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Antimicrobial Resistance: Unexplained Failure to Antibiotic Therapy in a Case at Maluti Adventist Hospital Berea Lesotho

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Authors' contributions

This work was carried out in collaboration between both authors. Author LN wrote the first draft of the manuscript and managed the literature searches. Author ABN designed the study and wrote the protocol. Both authors read and approved the final manuscript.

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Case Report

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ABSTRACT

Aim: The aim of the present study was to highlight the presence and problem of antimicrobial resistance in our setting.
Case Presentation: We present a 17-year old female with yellow offensive vaginal discharge, itchiness and lower abdominal pain of about two-weeks duration. She was treated with antibiotics based on laboratory results of urine and high vaginal swabs. However, the symptoms persisted despite the treatment and high adherence to the medications.
Discussion: Antimicrobial Resistance (AMR) presents a painful risk to human health and life around the globe. The efficacy and effectiveness of antimicrobial agents are now under massive threat from increasing resistance of disease pathogens to antimicrobial agents. The unexplained failure of antibiotic therapy occurred despite the prescription being based on sensitivity results from swab culture on two separate occasions.
Conclusion: There is need for high index of suspicion of antimicrobial resistance by health workers. There is also need for rational prescription, dispensing and use of antimicrobial agents. Patients need increased access to high quality antimicrobial medicines and more awareness of the development, spread and prevention of antimicrobial resistance.

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1. INTRODUCTION

Antimicrobial Resistance (AMR) presents a painful risk to human health and life around the globe. Effective antimicrobial agents make it possible to treat infections [1]. However, the effectiveness of antimicrobial agents is now under massive threat from increasing resistance of disease pathogens to antimicrobial agents. Global AMR shows no signs of decline though it may perhaps shift direction [2]. Numerous attempts have been made to delineate the diverse aspects of AMR and possible solutions required to deal with this global challenge have been tried. At present, the multifaceted etiology of AMR means that many factors are at play. Key drivers of AMR include over prescription of antibiotics, under- or over-dispensing of antibiotics, inadequate diagnostic testing, suboptimal adherence to medication regimens and rampant use of antibiotics in animal health and agricultural settings where they are often used to promote growth rather than treating illness. Further, another under-recognized driver of AMR is poor quality medicines which has led to treatment failure as well as escalating AMR [3]. AMR is a global public health threat and a danger that continues to escalate. Resistant strains of bacteria adversely impact the entire population. However, until recently the increasing trend in drug resistant infection amongst infants and children, including adolescents, have gone relatively unrecognized [4].

2. CASE PRESENTATION

A 17-year-old high school girl presented at the outpatient department of Maluti Adventist Hospital (MAH) Mapoteng, Berea district in Lesotho on 26/09/2019. She complained of yellowish offensive vaginal discharge, itchiness and lower abdominal pain all of about two weeks' duration. There were no urinary symptoms. She had no previous history of any chronic illness or surgical procedures. She was sexually active but use of condom was unknown. She lived with her mother who was not married and had no other siblings. On examination, she was healthy looking. She had mild lower abdominal tenderness. Genitourinary examination, showed foul smelling yellowish vaginal discharge. The diagnoses of urinary tract infection and pelvic inflammatory disease were made.

Urinalysis, urine and high vaginal swab culture and sensitivity tests were done. Urine biochemistry results showed trace of blood, 2+ leucocytes, negative for ketones, glucose and protein, pH 5, and specific gravity 1.020. Urine microscopy results showed white blood cells 20-30 per HPF, red blood cells 0, scanty bacteria, and epithelial cells 2+. There were no laboratory evidence of candida or other fungal infections. Based on these results the patient was put empirically on amoxicillin 500mg three times a day for a week while waiting for culture and sensitivity results. Five days later, culture and sensitivity results showed growth of gram negative bacilli. This was a *Proteus* species which was resistant to chloramphenicol, erythromycin, ciprofloxacin, cefotaxime and colistin. It had intermediate sensitivity to amikacin, gentamycin and meropenem with full susceptibility to co-amoxyclav, vancomycin, cefdopoxime and clarithromycin. The patient was then placed on oral co-amoxyclav 625mg three times daily for 10 days. On the 10th day of antibiotic treatment, the patient was followed up and reviewed. She reported that yellowish PV discharge was still present but the itching and lower abdominal pain had resolved. She reported that the discharge had not decreased at all and it was as though she had not taken any antibiotic treatment. The same treatment was prolonged by an additional five days. Despite increasing the treatment duration, the patient's condition remained the same. She did not respond to antibiotic treatment despite the sensitivity test which showed that this antibiotic was indeed effective against this causative microorganism. The culture and sensitivity test of the vaginal discharge was repeated on 25th October 2019 and the result showed a mixed pure growth of *Klebsiella* species and *Proteus* species. *Klebsiella* species was resistant to amoxicillin, had intermediate sensitivity to colistin and was susceptible to chloramphenicol, ciprofloxacin, cefotaxime, amikacin, gentamycin and nalidixic acid. *Proteus* species on this swab was resistant to chloramphenicol, vancomycin, and nitrofurantoin, but had intermediate sensitivity to co-amoxyclav and was susceptible to nalidixic acid. The patient was then prescribed high dose oral co-amoxyclav 1.2g three times daily and nalidixic acid 500mg four times daily for a week. After treatment completion, the yellowish vaginal discharge was still present but offensive smell had significantly reduced. The cause of treatment failure was unexplained as the patient had good medicine adherence as instructed by the pharmacist. The patient

