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CASE SERIES

Is *Propionibacterium acnes* becoming the most common bacteria in delayed infections following adolescent idiopathic scoliosis surgery?

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Abstract

Study design Retrospective review of hospital charts.

Objective (1) To determine the microbiological profile of patients with surgical site infections following posterior spinal fusion surgery (PSF) for Adolescent Idiopathic scoliosis (AIS). (2) To study the treatment outcome of patients with surgical site infections (SSI) following surgery for AIS. (3) To identify the key differences in presentation and management of acute and delayed SSI following AIS surgery.

Summary of background data There has been increasing evidence of the role of *P. acnes* in deep surgical site infections. Literature related to this is abundant in relation to shoulder arthroplasty; however, it is sparse in relation to spine surgery.

Methods We conducted a retrospective review of all patients treated for AIS during a 5-year period (2010–2014) at our institution, with a minimum of 2-year follow-up after the index surgery. Patients with a postoperative infection following their index surgery were included. Charts of AIS patients with post-op infections were reviewed for details of the index surgery, time to presentation of the infection, presenting signs/symptoms, microbiology details, details of surgical and antibiotic treatment, and outcomes.

Results Nine (2.8%) post-op infections were identified out of 315 cases for AIS during this period. Seven (2.2%) involved *P. acnes*. Two (0.6%) involved MSSA. The average time for cultures to show growth was 6.1 days (range 5–8 days) in *P. acnes* group and 2–3 days in MSSA group. Patients with *P. acnes* infections were treated with implant removal, debridement and antibiotics. All patients achieved solid fusion except two patients from the *P. acnes* group had pseudoarthrosis and had to undergo revision fusion.

Conclusion *Propionibacterium acnes* was the single most common bacteria isolated from delayed surgical site infection following PSF in AIS patients. Optimal treatment consists of debridement, implant removal and antibiotics. These patients have high incidence of pseudoarthrosis.

Level of evidence Level IV.

Keywords P acnes · Surgical site · Delayed · Scoliosis · Surgery · Infections

Introduction

Infection after spine surgery is a devastating complication and can ruin the most desirable results of meticulously performed surgeries. This issue can be more devastating in extensive spinal deformity correction surgeries. Infection rates after deformity surgery range from 1.7% [1] to 6.9% [2]. With the advent of modern antibiotic prophylaxis, the incidence of perioperative infections with gram-positive organisms has been reduced drastically. However, what seems to be more concerning now is the increasing prevalence of late infections caused by skin commensals [1, 3–5].

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One of the increasingly relevant skin flora is *Propionibacterium acnes* (*P. acnes*). *Propionibacterium acnes* is a slow-growing aero tolerant anaerobic gram-positive organism that lives on sebum secreted by sebaceous glands [6] (Fig. 1). Traditionally, *P. acnes* was thought to only cause acne; however, in the recent years, it has been held responsible for causing perioperative infections in various organ systems like bone and joint surgery [7, 8], ocular [9] and dental [10] surgical procedures. Being rich in sebaceous glands, the skin of forehead, shoulder, neck and lumbar spine area has a high concentration of *P. acnes* [11] (Figs. 2, 3). This can possibly explain why *P. acnes* infections in orthopedic practices are commonly seen in shoulder and spine surgery. In surgeries, where instrumentation is required, *P. acnes* can be a significant latent pathogen because of its ability to form biofilms around implanted orthopedic devices [12].

The literature on *P. acnes* infection in spine surgery is sparse. We present our experience with late post-operative surgical site infections (SSI) in posterior instrumented fusions for pediatric deformity. In our series, *P. acnes* has been the most common organism isolated in such late SSI. Our goal is to inform and educate spine surgeons to *P. acnes*, on its incidence, presentation, and treatment options to address these late infections. We hope to initiate a discussion to develop strategies for preventing these infections.

