Open Forum Infectious Diseases

BRIEF REPORT

Clinical Characteristics and Outcomes Among Individuals With Spinal Implant Infections: A Descriptive Study

Sanjiv M. Baxi,[1,2] Makeda L. Robinson,[3] Marie F. Grill,[4] Brian S. Schwartz,[1,5] Sarah B. Doernberg,[1] and Catherine Liu[1]

[1]Department of Medicine, Division of Infectious Disease, University of California, San Francisco, [2]School of Public Health, University of California, Berkeley, and [3]Department of Medicine, Division of Infectious Diseases and Geographic Medicine, Stanford University, California; [4]Department of Neurology, Mayo Clinic, Phoenix, Arizona; and [5]School of Medicine, University of California, San Francisco, California

Little is known about the clinical presentation and outcomes associated with spinal implant infections. Here, we describe a single center's experience in a retrospective cohort of 109 individuals with spinal implant infections, including clinical, microbiological, therapeutic, and outcome data.

Keywords. spinal implant infection; infectious diseases consultation; surgical site infections; vertebral osteomyelitis; discitis.

Spinal surgeries involving implants have become increasingly common in the United States over the past 20 years [1–3]. Spinal implant infection is an important complication, arising in 2%–5% of spinal interventions and associated with significant patient morbidity [4–6]. Insufficient guidance is available for the management of spinal implant infections. This is largely due to the limited data regarding the clinical presentation, natural history, microbiology, and outcomes of individuals with this complication. Understanding the clinical manifestations and microbiologic features of these infections may provide opportunities to improve the management of spinal implant infections. In this study, we describe the clinical characteristics and outcomes of patients with spinal implant infections in a single tertiary referral medical center.

Received 20 March 2016; accepted 23 August 2016.

Prior presentation: This paper was presented, in part, at IDWeek 2013 in San Francisco, California, from 2–6 October 2013.

Correspondence: S. M. Baxi, University of California San Francisco, Division of Infectious Diseases, 513 Parnassus Avenue, Med Sci Room 419, San Francisco, CA 94143 (sanjiv.baxi@ucsf.edu).

Open Forum Infectious Diseases®

DOI: 10.1093/ofid/ofw177

METHODS

Study Population

This was a single-center, retrospective descriptive cohort at the University of California San Francisco (UCSF). Individuals were included if they had spinal surgery performed at UCSF, had a spinal implant, and if they met the National Healthcare Safety Network definition of surgical site infection between January 2009 through July 2013 [7].

Measurements and Definitions

Demographic, clinical, microbiologic, treatment, and outcome data were collected from the electronic medical record. Individuals were only included once (a second infection during the study period was considered to be a recurrence). Since July 2010, treatment has been determined using a standardized protocol (SOP), developed to provide guidance on antibiotic selection and duration, including oral suppressive therapy. Prior to 2010, participants were managed per provider discretion. Early and late-onset spinal implant infections were defined as those occurring more than 30 days or 30 days or longer after the implant was placed, respectively.

Outcomes

Participant vital status was determined by manual chart review, search of public internet-based death records, search of the National Center for Health Statistics national death index (through 2012), and search of the Social Security Administration death master file (through 2013). Need for repeat surgery was defined as spinal surgery performed at the affected vertebral levels during the study period for any reason (planned or unplanned). Recurrence of infection was defined as any infection (by any organism) at the affected vertebral levels during the study period. All outcomes were considered through 365 days.

Statistical Analysis

Univariate analyses were performed using Fisher exact test for categorical data and *t* tests for continuous data to compare variables. With respect to outcomes, Cox proportional hazards models were used, and tied survival times were addressed using the Efron method [8]. All statistical procedures were conducted using R version 3.2.2 (Vienna, Austria). The UCSF Committee for Human Research approved this study.

RESULTS

Clinical Features

A total of 109 individuals with spinal implant infection were identified during the study period. Full clinical data are summarized in Table 1. The mean age was 56 years, 48/109 (44%) were immunocompromised, and 58/109 (53%) had a history of prior spinal surgery. At presentation, inflammatory markers were

