key clinical and diagnostic features of SIIs, including principles of management. Given the scarcity of high-quality

studies specific to SIIs, much of the current guidance is extrapolated from the periprosthetic joint infection (PJI) literature and low-level studies on SIIs. We sought to provide useful guidance and expert interpretation of the best-available evidence through a multidisciplinary perspective.

EARLY POSTOPERATIVE INFECTIONS

A 69-year-old female with foraminal stenosis and degenerative listhesis underwent an L4/5 laminectomy and transforaminal interbody fusion. A week after surgery, she presented to the emergency department due to fever, worsening back pain, and radiculopathy. Blood tests showed a C-reactive protein (CRP) level of 250 mg/L (normal, <5 mg/L). Magnetic resonance imaging (MRI) revealed a rim-enhancing fluid collection at the level of the laminectomy with extension into the epidural canal (Figure 1). The fluid collection was aspirated; culture of the aspirate grew penicillin-susceptible *Staphylococcus lugdunensis*. Subsequently, thorough surgical debridement and laminectomy of L2 was performed. Multiple intraoperative cultures were positive for *S lugdunensis*, and the patient was started on intravenous (IV) benzylpenicillin at 12 million units every 24 hours for 2 weeks. Oral levofloxacin 500 mg plus rifampin 450 mg twice a day were then administered for an additional 10 weeks. Three months after completing the antibiotic treatment, CRP had normalized and the patient was pain-free.

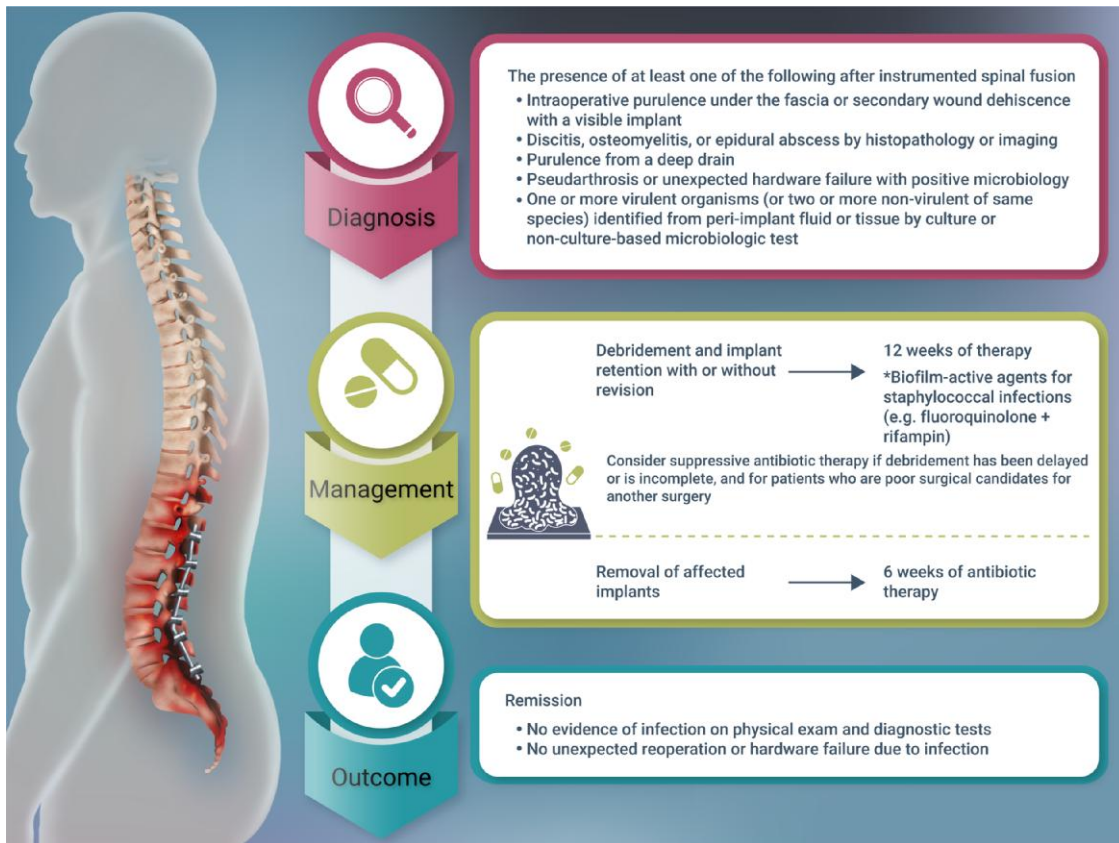
This case illustrates early postoperative SII. While some authors consider infections occurring within 6 weeks as early infections [4, 5], we consider a time frame up to 90 days as early-onset, in line with the National Healthcare Safety

