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CASE REPORT
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Case Report: *Kingella kingae* causing prosthetic joint infection in an adult

Katherine Wensley[1], Damian McClelland[1,*], Natalie Grocott[1], Gopikanthan Manoharan[1] and Seema Desai[2]

Abstract

Introduction. *Kingella kingae* is a Gram-negative micro-organism that is rarely isolated as a pathogen in the adult population. Although widely reported to affect prosthetic heart valves, there have been no previously reported cases of *K. kingae* infecting prosthetic joints in adults.

Case Presentation. A 61-year-old patient with a history of rheumatoid arthritis presented with insidious onset of pain and swelling in her right shoulder, which had progressed to a discharging sinus. The patient had undergone a total shoulder replacement 11 years previously and had not developed any prior post-operative infections. She had been taking anti-TNF medication for 5 years prior to review for her rheumatoid disease. The patient underwent a two-stage revision replacement procedure, including implant removal, sinus excision and debridement. Deep tissue samples grew *K. kingae* post-operatively. The patient was commenced on intravenous ceftriaxone for 14 days, followed by a further 28 days of oral ciprofloxacin. A second-stage custom shoulder replacement was undertaken 10 months following the first stage and the patient made a good functional recovery.

Conclusion. The authors suggest that clinicians should be attuned to *K. kingae* as a potential pathogen for prosthetic joint infection, particularly in patients who are immunosuppressed. Two-stage revision procedures can ensure a favourable outcome and eradication of this pathogen from the joint. Beta lactams remain the principal antibiotic of choice.

DATA SUMMARY

No data were generated, or reused, in this case report.

INTRODUCTION

Kingella kingae was previously considered to be part of the normal oropharyngeal flora [1], but due to improved culture techniques for this fastidious organism, it has recently been acknowledged as an emergent pathogen in the paediatric population, where it typically affects bones and joints [2]. There are very few reported cases in the adult population, where it typically causes endocarditis, spondylodiscitis or bacteraemia [3]. We present a previously unreported case of *K. kingae* prosthetic joint infection in a patient with inflammatory joint disease. Clinicians should be attuned to *K. kingae* as a potential cause of prosthetic joint infection, particularly in patients who are immunosuppressed due to immune suppressive medications. Operating surgeons must obtain deep tissue samples using sterile instruments during surgery and send them to a microbiology laboratory for culture and identification of the pathogen.

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Keywords: *Kingella kingae*; prosthetic joint infection; immunocompromised.
Abbreviations: BD, equivalent to twice a day; CLED, cystine–lactose–electrolyte-deficient; EUCAST, European Committee on Antimicrobial Susceptibility Testing; FAB, fastidious anaerobe broth; MALDI-TOF MS, matrix-assisted laser desorption/ionization time-of-flight mass spectrometry; MDT, Multi-Disciplinary Team; TDS, three times a day.

CASE PRESENTATION

A 61-year-old lady with a history of rheumatoid arthritis since 1986 was referred to the orthopaedic surgical clinic by her treating rheumatologist. She had a total shoulder replacement implanted 11 years previously at a different hospital trust and did not have any delayed healing or episodes of infection post-operatively. On attendance at the orthopaedic clinic, she reported a 1 month history of pain and swelling in the shoulder, which had progressed to an intermittently discharging sinus over the posterior aspect of her shoulder. She had not recently undergone any dental intervention or other surgical procedures, and had otherwise been systemically well throughout this period. X-rays revealed elevation of the humeral head consistent with rotator cuff failure. The replacement head had also migrated medially due to failure of the supporting glenoid bone and there was osteolysis around the humeral implant (Fig. 1.).

The patient had been on immunosuppressive medications, which included anti-TNF medication and methotrexate for rheumatoid arthritis for the previous 5 years, and was not taking antibiotics at the time of presentation to the clinic. Initial superficial wound swabs were taken for culture at this clinic attendance, all of which revealed no growth at this stage.

