

Emphysematous cystitis in feline caused by *klebsiella oxytoca* multi-resistant producer of extended spectrum betalactamases associated with *enterococcus* sp. - case report

Cistite enfisematosa em felino causada por *klebsiella oxytoca* multirresistente produtora de betalactamases de espectro estendido associada a *enterococcus* sp. – relato de caso

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ABSTRACT

Over the years, resistance to antimicrobials has become one of the world's biggest public health problems. This problem deserves attention not only in medicine but also in veterinary medicine since microorganisms have zoonotic potential. For that reason, this study aims to report a case of feline emphysematous cystitis caused by a multiresistant

Klebsiella oxytoca Extended Spectrum Beta-lactamase (ESBL) producer associated with an *Enterococcus* sp. We treated the animal at the Veterinary Hospital of the Universidade Federal de Mato Grosso, campus Sinop, Mato Grosso, Brazil and the microorganisms were identified by employing morphotintorial characteristics and biochemical tests at the Animal Health Laboratory of the same institution. We performed the antimicrobial sensitivity test using the Kirby and Bauer method, where we identified resistance to several antimicrobial classes. For phenotypic detection of ESBL production in the *Klebsiella oxytoca* strain, we performed Disk Approximation, Three-dimensional Extract Test and Minimum Inhibitory Concentration tests using the Etest® tape. This case draws attention because they are bacteria commonly isolated in nosocomial infections in humans only and, for that reason, it emphasizes the importance of working with antimicrobial resistance in the concept of One Health

Keywords: antimicrobial resistance one health, public health.

RESUMO

Com o passar dos anos a resistência aos antimicrobianos tornou-se um dos maiores problemas de saúde pública a nível mundial, esse problema merece atenção não apenas na medicina humana, mas também na medicina veterinária, uma vez que os microrganismos apresentam potencial zoonótico. Tendo em vista tal cenário este trabalho tem como objetivo relatar um caso de cistite enfisematosa em paciente felino ocasionada por *Klebsiella oxytoca* multirresistente e produtora de β -lactamases de Espectro Estendido (ESBL) associada a *Enterococcus* spp. O animal foi atendido no Hospital Veterinário da Universidade Federal de Mato Grosso/campus Sinop – MT e os microrganismos foram identificados por meio das características morfotintoriais e provas bioquímicas no Laboratório de Sanidade Animal da mesma instituição. O teste de sensibilidade aos antimicrobianos foi realizado pelo método Kirby e Bauer, no qual foi possível constatar resistência a várias classes de antimicrobianos. Para detecção fenotípica da produção de ESBL na cepa de *Klebsiella oxytoca* foram feitos os testes de Aproximação em Disco, Teste do Extrato Tridimensional e Concentração Mínima Inibitória por meio da fita Etest®. Esse caso chama atenção por serem agentes bacterianos comumente isolados nas infecções nosocomiais em humanos e ressalta a importância de trabalhar a resistência aos antimicrobianos no conceito de Saúde Única.

Palavras-chave: saúde única, resistência aos antimicrobianos, saúde pública.

1 INTRODUCTION

Urinary tract infection is characterized by the presence and multiplication of microorganisms in urine (MONTEIRO et al., 2013). Urinary tract infection that is located in the urinary bladder is called cystitis. Emphysematous cystitis is a complication characterized by air in the wall of the urinary bladder, which is diagnosed by imaging, and this condition occurs due to infection with gas-producing bacteria (GABE et al., 2018).

Although it may have a viral or fungal etiology, most urinary tract infections are originated from bacteria. Most of the time, these conditions involve only one strain of bacteria, even though 20 to 30% of cases are mixed infections (MONTEIRO et al., 2013). These infections are usually ascendant and involve opportunistic bacteria (FERREIRA et al., 2014). The microorganisms that stand out the most in this infectious process are enterobacteria, such as *Escherichia coli* and *Klebsiella* spp, accompanied by other agents such as *Pseudomonas* spp, *Staphylococcus* spp, *Streptococcus* spp and *Enterococcus* spp (DE OLIVEIRA et al., 2019).