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Network [3]. Symptoms include worsening back pain, wound drainage or dehiscence, fever, and other systemic manifestations [6]. However, these are not specific to SII. Distinguishing physiological wound drainage from infection is challenging. Wound drainage within 2 weeks can be normal, and is more likely to represent infection if it persists longer [7, 8]. Infection typically begins in the posterior part of the spine (ie, posterior epidural space, operative site such as laminectomy area, back/neck muscle, subcutaneous tissue), from which it may spread anteriorly (ie, anterior epidural space, paravertebral space, intervertebral disc space, vertebral body, prevertebral space) [9].

The initial workup of patients suspected of early SII should include plain radiography to assess implant location and integrity, fusion status, and spinal stability [10]. This is a relatively low-cost and accessible imaging modality but provides insufficient assessment of soft tissues. Therefore, it is of limited value for diagnosing and assessing the extent of infection [10]. MRI is currently the imaging modality of choice for diagnosis of non-implant-associated spinal infections due to its high sensitivity and specificity [11, 12]. However, these metrics cannot be extrapolated to SII due to metal artifacts and postoperative changes that affect diagnostic performance; it is hard to predict how much the images will be degraded by the implant artifacts.

There are limited data on the accuracy of MRI in early postoperative SII [13–15]. One study showed that the sensitivity and specificity of MRI in these types of infections were 71% and 83%, respectively [16]. The presence of deep infections, such as osteomyelitis or abscesses beneath the fascia, is diagnostic of SII (Box 1).

Surgical debridement is necessary for SII according to the Spine Working Group of the Second International Consensus Meeting on Musculoskeletal Infection [17]. Aggressive debridement with implant retention is an acceptable treatment strategy for early infections with stable implants [17]. While some surgeons choose to replace the implants during the operation, it is unclear if this improves patient outcomes. With regard to bone grafts placed during the index surgery, there is no direct evidence comparing bone graft removal with retention at debridement. However, most experts suggest that loose bone grafts be removed [17, 18]. This recommendation is based on the theoretical concern that unincorporated bone grafts lack a blood supply and may therefore be a nidus for infection.

Identifying the microorganism(s) responsible for infection is critical in the optimal management of SII. Empiric antibiotic treatment of postoperative wound drainage without surgical intervention is not advised. In a study of patients who called

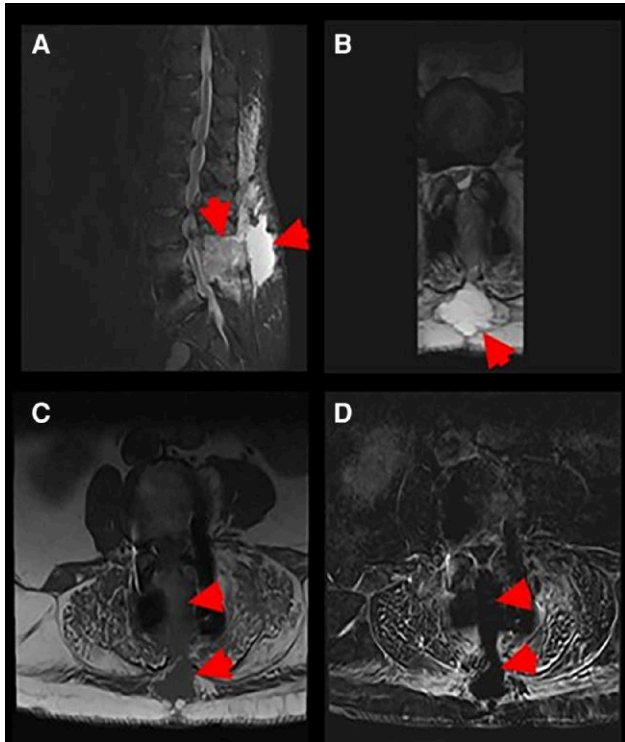


Figure 1. MRI findings in early postoperative infections. Sagittal STIR (A), axial T2-weighted (B), axial unenhanced T1-weighted (C), and axial subtraction contrast-enhanced T1-weighted (D) images show a localized fluid collection posteriorly in the soft tissues at the L4/L5 level and a non-liquified collection more anteriorly. There is mild surrounding contrast enhancement. Abbreviations: MRI, magnetic resonance imaging; STIR, short tau inversion recovery.