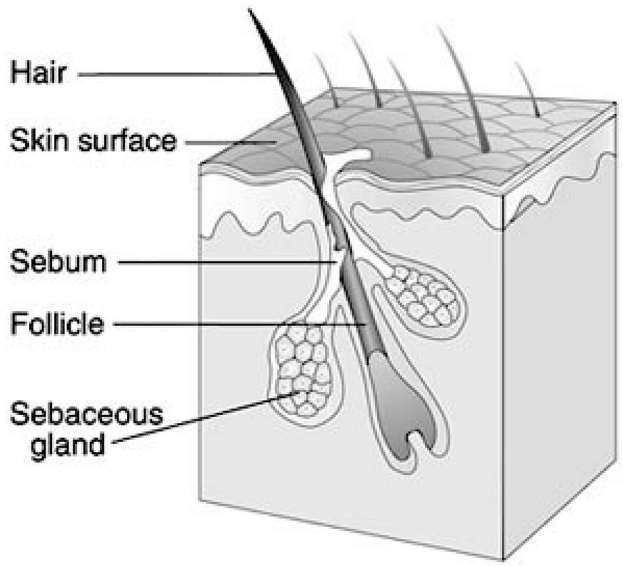

Fig. 1 Diagram demonstrating the structure of a normal pilosebaceous unit. (Image from the National Institute of Arthritis and Musculoskeletal and Skin Diseases, U.S. National Institutes of Health, Bethesda, Maryland.)

Materials and methods

After obtaining approval from the institutional review board, we conducted a retrospective review of all patients treated for AIS during a 5-year period (2010–2014) at our institution, with a minimum of 2-year follow-up after the index surgery. There were 315 consecutive Adolescent idiopathic scoliosis (AIS) patients operated at our center during this period. All these patients had received cefazolin IV within 30 min prior to skin incision and stainless steel implants were used for deformity correction. Patients with a postoperative infection following their index surgery were included. Charts of AIS patients with post-operative infections were reviewed for details of the index surgery, time to presentation of the infection, presenting signs/symptoms, microbiology details, details of surgical and antibiotic treatment, and outcomes.

Results

Nine (2.8%) post-operative infections were identified out of 315 cases for AIS during this period. Seven (2.2%) involved *P. acnes*, including one that was a polymicrobial infection with *P. acnes*, Acinetobacter and Staph epidermidis. Two (0.63%) of the infections were due to Methicillin sensitive *Staphylococcus aureus*, MSSA. The average time to presentation for the *P. acnes* infection was 25.7 months (range 11–56 months), and the most common presenting symptom was dull back pain. Gradually these developed boggy swelling around the operative site. ESR and CRP levels were elevated in these patients. At this time, a clinical diagnosis of delayed surgical site infection was made and patients were advised surgery for debridement and implant removal. The average time for diagnosis of infection after the index surgery was 32 months (range 14–66 months) with the average time between onset of symptoms and diagnosis was 7 months (range 1–22 months). All patients with *P. acnes* infection were treated with implant removal and antibiotics as per recommendations from infectious disease specialist. A set of two deep cultures were taken from the surgical wound at the time of debridement. Notably prophylactic antibiotics at the time of this surgery were withheld until the time that the cultures were drawn. Post operatively each patient was given broad-spectrum antibiotics until the cultures were positive for *P. acnes*. The time for cultures to be positive was average 6.1 days (range 5–8 days) in our series. Once culture and sensitivity reports were available, antibiotics were converted to IV penicillin.

