Received: 25 October 2023 | Revised: 30 November 2023 | Accepted: 14 December 2023

DOI: 10.1002/ccr3.8402

CASE REPORT

Clinical Case Reports Open Access WILEY

A rare case of multi-drug resistant *Raoultella ornithinolytica*-induced sepsis in a healthy young man in Uganda

Elias Rugaatwa Ndibarema[1,2] | **Ronald Olum**[1,3,4] | **Joseph Ogavu**[1,2] | **Anthony Makhoba**[1,2]

[1]Department of Medicine, St Francis Hospital Nsambya, Kampala, Uganda

[2]Mother Kevin Postgraduate Medical School, School of Medicine, Uganda Martyrs University, Kampala, Uganda

[3]School of Public Health, Makerere University, Kampala, Uganda

[4]School of Public Health, Imperial College London, United Kingdom

Correspondence
Elias Rugaatwa Ndibarema, Department of Medicine, St Francis Hospital Nsambya, Kampala, Uganda.
Email: eliasndibarema@gmail.com

Key Clinical Message

Antimicrobial resistance (AMR) is a public health challenge. It causes unresponsiveness to treatment with antimicrobials, leads to sepsis, septic shock, and increased hospital mortality. This is compounded by new multidrug resistant organisms. We present and discuss a case of sepsis caused by a rare multi-drug resistant bacterium *Raoultella ornithinolytica*.

Abstract

Antimicrobial resistance is a major public health concern worldwide, associated with nearly 5 million deaths. The highest mortality attributed to AMR is seen in sub-Saharan Africa. *Escherichia coli, Staphylococcus aureus, Klebsiella pneumoniae*, *Streptococcus pneumoniae*, *Acinetobacter baumannii*, *and Pseudomonas aeruginosa* contribute to most deaths attributed to AMR globally. However, other uncommon microorganisms have been implicated. Few cases of resistant, extended-spectrum beta-lactamase (ESBL) producing *Raoultella ornithinolytica* have been reported to cause sepsis worldwide. To our knowledge, no case of *R. ornithinolytica*-induced sepsis has been reported in our settings. We report a case of sepsis due to *R. ornithinolytica* in an injured young adult. We received a 36-year-old man, a professional banker involved in a road traffic accident 2 h before admission. He sustained a deep degloving wound on the right ankle with exposure of the lateral malleolus and presented with severe pain, and bleeding at the injury site. x-Rays confirmed a comminuted intra-articular distal tibia and fibular fracture. Surgical debridement and external fixation were aseptically done on the same day. Below knee amputation was done on the 7th day post-admission due to extensively injured and infected limb with sepsis. Local pus culture isolated ESBL-positive *R. ornithinolytica* susceptible only to meropenem, ciprofloxacin, and amikacin. Introducing these antibiotics on the 11th post-admission day averted sepsis and enhanced patient recovery. With the threat of AMR, newly emerging highly resistant microbes should be expected and suspected. Early recognition of sepsis and its focus and precise intervention with antimicrobials guided by specimen culture and susceptibility profile is highly recommended and

should be standard practice. It highly reduces morbidity and mortality due to sepsis.

