

Hip Joint Infections Caused by Multidrug-Resistant Enterobacterales Among Patients With Spinal Cord Injury: Experience of a Reference Center in the Greater Paris Area

B. Davido,^{1,2} L. Noussair,³ F. El Sayed,⁴ K. Jaffal,¹ H. Le Liepvre,⁵ D. Marmouset,⁶ T. Bauer,⁶ J. L. Herrmann,^{2,3} M. Rottman,^{2,3} A. C. Cremieux,^{2,7} and A. Saleh-Mghir^{1,2}

¹Service des Maladies Infectieuses, Université Paris-Saclay, Hôpital Raymond Poincaré, Assistance-Publique des Hôpitaux de Paris, Garches, France, ²UMR UVSQ INSERM U1173, UFR Simone Veil des Sciences de la Santé, Montigny le Bx, France, ³Laboratoire de Microbiologie, Université Paris-Saclay, Hôpital Raymond Poincaré, Assistance-Publique Des Hôpitaux De Paris, Garches, France, ⁴Laboratoire de Microbiologie, Université Paris-Saclay, Hôpital Ambroise Paré, Assistance-Publique des Hôpitaux de Paris, Boulogne-Billancourt, France, ⁵Medecine Physique et reeducation, Université Paris-Saclay, Hôpital Raymond Poincaré, Assistance-Publique des Hôpitaux de Paris, Garches, France, ⁶Service d'Orthopédie, Université Paris-Saclay, Hôpital Ambroise Paré, Assistance-Publique des Hôpitaux de Paris, Boulogne-Billancourt, France, and ⁷Service de Maladies Infectieuses, Université Paris Nord, Hôpital Saint-Louis, Assistance-Publique des Hôpitaux de Paris, Paris, France

Background. We aimed to describe the management and treatment of hip joint infections caused by multidrug-resistant Enterobacterales among patients with spinal cord injury (SCI).

Methods. We included all hip joint infections associated with grade IV decubitus ulcers caused by extended-spectrum beta-lactamase producing Enterobacterales (ESBL-PE) and carbapenemase-producing Enterobacterales treated in a reference center for bone and joint infections over 9 years in a retrospective study.

Results. Seventeen SCI patients with ischial pressure ulcers breaching the hip capsule (mean age 52 ± 15 years) were analyzed. In 16 patients, paraplegia was secondary to trauma and 1 was secondary to multiple sclerosis. Infections were mostly polymicrobial ($n = 15$; 88.2%), notably caused by *Klebsiella pneumoniae* ($n = 10$) and *Staphylococcus aureus* ($n = 10$). The carbapenemases identified were exclusively OXA-48-type ($n = 3$) including 2 isolates coexpressed with ESBL-PE within the same bacterial host. Multidrug-resistant Enterobacterales were commonly resistant to fluoroquinolones ($n = 12$; 70.6%). Most therapies were based on carbapenems ($n = 10$) and combination therapies ($n = 13$). Median duration of treatment was 45 (6–60) days. Of 17 cases of hip joint infections, 94.1% ($n = 16$) benefited from a femoral head and neck resection. Infection control was initially achieved in 58.8% ($n = 10$) of cases and up to 88.2% after revision surgeries, after a median follow-up of 3 (1–36) months.

Conclusions. Hip infections among SCI patients caused by multidrug-resistant Enterobacterales are often polymicrobial and fluoroquinolones-resistant infections caused by *Klebsiella pneumoniae* and *S aureus*, highlighting the need for expert centers with pluridisciplinary meetings associating experienced surgeons, clinical microbiologists, and infectious disease specialists.

Keywords. bone; carbapenemase; ESBL; infection; spinal cord.

The most recent estimate in 2020 of people living with spinal cord injury (SCI) in the United States is approximately 296 000 individuals, with an annual incidence of 17 900 new cases each year [1]. In Europe, the incidence of traumatic SCI is between 16 and 19.4 per million habitants [2], whereas approximately half of the SCIs are related to a traumatic etiology. The first 2 causes of infection in such patients

involve the urinary tract followed by pressure ulcers [3]. In recent studies, some experts estimated the complication rate of late-stage pressure ulcers to be 17.3%, including contiguity osteomyelitis [4], with pelvic osteomyelitis or osteoarticular hip involvement.