Initially, the patient did not wish to undergo revision surgery and instead wished to consider management with suppressant antibiotic therapy, but after further consideration, she decided to proceed with a revision procedure. A two-stage procedure was planned that initially comprised implant removal, debridement, temporary spacer insertion and empirical intravenous antibiotic therapy post-operatively, followed by reimplantation of a custom-made prosthesis at a later second stage. At the first-stage operation, the implant was removed, the sinus was excised, and an extensive debridement and washout was performed. A large loculated collection and copious infected tissue were noted. Seven deep tissue samples were obtained with sterile instruments and sent to the microbiology laboratory for culture and sensitivity testing in a sterile container. An antibiotic-loaded cement spacer (model H48G, Synicem Shoulder Spacer, Lima Orthopaedics UK Ltd, Letchworth Garden City, UK) loaded with 1.50 g of gentamicin was inserted to maintain tissue tension and joint alignment. The patient was started empirically on IV flucloxacillin 2 g QDS following surgery since Gram-positive organisms are the commonest pathogens in prosthetic joint infections, while awaiting results from the intra-operative samples.

Tissue samples were homogenized using a vortex machine with the addition of saline broth and were plated on the blood, cystine–lactose–electrolyte-deficient (CLED) and chocolate agar. Further, fastidious anaerobe broth (FAB) was also inoculated for each sample and was read each day for a total of 5 days of incubation. *K. kingae* was isolated from two out of seven tissue samples at 48 h from the blood plate and subsequently identified using matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS) technology. One out of the two positive tissue samples, with further FAB, isolated a similar pathogen. Ciprofloxacin, amoxicillin and ceftriaxone etests were set up, and the organism was detected to be sensitive to all as per European Committee on Antimicrobial Susceptibility Testing (EUCAST) guidelines. Antibiotics at this stage were rationalized as per microbiology advice and the patient was commenced on intravenous ceftriaxone 2 g once a day for 14 days, followed by a further 28 days of oral ciprofloxacin 500 mg BD (equivalent to twice a day) to complete a total 6-week course. A transthoracic echocardiogram was performed in view of the risk of endocarditis, and this was negative.

The second-stage procedure for implantation of the definitive prosthesis (custom-made Lima shoulder, Lima Orthopaedics UK Ltd, Letchworth Garden City, UK) was performed 10 months following the first stage (with two delays due to anaesthetic concerns and the presence of pressure ulcers). At the second-stage procedure, there was no evidence of an active infective process and implantation of the new custom-made prosthesis was undertaken. Three deep tissue samples were obtained using sterile instruments and sent to the microbiology laboratory for culture and sensitivity testing. Samples were processed in a similar manner as previously stated with additional broth incubation for 5 days. The patient was commenced empirically on intravenous vancomycin,

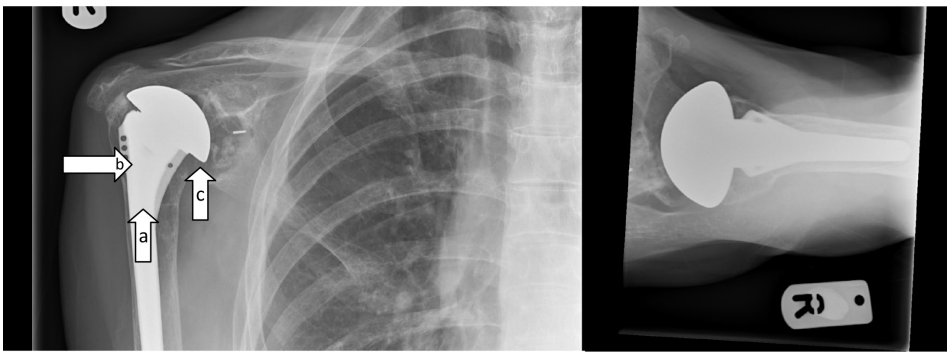

Fig. 1. X-rays taken at initial consultation demonstrating elevation of the humeral head (a), medialization of the glenoid implant (b) and osteolysis around the humeral implant (c).

dosed as per the local vancomycin calculator, and co-amoxiclav 1.2 g TDS (three times a day), as per the local hospital guidelines for revision surgery post-operatively. No pathogens were isolated from any deep tissue specimens following a final read at 5 days. The patient was subsequently discussed in the Bone Infection MDT (Multi-Disciplinary Team) meeting and it was advised that the antibiotics be rationalized to oral ciprofloxacin 500 mg BD to complete the 6-week post-operative period because the patient was immune suppressed and had a high risk of relapse.