KEYWORDS

ESBL, multi-drug resistance, *Raoultella ornithinolytica*, sepsis

1 | INTRODUCTION

Antimicrobial resistance (AMR) is a significant public health concern worldwide. In 2019 alone, nearly 5 million deaths were associated with AMR, and 1.27 million deaths were attributed to AMR due to bacterial pathogens.[1] By 2050, AMR will cost 10 million lives yearly and a cumulative financial loss of 100 trillion US dollars if actions to curb its development are not urgently instituted.[2] Low- and middle-income countries (LMICs) suffer the greatest burden, with the highest number of deaths attributed to AMR in sub-Saharan Africa.[1,3] Six major pathogens, namely, *Escherichia coli, Staphylococcus aureus, Klebsiella pneumoniae*, *Streptococcus pneumoniae*, *Acinetobacter baumannii*, *and Pseudomonas aeruginosa* contribute to the majority of deaths attributed to AMR globally.[1] However other uncommon microorganisms have been implicated. *Raoultella ornithinolytica* (*R. ornithinolytica*) is a gram-negative encapsulated facultative anaerobic bacterium[4] that was first discovered in 1989 and named *Klebsiella ornithinolyticus*. It was later reclassified to the genus *Raoultella* based on the presence of *16Sr-RNA* and *rpoB* genes that were different from those of *Klebsiella*.[5] *R. ornithinolytica* has been found in water environments, soil, insects, and fish.[6] It has been shown to cause histamine toxicity associated with fish (Scombroid syndrome) because it expresses histidine decarboxylase, which converts histidine to histamine,[7] leading to skin manifestations (flushing, pruritus.) headache, and abdominal cramping. *R. ornithinolytica* has been reported to cause bacteremia and sepsis in a few soft tissue and urinary tract infections.[8] It has previously been regarded as an opportunistic infection affecting immunocompromised persons such as preterm babies,[9] neonates, children,[10] elderly, cancer patients, and those undergoing invasive procedures.[4] Cases of *R. ornithinolytica* in healthy immunocompetent persons have rarely been reported.[4]

Very few cases of extended-spectrum beta-lactamase (ESBL) producing *R. ornithinolytica* have been reported worldwide.[11,12] These were isolated in rivers in Italy and Switzerland. ESBL is an enzyme bacteria produce to become resistant to extended-spectrum penicillin,[13] cephalosporins, and monobactams, except for cephamycins and carbapenems. To our knowledge, no case of ESBL positive *R. ornithinolytica*-induced sepsis has been reported in our settings. We present and discuss the first case of sepsis caused by a culture-isolated ESBL-producing *R. ornithinolytica* at a tertiary hospital in Uganda.

2 | CASE PRESENTATION

We received a 36-year-old male patient, a professional banker, who sustained a road traffic accident 2 h before admission. He reportedly fell off a motorcycle where he was a passenger and was thrust into a sideway water trench after a head-on collision with another motorcycle. He sustained a deep degloving wound on the right ankle with exposure of the lateral malleolus and presented with severe pain and bleeding at the injury site. He was otherwise anxious and restless, with a blood pressure of 125/67 mmHg, a pulse of 80 beats/min, a temperature of 37.8°C, a respiratory rate of 18 breaths/min, and oxygen saturation of 99% in room air (Figure 3). Lateral and anteroposterior x-rays confirmed a comminuted intra-articular distal tibia and fibular fracture (Figure 1). Surgical debridement and external fixation were done on the same day by the orthopedic surgery team in the main theater, observing strict aseptic technique as per the hospital theater protocol. He was thereafter admitted to the high dependence unit (HDU) for close monitoring and postoperative care. However, the patient reported fevers on the first postoperative day, while in the HDU. A local right lower limb examination revealed a grossly soiled dressing with an offensive smell and pus discharge from the insertion points of external fixators. Capillary refill of more than 4 s, loss of sensation on the medial aspect of the dorsum and plantar aspect of the foot, and the dorsalis pedis pulse were not appreciable. He was generally weak and lethargic with a Glasgow coma scale of 14, breathing at 22 breaths/min with a temperature of 39.5°C, pulse 115 bpm, and blood pressure 123/67 mmHg (Figure 3). A clinical bedside diagnosis of sepsis (injury site infection focus) was made with quick-SOFA score of 2/3. A pus swab was taken from the site for culture. BACTEC 9050 automated culture system was used, and species identified by Vitek-2 Compact system. Serial full blood hemogram and clinical vital signs were then taken (Figures 3 and 4).

An assessment of peripheral CT-angiography (done on first postoperative day) showed occlusion of the right