The most common microorganisms involved in osteomyelitis due to pressure ulcers among SCI patients are *Staphylococcus aureus* and *Enterococcus faecalis* (approximately 77%), followed by anaerobes (40%) and Enterobacterales (20%) [5, 6]. In 2018, the Infectious Disease Society of America (IDSA) distributed a survey among a large panel of specialists that revealed widely divergent diagnostic and treatment approaches of osteomyelitis associated with pressure ulcers [7].

Bone and joint infections (BJIs) are considered to be among the most serious and difficult to treat infections, with protocols often recommending a combination of debridement surgery and prolonged courses of antimicrobial therapy, and most of the literature relates to prosthetic joint infection [8]. It is even more complex among SCI patients sometimes

Received 18 February 2022; editorial decision 11 April 2022; accepted 13 April 2022; published online 17 April 2022

Correspondence: B. Davido, MD, Msc, Service des Maladies Infectieuses, Université Paris-Saclay, Hôpital Raymond Poincaré, AP-HP, 104 Boulevard Raymond Poincaré, 92380 Garches, France (benjamin.davido@aphp.fr).

Open Forum Infectious Diseases®

© The Author(s) 2022. Published by Oxford University Press on behalf of Infectious Diseases Society of America. This is an Open Access article distributed under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs licence (<https://creativecommons.org/licenses/by-nc-nd/4.0/>), which permits non-commercial reproduction and distribution of the work, in any medium, provided the original work is not altered or transformed in any way, and that the work is properly cited. For commercial re-use, please contact journals.permissions@oup.com
<https://doi.org/10.1093/ofid/ofac209>

requiring large debridement surgery with variable antimicrobial therapy duration [5], sometimes considered as being over treated [7].

In BJIs, commonly encountered susceptible microorganisms can be easily treated using a combination therapy including fluoroquinolones (FQs), due to its high oral bioavailability and bone diffusion [9]. However, FQ resistance is increasing, and it is very frequent among extended spectrum beta-lactamase-producing Enterobacterales (ESBL-PE) and may be associated with poorer outcomes [10, 11].

Considering the worldwide spread of ESBL-PE [12, 13], with concomitantly a worldwide increase of carbapenemase-producing Enterobacterales (CPE) [14], physical medicine and rehabilitation physicians will inevitably be faced with the management of those rare but complex osteomyelitis cases among SCI patients that are most exposed to healthcare-associated infections and antimicrobials.

To our knowledge, there is no reported case series addressing the management of contiguity hip joint infections caused by multidrug-resistant Enterobacterales (ESBL-PE and CPE) in SCI patients. New data are always appreciated to support their specific care, which prompts us to share our experience in their management.

METHODS

Compliance With Ethical Standards

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Ethical Approval and Informed Consent

The research was conducted in accordance with the Declaration of Helsinki as well as national and institutional standards. No patient included in the study expressed opposition to the use of clinical data in this retrospective study.

Setting

A retrospective study was conducted in a French reference center for BJIs treatment serving the Greater Paris area, organized around weekly multidisciplinary meetings with an infectious disease specialist, an orthopedic surgeon, a microbiologist, and a pharmacist. All SCI adults of documented hip osteomyelitis due to ESBL-PE and/or CPE from January 2011 to January 2020 were identified using the laboratory information system (GLIMS v8; MIPS, Belgium).

During this 9-year period, our center managed approximately 2500 BJIs, in contrast with approximately 550 SCI patients admitted every year for rehabilitation. The center is part of the Assistance-Publique des Hôpitaux de Paris (AP-HP) group,

with Hôpital Raymond Poincaré being a center of expertise in neurological impairment, including patients with paraplegia and pressure ulcers. This patient population is frequently colonized by multidrug-resistant organisms with an incidence that can reach up to twice the value observed in French healthcare facilities. Indeed, the incidence of ESBL-PE in rectal swab screening was 1.39 per 1000 patient-days, compared with a national average of 0.59 per 1000 patient-days in the general population. Furthermore, Hôpital Raymond Poincaré reported a high antibiotic consumption for inpatients from 741 to 505 defined daily doses (DDD) during the same period, versus from 377 to 306 DDD per 1000 patient-days in comparison with all other French healthcare-facilities. These numbers are mostly explained by 2 factors: first, the population served by Hôpital Raymond Poincaré, which specializes in the care for highly resistant organisms and hosts a dedicated 8-bed unit caring for CPE-infected patients, including many war-injured patients with complex multidrug-resistant BJIs; and second, the large number of complex BJI inpatients benefitting from prolonged high-dose combination antimicrobial therapies.