In the two patients who had infection due to MSSA, the average time to presentation was 3 weeks. Both of these

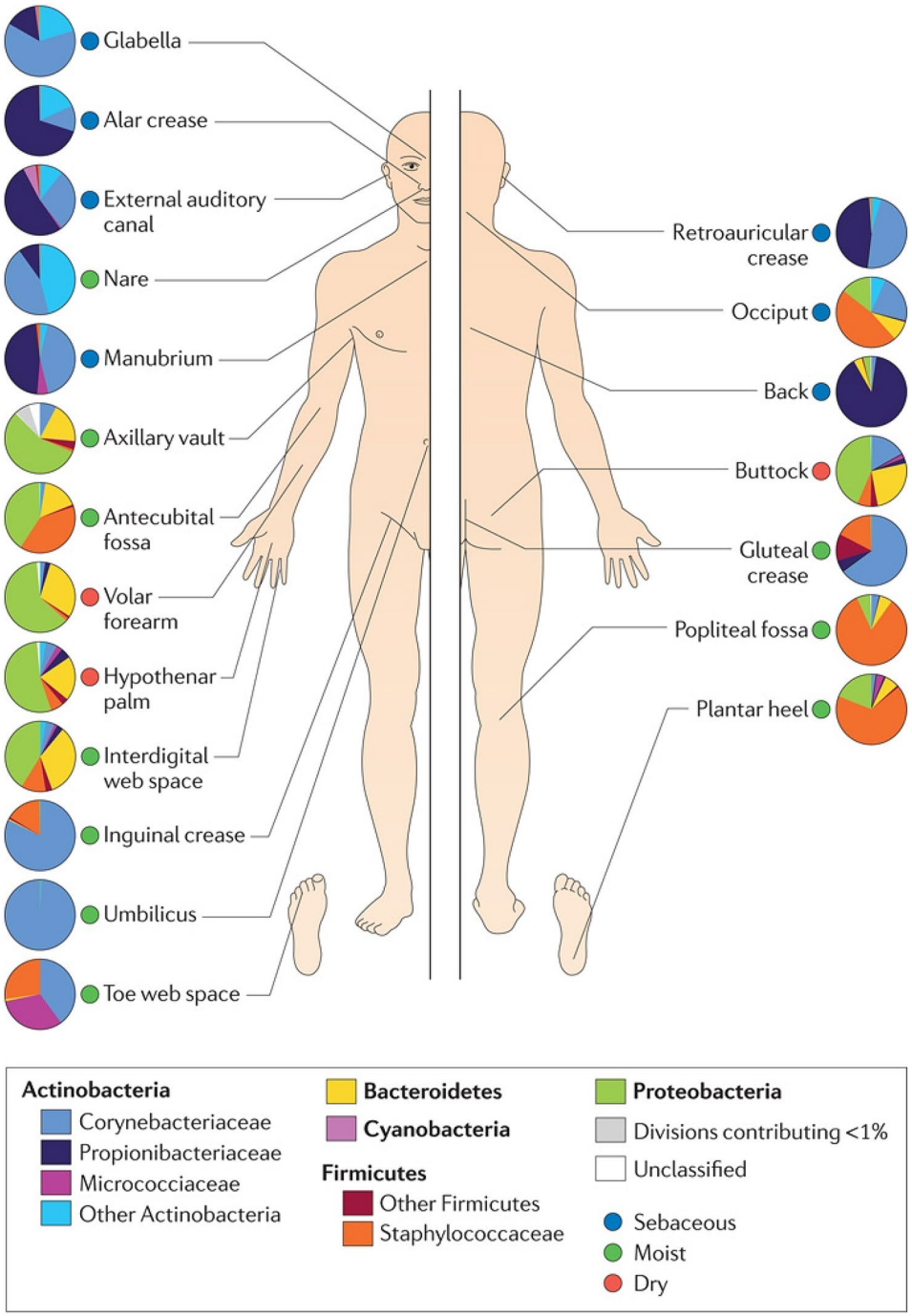

Fig. 2 Distribution of bacteria on human skin (Reproduced with permission from Macmillan Publishers Ltd: Grice EA, Segre JA. The skin microbiome. Nat Rev Microbiol. 2011 Apr;9 [4]:244–53. Copyright [2011]. http://www.nature.com/nrmicro/index.html)

patients presented with wound drainage. These patients were treated with irrigation and debridement with retention of spinal implants. These patients were treated with 4–6 weeks of intravenous antibiotics followed by 1 year of oral antibiotics. These patients did not require implant removal at the debridement surgery nor require implant removal at final follow-up.