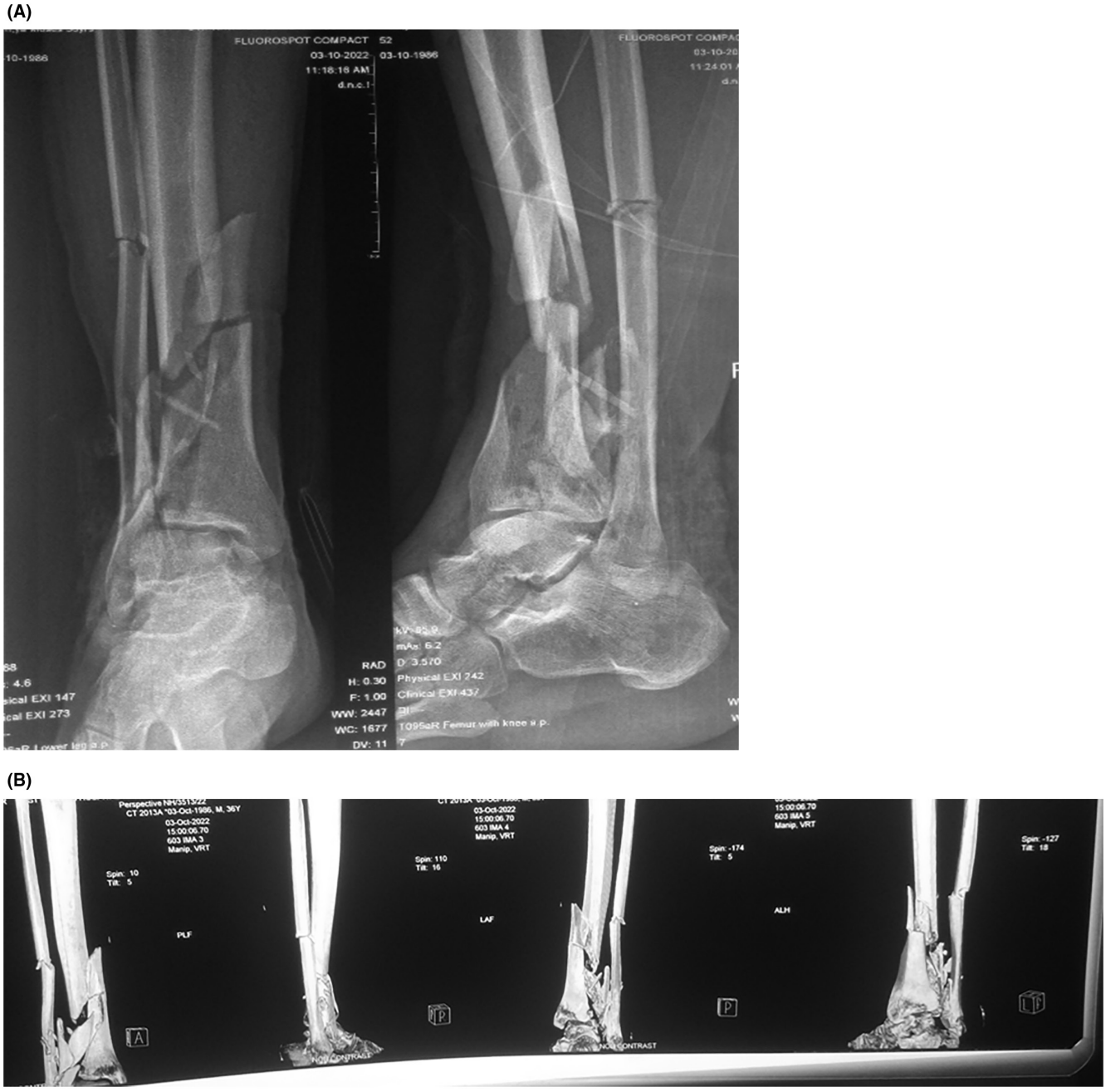


FIGURE 1 (A) x-Rays showing right distal tibia and fibula fractures. (B) 3D reconstruction of CT scan images showing right distal tibia and fibula fractures.

posterior tibial artery at the fracture site (Figure 2). Throughout postoperative Days 1–7, the patient had persistent fevers and tachycardia (Figure 3). He registered reduced urine output on 6th and 7th postoperative days at 400mLs and 350mLs in 24 h, respectively. He was therefore diagnosed with sepsis (infected crushed limb focus) with a SOFA score of 4: lethargy scored1 and urine output less than 500 in 24 hours scored3.[14] On the 7th day postoperative, the plastic surgeon recommended right below knee amputation (BKA) due to extensive soft tissue and bone injury with extensive infection and worsening clinical examination findings. BKA was done 7 days post-injury and post-debridement, and external fixation.