Microbiological Methods

At least 3 intraoperative samples of bone and tissue were collected (MED-Extremes) and processed using a bead mill as previously reported [15]. Cultures were performed on solid media with 5 days incubation under aerobic, anaerobic, and CO₂ atmospheres and a 14-day broth enrichment on blood culture media (Bactec Peds Plus media and Lytic Anaerobic media on a Bactec FX instrument; BD Diagnostic, Sparks, MD).

Bacterial identification of all cultured microorganisms was performed by MALDI-TOF mass spectrometry (MALDI Biotyper; Bruker Daltonique, Wissenbourg, France), and susceptibility testing was performed by Kirby-Bauer disk diffusion and diameters digitized using the SIRSCAN system (I2A, Montpellier, France), and interpreted according to the French implementation (Société Française de Microbiologie a créé un Comité de l'Antibiogramme [CA-SFM]) of the European Committee on Antimicrobial Susceptibility Testing (EUCAST) guidelines in use at the time of analysis.

Confirmation of ESBL activity was provided by testing the synergy between clavulanate and third-generation cephalosporins with cloxacillin inhibition of the chromosomal cephalosporinase in AmpC-producing microorganisms according to CA-SFM. Carbapenemase-producing Enterobacterales were suspected on diminished carbapenem diameters and global resistance profile on clinical isolates and confirmed by a carbapenem hydrolysis assay. The molecular identification of the carbapenemase was achieved by immunoenzymatic assays or molecular detection assay (Xpert1 Carbapenemase Test; Cepheid, Maurens-Scopont, France), and cases negative for OXA-48-like, New Delhi metallo- β -lactamase, Verona integron-encoded metallo- β -lactamase, *K pneumoniae*

carbapenemase, or imipenemase were sent to the French national reference center for antimicrobial resistance for further exploration. On demand minimum inhibitory concentrations of relevant antimicrobial agents were confirmed using ellipsometry (E-test, bioMérieux, Marcy l’Etoile, France or Liophilchem, I2A) according to EUCAST breakpoints.

Definitions

Bone and joint infection was defined by both imaging with an articular involvement and a microbiologically positive bone biopsy. We purposefully excluded isolated pelvic osteomyelitis without hip arthritis, which is a different clinical entity treated with negative pressure therapy associated when needed with flap coverage [17]. Bone and joint infection caused by multidrug-resistant Enterobacterales was defined as microbiological documentation with 1 or more intraoperative tissue samples or joint fluid positive for ESBL-PE or CPE. Treatment success was defined as the absence of local or systemic signs of infection, including delayed wound healing and the absence of relapse requiring additional surgery within 3 months. Cases that did not meet the above-mentioned criteria were classified as “primary failure”, and outcome was evaluated at the time of failure. Secondary success was evaluated according to the same criteria 3 months after the last surgery in cases in which primary failure occurred.

Data Collection

The following data were collected: patient characteristics (age, sex, comorbidities, Charlson score [18], hospitalization and stay abroad for more than 1 month within previous 6 months, hospital length of stay [LOS], digestive tract colonization); infection characteristics (presence of an implant or foreign body, site of infection, species of the causative microorganism and mechanism of resistance, its resistance to FQs); treatment characteristics (number of procedures including the present one, surgical strategy, antimicrobial therapy, and duration); and outcome and time frame of its evaluation (months).

Statistical Analysis

Descriptive results were expressed using the median and range for continuous variables, where appropriate, and as the number (percentage) for categorical variables. Analyses were performed using Microsoft Excel 2018 (Microsoft Corp., Redmond, WA).

RESULTS

Study Population and Infection Characteristics

During the study period, the center did manage approximately 185 patients for hip infections, while we observed 101 BJIs caused by multidrug-resistant Enterobacterales. After exclusion of non-SCI patients, we analyzed 17 patients (16.8%) whose details are presented in Table 1.

The sex ratio (male/female) was 8:1 with a mean \pm standard deviation age of 52 ± 15 years. The median Charlson comorbidity score was 1 (range, 0–6) and the median LOS was 30 (range, 10–69) days.

Infection sites were exclusively the hip ($n = 17$), including 1 external fixator on 1 prosthesis. Sixteen patients suffered from traumatic paraplegia and 1 multiple sclerosis with spinal cord disorder responsible for ischial pressure sore. The majority of patients had previously been hospitalized within the previous 6 months ($n = 12$; 70.6%), and all carriers of CPE ($n = 3$) had returned from countries with a high rate of multidrug-resistant Enterobacterales.