One patient with delayed infection did not grow any organism on culture. Since this patient's clinical presentation was consistent with *P. acnes* infection, we treated him with debridement, implant removal and IV antibiotics. This patient was lost to follow up 3 months after revision surgery. Eight patients were followed up for an average period of 64 months (range 32–120 months) from the index surgery. Six patients (four *P. acnes*, two MSSA) achieved solid fusion without any additional procedure. There were two patients who were diagnosed to have pseudoarthrosis at the time of surgical debridement. They were managed with same protocol of debridement, implant removal and antibiotics. Revision instrumented fusion was done at the end of antibiotic

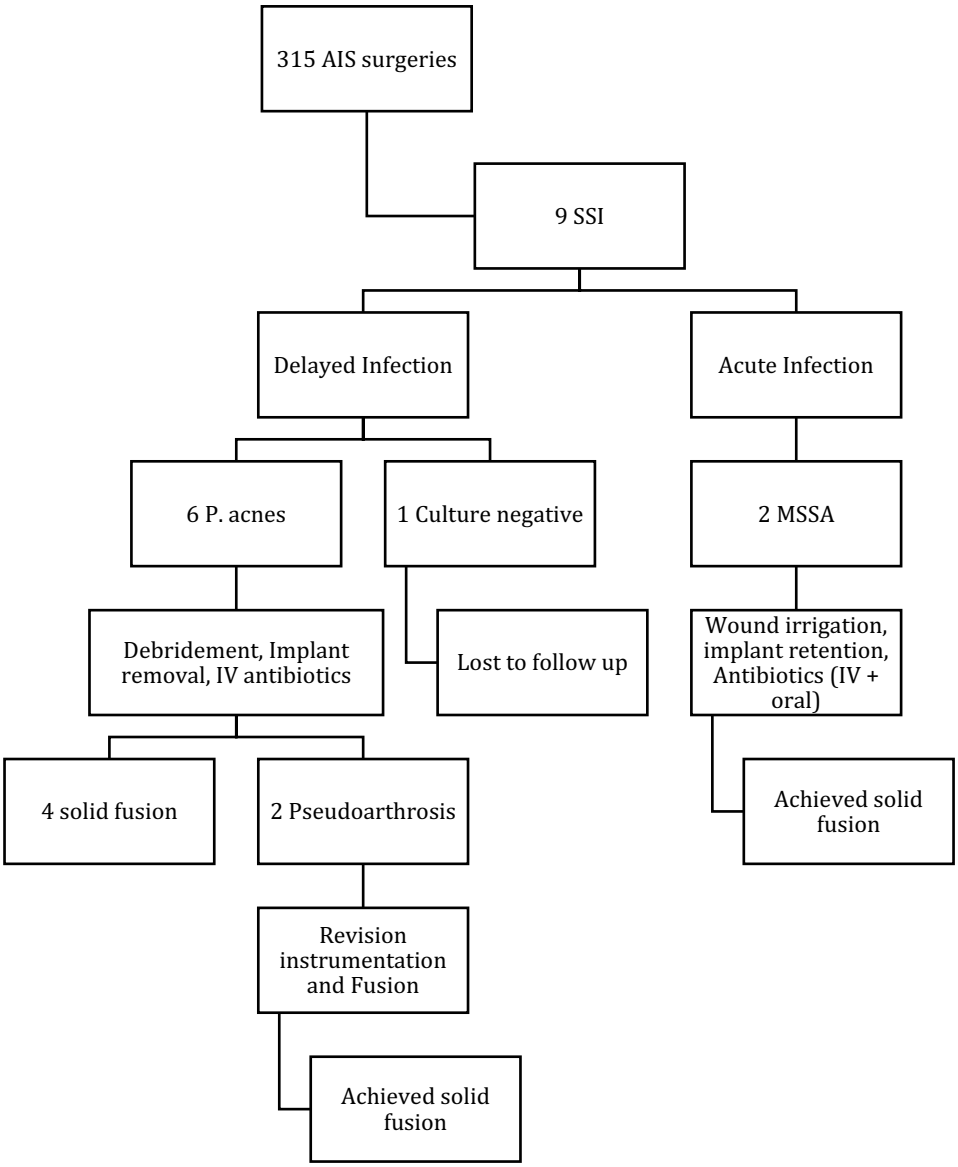

Fig. 3 Distribution of patients with surgical site infection, their management and final outcome