The first 8 days of empiric intravenous antibiotics (flucloxacillin–amoxicillin 500 mg 8 hourly, metronidazole 500 mg 8 hourly, and linezolid 600 mg 12 hourly) did not avert the progression of sepsis. Results of the pus culture from the infected crushed limb isolated ESBL-positive *R. ornithinolytica* susceptible to only meropenem, ciprofloxacin, and amikacin (Table 1). In addition to beta-lactam ring antibiotics, this bacterium was also resistant to gentamycin, co-trimoxazole,

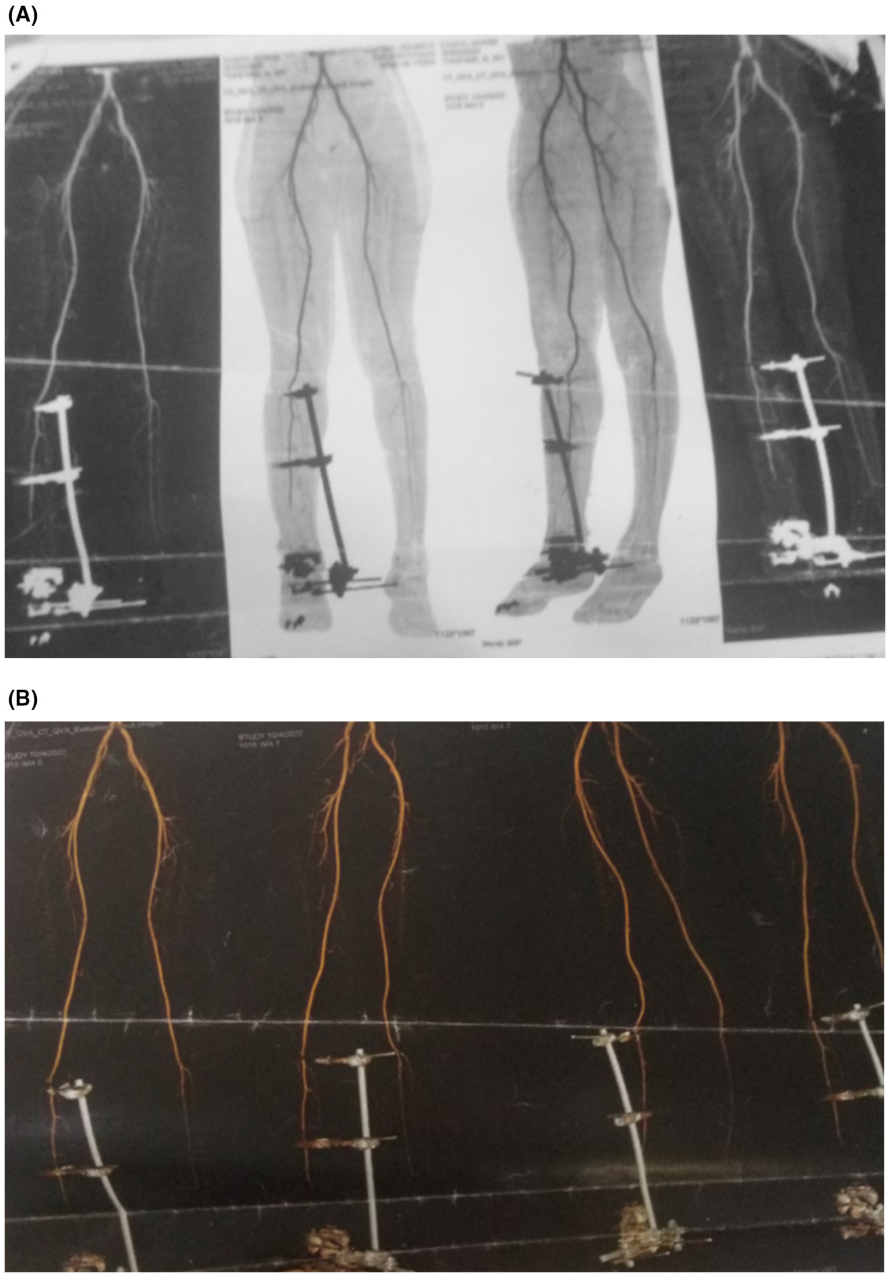
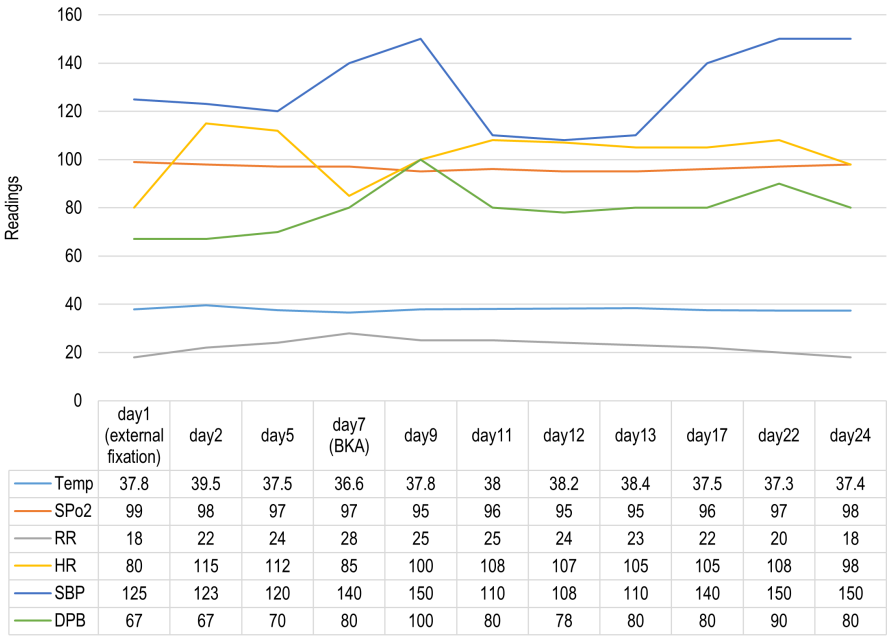