Table 1. Baseline Characteristics of Individuals With Spinal Implant Infections

Characteristic	All Patients (N = 109)
Age, mean years (SD)	56.1 (18.2)
Race/Ethnicity	
White	92 (84.4)
Hispanic	7 (6.4)
African-American	4 (3.7)
Asian	3 (2.8)
Native American	1 (0.9)
Other	2 (1.8)
Female gender	56 (51.4)
Smoking status	
Current	8 (7.3)
Former	42 (38.5)
Never	59 (54.1)
Diabetes mellitus	16 (14.7)
Chronic kidney disease	7 (6.4)
Cirrhosis	2 (1.8)
HIV/AIDS	3 (2.8)
Injection drug use	1 (0.9)
Immunological abnormality[a]	48 (44.0)
Receipt of immunosuppressive medications[b] (iatrogenic immunocompromised)	15 (13.8)
Surgical service	
Orthopedics	48 (44.0)
Neurosurgery	57 (52.3)
Combined	4 (3.7)
Surgical approach	
Posterior	93 (85.3)
Anterior	4 (3.7)
Combined	12 (11.0)
Depth of infection	
Superficial only (dermis and above)	14 (12.8)
Subdermal (from dermis to fascia)	13 (11.9)
Deep (below fascia)	81 (74.3)
Unknown	1 (0.9)
Surgical procedure preceding infection	
Primary	49 (45.0)
Revision	60 (55.1)
Infection timing	
Early (<30 days post-surgery)	80 (73.4)
Late (≥30 days post-surgery)	29 (26.6)
Vertebral bodies involved, mean bodies (SD)	5.3 (4.4)
Past history of any spinal surgery	58 (53.2)
Documented back pain at presentation	49 (45.0)
Neurological deficit at presentation	9 (8.3)
Past osteomyelitis/discitis	6 (5.5)
C-reactive protein at diagnosis (perioperative), mean mg/L (SD)	89.8 (78.8) (n = 86)
Erythrocyte sedimentation rate at diagnosis, mean mm/hr (SD)	57.4 (27.8) (n = 85)
White blood cell count at diagnosis, mean cells x10^9 per liter (SD)	10.1 (4.7)
Pathogen	
Methicillin-resistant *Staphylococcus aureus*	12 (11.0)
Methicillin-susceptible *Staphylococcus aureus*	23 (21.1)
Staphylococcus epidermidis	9 (8.3)
Polymicrobial[c]	46 (42.2)
Enteric gram-negative bacilli	3 (2.8)
Enterococcus	3 (2.8)
Propionibacterium acnes	2 (1.8)
Pseudomonas	1 (0.9)
Streptococcus	1 (0.9)
Culture negative at surgery	6 (5.5)
Other[d]	3 (2.8)
Positive blood cultures at presentation matching spinal isolate	15 (13.4)
Duration of intravenous therapy, mean days (SD)	33.1 (23.8)
Use of rifampin in treatment	53 (48.6)
Inpatient infectious diseases consultation	96 (88.1)
Removal of implant	13 (12.3)
Placement of new spinal implant	15 (13.8)
Outcomes	
Recurrence of infection	9 (8.3)
Need for repeat surgery	22 (20.2)
One year all-cause mortality	5 (5.6)
Composite outcome (at least 1 of the 3 above)	28 (24.8)
Time to recurrence of infection, mean days (SD)[e]	62.9 (48.0)
Time to repeat surgery, mean days (SD)[e]	49.5 (55.4)
Time to mortality, mean days (SD)[e]	61.4 (86.4)
Time to composite outcome, mean days (SD)[e]	62.9 (83.8)

All values reported as N (%) unless otherwise stated.

Abbreviations: AIDS, acquired immunodeficiency syndrome; HIV, human immunodeficiency virus; SD, standard deviation.

[a] Defined as having HIV/AIDS, active malignancy, autoimmune disease, or immunodeficiency.

[b] Defined as receiving >2 weeks of corticosteroids, biological agent, or chemotherapy.

[c] Any operative specimen with more than 1 organism was considered polymicrobial.

[d] Includes *Corynebacterium* spp. and *Cryptococcus* spp.

[e] Limited to those who experienced the outcome.

elevated with mean C-reactive protein (CRP) significantly higher among those with early vs late-onset infection ($P < .001$). The mean white blood cell count (WBC) was in the normal range. Ninety-six (88%) patients received inpatient infectious diseases (ID) consultation.

Microbiology

The most common cause of monomicrobial infection was *Staphylococcus aureus*, accounting for 32% of infections. Monomicrobial infection due to gram-negative organisms was seen in only 4 (4%) cases. Forty-six infections (42%) were polymicrobial, and 21 of these (46%) contained at least 1 gram-negative organism. Fifteen (13%) individuals had positive blood cultures, of which 53% were due to *S. aureus* (37% of these were methicillin resistant [MRSA]). Other organisms isolated from blood culture included *Corynebacterium* spp. (n = 1), *Staphylococcus epidermidis* (n = 1), *Escherichia coli* (n = 1), *Pseudomonas aeruginosa* (n = 1), *Enterococcus* spp. (n = 1), and polymicrobial (n = 2). There were no significant differences in microbiology between early vs late-onset infections ($P = .20$).