The patient completed the course of antibiotics and recovered post-operatively with no further complications from the shoulder perspective. She continued to make progress, and her range of motion at the shoulder joint improved slowly. However, her post-operative physiotherapy was limited to over-the-phone sessions during the coronavirus disease 2019 (COVID-19) crisis and 7 months post-surgery the patient fell, sustaining a closed, right tibial shaft fracture that was successfully managed non-operatively in serial casts, although this further limited her shoulder rehabilitation. Twelve months post-operatively, her radiographs were satisfactory (Fig. 2) and she had regained function to a level beyond her pre-operative range. Her inflammatory markers were CRP 36.6, ESR 59 (consistent with her rheumatoid clinical picture), and WCC 6.8; and her clinical shoulder scores were 36 for the Oxford shoulder score, with a Constant score of 43.

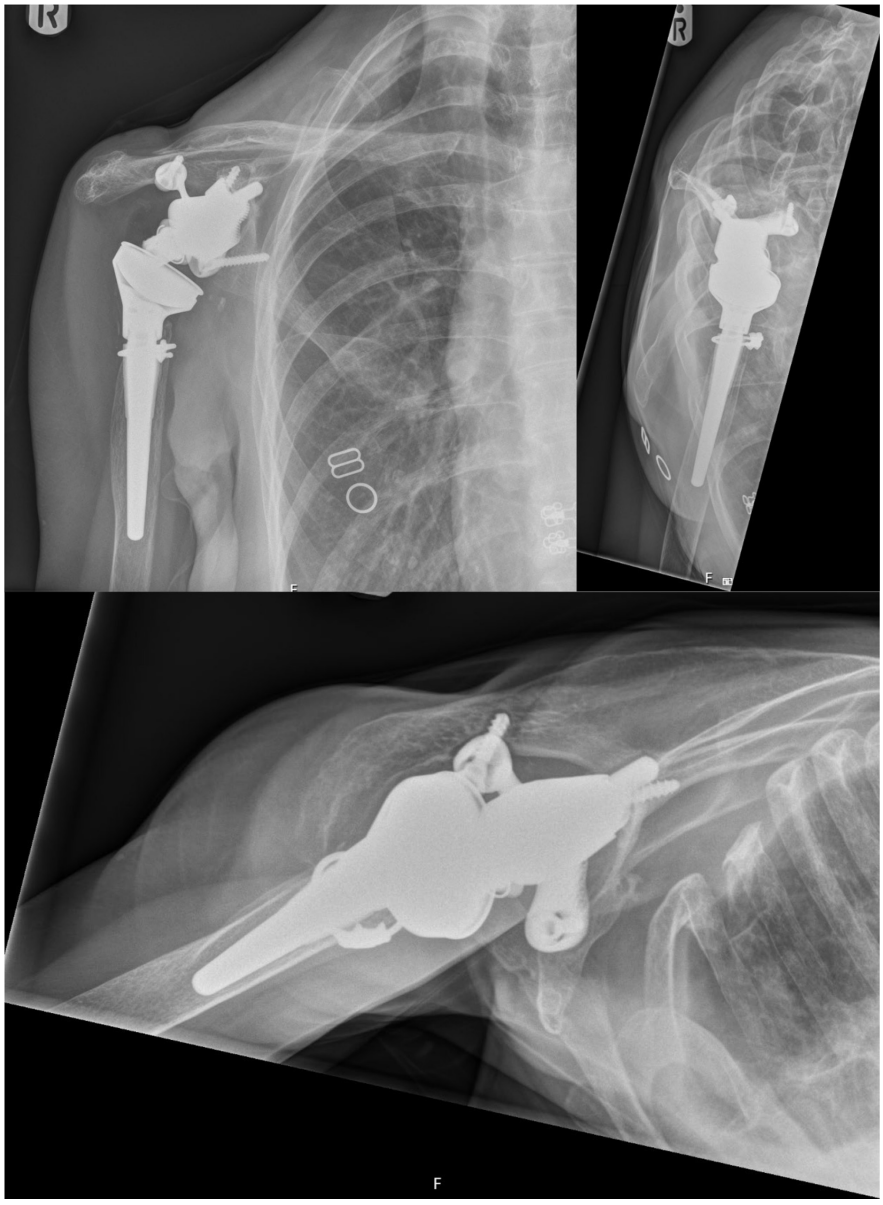

Fig. 2. X-ray images taken 12 months post-operatively, demonstrating satisfactory prosthesis position.

At 14 months post-second stage surgery, the patient was admitted with sepsis, with the likely focus originating from a right foot ulcer that had led to osteomyelitis. Superficial ulcer swabs from the right foot isolated *Staphylococcus aureus* (MSSA). The patient declined any further ongoing treatment and elected to return home with her family for palliative care.

DISCUSSION

K. kingae is a Gram-negative member of the notoriously difficult-to-culture HACEK group (*Haemophilus* species, *Aggregatibacter* species, *Cardiobacterium hominis*, *Eikenella corrodens* and *Kingella* species) of micro-organisms and a component of the normal oropharyngeal flora in children. In the past two decades, we have seen improved laboratory methods for isolating fastidious organisms, leading to increased isolation of rare pathogens from tissue samples. Consequently, there has been greater recognition of its importance as a paediatric pathogen, where it is speculated that *K. kingae* passes into the bloodstream through mucosal lesions caused by upper respiratory tract viral infections. It is known that *K. kingae*, particularly as a fastidious organism, tends to grow slowly on conventional solid culture medium, which might be why the potential of this pathogen in various clinical conditions is underestimated, especially in patients who are immunosuppressed [4]. Additionally, Gram staining on tissues could fail to detect the presence of this organism in a high percentage of cases [2, 5].