FIGURE 2 (A, B) CT angiography images showing occlusion of the right posterior tibial artery at the fracture site.

tetracycline, and tobramycin. Intravenous meropenem 1000 mg 8 hourly was introduced on Day 4 post-BKA based on the pus culture and susceptibility results, and the patient registered a steady improvement in clinical condition. Renal function improved on antibiotics and fluid therapy, with urine volumes of ≥800mLs/day by Day 20. Figures 3 and 4 summarize the patients' clinical vitals and laboratory results during hospitalization. The patient was also transfused twice (on Days 5- and 22-day post-injury) due to sepsis-related anemia. The patient spent 30 days in the hospital and was discharged in a fairly good general condition to continue BKA stump wound dressing from the outpatient theater and orthopedic review as an outpatient.

3 | DISCUSSION

This is the first recorded case of sepsis caused by ESBL-producing *R. ornithinolytica* in our settings. The existence of such highly resistant microbes in the environment poses a great danger to the humanity. This organism has been isolated in water bodies in Europe[11,12] and Hawaii[8] in soil, insects, ticks, and fish.[6] In the latter,



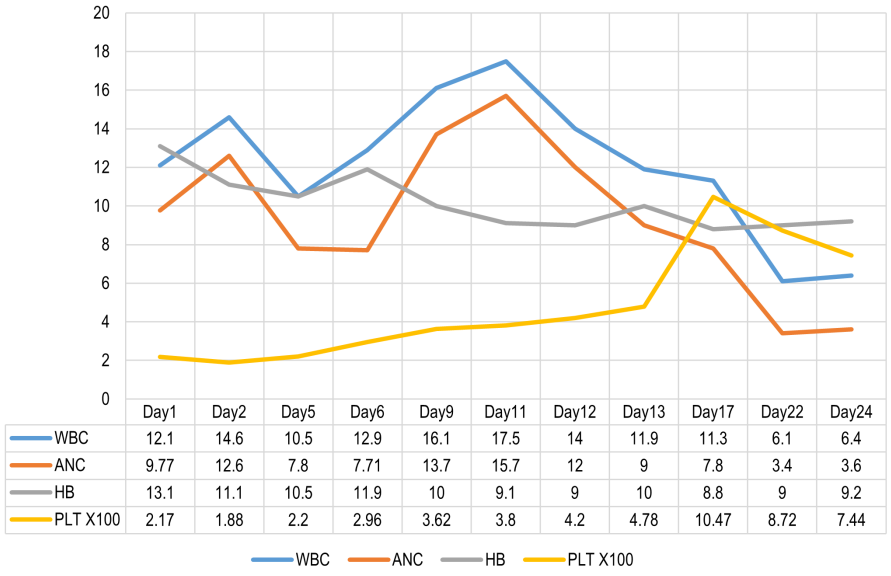
	day1 (external fixation)	day2	day5	day7 (BKA)	day9	day11	day12	day13	day17	day22	day24
Temp	37.8	39.5	37.5	36.6	37.8	38	38.2	38.4	37.5	37.3	37.4
SPo2	99	98	97	97	95	96	95	95	96	97	98
RR	18	22	24	28	25	25	24	23	22	20	18
HR	80	115	112	85	100	108	107	105	105	108	98
SBP	125	123	120	140	150	110	108	110	140	150	150
DPB	67	67	70	80	100	80	78	80	80	90	80