Treatment and Outcomes

Tailoring of antibiotic regimens was based on an SOP. Overall, the mean duration of intravenous antibiotics was 33.1 days. This duration did not significantly differ by organism or SOP use. The mean duration of oral antibiotic treatment was not calculated given that 24 individuals (22%) remained on indefinite antibiotic suppression. Rifampin was used in 53 (49%) infections in total; in most Staphylococcal infections (26/44) and polymicrobial infections (24/46, all of which contained at least 1 Staphylococcal species); and in 1 case each of a culture-negative, *Enterococcus* species and *Corynebacterium* species infections. With respect to recurrence, 6/9 (67%) were due to monomicrobial gram-positive organisms and none were due to monomicrobial gram-negative organisms. In the setting of repeat surgery, 11/22 (50%) of the individuals had monomicrobial gram-positive organisms (7/11, or 64%, were due to methicillin-sensitive *S. aureus*[MSSA]) and 1 (4.5%) had a monomicrobial gram-negative organism. Finally, 14/28 (50%) individuals who experienced 1 of the 3 outcomes had a monomicrobial gram-positive infection. Of these, 9/14 (64%) were due to MSSA.

ID consultation resulted in more rifampin use ($P = .002$) and longer duration of intravenous (IV) antibiotic therapy ($P < .001$, mean duration of IV therapy for ID consult vs none was 36.6 vs 7.6 days, respectively). Twenty-two individuals required repeat surgery, 9 had recurrence of infection (all also had repeat surgery), 5 died, and 28 had at least 1 of these outcomes. Given the exploratory nature of this study, several variables were considered to better understand possible determinants of outcomes in spinal implant infections. There were no statistically significant differences in univariate Cox regressions for recurrence of infection, need for repeat surgery, 1-year all-cause mortality, or a composite of these outcomes by use vs no use of the SOP (hazard ratio [HR] 0, $P = 1$; HR 1.32, $P = .56$; HR 0 $P = 1$; HR 0.96, $P = .92$, respectively), for early vs late-onset infections (HR 2.18, $P = .25$; HR 1.04, $P = .93$; HR 1.87, $P = .50$; HR 1.12, $P = .79$, respectively), rifampin use (HR 0.52, $P = .36$; HR 0.88, $P = .76$; HR 0.26, $P = .23$; HR 0.79, $P = .53$, respectively), infection depth (HR 0.94, $P = .89$; HR 1.48, $P = .28$; HR 4.33, $P = .24$; HR 1.72, $P = .12$, respectively), antibiotic suppression (HR 0.88, $P = .87$; HR 0.51, $P = .28$; HR 2.20, $P = .39$; HR 0.70, $P = .48$, respectively), or implant removal (HR 4.32, $P = .05$; HR 1.73, $P = .99$; HR 1.90, $P = .57$; HR 1.69, $P = .29$, respectively).

DISCUSSION

Indications for spinal surgeries are increasing as technology advances and the population ages. An understanding of the clinical characteristics of spinal implant infections and their relationship to outcomes is important to inform the development of infection prevention and diagnostic and management strategies. In this large retrospective cohort of patients with spinal implant infections, we identified several important features. These patients are medically complex; half of them were immunocompromised and more than half had a history of prior spinal surgery. While Staphylococcal species were the predominant organisms in monomicrobial infections, in contrast to prior studies, most patients had polymicrobial infections [4, 5, 9, 10]. This finding may be attributable to the volume of lumbosacral surgical interventions performed at this institution [11]. Spinal implant infections are associated with significant morbidity, with 25% of our patients experiencing at least 1 of the following: recurrent infection, need for repeat surgery, or death. Infection timing, rifampin use, infection depth, indefinite antibiotic suppression, and removal of implant did not influence these outcomes. A notable exception to this is the increased risk of recurrence associated with implant removal, but this likely temporally reflects removal of the hardware due to recurrence as opposed to recurrence due to failure to remove the hardware.