More recently, *K. kingae* has been noted as a pathogen in the adult population, most often in immunocompromised individuals, where it has been noted to cause endocarditis, spondylodiscitis or bacteraemia [2]. Although widely reported to affect prosthetic heart valves [6], to our knowledge, there have been no previously reported cases of *K. kingae* infecting prosthetic joints.

The rate of prosthetic shoulder joint infections in the general adult population ranges between 1–4% [7] and the causative pathogens are usually *Cutibacterium acnes*, *Staphylococcus aureus* and *Staphylococcus epidermidis* [1]. Due to an ageing population and the associated rise in the number of prosthetic shoulder replacements being performed [8], the rate of prosthetic joint infection cases is also likely to increase, and hence knowledge concerning potential pathogens is of increasing consequence.

Collaboration between the surgical team and microbiology colleagues is vital in ensuring optimal management when *K. kingae* is isolated. Penicillins are usually effective in treatment, as are broad-spectrum second- or third-generation cephalosporins [9–11]. Consequently, *K. kingae* is generally susceptible to broad-spectrum empirical antibiotic therapy, which is frequently administered prior to diagnosis due to the slow growth of the organism, delaying pathogen identification. 16S rDNA gene sequencing could assist in identification even after antibiotic use and can significantly reduce time to diagnosis [12]. Alternatively, the literature suggests that identification of *K. kingae* can be further improved by using blood culture broth, whereby joint fluid or pus obtained from the joint is directly inoculated into blood culture broth in theatre, which decreases the concentration of *K. kingae* growth-inhibiting factors normally present in synovial fluid [5]. This technique should therefore be considered in patients with prosthetic joint infection who are deemed to be at higher risk due to being on immunosuppressants.

CONCLUSION

K. kingae is a rare cause of prosthetic joint infection, but should be considered as a potential pathogen in adults who are immunocompromised. The authors present a case where *K. kingae* was identified as a likely pathogen infecting a primary shoulder joint replacement that was successfully treated with antibiotics and a two-stage revision surgical technique. Multidisciplinary collaboration is vital in optimizing medical and surgical outcomes in such cases.