FIGURE 3 Trends in clinical and vital signs of the patient during admission. BKA, below knee amputation.

TABLE 1 Gram stain, culture, and drug susceptibility results of the patient.

Sample	Gram stain	Isolates	Susceptible	Resistant
Pus	Gram negative rods	*Raoultella ornithinolytica*—ESBL positive	Amikacin, meropenem, and ciprofloxacin	Gentamycin, Cotrimoxazole, all penicillin, and cephalosporins
Blood	Not applicable	No growth after 5 days of incubation	Not applicable	Not applicable

Note: Extended spectrum beta lactamases (ESBL) producing bacteria are resistant to all forms of penicillin and cephalosporins and are also resistant to all beta-lactamase inhibitor combinations.



	Day1	Day2	Day5	Day6	Day9	Day11	Day12	Day13	Day17	Day22	Day24
WBC	12.1	14.6	10.5	12.9	16.1	17.5	14	11.9	11.3	6.1	6.4
ANC	9.77	12.6	7.8	7.71	13.7	15.7	12	9	7.8	3.4	3.6
HB	13.1	11.1	10.5	11.9	10	9.1	9	10	8.8	9	9.2
PLT X100	2.17	1.88	2.2	2.96	3.62	3.8	4.2	4.78	10.47	8.72	7.44

FIGURE 4 Trends in full hemogram results of the patient during admission. ANC, absolute neutrophil count (×1000cells/cc); HB, hemoglobin concentration in g/dL; WBC, white blood cells (×1000cells/cc); PLT, platelets (×1000 cells/cc).

it has been associated with the scombroid syndrome. The peculiarity of this case comes from the patient's report of being thrust into a roadside water trench following the road crush. This could have been the source of wound contamination with *R. ornithinolytica*, which later progressed to sepsis. This bacterium is majorly opportunistic, affecting the immunocompromised and those undergoing invasive procedures.[4] Cases of wound

and skin sepsis, pneumonia, pleural effusions, meningitis, cerebral abscess[15]; urinary tract, gastrointestinal, hepatobiliary,[16] and ENT[17] infections have been documented. Mortality of up to 5% due to *R. ornithinolytica* has been reported.[15] In our environment, it is possible that this organism has been infecting humans and treated empirically (without isolation by culture) and developed extensive resistance over time, or a highly resistant ESBL-producing strain has existed in our water bodies for decades.

Sepsis is a life-threatening organ dysfunction due to dysregulated host response to an infection.[18] Organ dysfunction can be identified as an acute change in total SOFA score of ≥2 points consequent to the infection. Sepsis is a medical emergency as it rapidly progresses to septic shock, with mortality as high as 30% in hospitalized patients and 50%–60% in ICU.[18,19] Early recognition of sepsis and interventions such as optimal antimicrobial therapy, fluid resuscitation, and source control are essential for survival. AMR causes clinical unresponsiveness to treatment and rapid evolution to sepsis and septic shock. Patients with resistant pathogens have been found to have a higher risk of hospital mortality.[20] For *R. ornithinolytica*, prognosis in highly variable depending on the patient's overall health status and focus of infection and outcomes are not poor when prompt proper therapy is initiated.[21]