Infections were mostly polymicrobial ($n = 15$; 88.2%), notably caused by *K pneumoniae* ($n = 10$) and *S aureus* ($n = 10$), followed by ESBL-producing *Escherichia coli* ($n = 5$). All carbapenemases were of the OXA-48-type ($n = 3$), hosted each by *K pneumoniae*, *E coli*, and *Klebsiella aerogenes* and caused resistance to all carbapenems. Multidrug-resistant Enterobacterales were mainly resistant to FQ. Indeed, resistance was observed in 70.6% of ESBL-PE and CPE ($n = 12$).

Surgical Management

The median number of surgical procedures was 2 (range, 1–10). Of 17 cases of hip joint infections, 16 (94.1%) benefited from a femoral head and neck excision as illustrated in Figure 1, and 1 debridement with saline lavage that resulted in failure.

Antimicrobial Susceptibilities, Treatments, and Outcomes

Antibiotic susceptibility differed widely between isolates from different patients (see Table 1). Patients were most often treated with combination therapies—dual therapy ($n = 8$) or triple therapy or more ($n = 5$)—and rarely with monotherapy ($n = 4$). The most prescribed antimicrobial therapy was based on carbapenems ($n = 10$), the recommended therapy for ESBL-PE. Median duration of treatment was 45 (6–60) days.

Primary treatment was successful in 10 patients (58.8%) with a median follow-up of 3 (1–36) months. Five patients required a subsequent surgery to achieve infection control, and 2 patients died several months after the treatment including 1 with a chronic fistula. Moreover, there was a trend for a poorer outcome in patients infected by *K pneumoniae* isolates (success $n = 4$ of 10) versus other microorganisms ($n = 6$ of 7).

DISCUSSION

To the best of our knowledge, literature is scarce about the natural history of BJIs among SCI patients [19–21]. In addition, only a few reports detailed the microbiological documentation, with the exception of pelvic osteomyelitis [5–7]. Moreover, little is known about BJIs caused by multidrug-resistant Enterobacterales, with experts agreeing that their management relies on orthopedic implants removal [11, 22, 23]. Following

Table 1. Cases Summary

N	Year	Sex	Age (Years)	Comorbidities	Admission in Previous 6 Months	Stay Abroad	Colonization	Implant	Surgical Strategy	Number of Procedures	Microorganisms	FQ	Antimicrobial Therapy	Hospital LOS (Days)	Outcome	Follow-up (Months)
1	2019	M	79	Myeloma, traumatic paraplegia	Yes	No	ESBL <i>Klebsiella pneumoniae</i>	No	Right femoral head and neck excision	1	ESBL <i>K pneumoniae</i>	R	MEM (16 days), followed by CAZ/AVI + TEM (7 days)	69	Failure (chronic fistula) then death	18
2	2018	F	58	Traumatic paraplegia	Yes	No	ESBL <i>Escherichia coli</i>	No	Right femoral head and neck excision	2	MRSA, ESBL <i>E coli</i> , <i>K pneumoniae</i> , <i>Bacteroides fragilis</i>	R	TZP + DAP (3 days) and finally MEM + CLI + RIF (33 days)	21	Favorable	24
3	2018	M	52	Traumatic paraplegia	Yes	No	ESBL <i>E coli</i>	No	Left femoral head and neck excision	2	ESBL <i>E coli</i> , <i>Pseudomonas aeruginosa</i>	R	TZP + DAP (4 days) and finally CAZ + SXT + CIP (44 days)	30	Favorable	6
4	2018	M	64	Traumatic paraplegia	No	Yes (Egypt)	ESBL <i>K pneumoniae</i> , ESBL <i>E coli</i> , OXA48- <i>E coli</i>	No	Right femoral head and neck excision	1	ESBL <i>E coli</i> , <i>Proteus mirabilis</i> , <i>Enterococcus</i> spp, ESBL <i>K pneumoniae</i>	R	MEM + DAP (7 days) and finally SXT + CLI (35 days)	62	Favorable	12
5	2017	M	59	Traumatic paraplegia	No	Yes (Thailand)	ESBL <i>E coli</i> , ESBL <i>K pneumoniae</i> , <i>Acinetobacter baumannii</i>	No	Right femoral head and neck excision	3	OXA48 <i>K pneumoniae</i> , MSSA and ESBL <i>K pneumoniae</i>	R	IMI + COL + DAP (30 days)	50	Failure (new surgery) then death	2
6	2017	M	50	Traumatic paraplegia, B hepatitis	No	No	ESBL <i>E coli</i>	No	Left femoral head and neck excision	3	MRSA, <i>P mirabilis</i> , <i>Streptococcus</i> spp, ESBL <i>K pneumoniae</i> , <i>Enterococcus avium</i>	S	MEM + DAP (40 days)	25	Failure (new surgery)	2
7	2017	M	46	Traumatic paraplegia	Yes	No	No	External Fixator	Right femoral head and neck excision	2	<i>Enterococcus faecalis</i> , ESBL <i>E coli</i>	R	MEM (45 days)	25	Failure (new surgery)	2
8	2017	M	73	Traumatic paraplegia, diabetes, hypertension	No	No	No	No	Right femoral head and neck excision	1	ESBL <i>K pneumoniae</i>	R	CAZ/AVI (45 days)	35	Favorable	3
9	2017	M	44	Traumatic paraplegia, diabetes, hypertension	Yes	No	ESBL <i>K pneumoniae</i>	No	Right femoral head and neck excision	10	ESBL <i>K pneumoniae</i> , <i>P mirabilis</i> , <i>Bacteroides fragilis</i> , MRSA, <i>actinomyces</i>	S	ATM + MTZ + CIP + DAP (60 days)	35	Failure (new surgery)	2
10	2017	M	50	Traumatic paraplegia	No	No	No	No	Left femoral head and neck excision	3	ESBL <i>Enterobacter cloacae</i> , MSSA	S	MEM + RIF (45 days)	31	Favorable	6
11	2017	M	54	Traumatic paraplegia	Yes	No	No	No	Left femoral head and neck excision	3	<i>P mirabilis</i> , <i>Enterococcus faecium</i> and ESBL <i>K pneumoniae</i>	R	MEM + DAP + FOS (45 days)	60	Failure (new surgery)	1
12	2016	M	49	Diabetes, multiple sclerosis	Yes	No	No	No	Right femoral head and neck excision	2	OXA48/ESBL <i>E coli</i> , <i>P mirabilis</i>	S	FOS + CIP (45 days)	21	Favorable	24
13	2015	M	29		Yes	Yes (Morocco)	OXA48/ESBL	No	Right femoral	10	OXA48/ESBL <i>K mirabilis</i>	I	TZP (3 days) and	35	Favorable	36