therapy and they eventually achieved solid fusion. These two patients had normalization of the ESR and CRP prior to revision surgery. The details of all nine patients with postoperative infection patients are shown in Table 1.

Discussion

In our series, patients with *P. acnes* infections took several months to years to present with infection versus patients with MSSA acute infections, who presented within 3 weeks of the index operation. This can be attributable to the formation of biofilms around orthopedic implants by *P. acnes* [24]. Unfortunately, biofilm forming species have been correlated with worse outcomes than those that do not form biofilms [12, 25]. These biofilms protect the bacteria from phagocytosis and also prevent antibodies and antibiotics from reaching the bacteria [26]. This also keeps the bacteria relatively isolated from the immune system [27, 28]. Hence, most patients with postoperative *P. acnes* infection lack the classical inflammatory response of pain, redness, elevated temperature and rather present with unexplained dull aching pain and swelling [29, 30]. All of our patients with *P. acnes* infection presented with dull back pain and swelling.

Possible routes of late infections in spine include hematogenous seeding [13] or activation of dormant organisms that were implanted at the time of surgery [14]. However, some researchers believe that late activation of implanted bacteria during surgery remains the major route of entry in delayed infections while claiming hematogenous seeding is

Table 1 Details of patients with surgical site infection following surgery for Adolescent Idiopathic Scoliosis

Sr No.	Age (index)	Gender	Co morbities	Surgery	Onset of symptoms	Time to diagnosis	Delay in diagnosis	Initial ESR at time of diagnosis	CRP at time of diagnosis	Sxs at inxn	Number of cultures	Organism	Culture positive day	Intra op findings	Outcome at final Follow-up	Duration of follow-up from index surgery
1	13	F	Nil	T2-T12 PSF	23 months	26 months	3m	35	NA	Mild back pain, swelling of low back	2 sets	MSSE, Acinetobacter, Stap epidermidis, Pacnes	8 days	"Mucinous material", sinus tract to hardware	Solid fusion, wound healed well	78 months
2	17	F	Dm Type 1	T4-L1 PSF	12 months	18 months	6	NA	NA	Mild back pain, swelling of low back	4 sets	*P. acnes*	6	Frank Pus	3 level pseudo arthrosis, T 7-8, T8-9, T9-10 re operated in 2015 with revision fusion T 7 - T11 2015	66 months
3	15	M	Nil	T2-L1 PSF	8 months	14 months	6	42	3.6	Back pain, malaise	4 sets	*P. acnes*	6	Small amount of cloudy fluid, mucinous material	Developed progressive deformity, pseudoarthrosis, Revision instrmentation and fusion done on jan 2015, solid fusion there after	66 months

Table 1 (continued)