The patient exhibited clinical unresponsiveness to flucloxacillin-amoxicillin, metronidazole, and linezolid. All laboratory and clinical markers of infection worsened until meropenem was introduced based on the isolation of ESBL-positive *R. ornithinolytica* and antimicrobial susceptibility testing (AST). Cases of sepsis due to multidrug-resistant *R. ornithinolytica* have been reported in Ghana[22] and China,[4] and as a local infection in Ireland.[23]

3.1 | Conclusion and recommendation

With the threat of AMR, newly emerging highly resistant microbes should be expected and suspected. Early recognition of sepsis (and its focus) in the wake of AMR and precise intervention with antimicrobials guided by specimen culture and susceptibility profile is highly recommended and should be standard practice. It highly reduces morbidity and mortality due to sepsis.

3.2 | Limitations

Due to laboratory inadequacies, we did not do serum lactate levels in the first hour of diagnosis of sepsis, as recommended by the surviving sepsis campaign.[14]

AUTHOR CONTRIBUTIONS

Elias Rugaatwa Ndibarema: Conceptualization; data curation; formal analysis; funding acquisition; investigation; methodology; project administration; resources; validation; visualization; writing – original draft; writing – review and editing. **Ronald Olum:** Writing – review and editing. **Joseph Ogavu:** Project administration; supervision. **Anthony Makhoba:** Supervision.

ACKNOWLEDGMENTS

We appreciate the great contribution by the patient for volunteering the data and providing consent to publish this work.

FUNDING INFORMATION

No funding was obtained.

CONFLICT OF INTEREST STATEMENT

Authors have no conflict of interest to declare.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ETHICS STATEMENT

This case number AMR0094 was identified as part of the larger study on Antimicrobial Resistance in Sepsis patients ongoing at St. Francis Hospital Nsambya (SFH). The study was approved by the SFH Research Ethics Committee, approval No. SFHN-2022-52. Informed consent was obtained from AMR0094 to participate in the study.

CONSENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

ORCID

Elias Rugaatwa Ndibarema https://orcid.org/0000-0003-1520-5706
Ronald Olum https://orcid.org/0000-0003-1289-0111

REFERENCES

1. Antimicrobial Resistance Collaborators. Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. *Lancet*. 2022;399(10325):629-655. doi:10.1016/S0140-6736(21)02724-0
2. O'Neill J. Tackling drug-resistant infections globally: final report and recommendations. 2016.
3. Sulis G, Sayood S, Gandra S. Antimicrobial resistance in low- and middle-income countries: current status and future directions. *Expert Rev Anti Infect Ther*. 2022;20(2):147-160. doi:10.1080/14787210.2021.1951705
4. Chen X, Zhou X, Cao J, Ma K, Xia Z. A case report of community-acquired *Raoultella ornithinolytica* infection in