Funding information
This work received no specific grant from any funding agency.

Author contributions
D. M.: conceptualization, data curation, methodology, supervision, validation, writing – original draft, writing – review and editing. K. W.: data curation, methodology, validation, writing – original draft, writing – review and editing. N. G.: data curation, methodology, validation, project administration, resources, writing – original draft, writing – review and editing. G. M.: data curation, methodology, validation, writing – original draft, writing – review and editing. S. D.: conceptualization, data curation, methodology, supervision, validation, writing – original draft, writing – review and editing.

Conflicts of interest
The authors declare that there are no conflicts of interest.

Ethical statement
Ethical approval was not required for this case report.

Consent to publish
All personal identifiers in this case report have been removed to ensure anonymity of the patient. A written consent form was completed by the patient for publication.

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Peer review history

VERSION 2

Editor recommendation and comments

https://doi.org/10.1099/acmi.0.000559.v2.3

Lindsey Tolman; University at Albany, UNITED STATES

Date report received: 20 June 2023
Recommendation: Accept

Comments: Reviewer comments have been satisfactorily addressed and sufficient methodology detail added to the revised submission.

SciScore report

https://doi.org/10.1099/acmi.0.000559.v2.1

iThenticate report

https://doi.org/10.1099/acmi.0.000559.v2.2

Author response to reviewers to Version 1

Mr Damian McClelland

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Editor-in-chief

Access Microbiology

14/05/2023

Dear Editor-in-Chief,

We are grateful for your reviewing team's consideration and comments for our manuscript "Case Report: Kingella kingae causing prosthetic joint infection in an adult".

We have endeavoured to address the feedback and comments suggested by your reviewers as follows, and we thank you for your further consideration of our work for publication.

Editorial Office requirements

Comment: Upload figures in file inv

Answer: We have uploaded both figures as individual files as advised in addition to the figures being included in the manuscript.

Reviewer 1: Points to be reviewed

Comment: Species name needs to be italicised.

Answer: Species name has been italicised throughout the manuscript as suggested.

Comment: There is no need to put K. kingae in brackets, as the general rule of thumb in microbiology is to state it once in full and then subsequently shortened.

Answer: The manuscript has been amended as suggested.

Comment: Line 42: rephrase to "patients who are immune compromised"

Answer: The manuscript has been amended as suggested. Line 44.

Comment: Line 42: the authors might want to elaborate on what they mean by adherence to specific culture and isolation techniques.

Answer: The manuscript has been amended to clarify the original statement and now reads: "Operating surgeons must obtain deep tissue samples using sterile instruments during surgery and send to a microbiology laboratory for culture and identification of the pathogen." Line 44-46.

Comment: Line 48: "our clinic" - name the clinic, is this a surgical clinic/microbiology clinic?

Answer: The manuscript has been amended to specify the clinic and now reads "…the orthopaedic surgical clinic by her treating rheumatologist". Line 50.

Comment: Line 55: as this is a microbiology journal it might be worth describing what medialisation is

Answer: The manuscript has been updated to clarify medialisation and now reads: "The replacement head had also migrated medially due to failure of the supporting glenoid bone and there was osteolysis around the humeral implant (Fig 1.)." Line 58-60.

Comment: Figure 1: please use arrows to point out what you're describing

Answer: Arrows have been added to figure 1 and the corresponding legend has been updated to reflect the addition of the arrows.

Comment: Line 62: were these swabs of the sinus and pus? Please clarify.

Answer: The manuscript has been updated to clarify that the swabs were superficial swabs that were taken from the wound and now reads: "Initial superficial wound swabs were taken for culture at this clinic attendance, all of which revealed no growth at this stage." Line 68-70.

Comment: Line 71: What antibiotics had she been put on that were stopped? How long had she received them for and what route of administration?

Answer: This line has been removed from the manuscript to aid clarity.

Comment: Line 73: should read "at first stage"

Answer: The manuscript has been amended as suggested. Line 78.

Comment: Line 76&94: how many tissue samples?