Sr No.	Age (index)	Gender	Co morbities	Surgery	Onset of symptoms	Time to diagnosis	Delay in diagnosis	Initial ESR at time of diagnosis	CRP at time of diagnosis	Sxs at inxn	Number of cultures	Organism	Culture positive day	Intra op findings	Outcome at final Follow-up	Duration of follow-up from index surgery
4	16	M	CKD Stage 2	T2-L2 PSF	56 months Epidermoid cyst that did not heal	66 months	10	65	2.9	Epidermoid cyst that was drained but the wound didn't heal	4 sets	*P. acnes*	6	Gross pus	Solid Fusion, No Symptoms	120 months
5	12	F	Nil	T2-T12 PSF	12 months	14 months	2	58	4.8	Low grade back pain	1 set	*P. acnes*, Coagulase negative Staph warneri	6	Biofilm, No pus	Solid Fusion, No Symptoms	58 months
6	17	M	Nil	T2-T12 PSF	11 months	33 months	22	64	6.8	Localized swelling, slight back pain	2 sets	*P. acnes*	5	Pus and biofilm	Solid Fusion, No Symptoms	47 months
7	15	M	Nil	T11-L3 PSF	58 months	59 months	1	71	10.1	Localized swelling, slight back pain, drainage	2 sets	No Growth after 2 weeks		Pus throught the wound	Loss to follow-up on sept 2015. was on IV antibiotics till then (3 months post debridement)	
8	14	F	Nil	PSF T10-L3	3 weeks	3 weeks	0	87	4.9	Wound drainage	2 sets	MSSA	3	Gross pus	Solid Fusion	48 months

Table 1 (continued)

Sr No.	Age (index)	Gender	Co morbities	Surgery	Onset of symptoms	Time to diagnosis	Delay in diagnosis	Initial ESR at time of diagnosis	CRP at time of diagnosis	Sxs at inxn	Number of cultures	Organism	Culture positive day	Intra op findings	Outcome at final Follow-up	Duration of follow-up from index surgery
9	17	M	Nil	PSF T2-L1	3 weeks	3 weeks	0	45	5.8	Drainage, increased pain	2 sets	MSSA	2	Scant sero sangiou-nous dis-charge	***Clinda resistant, prior topical clinda for back acne***	32 months

Table 2 Various studies showing time taken for *P. acnes* to grow on culture

Author	Surgery type	Time for *P. acnes* to grow on culture media
Bémer P [31]	Spine	7–14 days
Butler-Wu [32]	Periprosthetic joint infections	13 days
Matsen [16]	Shoulder	17 days

a doubtful concept [1]. Currently, routine skin preparation methods seem to be inadequate for removal of this organism at the incision site. It has been hypothesized that these organisms enter the operative site at the time of incision during the index surgery and contaminate implanted orthopedic devices, subsequently producing biofilms that make them resistant to antibiotics [11, 15, 16]. In one retrospective analysis, Nandyala et al. showed tissue contamination with skin commensals occurred in up to 23% of patients and the most common bacteria isolated from the tissue cultures was *P. acnes* [17]. Literature supporting this philosophy has been published in relation to primary [18] as well as revision shoulder arthroplasty [19]. In the McGoldrick et al. series, a substantial number of patients undergoing revision shoulder arthroplasty for stiffness or component loosening that were presumed to be aseptic were infected with *P. acnes*. Similar findings have also been seen with primary lumbar disc herniation, where in *P. acnes* have been cultured from herniated nucleus pulposus collected during surgery [20–23].

Two of our *P. acnes* infection patients were diagnosed with pseudoarthrosis when implants were removed for debridement. *P. acnes* is increasingly found in revision spine surgeries for pseudoarthrosis. Shifflett et al., in their series of 578 cases of presumed aseptic revision spine surgeries, found that *P. acnes* was the most common organisms cultured from the surgical wounds. *P. acnes* was three times more common than any other organism. In their series, more than 54.2% patients with primary diagnosis of pseudoarthrosis had positive cultures for *P. acnes*. The average time between the index and the revision surgery was 57.6 months which again reiterates the slow and indolent nature of these infections [31]. This suggests that infections with slow-growing organism like *P. acnes* may have a significant impact in slowing or arresting fusion in spine surgery. Multiple deep cultures should be taken from the wound and should be cultured on an anaerobic liquid medium like thioglycolate broth for up to 14 days or longer to detect *P. acnes* [16, 32, 33] (Table 2). In our study, two deep cultures were taken from the surgical site at the time of surgical debridement and implant removal and inoculated on thioglycolate broth. The average time for *P. acnes* to be positive on culture was 6.1 days (range 5–8 days). We attribute the early growth

in culture to high bacterial burden in our patients. However, we still recommend holding cultures for a minimum of 14 days to account for slow-growing organisms before declaring cultures to be negative.