a healthy, young individual. *BMC Infect Dis*. 2021;21(1):1095. doi:10.1186/s12879-021-06799-w
5. Sękowska A, Dylewska K, Gospodarek E, Bogiel T. Catheter-related blood stream infection caused by *Raoultella ornithinolytica*. *Folia Microbiol (Praha)*. 2015;60(6):493-495. doi:10.1007/s12223-015-0390-2
6. Hajjar R, Ambaraghassi G, Sebajang H, Schwenter F, Su SH. *Raoultella ornithinolytica*: emergence and resistance. *Infect Drug Resist*. 2020;13:1091-1104. doi:10.2147/IDR.S191387
7. Kanki M, Yoda T, Tsukamoto T, Shibata T. *Klebsiella pneumoniae* produces no histamine: *Raoultella planticola* and *Raoultella ornithinolytica* strains are histamine producers. *Appl Environ Microbiol*. 2002;68(7):3462-3466. doi:10.1128/AEM.68.7.3462-3466.2002
8. Nakasone ES, Kaneshiro R, Min K, Tokeshi J. Emergence of *Raoultella ornithinolytica* on O'ahu: a case of community-acquired *R. Ornithinolytica* urinary tract infection. *Hawaii J Med Public Health*. 2015;74(5):174-175. Available at: http://www.ncbi.nlm.nih.gov/pubmed/26019987
9. Ozkan EA. A rare case of a newborn with urinary tract infection by *Raoutella ornithinolytica*. *Am J Health Res*. 2014;2(6):375. doi:10.11648/j.ajhr.20140206.19
10. Büyükcam A, Liste Ü, Bıçakçıgil A, Kara A, Sancak B. A case of *Raoultella ornithinolytica* urinary tract infection in a pediatric patient. *J Infect Chemother*. 2019;25(6):467-469. doi:10.1016/j.jiac.2018.12.011
11. Piccirilli A, Pompilio A, Rossi L, et al. Identification of CTX-M-15 and CTX-M-27 in antibiotic-resistant gram-negative bacteria isolated from three rivers running in central Italy. *Microb Drug Resist*. 2019;25(7):1041-1049. doi:10.1089/mdr.2019.0016
12. Zurfluh K, Hächler H, Nüesch-Inderbinen M, Stephan R. Characteristics of extended-spectrum β-lactamase- and carbapenemase-producing Enterobacteriaceae isolates from rivers and lakes in Switzerland. *Appl Environ Microbiol*. 2013;79(9):3021-3026. doi:10.1128/AEM.00054-13
13. Teklu DS, Negeri AA, Legese MH, Bedada TL, Woldemariam HK, Tullu KD. Extended-spectrum beta-lactamase production and multi-drug resistance among Enterobacteriaceae isolated in Addis Ababa, Ethiopia. *Antimicrob Resist Infect Control*. 2019;8(1):39. doi:10.1186/s13756-019-0488-4
14. Singer M, Deutschman CS, Seymour CW, et al. The third international consensus definitions for sepsis and septic shock (Sepsis-3). *JAMA*. 2016;315(8):801. doi:10.1001/jama.2016.0287
15. Seng P, Boushab BM, Romain F, et al. Emerging role of *Raoultella ornithinolytica* in human infections: a series of cases and review of the literature. *Int J Infect Dis*. 2016;45:65-71. doi:10.1016/j.ijid.2016.02.014
16. Seixas R, Alves A, Selaru A, Vanzeller M, Shiang T, Conde S. *Raoultella ornithinolytica* in MALT-type non-Hodgkin lymphoma. *Eur J Case Rep Intern Med*. 2021;8(11):003023. doi:10.12890/2021_003023
17. Cavaliere M, Bartoletti G, Capriglione P, et al. Unusual localization of an emergent bacterium, *Raoultella Ornithinolytica*. *Case Rep Med*. 2020;2020:1-3. doi:10.1155/2020/1710271
18. World Health Organization. SEPSIS, Fact Sheets. 2020.
19. Bauer M, Gerlach H, Vogelmann T, Preissing F, Stiefel J, Adam D. Mortality in sepsis and septic shock in Europe, North America and Australia between 2009 and 2019–results from a systematic review and meta-analysis. *Crit Care*. 2020;24(1):239. doi:10.1186/s13054-020-02950-2
20. Reinhart K. How Antimicrobial Resistance Ampli fi es the Burden of Sepsis. 2021 By Keynote Contributor 1–6.
21. Haruki Y, Hagiya H, Sakuma A, Murase T, Sugiyama T, Kondo S. Clinical characteristics of *Raoultella ornithinolytica* bacteremia: a case series and literature review. *J Infect Chemother*. 2014;20(9):589-591. doi:10.1016/j.jiac.2014.05.005
22. Tayo A, Nyame K. Sepsis from multisystem infection with multidrug-resistant *Raoultella ornithinolytica*. *Cureus*. 2022;14(1):e20975. doi:10.7759/cureus.20975
23. Goodman D, Murphy D, Dorairaj J. Case study: soft tissue infection with *Raoultella ornithinolytica*. *JPRAS Open*. 2022;33:17-20. doi:10.1016/j.jpra.2022.04.004

How to cite this article: Ndibarema ER, Olum R, Ogavu J, Makhoba A. A rare case of multi-drug resistant *Raoultella ornithinolytica*-induced sepsis in a healthy young man in Uganda. *Clin Case Rep*. 2024;12:e8402. doi:10.1002/ccr3.8402