Table 1. Continued

N	Year	Sex	Age (Years)	Comorbidities	Admission in Previous 6 Months	Stay Abroad	Colonization	Implant	Surgical Strategy	Number of Procedures	Microorganisms	FQ	Antimicrobial Therapy	Hospital LOS (Days)	Outcome	Follow-up (Months)
				Traumatic paraplegia			<i>Klebsiella aerogenes</i> OXA48 <i>E coli</i>		head and neck excision		<i>aerogenes</i> , MSSA, <i>Corynebacterium amycolatum</i>		finally LVX (3 days)			
14	2014	F	73	Traumatic paraplegia, PAOD	Yes	No	ESBL K <i>pneumoniae</i>	Prosthesis	Implant removal and right femoral head and neck excision	3	ESBL K <i>pneumoniae</i> , MRSA	R	IMI + VAN (45 days)	10	Favorable	12
15	2012	M	27	Traumatic paraplegia	Yes	No	No	No	Right hip surgical debridement	3	MRSA, ESBL K <i>pneumoniae</i>	R	IMI + VAN (45 days)	10	Failure (new surgery)	3
16	2011	M	25	Traumatic paraplegia	Yes	No	No	No	Right femoral head and neck excision	2	ESBL <i>E cloacae</i> , MSSA, <i>E faecalis</i>	S	IMI, GEN (12 days) and finally IMI + LVX (21 days)	21	Favorable	3
17	2011	M	52	Traumatic paraplegia	No	No	No	No	Right femoral head and neck excision	1	ESBL <i>E cloacae</i> , MSSA	R	IMI + AMK (10 days) and finally IMI (20 days)	14	Favorable	3

Abbreviations: AMK, amikacin; ATM, aztreonam; CAZ, ceftazidime; CAZ/AVI, ceftazidime-avibactam; CEF, cefepime; CIP, ciprofloxacin; CLI, clindamycin; COL, colistin; DAP, daptomycin; ESBL, extended-spectrum beta-lactamase; FOS, fosfomycin; FQ, fluoroquinolone; FUS, fusidic acid; GEN, gentamicin; I, intermediate; IMI, imipenem; LOS, length of stay; LVX, levofloxacin; MEM, meropenem; MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-susceptible *Staphylococcus aureus*; MTZ, metronidazole; PAOD, peripheral arterial obstructive disease; R, resistant; RIF, rifampicin; S, susceptible; SXT, trimethoprim/sulfamethoxazole; TEM, temocillin; TGC, tigecycline; TZP, piperacillin/tazobactam; VAN, vancomycin; VRE, vancomycin-resistant enterococci.