All *P. acnes* patients who did not have pseudoarthrosis were clinically cured with the approach of surgical debridement, implant removal followed by antibiotic therapy. Two patients were found to have pseudoarthrosis at the time of surgical debridement. Yet, we followed our standard protocol of implant removal and antibiotic therapy for these patients and revision instrumented fusion surgery done at a later date. These patients were not braced, and were scheduled once lab parameters of CRP and ESR had normalized. Both of the patients were operated by 6 months post implant removal. Retaining implants in deep infections has a risk of recurrence of infection. In a series of 15 patients with AIS with late post-operative infections, Silvestre et al. tried to salvage implants in six patients who presented with less severe clinical signs of infection. They treated these patients with debridement, pulse irrigation and continuous suction irrigation. At a mean duration of 11 months, they had to perform implant removal on all these patients due to recurrence or persistence of infection [34]. Maruo et al. have shown that *P. acnes* is a significant risk factor in treatment failure of surgical site infections leading to instrumentation removal [35]. Because instrumentation removal before full fusion can lead to a loss of correction in idiopathic scoliosis [36], preventing or rapidly diagnosing and treating *P. acnes* infections can help prevent unnecessary complications and revision surgery.

In contrast, the two patients with MSSA infections presented 3 weeks after the index surgery. They were treated with wound lavage and IV antibiotics for 4–6 weeks followed by oral antibiotics for up to 1 year duration. Notably, these patients did not need implant removal and achieved solid fusion at final follow-up. Table 3 demonstrates key differences between *P. acnes* and MSSA surgical site infection in our series.

We used stainless steel implants in all our patients. Stainless steel has higher stiffness and is not notch sensitive as compared to titanium [37, 38]. In our experience, we can apply a higher corrective force and thus gain better deformity correction with stainless steel implants. Some reports state that use of stainless steel implants in spine surgery was associated with higher incidence of SSI in spine surgery [34, 39]. However, in another study, Wright et al. have shown that the type of metal, stainless steel, titanium, or cobalt chrome/titanium, does not affect the risk of SSI in scoliosis surgery [40]. As of today, we still continue to use stainless steel implants for deformity correction surgery in AIS.

Future research could be directed with the following questions:

1. Is the rise in incidence of *P. acnes* infections due to improved microbiological techniques to detect it?
2. Is there a change in the virulence of *P. acnes*? Has *P. acnes* made the transition from a skin commensal to an actual pathogen in surgical site infections? [41–43]
3. Are there particular strains of *P. acnes* that are more likely to be causative in surgical site infections?
4. With the increasing number of *P. acnes* infections, do we need to change our protocols of prophylactic antibiotics to prevent *P. acnes* infections in spine surgery?

From January 2005 onwards, we have been using our institutional infection control protocol for all spinal fusion cases following which SSI rates for all cervical, thoracic, and lumbar instrumented cases combined decreased from 3.9% (97/2473) to 0.93% (57/6158) ($p < 0.0001$) [44]. The protocol consists of

Table 3 Key differences between acute and delayed SSI in posterior spinal surgery in AIS patients

	Acute infections	Delayed infections
Number of patients	Two (MSSA)	Seven (six *P. acnes*, one Culture negative)
Time to presentation after index surgery	3 weeks	25.7 months (range 11–56 months)
Time to diagnosis after index surgery	3 weeks	32 months (range 14–66 months)
Symptoms	Back pain, wound drainage	Dull back pain and swelling
Lab markers	Elevated ESR and CRP	Relatively lesser rise in ESR and CRP
Treatment	Wound irrigation and antibiotics	Debridement, implant removal, antibiotics
Cultures	Positive in 2–3 days	Positive in 6.1 days (range 5–8 days)
Gram stain	Gram positive cocci	Negative
Antibiotic regimen	6 weeks IV Antibiotics + 1-year Oral Antibiotics	Penicillin G IV + Pen V Oral; Vancomycin; Clindamycin
Complications	None	2 cases of pseudoarthrosis, required revision instrumentation and fusion