their treating physician with non-purulent postoperative wound drainage without systemic symptoms, an antibiotic prescription did not reduce the incidence of surgical intervention or the development of infection [8]. Therefore, if a patient is hemodynamically stable, antibiotics should be withheld until surgical intervention can be performed and deep specimens collected for aerobic and anaerobic bacterial cultures. Based on data in PJI, to maximize culture yield, at least 3 tissue or fluid specimens should be collected for aerobic and anaerobic bacterial cultures if inoculated in blood culture bottles, or 4, if routine plate and broth cultures are used [19]. In addition to bacteria, tissue or fluid culture in blood culture bottles will recover *Candida* species [20]. Special cultures for fungal and mycobacterial etiologies should not be routinely performed, as these infections are exceedingly rare [20, 21]. Isolation of a virulent bacteria such as *Staphylococcus aureus* from deep specimens is diagnostic of SII. Nonvirulent bacteria, such as coagulase-negative staphylococci, may be considered clinically significant and pathogenic if isolated in multiple specimens.

Among hemodynamically unstable patients, empiric antibiotic therapy should cover gram-positive bacteria, including

Box 1. Suggested Diagnostic Criteria of Spinal Implant Infection^a

The presence of at least one of the following criteria after instrumented spinal fusion:

- Intraoperative purulence under the fascia or secondary wound dehiscence with a visible implant
- Discitis, osteomyelitis, or epidural abscess by histopathology or imaging (eg, computed tomography, magnetic resonance imaging, positron emission tomography)
- Purulence from a deep drain
- Pseudarthrosis or unexpected hardware failure with positive microbiology
- One or more virulent organisms identified from peri-implant fluid or tissue by culture or non-culture microbiologic test
- Two or more identical non-virulent organisms identified from peri-implant fluid or tissue by culture or non-culture microbiologic test

^aAdapted from the National Healthcare Safety Network (NHSN) surveillance definition for surgical site infections during spinal fusion surgeries [3].

Note: These suggested criteria have not been validated and should be considered guidance rather than strict rules. Clinical judgment remains crucial in diagnosis. The studies discussed in this review used different definitions of spinal implant infection, underscoring the need for standardization in future research to facilitate more consistent comparison and analysis of outcomes.

methicillin-resistant *S aureus* [22]. The proportion of infections with gram-negative bacteria can be as high as 19%, particularly in infections involving the lumbosacral region [23, 24]. Therefore, expanded coverage is also reasonable. Once culture and susceptibility results are available, antibiotic therapy should be tailored accordingly. The definitive antimicrobial regimen should be guided by microbial etiology, antimicrobial susceptibility patterns, and patient-specific factors. Table 1 shows the most frequently isolated pathogens and suggested antibiotic treatments [4, 25].

The route of antibiotic administration depends upon several factors, including severity of infection, association with other infectious syndromes, and comorbidities. Intravenous administration is typically initiated due to its rapid onset of action and predictable pharmacokinetics. Oral antibiotics are a viable option for completion of therapy. The Oral versus Intravenous Antibiotics for Bone and Joint Infection (OVIVA) trial demonstrated the effectiveness of this approach, although a small minority of the study population had SIIs [26]. The choice of oral therapy depends on the availability of bioavailable drugs and patients' gastrointestinal function. Furthermore, agents

Table 1. Frequently Isolated Pathogens in Spinal Implant Infections Based on Timing From Surgery and Suggested Antibiotic Treatment

