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REVIEWER'S REPORT

Manuscript No.: 56052

Title: Carbapenem-Resistant Klebsiella pneumoniae Prosthetic Hip Infection Following a Pelvic Pressure Ulcer: Therapeutic Value of Ceftazidime– Avibactam

Recommendation:
Accept as it is …….
Accept after minor revision……Yes……
Accept after major revision ……
Do not accept (*Reasons below*) ……

Rating	Excel.	Good	Fair	Poor
Originality	•			
Techn. Quality	•			
Clarity	•			
Significance	•			

Reviewer Name: Dr. Sireesha Kuruganti **Date:** 05/02/2026

Detailed Reviewer's Report

Here's an in-depth review of the manuscript, with references to line numbers where appropriate:

General Comments:

This manuscript presents a compelling case report on a carbapenem-resistant Klebsiella pneumoniae (CRKP) prosthetic hip infection (PJI) following a pelvic pressure ulcer, successfully treated with ceftazidime-avibactam. The authors effectively highlight a critical clinical challenge and a valuable therapeutic solution. The narrative flows logically, from introduction to case report, discussion, and conclusion. The emphasis on hematogenous spread from a distant infectious focus is well-supported and offers an important clinical insight.

Specific Feedback:

Title (Lines 1-5):
"Carbapenem-Resistant Klebsiella pneumoniae Prosthetic Hip Infection Following a Pelvic Pressure Ulcer: Therapeutic Value of Ceftazidime-Avibactam" - The title is accurate, concise, and clearly reflects the content of the manuscript. It effectively conveys the main points of the case.

Abstract (Lines 7-24):
The abstract is well-structured and summarizes the case, its diagnostic complexity, therapeutic difficulties, and the successful outcome with ceftazidime-avibactam.
Line 13: "strongly suggesting hematogenous spread from the remote infectious focus." This is a key conclusion that is well-supported in the discussion.
Lines 23-24: "supporting its role as a valuable treatment option for severe prosthetic joint infections due to carbapenem-resistant Enterobacterales." This concluding statement accurately reflects the study's primary contribution.
Keywords (Lines 26-28): The keywords are appropriate and will aid in searchability.

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Introduction (Lines 31-50):

Lines 31-34: The introduction sets the stage by emphasizing the seriousness of PJIs, particularly those caused by multidrug-resistant Gram-negative bacteria like CRKP. This provides necessary context.

Lines 36-39: "In some patients, PJI may occur through hematogenous dissemination from a distant infectious focus. Pelvic pressure ulcers, especially when complicated and heavily colonized by resistant organisms, may constitute an underrecognized source of bacteremia and subsequent prosthetic infection." This is a crucial point and a central theme of the manuscript. The authors effectively introduce the hypothesis of hematogenous spread from pressure ulcers.

Lines 41-43: The introduction of ceftazidime-avibactam as a new therapeutic opportunity is timely and relevant.

Lines 45-50: The authors clearly state the purpose of the case report, focusing on the pathophysiological mechanism and the beneficial role of ceftazidime-avibactam. This provides a clear roadmap for the reader.

Case Report (Lines 52-96):

Lines 52-57: The patient's demographics, comorbidities (poorly controlled diabetes, chronic kidney disease, pelvic trauma leading to bed confinement), and initial presentation with a complicated pelvic pressure ulcer are clearly described. These comorbidities are important for understanding the patient's susceptibility to such a severe infection.

Lines 59-62: The initial clinical findings (perineal pain, necrosis, right hip pain, fever), radiological assessment (femoral neck fracture, subcutaneous emphysema, pelvic abscess), and laboratory results (severe inflammation, leukocytosis) are well-documented, providing a comprehensive picture of the patient's condition.

Lines 63-65: The isolation of CRKP and Enterococcus faecalis from the necrotic area is critical. The mention of "antibiogram in Table 1" indicates that important data might be missing from this text. If Table 1 is meant to be included, its absence in this document should be noted. If it's merely a past reference, that should be clarified.

Lines 67-68: Initial management with colistin and imipenem, along with hyperbaric oxygen therapy, and subsequent improvement, provides a baseline for later comparison when these therapies fail for the PJI.

Lines 69-70: The timeline of the total hip arthroplasty (THA) implantation one month after initial management is important.

Lines 72-76: The development of fever, local inflammation, and worsening laboratory markers (leukocytosis, CRP) ten days post-surgery clearly indicates a new infection.

Lines 78-79: The isolation of CRKP from both superficial and deep pus samples, along with Enterococcus faecalis from the superficial site, reinforces the strong suspicion of PJI. The identification of the same CRKP strain is a crucial piece of evidence for the hematogenous spread hypothesis.

Lines 80-81: The continuation of colistin and imipenem, and only transient improvement, highlights the resistance challenge.

Lines 83-87: The chronic nature of the infection, persistent purulent discharge over three years, deep collection, and eventual septic loosening necessitating prosthesis removal, clearly demonstrate the severity and recalcitrance of the PJI. Re-isolation of CRKP with the same resistance profile from the explanted material further strengthens the argument for a persistent infection from the original source.

Lines 89-94: The detailed antibiotic susceptibility testing results are vital. The extensive resistance to various beta-lactams, carbapenems, aminoglycosides, fluoroquinolones, and trimethoprim-sulfamethoxazole underscores the limited therapeutic options. The fact that "colistin remained the only active agent" initially, but later failed, sets the stage for the introduction of ceftazidime-avibactam.