1. Chlorhexidine wash (HIBICLENS -Mölnlycke Health Care, Norcross, GA) wash to the surgical site on the night before and morning of surgery.
2. Surgical site is scrubbed with Chlorhexidene solution for three minutes, wiped with 70% isopropyl alcohol and painted with ChloraPrep (2% Chlorhexidene gluconate, 70% isopropyl alcohol) solution and allowed to dry. The surgical site is draped and covered with Ioban (3 M Health care).
3. Perioperative antibiotics: all patients receive preoperative intravenous antibiotics consisting of Cefazolin—a first generation cephalosporin. In patients with an allergy to cephalosporins, vancomycin is utilized. All patients have antibiotics redosed intraoperatively every 3–4 h. All intravenous antibiotics are discontinued at 48 h after surgery or earlier if the patient is discharged within 48 h.
4. Copious wound irrigation with normal saline antibiotic solution containing 50,000 units of Bacitracin in 3 L of normal saline.
5. Local, intra-wound antibiotic delivery (deep and subcutaneous) with vancomycin powder (this is a recent infection control measure instituted by our team in January 2014).
6. Meticulous, layered wound closure.
7. Closed suction drains are routinely utilized. Drains are generally removed 1–3 days after surgery, while the dressing on the wound is kept intact.
8. Bacitracin ointment over the wound.
9. Iodine impregnated 1 inch Steri strips applied on top of the ointment.
10. Sterile dressing using gas permeable barrier (Opsite Films- Smith and Nephew, Fort Worth, TX).
11. Wound dressings are never changed and removed after 5 days and then wounds are left open to air.

In 2014, following the study period, we started adding 2 g of vancomycin powder with crushed cancellous bone allograft used for fusion in the AIS surgeries. Local Vancomycin powder in dose of 2 gm has found to be safe and effective in reducing infection rate in spine surgery from 2.6% to 0.2%. Despite high local concentrations up to 1457 µg/ml, vancomycin has shown minimal systemic absorption with no systemic side effects as would otherwise be seen with its intravenous use [45, 46]. In our experience, we have not encountered any *P. acnes* infection in AIS patients after this intervention. It is possible that local vancomycin applied in the wound has inhibitory effect on *P. acnes*. Patients with acne lesions posted for scoliosis surgery are sent for a dermatology consult. We start them on oral Tetracyline antibiotic for 2 weeks before the surgery and continue the same for 1 week after the surgery. These points can be a future direction for research in terms of prevention of *P. acnes* infections in Posterior instrumented spinal fusion surgeries in AIS.

Conclusions

- *Propionibacterium acnes* is the most common skin commensal on the back
- Cultures should be held for a minimum of 14 days to improve the likelihood of diagnosis of a latent organism like *P. acnes*
- *Propionibacterium acnes* infections usually presented late because of their ability to form biofilms and avoid immune detection
- Treatment of *P. acnes* infections involves debridement, instrumentation removal and antibiotics

Author contributions Study conceptualization: RSB, TLL, MPK, SSB, CCK; Methodology: MPK, SSB, CCK, TLL, RSB; Formal Analysis and investigation: MPK, SSB, CCK, TLL, RSB; Writing of first draft of Manuscript: MPK, SSB, CCK, TLL, RSB; Review, editing and final approval of manuscript: RSB, TLL, MPK, SSB, CCK, TLL; Funding: None; Resources: None; Supervision: RSB.

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Compliance with ethical standards

Conflict of interest No conflicts of interest.

Ethical approval Institutional IRB approval obtained. The study was conducted in compliance with the Ethical standards.

Informed consent Study is a retrospective chart review so informed consent has been waived off.

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