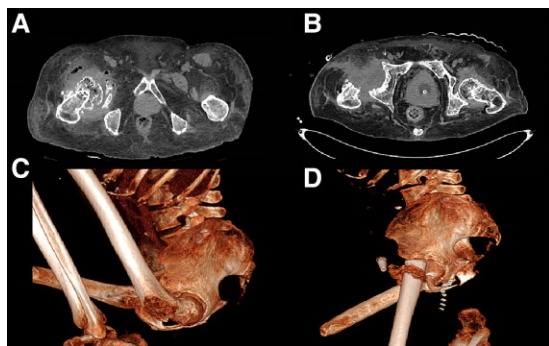


Figure 1. Pre- and postoperative computed tomography (CT) scan documentation of head and neck resection surgery. Patient number 1: preoperative CT-scan showing large intracapsular gas collections and multiple geodes within the right femoral head (A). Femoral head and neck resection left an extensive synovitis with a fistulous tract that caused a relapse (B). Patient number 3: 3-dimensional CT scan reconstruction showing left trochanteric osteomyelitis with bone loss (C), and postoperative femoral head and neck resection with removal of the diseased bone tissue (D).

up on our previous reports of native ESBL-PE and CPE BJIs [24, 25], we report an original case series of hip joint infections caused by multidrug-resistant Enterobacterales among SCI patients.

Our study revealed a primary success rate of 58.8% for a deemed difficult-to-treat infection, with up to 88.2% success after repeated surgery. This result is remarkable because this subset of infections caused by multidrug-resistant Enterobacterales could be expected to be therapeutically more challenging than cases caused by susceptible organisms. Ohlmeier et al [21] reported 21 of 59 SCI patients infected by susceptible microorganisms, successfully treated by a single surgery using the same technique of femoral head and neck resection. The procedure has the advantage of significantly reducing the LOS and the number of subsequent surgeries in case of recurrent pressure ulcers [19]. Indeed, in such a population of SCI, it is common that patients require a revision surgery, with a median number of surgeries in our cohort of 2 procedures in comparison to 2.6 as reported by Ohlmeier et al [21].

Although our work focuses on multidrug-resistant Enterobacterales, especially *K pneumoniae*, the second species of microorganisms observed was *S aureus*. Staphylococci has been previously described as a major bacteria involved in pressure ulcers complications among SCI cases [5, 6] but also in the global epidemiology of osteomyelitis [26]. Of note, given the limited sample size, we could not perform statistical analysis, but there was a trend towards poorer outcome for *K pneumoniae* hip infections, as previously supported in our work regarding ESBL-PE BJIs [25].

It is noteworthy that we commonly used carbapenems against BJIs caused by multidrug-resistant Enterobacterales. However, some circumstances required last-resort antibiotics

(fosfomycin, tigecycline, and colistin) [27], and also a novel antibiotic (ceftazidime-avibactam), effective against ESBL-PE and most CPE. Those treatments were chosen considering the high rate of FQs-resistant strains (70.6%).

Concerning the duration of treatment, we prescribed a median duration of antibiotics of 45 days as recommended by the guidelines issued by the Infectious Diseases Society of America regarding the treatment of native osteomyelitis [28]. Such long treatment duration might explain our median LOS (30 days); meanwhile, LOS of rehospitalization averages approximately 18 days among SCI patients according to the National SCI Statistical Center in the United States [29].