reported not to have taken any other medicines or herbal remedies which would have interacted with the antibiotics. Also, the patient reported to be sexually inactive throughout the duration of her treatment. Despite these treatment courses, the patient still reported yellowish and offensive vaginal discharge though less in severity when compared to when she first came to the hospital. However, her family expressed concern about whether or not she would completely recover from this infection.

3. DISCUSSION

This case demonstrated an unexplained failure of antibiotic therapy despite the prescription being based on sensitivity results from swab culture on two separate occasions. This unexplained failure of antibiotic therapy could be due to several factors including patient and health systems factors as well as medicine quality. Patient factors might include compliance to prescribed therapy and possibility of re-infection. However, the patient had good adherence but did not respond to the antibiotic regimens. A study showed the importance of patient adherence on antimicrobial drug dosing which will in effect affect the clinical response [5]. Re-infection was a possibility since there was a new microorganism (*Klebsiella*) discovered in the second culture of vaginal discharge that was not previously present in the first culture. Re-infection hinders or prevents good response to antibiotic therapy mainly due to high microbial load and also escalating microbes developing resistance to antibiotics that were previously effective. Antibiotics kill sensitive bacteria but allow resistant pathogen to remain which then reproduce and thrive through natural selection [2].

Furthermore, the quality of medicines affects patients' response to therapy [6]. Poor quality medicines could lead to sub-therapeutic doses and potentially result in treatment failure [7]. However, the medicines supplied to the hospital were pre-qualified and were being regulated by the Lesotho National Pharmacotherapeutics Committee before use to ensure high quality and standard. Poor quality medicines could be the result of degradation by improper storage or distribution, but also from poor manufacturing practices either inadvertently or deliberately. Hence the therapeutic benefit of antibiotics relies on good quality manufacturing, distribution and storage within the supply chain. Fortunately, the storage condition in the hospital was generally optimal with constant electricity. Evidence has shown that exposure to sub therapeutic levels can promote the development of resistance strains with increased virulence that could give rise to deadlier infections [8]. In this manner substandard or falsified medicines could help to accelerate AMR [8]. Early findings reported that pathogens exposed to sub-therapeutic levels of antibiotics in vitro could potentially give rise to a pathogen not only becoming resistant to one drug but to multiple other antibiotics as well [7]. In our setting, there was no obvious problem with the storage and distribution.

A comprehensive analysis conducted in 2018 found that more than 12% of antibiotics circulating in low and middle income countries are substandard or falsified and WHO estimates that globally, around 30 billion US dollars are wasted each year on medicines that do not work [9]. In fact, 1 in 10 medicines in low- and middle-income countries are substandard. However, detection of these poor quality medicines in our setting remains a huge challenge due to limited resources. Healthcare professionals and patients often use these medicines without the knowledge that they are substandard due to similar packaging. It is only after analytical testing that fault is identified.

The consequences of AMR are most severe for people with low incomes and other vulnerable groups such as children and adolescents. This was observed in a Tanzanian study which showed a high level (13.9%) of laboratory confirmed infection in the bloodstream despite about two-third of the population having got antibiotics before the blood culture [10]. AMR does not only affect adults but also children and adolescents as well. The quality of medicines could have huge impact on the emergence of drug resistance. The occurrence of AMR amongst children and adolescent has an academic impact and hinders their attainment of a good education since these children are often absent from school due to frequent visits to the health centers. Therefore, AMR amongst children and adolescents in school may have an impact on the attainment of the sustainable development goal (SDG) 4, Quality Education. Hence, there is a need for more research to look into how AMR in children and adolescent may affect their education which in the future may have an impact on their employment opportunities.

4. CONCLUSION

AMR is an increasing threat to global health. This case demonstrated a local case of AMR in

an adolescent girl who despite receiving all prescribed medicines based on clinical and laboratory results yet the infection did not clear. This calls for high index of suspicion of antimicrobial resistance especially when there is poor response during early initiation of antimicrobial therapy. Therefore, more work needs to be done by health care professionals to ensure that patients receive the right and high quality antimicrobial agents in the right dosage, frequency and duration to reduce the risk of antimicrobial resistance. The community should also be educated on how to suspect and prevent spread of AMR.

CONSENT

Informed written consent was obtained from the patient and parent.

ETHICAL APPROVAL

This research was approved by the Ministry of Health Research and Ethics Committee Lesotho with reference number ID 55-2022.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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