Timing	Microorganisms	Intravenous Antibiotics ^a	Oral Antibiotics ^a
Early postoperative infections	<i>Staphylococcus aureus</i> , <i>Staphylococcus epidermidis</i>	Cefazolin 2 g every 8 h	Ciprofloxacin 750 mg 2x/d or levofloxacin 500 mg 2x/d with rifampin 600 mg/d
		Nafcillin/oxacillin 2 g every 4 h	Clindamycin 600 mg 3x/d
	<i>Streptococcus</i> species	Vancomycin target AUC 400–600 mg*h/L	Doxycycline or minocycline 100 mg 2x/d
		Dalbavancin 1500 mg every 2 wk	TMP-SMX (20 mg/kg/d TMP component)
Chronic infections	<i>S epidermidis</i>	Daptomycin 8–12 mg/kg/d	Cefadroxil 1 g 2x/d
			All preferably in combination with rifampin
	<i>Cutibacterium acnes</i>	Benzylpenicillin 24 million units/d	Amoxicillin 1 g 3x/d
		Ceftriaxone 2 g/d	
Chronic infections	Gram-negative bacteria	Ceftriaxone 2 g/d	Ciprofloxacin 750 mg 2x/d
		Cefepime 2 g every 12 h	TMP-SMX (20 mg/kg/d TMP component)
	<i>Enterococcus</i> species	Ertapenem 1 g/d	
		Meropenem 1 g every 8 h	
Chronic infections	<i>S epidermidis</i>	Ampicillin 2 g every 4 h	Linezolid 600 mg 2x/d
		Vancomycin target AUC 400–600	Tedizolid 200 mg/d
	<i>Cutibacterium acnes</i>	Dalbavancin 1500 mg every 2 wk	Amoxicillin 1 g 3x/d
		Daptomycin 8–12 mg/kg/d	
Chronic infections	<i>S epidermidis</i>	Cefazolin 2 g every 8 h	Ciprofloxacin or levofloxacin 750 mg 2x/d with rifampin 600 mg/d
		Vancomycin target AUC 400–600	Clindamycin 600 mg 3x/d
	<i>Cutibacterium acnes</i>	Dalbavancin 1500 mg every 2 wk	Doxycycline or minocycline 100 mg 2x/d
		Daptomycin 10 mg/kg/d	TMP-SMX (320 mg TMP component) 2x/d
Chronic infections	<i>S epidermidis</i>		Cefadroxil 1 g 2x/d
			Amoxicillin 1 g 3x/d
	<i>Cutibacterium acnes</i>	Benzylpenicillin 24 million units/d	Doxycycline or minocycline 100 mg 2x/d
		Ceftriaxone 2 g/d	Cefadroxil 1 g 2x/d

Monomicrobial infections represent 60% of early infections, while 25% are polymicrobial and the rest are culture-negative. Infections with gram-negative bacteria and *Enterococcus* species are common in surgeries involving the lumbosacral region (20% of cases). The percentages presented are approximations derived from the various studies cited. Precise figures are unavailable due to inconsistent definitions of infection timing across studies, mixing of early and late infection cases in some reports, and inclusion of data from non-instrumented spinal fusion surgery alongside instrumented cases.

Abbreviations: AUC, area under the receiver operating characteristic curve; TMP-SMX, trimethoprim/sulfamethoxazole.

^aOral β -lactams are reasonable options but may have low bioavailability. Rifampin was reported to interact with doxycycline and TMP-SMX but the clinical impact of this is unclear. The antibiotic dosages provided assume normal kidney function. Adjust doses for patients with impaired kidney function. Some papers have recommended doses of up to 960 mg TMP component 3x/d for TMP-SMX. These are select antibiotic regimens and do not constitute an exhaustive list.

with activity against biofilms are preferred if the implant is retained. A retrospective study of *S aureus* SII showed that recurrence rates were lower in patients who were treated with a rifampin-containing regimen [27]. Another study showed that biofilm-active antibiotic regimens were associated with improved treatment compared with regimens without biofilm-active antibiotics [28]. These studies included a heterogeneous patient population with varied surgical and medical management approaches. The results are most likely confounded by indication bias. Despite a low level of evidence, the benefits of improved treatment success probably outweigh the risks of antibiotic side effects. Antibiotics considered to exhibit antibiofilm activity in vitro include fluoroquinolones, tetracyclines, daptomycin, and fosfomicin [29]. However, clinical studies have mostly focused on fluoroquinolones and rifampin [28, 30, 31].

The optimal duration of antibiotic therapy remains a subject of debate. In patients whose affected implants have been explanted and in whom there are no associated abscesses, 6 weeks of therapy is sufficient consistent with treatment of native vertebral osteomyelitis [32]. For SIIs managed with implant retention, most studies use approximately 12 weeks of therapy [22, 23, 33]. Some studies suggest that fixed durations of up to 12 weeks are sufficient, while 1 study noted that suppressive

antibiotic therapy (SAT) up to a year improved outcomes [5, 34–37]. Perhaps the best evidence for the duration of therapy for implant-associated infections managed with implant retention is the Duration of Antibiotic Treatment in Prosthetic Joint Infection (DATIPO) trial for PJI, which showed 6 weeks to be not noninferior to 12 weeks of therapy [38]. Adapting results of this trial to SIIs, antibiotic therapy should be administered for a minimum of 12 weeks. Further research is needed to define the optimal duration of therapy for SIIs managed with implant retention, including the need for SAT. Risk factors for treatment failure remain unclear, making it difficult to identify patients who might benefit from SAT [22, 39]. While there is no strong evidence for routine SAT, we suggest that SAT be considered when surgical debridement has been delayed for several weeks, surgical debridement was not performed or was incomplete, and for those who are poor surgical candidates for another surgery.