Answer: The number of tissue samples taken have been added to the manuscript. These are "seven" and "three" respectively. Lines 80 & 109.

Comment: Line 79: how many grams of gentamicin?

Answer: 1.50g of Gentamicin. Line 84.

Comment: Line 81: why was fluclox chosen?

Answer: The manuscript has been amended to clarify why fluclox was chosen and now reads: "The patient was started empirically on IV Flucloxacillin 2g QDS following surgery since gram positive organisms are the commonest pathogens in prosthetic joint infections, while awaiting results from the intra-operative samples." Line 85-88.

Comment: Line 82: this needs to be elaborated on extensively as this is a microbiology journal. How were the samples processed, were tissues homogenised? What medium - blood culture bottles/agar? How long was incubation, at what day did the cultures come up positive, what antimicrobial susceptibility tests were performed? How many tissue samples out of the total were positive? This is important information.

Answer: The manuscript has been amended to expand and clarify the initial statement and now reads: "Tissue samples were homogenized using a vortex machine with addition of saline broth and were plated on the blood, CLED and chocolate agar. Further, FAB (Fastidious Anaerobe Broth) was also inoculated for each sample and was read each day for a total of five days of incubation. *K. kingae*was isolated from two out of seven tissue samples at 48 hours from the blood plate and subsequently identified using MALDI-TOF technology. One out of the two positive tissue samples, with further FAB isolated a similar pathogen. Ciprofloxacin, amoxicillin and ceftriaxone etests were set up, and the organism was detected to be sensitive to all as per EUCAST guidelines. Antibiotics at this stage were rationalized as per microbiology advice and the patient was commenced on intravenous ceftriaxone 2g once a day for 14 days, followed by a further 28 days of oral ciprofloxacin 500mgs BD to complete a total 6 weeks course." Line 90-100.

Comment: Line 96-97: why were these IV antibiotics chosen when the patient had IV ceftriaxone at first stage?

Answer: The manuscript has been amended to explain the choice of antibiotic and now reads: "The patient was commenced empirically on intravenous vancomycin, dosed as per the local vancomycin calculator, and co-amoxiclav 1.2 g TDS, as per the local hospital guidelines for revision surgery post-operatively. All deep tissue specimens did not isolate any pathogen following a final read at five days. The patient was subsequently discussed in the Bone Infection MDT meeting and was advised to rationalize antibiotics to oral ciprofloxacin 500mgs BD to complete 6 weeks post operatively due to the patient being immune suppressed and having a high risk for relapse." Line 112-119.

Comment: Line 97: it would be interesting to know if these samples were put up for prolonged incubation/additional culture medium based on the organism?

Answer: The manuscript has been amended to address the incubation query as follows: "Samples were processed in a similar manner as previously stated with additional broth incubation for five days. The patient was commenced empirically on intravenous vancomycin, dosed as per the local vancomycin calculator, and co-amoxiclav 1.2 g TDS, as per the local hospital guidelines for revision surgery post-operatively. All deep tissue specimens did not isolate any pathogen following a final read at five days." Line 111 – 116.

Comment: Figures 2 and 3 seem unnecessary for this journal. It would be interesting to see a Gram-stain of the isolate or what it looks like on agar plates?

Answer: Unfortunately, the authors do not have the suggested figures, though figure three has been removed form the manuscript as suggested. The authors feel that Figure 2 assists in evidencing an appropriate revision procedure and supports the post-operative results suggested in the manuscript.

Comment: Line 117: Staphylococcus aureus, not Staph aureus. Italicise.

Answer: The manuscript has been amended as suggested. Line 137.

Comment: Line 115: generalised sepsis? Surely just sepsis.

Answer: The manuscript has been altered as suggested. Line 135.

Comment: Line 116: what kind of culture? Tissue/swabs? Be more specific.

Answer: The culture has been added and the manuscript now reads: "Superficial ulcer swabs from the right foot isolated *Staphylococcus aureus*(MSSA)." Line 136-137.

Comment: Line 140: Propionibacterium has been reclassified as Cutibacterium acnes, please change.