Urinary tract infection of bacterial origin is uncommon in cats. However, the disease can occur in these animals when they undergo a probing process for urethral clearance. This is explained by the fact that this procedure favors the entry of microorganisms into the urinary tract (RECHE JR et al., 1998). Urinary tract infection is characterized by the presence and multiplication of microorganisms in the urine (MONTEIRO et al., 2013). Urinary tract infection that is located in the urinary bladder is called cystitis. Emphysematous cystitis is a complication characterized by air in the wall of the urinary bladder, which is diagnosed by imaging, and this condition occurs due to infection with gas-producing bacteria (GABE et al., 2018).

Characterized as the ability of the microorganism to multiply in the presence of therapeutic or greater doses of the drug, antimicrobial resistance has become a much-discussed topic in recent years, and it is a matter of concern in both human and veterinary medicine (SFACIOTTE et al., 2014).

In this context, urinary tract infections deserve special attention since they are one of the main reasons for using antimicrobials in veterinary medicine (DORSCH et al., 2015), often inappropriately. As a result, the detection of resistant microorganisms isolated from urinary tract infections is increasing (MARQUES et al., 2018). Furthermore, many of the pathogens isolated from these infections cause diseases in humans, which results in the insertion of essential drugs from human medicine into the routine of the veterinary clinic (GUARDABASSI et al., 2004; MARQUES et al., 2018; WHO, 2017).

The intimate contact of dogs and cats with their tutors and family members is also on the rise, which is a cause of concern and importance of this topic for public health since studies show that these animals can share bacteria with the human beings they live with (JOHNSON et al., 2009; POMBA et al., 2017). Because of this scenario, this work

aims to report a case of *Klebsiella oxytoca*, producer of extended-spectrum β -lactamases, associated with an *Enterococcus* sp causing emphysematous cystitis in a feline.

2 CASE REPORT

The patient, feline, mixed breed, male, two years old, neutered, arrived at the Veterinary Hospital of Universidade Federal do Mato Grosso, Sinop campus, presenting dysuria, pollakiuria, hematuria and strangury. The animal had a urethral obstruction in its clinical history and had previously undergone a process of clearance through urethral catheterization. Through the ultrasound examination, it was possible to detect emphysematous cystitis. We collected a urine sample using the cystocentesis method, divided into two aliquots. A part was sent for urinalysis, where the presence of bacteria was found in abnormal amounts in the urine (+ + + + +). The other portion of the sample was sent to the Animal Health Laboratory of the Veterinary Hospital of UFMT, Sinop, to proceed with the culture and antimicrobial susceptibility test.

The first step of the bacterial isolation process was inoculating the urine sample in Brain Heart Infusion (BHI) broth under aerobic conditions at 37°C for 24 hours. After this period, the sample was seeded on Muller-Hinton Agar under aerobic conditions at 37°C for 24h.

When evaluating the colony growth pattern on Muller-Hinton Agar, we noticed the presence of two distinct colonies, suggesting the presence of two different microorganisms. Therefore, the Gram staining method was performed in both colonies, in which we identified that one microorganism was a Gram-negative rod and the other was a Gram-positive cocco.

To identify the Gram-negative rod, we evaluated the fermentation profile on Mac Conkey Agar, Eosin-Methylene Blue Agar and analysis of the following biochemical tests: Triple Sugar Iron Agar, Simmons Citratto Agar, SIM Agar, Lysine Decarboxylase Broth, and MR- VP. As for identifying Gram-positive cocci, we used the following tests: Catalase Test, Growth in BHI Broth 6.5% NaCl, Growth in Blood Agar and Muller-Hinton Agar at 37°C and 45°C, Bile-Esculin Agar and Optochin Test. By observing the test results, we identified the Gram-negative rod as *Klebsiella oxytoca* and the Gram-positive cocco as *Enterococcus*.

After being isolated, the bacterial strains were submitted to the antimicrobial susceptibility test. We performed this examination according to the Kirby-Bauer Method,

following the criteria and parameters for evaluation recommended by the Clinical and Laboratory Standards Institute (CLSI, 2020).