In our findings, the sex ratio (male/female) of 8:1 is concordant with the data observed by the National SCI Statistical Center, where approximately 80% of new cases are male considering their higher risk behavior [29]. Nevertheless, our study presents some limitations. First, it is a relatively limited sample size ($n = 17$) but for a rare condition from a center of reference for the treatment of complex BJIs among SCI patients. Second, the retrospective nature of the study did not allow an exhaustive list of the received antimicrobial therapies by the orthopedic surgeons. Third, these patients were coming for different and multiple centers of rehabilitation with prescriptions for antibiotics, most of them time over-the-counter medications, including for positive urinary samples, which made it difficult to draw conclusions of the actual contribution of antimicrobial therapy in addition to surgery. Fourth, the short median follow-up of 3 months is mostly due to the broad catchment area of our specialized centers, limiting the interpretation of the endpoint, considering that the average time until recurrence can reach up to 2 years [20]. However, from our previous experience, those failures typically appear within the next 6 weeks after surgery and are easily re-addressed to our center of expertise in case of relapse. Moreover, these infections do not involve implant-related biofilm formation and are not, in our experience, subject to delayed failure. Moreover, it is difficult to ensure such a prolonged follow-up among patients of impaired mobility who often reside far away and require rehabilitation centers. Fifth, phenotypes of the microorganisms included are heterogeneous and polymicrobial, which makes it difficult to interpret the value of the different antibiotic strategies used, but the homogeneity of the surgical procedure largely based on femoral head and neck excision supports its reproducibility.

CONCLUSIONS

In the present series of SCI patients suffering from hip infections, osteomyelitis were caused by multidrug-resistant Enterobacterales, including *K pneumoniae* and *S aureus*, that were mainly fluoroquinolones-resistant. Although patients had few comorbidities, they required aggressive surgery relying

on femoral head and neck excision with multiple revision to improve definite outcome, highlighting the need for expert centers with pluridisciplinary meetings with experienced specialists. Infectious disease specialists familiar with the use of broad-spectrum antibiotics are crucial to ensure their proper use in combination, with appropriate dosage and duration. Further data are needed to evaluate the impact of shorter treatment duration with novel drugs on the outcome.

Notes

Author contributions. B. D., L. N., T. B., and A. C. C. designed the study. B. D. and F. E. S. supervised data collection and data management. B. D., H. L. L., D. M., J. L. H., and K. J. analyzed the data. B. D. and A. S.-M. prepared the first draft of the manuscript. M. R. was responsible for editing and proofreading the entire manuscript. All the authors participated in manuscript preparation and approved the final manuscript for publications. I confirm that all listed authors have contributed to this work and approved the paper.

Financial support. This work was carried out as part of our routine work.

Potential conflicts of interest. All authors: No reported conflicts of interest. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest.