The success rate of implant retention as treatment of SII ranges from 71% to 73% at 1 to 2 years. Most papers define success as implant survival without the need for further revisions [5, 7, 40, 41]. We prefer the term “remission” over “cure” to describe treatment success, as no diagnostic test can definitively rule out persistent infection when the implant is retained. Patients should be counseled as to warning signs of infection

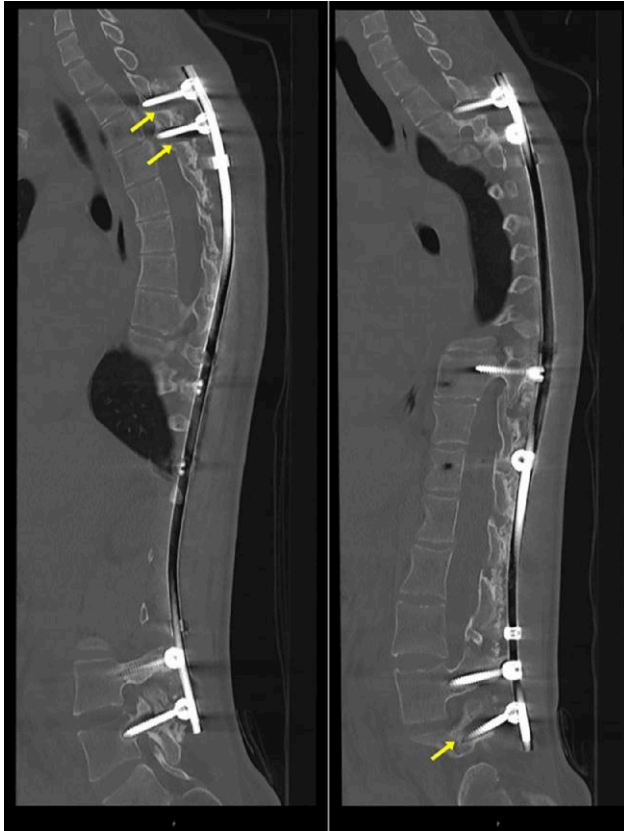


Figure 2. CT-scan findings in chronic spinal implant infection. Sagittal CT images showing diffuse osteolysis around the T3, T4, and L5 pedicle screws (arrows), in keeping with either aseptic mechanical loosening or infection. Abbreviation: CT, computed tomography.

recurrence, such as worsening neck or back pain, new weakness or numbness at the affected area, or unexplained fever (Box 2). Furthermore, clinicians should consider infection when there is pseudarthrosis or unexpected hardware failure. There is no literature investigating the utility of follow-up imaging of patients with SII. In studies involving patients with native vertebral osteomyelitis, follow-up imaging had poor correlation with clinical status and is therefore not recommended [42]. Repeating imaging is recommended in certain clinical situations, such as residual abscess or when persistent infection is suspected.

CHRONIC SPINAL IMPLANT INFECTIONS

A 28-year-old male presented with chronic upper back pain. He had undergone spinal fusion from T3-L4 for scoliosis 5 years before presentation. Computed tomography (CT) scan showed loosening of multiple screws and migration of screws towards the spinal canal in the upper thoracic spine (Figure 2). Scintigraphy and CRP were normal. He underwent complete removal of the spinal implant due to suspected aseptic mechanical

Box 2. Key Talking Points With Patients

Acquisition

- Discuss the rate of surgical site infection according to national data and available literature
- Emphasize that no one is to blame for infection
- Sample question and answer:
 - How did I get the infection?
 - While we take every precaution to prevent infection, a small percentage of cases (~3%) may still develop an infection despite our best efforts. This is not due to negligence or fault on anyone's part, but rather an unfortunate risk that comes these invasive surgical procedures. Research is ongoing to determine how to lower this risk, but at the current time, this is what can be achieved.

Diagnosis

- Highlight criteria in diagnosis of infection
- Talk about the microorganism(s) found in cultures
- Sample question and answer:
 - My cultures are negative, does that mean I don't have an infection?
 - We rely on multiple sources of information, including test results and what we observed during the operation itself. It's important to note that cultures may come back negative even when an infection is actually present.