Answer: The reclassification has been updated in the manuscript as suggested. Line 165.

Comment: Line 152: 16S rRNA gene sequencing or PCR?

Answer: This has been clarified in the manuscript and now reads "The use of 16s rDNA gene sequencing could assist in identification even after antibiotic use and can significantly reduce time to diagnosis." Line 177-178.

Comment: Line 155-157: this is a bit of a confusing sentence, please re-word - what do you mean? Expand. Also, have you looked at synovial biopsy vs fluid in PJI? In the cases you have reviewed have there been any cases of dry joints or do they all have sinuses? Was this patient offered radiologically-guided sample collection?

Answer: The section has been amended to assist with clarity and now reads: "Alternatively, literature suggests identification of *K. kingae*can be further improved by using blood culture broth, whereby joint fluid or pus obtained from the joint is directly inoculated into blood culture broth in theatre, which decreases the concentration of *K. kingae*growth inhibiting factors normally present in synovial fluid[5]." Line 178 – 182.

Comment: Line 157&164: when no organism has been identified at which point in the investigation?

Answer: The manuscript has been amended to clarify the initial statement and now reads: "This technique should therefore be considered in patients with prosthetic joint infection who are deemed at higher risk due to being on immune suppressants." Line 182 – 184.

Comment: Line 165: you mention synovial fluid culture again but this is not something that you have demonstrated here in this report, therefore I think this should be removed from the conclusion and just remain in the discussion.

Answer: The suggestion has been actioned and the line has been removed from the conclusion of the manuscript as suggested.

Reviewer 2: Points to be reviewed

Comment: line 99: please rephrase the sentence to be more clear

Answer: Line 99 has now been amended to clarify the post-operative pathway and now reads: "The patient completed the course of antibiotics and recovered post-operatively with no further complications from the shoulder perspective. She continued to make progress, and her range of motion at the shoulder joint improved slowly." – Lines 122 – 124.

Comment: please italicized the name of microorganisms for example line 117

Answer: All microorganism names have been italicized as suggested.

Comment: line 129 please add its before " growth" in the sentence "K. kingae is a particularly fastidious organism, and growth on"

Answer: The manuscript has been amended as suggested.

Comment: line 139-141 suggest to rephrase the sentence

Answer: Line 139-141 has been rephrased to assist with clarity and now reads: "The rate of prosthetic shoulder joint infections in the general adult population ranges between 1-4%[i]and the common causative pathogen associated usually are *Cutibacterium acnes*, *Staphylococcus aureus*and *Staphylococcus epidermidis*[1]." – Lines 164-166.

Comment: line 141 suggest use word "number" instead of "volumes"

Answer: The manuscript has been amended as suggested.

Comment: line 143 " use "are" instead of "is"

Answer: The manuscript has been amended as suggested.

Sincerely,

Mr Damian McClelland

Consultant Trauma and Orthopaedic Surgeon

VERSION 1

Editor recommendation and comments

https://doi.org/10.1099/acmi.0.000559.v1.5

Lindsey Tolman; University at Albany, UNITED STATES

Date report received: 25 April 2023
Recommendation: Minor Amendment

Comments: This is a study that would be of interest to the field and community. The reviewers have highlighted minor concerns with the work presented. Please ensure that you address their comments. Please provide more detail in the Methods section and ensure that software is consistently cited and its version and parameters included.

Reviewer 2 recommendation and comments

https://doi.org/10.1099/acmi.0.000559.v1.3

Nid'a Alshraiedeh; Jordan University of Science and Technology Faculty of Pharmacy, Nid'a Alshraiedeh Assistant Professor Department of Pharmaceutical Technology J, Irbid, JORDAN
https://orcid.org/0000-0002-4366-8532

Date report received: 19 April 2023
Recommendation: Minor Amendment

Comments: the case is written clearly with few suggestion: line 99: please rephrase the sentence to be more clear please italicized the name of microorganisms for example line 117 line 129 please add its before " growth" in the sentence "K. kingae is a particularly fastidious organism, and growth on" line 139-141 suggest to rephrase the sentence line 141 suggest use word "number" instead of "volumes" line 143 " use "are" instead of "is"