This study also highlights some of the challenges associated with diagnosis and management of spinal implant infection. Less than half of the patients presented with back pain, a minority had positive blood cultures, and most presented with a normal WBC count. Although the CRP was elevated on average, there was significant variability likely reflecting heterogeneity of both the patient population and the test itself. The erythrocyte sedimentation rate was less variable at the time of diagnosis but lacks specificity. Our findings are consistent with previously published data that raise concerns over the usefulness of inflammatory markers in diagnosing spinal implant infections given poor specificity [5, 12]. Implant removal and exchange was uncommon, necessitating prolonged courses of antibiotic therapy, and about 20% of patients were maintained on indefinite suppressive antibiotics.

A major strength of this study is the size of the cohort. In the setting of such a rare complication, this study adds to the published experience in the clinical presentation and management of such infections. The study included several different outcomes of clinical interest among highly medically complex patients who are increasingly undergoing advanced medical procedures. Finally, great care was taken to determine the outcomes for each participant, particularly with respect to the all-cause mortality.

There are also notable limitations. This study was performed in a single center that serves as a tertiary referral site for complex spinal cases, often for individuals with a prior history of surgery. Thus, these findings may not be universally generalizable. Among those who died, the issue of competing risks (eg, the inability to develop treatment failure or need for repeat surgery) is an important limitation. However, the number of patients who died was low (5/109) as were the proportions for the other outcomes. In order to address this to some degree, the composite result was used to capture more outcomes of interest. Complete individual-level antibiotic treatment data were not available.

In summary, despite limitations, this is a large study that contributes to the existing literature on the clinical presentation and outcomes of individuals presenting with spinal implant infection. These data support the need to establish multicenter interdisciplinary prospective collaborations to further investigate outcomes, risk factors, and strategies for prevention, diagnosis, and management of spinal implant infections.

Notes

Financial support. S. M. B. is supported by the UCSF Traineeship in AIDS Prevention Studies (National Institutes of Health, T32 MH-19105).

Potential conflicts of interests. All authors: No reported 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.

References

1. Deyo RA, Mirza SK. Trends and variations in the use of spine surgery. Clin Orthop Relat Res **2006**; 443:139–46.
2. Weinstein JN, Lurie JD, Olson PR, Bronner KK, Fisher ES. United States' trends and regional variations in lumbar spine surgery: 1992–2003. Spine **2006**; 31:2707–14.
3. Statistical Brief #170. Healthcare Cost and Utilization Project (HCUP). February 2014. Agency for Healthcare Research and Quality, Rockville, MD. Available at: www.hcup-us.ahrq.gov/reports/statbriefs/sb170-Operating-Room-Procedures-United-States-2011.jsp. Accessed 23 August 2016
4. Kasliwal MK, Tan LA, Traynelis VC. Infection with spinal instrumentation: review of pathogenesis, diagnosis, prevention, and management. Surg Neurol Int **2013**; 4(suppl 5):S392–403.
5. Kowalski TJ, Berbari EF, Huddleston PM, Steckelberg JM, Mandrekar JN, Osmon DR. The management and outcome of spinal implant infections: contemporary retrospective cohort study. Clin Infect Dis **2007**; 44:913–20.
6. Dubee V, Lenoir T, Leflon-Guibout V, Briere-Bellier C, Guigui P, Fantin B. Three-month antibiotic therapy for early-onset postoperative spinal implant infections. Clin Infect Dis **2012**; 55:1481–7.
7. CDC. Surgical Site Infection (SSI) Event. Available at: http://www.cdc.gov/nhsn/pdfs/pscmanual/9pscssicurrent.pdf. Accessed 23 June 2016.
8. Hertz-Picciotto I, Rockhill B. Validity and efficiency of approximation methods for tied survival times in Cox regression. Biometrics **1997**; 53:1151–6.
9. Collins I, Wilson-MacDonald J, Chami G, et al. The diagnosis and management of infection following instrumented spinal fusion. Eur Spine J **2008**; 17:445–50.
10. Lazennec JY, Fourniols E, Lenoir T, et al. Infections in the operated spine: update on risk management and therapeutic strategies. Orthop Traumatol Surg Res **2011**; 97(6 suppl):S107–16.
11. Abdul-Jabbar A, Berven SH, Hu SS, et al. Surgical site infections in spine surgery: identification of microbiologic and surgical characteristics in 239 cases. Spine **2013**; 38:E1425–31.
12. Baxi S, Malani PN, Gomez-Hassan D, Cinti SK. Association between follow-up magnetic resonance imaging and clinical status among patients with spinal infections. Infect Dis Clin Pract **2012**; 20:326–9.