References

- Jain NB, Ayers GD, Peterson EN, et al. Traumatic spinal cord injury in the United States, 1993–2012. *JAMA* **2015**; 313:2236–43.
- Scivoletto G, Miscusi M, Forcato S, et al. The rehabilitation of spinal cord injury patients in Europe. *Acta Neurochir Suppl* **2017**; 124:203–10.
- Dinh A, Saliba M, Saadeh D, et al. Blood stream infections due to multidrug-resistant organisms among spinal cord-injured patients, epidemiology over 16 years and associated risks: a comparative study. *Spinal Cord* **2016**; 54: 720–5.
- Larson DL, Hudak KA, Waring WP, Orr MR, Simonelic K. Protocol management of late-stage pressure ulcers: a 5-year retrospective study of 101 consecutive patients with 179 ulcers. *Plast Reconstr Surg* **2012**; 129:897–904.
- Rigazzi J, Fährndrich C, Osinga R, et al. Osteomyelitis and antibiotic treatment in patients with grade IV pressure injury and spinal cord lesion—a retrospective cohort study. *Spinal Cord* **2022**. doi: 10.1038/s41393-022-00758-1.
- Brunel AS, Lamy B, Cyteval C, et al. Diagnosing pelvic osteomyelitis beneath pressure ulcers in spinal cord injured patients: a prospective study. *Clin Microbiol Infect* **2016**; 22:267.e1–8.
- Kaka AS, Beekmann SE, Gravely A, Filice GA, Polgreen PM, Johnson JR. Diagnosis and management of osteomyelitis associated with stage 4 pressure ulcers: report of a query to the emerging infections network of the Infectious Diseases Society of America. *Open Forum Infect Dis* **2019**; 6:ofz406.
- Minassian AM, Osmon DR, Berendt AR. Clinical guidelines in the management of prosthetic joint infection. *J Antimicrob Chemother* **2014**; 69(Suppl 1):i29–35.
- Rissing JP. Antimicrobial therapy for chronic osteomyelitis in adults: role of the quinolones. *Clin Infect Dis* **1997**; 25:1327–33.
- Martínez-Pastor JC, Vilchez F, Pitart C, Sierra JM, Soriano A. Antibiotic resistance in orthopaedic surgery: acute knee prosthetic joint infections due to extended-spectrum beta-lactamase (ESBL)-producing Enterobacteriaceae. *Eur J Clin Microbiol Infect Dis* **2010**; 29:1039–41.
- Rodríguez-Pardo D, Pigrau C, Lora-Tamayo J, et al. Gram-negative prosthetic joint infection: Outcome of a debridement, antibiotics and implant retention approach. A large multicentre study. *Clin Microbiol Infect* **2014**; 20:O911–9.
- Magiorakos A-P, Srinivasan A, Carey RB, et al. Multidrug-resistant, extensively drug-resistant and pandrug-resistant bacteria: an international expert proposal for interim standard definitions for acquired resistance. *Clin Microbiol Infect* **2012**; 18:268–81.
- McDanel J, Schweizer M, Crabb V, et al. Incidence of extended-spectrum β -lactamase (ESBL)-producing *Escherichia coli* and *Klebsiella* infections in the United States: a systematic literature review. *Infect Control Hosp Epidemiol* **2017**; 38:1209–15.
- van Duin D, Doi Y. The global epidemiology of carbapenemase-producing Enterobacteriaceae. *Virulence* **2017**; 8:460–9.
- Roux AL, Sivadon-Tardy V, Bauer T, et al. Diagnosis of prosthetic joint infection by beadmill processing of a periprosthetic specimen. *Clin Microbiol Infect* **2011**; 17:447–50.
- Tenover FC, Raney PM, Williams PP, et al. Evaluation of the NCCLS extended-spectrum beta-lactamase confirmation methods for *Escherichia coli* with isolates collected during Project ICARE. *J Clin Microbiol* **2003**; 41:3142–6.
- Andrianasolo J, Ferry T, Boucher F, et al. Pressure ulcer-related pelvic osteomyelitis: evaluation of a two-stage surgical strategy (debridement, negative pressure therapy and flap coverage) with prolonged antimicrobial therapy. *BMC Infect Dis* **2018**; 18:166.
- Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* **1987**; 40:373–83.
- Correa GI, Calderón WO, Roa RG, Guzmán LM, Burnier LA, Danilla SE. Proximal amputation of inferior extremity secondary to recurrent pressure ulcers in patients with spinal cord injuries. *Spinal Cord* **2008**; 46:135–9.
- Rubayi S, Gabbay J, Kruger E, Ruhge K. The modified Girdlestone procedure with muscle flap for management of pressure ulcers and heterotopic ossification of the hip region in spinal injury patients: a 15-year review with long-term follow-up. *Ann Plast Surg* **2016**; 77:645–52.
- Ohlmeier M, Bode A, Suero EM, et al. Outcome of subtrochanteric femur resection in patients with spinal cord injuries. *J Wound Care* **2018**; 27:774–8.
- Papadopoulos A, Ribera A, Mavrogenis AF, et al. Multidrug-resistant and extensively drug-resistant gram-negative prosthetic joint infections: role of surgery and impact of colistin administration. *Int J Antimicrob Agents* **2019**; 53:294–301.
- Pfang BG, García-Cañete J, García-Lasheras J, et al. Orthopedic implant-associated infection by multidrug resistant Enterobacteriaceae. *J Clin Med* **2019**; 8:220.
- Davido B, Noussair L, Saleh-Mghir A, et al. Case series of carbapenemase-producing Enterobacteriaceae osteomyelitis: feel it in your bones. *J Glob Antimicrob Resist* **2020**; 23:74–8.
- Davido B, Saleh-Mghir A, Rottman M, et al. Native bone and joint infections caused by extended-spectrum β -lactamase-producing Enterobacteriales: experience of a reference centre in the Greater Paris area. *Int J Antimicrob Agents* **2022**; 59:106497.
- Titécát M, Senneville E, Wallet F, et al. Bacterial epidemiology of osteoarticular infections in a referent center: 10-year study. *Orthop Traumatol Surg Res* **2013**; 99:653–8.
- Davido B, Bouchand F, Dinh A, et al. Reinforcement of an antimicrobial stewardship task force aims at a better use of antibiotics of last resort: the COLITIFOS study. *Int J Antimicrob Agents* **2017**; 50:142–7.
- Barbari EF, Kanj SS, Kowalski TJ, et al. Infectious Diseases Society of America (IDSA) clinical practice guidelines for the diagnosis and treatment of native vertebral osteomyelitis in adults. *Clin Infect Dis* **2015**; 2015:e26–46.
- Spinal cord injury (SCI) 2016 facts and figures at a glance. *J Spinal Cord Med* **2016**; 39:493–4.