Line 96: "Targeted therapy with ceftazidime--avibactam was initiated, leading to marked and sustained clinical improvement." This is the pivotal outcome of the case report.

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Discussion (Lines 98-150):

Lines 98-100: The discussion begins by reiterating the clinical significance of PJI and identifying high-risk patient populations.

Lines 100-104: The authors effectively transition to the concept of hematogenous seeding from distant infectious foci, citing Zimmerli et al. (1) and Tande and Patel (3). This strengthens the proposed mechanism in the reported case.

Lines 106-107: "In the present case, the pelvic pressure ulcer previously infected by multidrug-resistant K. pneumoniae and E. faecalis constituted a clear infectious focus." This direct link back to the patient's case is well-made.

Lines 107-109: The citation of other authors demonstrating pressure ulcers leading to severe sepsis and bone dissemination (4, 5) further supports the plausibility of the proposed mechanism.

Lines 111-114: The discussion of psoas abscesses and their association with hip PJI (Dauchy et al., 6) provides additional context for potential routes of spread in the pelvic region.

Lines 116-117: The presence of subcutaneous gas, a pelvic abscess, and inflammation in the patient further supports hematogenous dissemination, although this is an inferential link.

Lines 118-121: The authors acknowledge the absence of direct literature describing spread from pressure ulcers to THAs but generalize based on the known link between deep skin infections and prosthetic infections (1, 3). This is a reasonable extrapolation.

Lines 123-125: "The early postoperative infection of the THA by a CRKP strain identical to that previously isolated from the pressure ulcer further reinforces the hypothesis of hematogenous seeding." This is a crucial statement and the strongest evidence for hematogenous spread.

Lines 125-129: Referencing Zimmerli's recommendations (1) regarding bacteremia seeding prosthetic devices within the first three months post-implantation, and Tande and Patel's (3) work on Enterobacteriales colonizing prosthetic material during bacteremia, provides robust external validation for the proposed timeline and mechanism in the case.

Lines 131-133: The authors effectively underscore the challenges associated with treating bone, joint, and implant-associated infections caused by CRKP with conventional regimens.

Lines 135-136: "Several studies support the efficacy of ceftazidime–avibactam in these infections." This transitions to the effectiveness of the chosen therapy.

Lines 136-137: Schimmenti et al. (7) describing successful treatment of CRKP PJI with ceftazidime-avibactam provides direct supporting evidence.

Lines 139-140: Experimental data on robust bone penetration of ceftazidime-avibactam and its efficacy in an osteomyelitis model (Davido et al., 8) provide a scientific basis for its use.

Lines 142-144: The favorable response of severe osteoarticular infections, including discitis and vertebral osteomyelitis caused by KPC to ceftazidime-avibactam (De León-Borrás et al., 9), further supports its broad applicability and potential superiority over colistin in challenging sites.

Lines 146-148: The inclusion of "Nonetheless, vigilance remains necessary" and the mention of rapid emergence of resistance to ceftazidime-avibactam in certain KPC variants (Liu et al., 10) demonstrates a balanced and realistic perspective on the therapy, highlighting the need for appropriate use.

Lines 149-150: The discussion concludes by circling back to the patient's case, re-emphasizing the sustained clinical improvement with ceftazidime-avibactam and reinforcing the evidence for hematogenous dissemination from the ulcer, based on the consistent resistance profile of K. pneumoniae.

Conclusion (Lines 152-160):

The conclusion effectively reiterates the main findings and implications of the case report.

Lines 152-155: It summarizes the potential for hematogenous spread of CRKP from a pressure ulcer to a hip prosthesis, along with the diagnostic and therapeutic challenges of multidrug-resistant Gram-negative pathogens in PJI.

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Lines 157-158: It clearly states the clinical benefit of ceftazidime-avibactam and its role as an important therapeutic option for CRKP PJI.

Lines 159-160: The final sentence offers a pertinent clinical recommendation about early recognition and management of distant infectious foci, especially pressure ulcers, to prevent prosthetic contamination in high-risk patients. This adds a practical takeaway message.

References (Lines 162-181):

The references appear to be relevant and support the statements made in the manuscript. The formatting seems consistent.

Overall Strengths:

Clear and well-written narrative.

Strong emphasis and convincing evidence for hematogenous spread from a pressure ulcer, a potentially underrecognized source.

Highlights a crucial therapeutic solution (ceftazidime-avibactam) for a challenging infection.

Balanced discussion acknowledging potential limitations like resistance development.

Clinical relevance for orthopedic surgeons, infectious disease specialists, and geriatricians.

Potential Areas for Minor Improvement (if not already addressed in "Table 1"):

Antibiogram Data: While mentioned in the case report (Line 64) and susceptibility testing (Lines 89-94), a complete antibiogram, possibly in a table format, showing the detailed antimicrobial susceptibility of the Klebsiella pneumoniae isolate over time would significantly enhance the manuscript's data presentation. This would visually confirm the "same resistance profile" mentioned at various points.

Figure/Image: A clinical image of the pressure ulcer or radiological images of the PJI could potentially add visual impact and further illustrate the case. However, this is not essential for the scientific merit of the case report.

In conclusion, this is a well-presented and clinically significant case report that provides valuable insights into the pathophysiology and management of CRKP PJI, particularly emphasizing the role of ceftazidime-avibactam and the often-overlooked source of pressure ulcers.