When analyzing the susceptibility results in the *Klebsiella oxytoca* we observed resistance to fifteen antimicrobials (cephalothin, sulfazotrim, ciprofloxacin, enrofloxacin, gentamicin, ceftriaxone, neomycin, ceftazidim, norfloxacin, penicillin G, cefepime, ampicillin, aztreonam, azithromycin and tetracycline) sensitivity to five (cefoxitin, imipenem, ertapenem, chloramphenicol and amikacin) and intermediate sensitivity to one (amoxicillin + clavulanate).

In order to verify whether the strain *Klebsiella oxytoca* produced Extended Spectrum β -lactamases-ESBL, we carried out a Disk Approximation Test, Three-Dimensional Extract Test and Minimum Inhibitory Concentration Test using the Etest® tape (SANTIAGO, 2013). The results were positive.

Regarding *Enterococcus* sp, despite knowing its intrinsic resistance, we tested the same antimicrobials used for *Klebsiella oxytoca*. It was evidenced that this microorganism was sensitive only to amoxicillin + clavulanate, ampicillin and chloramphenicol.

We treated the patient at the discretion of the veterinarian responsible for the case, initially administering ampicillin 10mg/kg orally, twice a day, associated with the intravenous administration of meropenem 24mg/kg, once a day. Both drugs were used for seven days. Seven days after the end of treatment, the patient returned to the Veterinary Hospital with a recurrence. At that time, we treated the patient with meropenem 21mg/kg, subcutaneously, three times a day, for fourteen days. This treatment was successful, confirmed by urinalysis, whose result showed the absence of bacteria.

3 DISCUSSION

In the patient of the present report, it was possible to verify, through the clinical record, the history of urethral obstruction prior to the case of cystitis. The case confirms the findings of RECHE et al. (1998), in which all urine samples that showed bacterial growth (8%) were from male cats with a history of recurrent urethral obstruction since catheterization may favor the entry of bacteria into the urinary tract.

DORSCH et al. (2015) evaluated the prevalence of bacterial species and antimicrobial resistance in felines over ten years. This study reported that 10.6% of the

samples were infections by two agents, as in the case presented. The same study showed that 6.6% of their isolates were of the genus *Enterococcus* sp.

Klebsiella oxytoca has been considered an emerging pathogen in nosocomial infections in human medicine and is still poorly understood in veterinary medicine. It has been reported in cases of disseminated dermatitis in dogs (AQUINO; HERZIG, 2018), as well as osteomyelitis and septic shock, also in dogs (SELIŠKAR et al., 2007). In the study by SINGH et al. (2016), it was possible to verify that 58% of the *K. oxytoca* were ESBL producers, as well as the microorganism isolated in this case, which showed resistance to 71.4% of the antimicrobials tested.

POMBA et al. (2017) described the importance of evaluating this antimicrobial resistance related to companion animals as a public health problem since these agents have zoonotic potential and the ability for bacteria to transfer resistance genes. In recent years, reports of multidrug-resistant microorganisms in companion animals have grown, as has the contact of these animals with humans. This fact can be evidenced in the present work, considering that *Klebsiella* and *Enterococcus* are responsible for severe nosocomial infections in humans, which most of the time are resistant to several antimicrobials and, in this case, were isolated from a domestic feline.

The antimicrobial susceptibility test demonstrated its importance soon after the use of antimicrobials in the practice of medicine with the emergence of resistant strains (KONEMAN, 2012). However, it is often not requested in the clinical routine. The empirical prescription of antimicrobials without prior bacterial culture and susceptibility testing (antibiogram) is one of the main factors for selecting resistant microorganisms. The exam of culture and antibiogram was essential for the patient's treatment, as presented in this report, where it was possible to obtain success in the treatment even with multidrug-resistant microorganisms. (DA COSTA; SILVA JUNIOR, 2017).

4 CONCLUSION

Thus, the importance of culture and antibiogram for treating bacterial infections in animals is clear since antimicrobial resistance has progressively increased over the years, becoming a global health problem. It is worth mentioning that these pathogens can be transmitted between animals and humans, which shows the importance of the rational use of antimicrobials in veterinary and human medicine. Likewise, the report in question

highlights the need for multidisciplinary measures to prevent the emergence and spread of multidrug-resistant strains between animals and humans.

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