Treatment

- Avoid using the term “strong” in describing antibiotics; focus on appropriate antibiotics regardless of route
- Emphasize the minimum duration of therapy and the importance of adherence; avoid saying “forever” for treatment duration
- Sample question and answer:
 - How long will I be on antibiotics?
 - At the current time, the typical course of antibiotic treatment for this type of infection is at least 12 weeks. Based on current medical research, there is little evidence that extending antibiotic therapy beyond 12 weeks provides additional benefit in most cases. However, every patient is unique.
 - Depending on your specific circumstances and how you are responding to treatment, continuing antibiotics for longer than 12 weeks may be recommended.

Follow-up

- Introduce the concept of remission and instruct the patient to contact their treating physician if they experience symptoms of possible recurrence
- Educate patients on the limited utility of diagnostic tests in predicting recurrence or ruling out persistent infection
- Sample question and answer:

Box 2. Continued

- Am I cured? Should we repeat the tests to see if the infection is gone?
- Your infection is in remission. Unfortunately, no available imaging or blood tests reliably detect residual infection. However, we may use tests to monitor for recurrence of infection.

failure. Histopathology showed chronic inflammation with fibrosis but without neutrophils. Five days later, all 7 intraoperative cultures grew *Cutibacterium acnes*. He was treated with 6 weeks of oral amoxicillin and had no pain or recurrent findings of infection in 5 years of follow-up.

This case illustrates chronic infection. This type of SII typically presents with indolent pain, pseudarthrosis, and implant failure [43]. Diagnosis may be through unexpected positive intraoperative culture findings during presumed aseptic revision surgery [44]. While a proportion of chronic SIIs are diagnosed incidentally, infection is increasingly suspected preoperatively in cases of hardware failure and pseudarthrosis. The true incidence is unknown as there are no large, comprehensive epidemiologic studies. However, a systematic review revealed the prevalence of occult infection to be approximately 24% [44]. Patients who undergo instrumented spinal fusion for scoliosis at a young age seem to be at risk of occult infection as cause for hardware failure or pseudoarthrosis [45]. *Cutibacterium acnes* is the predominant organism in chronic infections [23, 46]. Due to the high prevalence of occult infection in unexpected hardware failure, it is good clinical practice to collect multiple specimens for aerobic and anaerobic bacterial cultures during revision surgery. In addition, the resected implants may be submitted for sonication (to sample surface biofilms) with aerobic and anaerobic cultures of the sonicate fluid performed [47, 48].

In contrast to acute infections, chronic or late infections are usually treated with implant removal, especially when the hardware has failed [17, 49]. In cases of long fusions (>3 levels), a 1- or 2-stage exchange may be needed to prevent fracture or progressive deformity [50]. Notably, it is unknown how implant exchange impacts infection recurrence. There are no studies on the optimal duration or type of antibiotic therapy for chronic infection. As with early infection, most studies have described a treatment duration of approximately 12 weeks if the implant has been revised, with some using SAT [5, 23, 37, 41]. Oral antibiotic therapy may be an effective treatment strategy for patients with infections due to *C acnes* [43].

CONCLUSIONS

Spinal implant infections present a formidable challenge, necessitating a multidisciplinary approach and careful consideration of patient factors. Early infections require surgical

debridement followed by antibiotic therapy based on culture results. In contrast, chronic infections frequently necessitate implant removal, particularly with hardware failure or pseudarthrosis. While the optimal duration of antibiotic therapy remains a subject of ongoing investigation, current evidence suggests a minimum of 12 weeks for implant-retained infections. The management of SIIs requires a delicate balance between preserving spinal stability and eradicating infection, underscoring the importance of a personalized, evidence-based approach tailored to each patient's unique circumstances.

Note

Potential conflicts of interest. R. P. reports grants from MicuRx Pharmaceuticals and Biofire. R. P. is a consultant to PhAST, Day Zero Diagnostics, Abbott Laboratories, Sysmex, Deepull Diagnostics, S.L., Netflix, Oxford Nanopore Technologies, and CARB-X. In addition, R. P. has a patent on a *Bordetella pertussis/parapertussis* PCR issued, a patent on a device/method for sonication with royalties paid by Samsung to Mayo Clinic, and a patent on an anti-biofilm substance issued. R. P. receives honoraria from Up-to-Date and the Infectious Diseases Board Review Course. All other authors report no potential conflicts. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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