Please rate the quality of the presentation and structure of the manuscript
Good

To what extent are the conclusions supported by the data?
Strongly support

Do you have any concerns of possible image manipulation, plagiarism or any other unethical practices?
No

Is there a potential financial or other conflict of interest between yourself and the author(s)?
No

If this manuscript involves human and/or animal work, have the subjects been treated in an ethical manner and the authors complied with the appropriate guidelines?
Yes

Reviewer 1 recommendation and comments

https://doi.org/10.1099/acmi.0.000559.v1.4

Leanne Cleaver; King's College London, Centre for Host Microbiome Interactions, Floor 17, Tower Wing, Guy's Hospital, Great Maze Pond, London, UNITED KINGDOM
https://orcid.org/0000-0002-7788-9384

Date report received: 17 April 2023
Recommendation: Major Revision

Comments: Thank you for the opportunity to review your case report which details a rare case of Kingella kingae in a prosthetic joint infection. Overall, this is well-structured and you have presented the case with good logic. However, this is lacking in microbiological detail in a few places which needs to be resolved. The final sentence of your conclusion is really key and I'm happy to see you have emphasised the importance of multidisciplinary collaboration in these cases. Points to be reviewed: - Species name needs to be italicised - There is no need to put K. kingae in brackets, as the general rule of thumb in microbiology is to state it once in full and then subsequently shortened. - Line 42: rephrase to "patients who are immune compromised" - Line 42: the authors might want to elaborate on what they mean by adherence to specific culture and isolation techniques - Line 48: "our clinic" - name the clinic, is this a surgical clinic/microbiology clinic? - Line 55: as this is a microbiology journal it might be worth describing what medialisation is - Figure 1: please use arrows to point out what you're describing - Line 62: were these swabs of the sinus and pus? Please clarify. - Line 71: What antibiotics had she been put on that were stopped? How long had she received them for and what route of administration? - Line 73: should read "at first stage" - Line 76&94: how many tissue samples? - Line 79: how many grams of gentamicin? - Line 81: why was fluclox chosen? - Line 82: this needs to be elaborated on extensively as this is a microbiology journal. How were the samples processed, were tissues homogenised? What medium - blood culture bottles/agar? How long was incubation, at what day did the cultures come up positive, what antimicrobial susceptibility tests were performed? How many tissue samples out of the total were positive? This is important information. - Line 96-97: why were these IV antibiotics chosen when the patient had IV ceftriaxone at first stage? - Line 97: it would be interesting to know if these samples were put up for prolonged incubation/additional culture medium based on the organism? - Figures 2 and 3 seem unnecessary for this journal. It would be interesting to see a Gram-stain of the isolate or what it looks like on agar plates? - Line 117: Staphylococcus aureus, not Staph aureus. Italicise. - Line 115: generalised sepsis? Surely just sepsis. - Line 116: what kind of culture? Tissue/swabs? Be more specific. - Line 140: Propionibacterium has been reclassified as Cutibacterium acnes, please change. - Line 152: 16S rRNA gene sequencing or PCR? - Line 155-157: this is a bit of a confusing sentence, please re-word - what do you mean? Expand. Also, have you looked at synovial biopsy vs fluid in PJI? In the cases you have reviewed have there been any cases of dry joints or do they all have sinuses? Was this patient offered radiologically-guided sample collection? - Line 157&164: when no organism has been identified at which point in the investigation? - Line 165: you mention synovial fluid culture again but this is not something that you have demonstrated here in this report, therefore I think this should be removed from the conclusion and just remain in the discussion.

Please rate the quality of the presentation and structure of the manuscript
Good

To what extent are the conclusions supported by the data?
Strongly support

Do you have any concerns of possible image manipulation, plagiarism or any other unethical practices?
No

Is there a potential financial or other conflict of interest between yourself and the author(s)?
No

If this manuscript involves human and/or animal work, have the subjects been treated in an ethical manner and the authors complied with the appropriate guidelines?
Yes

SciScore report

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iThenticate report

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