Chapter

Antibiotic Resistance of Pathogens of Cervical Lymphadenitis in Guinea Pig in Peru

Santos Wilton Calderón-Ruiz, Ronal Mescco, Edgar Valdez and Rubén Pinares

Abstract

The guinea pig (*Cavia porcellus*) is a small animal that provides a source of protein for the feeding of rural inhabitants of Peru. The frequency of pathogens associated with cervical lymphadenitis includes mainly pyogenic bacteria's Streptococcus sp., Staphylococcus sp. and Corynebacterium sp. The spread of these pathogens can be controlled by applying biosecurity with thorough disinfection and rest of ponds or cages. In this context, antibiotic resistance is a growing problem in veterinary and human medicine, disfavoring antibiotic therapeutic efficacy that can nullify the curative action during treatment. We describe the main bacteria isolated from cervical lymphadenitis can be very sensitive to bacitracin, polymyxin, vancomycin and gentamicin. Which will allow the proper use of antibiotics in guinea pigs, as well as an efficient control focused in One World One Health. Antimicrobial resistance against lymphadenitis in guinea pigs in vivo has not been well studied in the regions of Peru. Resistance to enrofloxacin, penicillin and oxytetracycline, the most widely used antibiotics by producers, is suspected without considering the specificity or the spectrum of their pharmacological action; which could represent a relevant public health problem at the regional level. For these considerations we suggest carrying out resistance tests with animals previously administered with fluoroquinolones and the new beta-lactams.

Keywords: guinea pig, pyogenic bacteria abscess, sepsis, antimicrobial resistance

1. Introduction

The guinea pig (*Cavia porcellus*) is a small indigenous animal that is raised for meat production in all the ecological levels of the coast, valleys and Andean Communities of Peru. guinea pig meat is the main source of protein with a lower level of fat, suitable for feeding rural residents and its demand is growing in Peruvian gastronomy due to its palatability and consumption habits [1]. However, the low level of knowledge about technical breeding and the epidemiological factors of the diseases of this species have a negative impact on health and productivity. The guinea pig is susceptible to various infectious diseases, the most common are caused by bacterial etiology [1, 2].

The Streptococcus equi subsp. Zooepidemicus a gram positive encapsulated coccus that produces beta hemolysis on blood agar [2] initially was associated with suppuration and abscess formation in the cervical lymph nodes (cervical lymphadenitis), which are evident on visual examination and palpation. Pathogens associated with cervical lymphadenitis include various species of bacteria. Streptococcus sp., Staphylococcus sp. and Corynebacterium sp. were isolated in 69.77, 20.93, and 9.30%, respectively [3], in another more recent study 91.9% of beta-hemolytic Streptococcus sp., 45.9% Staphylococcus sp. and 21.31% Klebsiella sp. were isolated [4], while in other study the most frequent pathogens isolated from cervical lymphadenitis were Streptococcus sp. (100%), Staphylococcus sp. (90%), Corynebacterium sp. (20%) and Salmonella sp. (20%) without influence of sex and age [5].

The pharmacological sensitivity of antibiotics against pathogens associated with cervical lymphadenitis was evaluated by in vitro halo inhibition. The most sensitive antibiotics against pyogenic pathogens the most sensitive were bacitracin, polymyxin, vancomycin and gentamicin and against beta hemolytic Streptococcus sp. were gentamicin and oxytetracycline [4].

The evaluation of antimicrobial susceptibility contributes to the correct clinical treatment and epidemiological control, in order to reduce antibiotic resistance problems of importance in therapeutics and public health. In this context, antibiotic resistance is a growing problem in veterinary medicine and therefore in human medicine, due to the lower antibiotic therapeutic efficacy that can nullify the curative action during treatment.

2. Lymphadenitis by the anatomical region and the affected organs

According to the anatomical region, craniocaudally and dorsoventrally direction, the abscesses can be can be localized and have several centimeters in diameter and contain an odorless yellow-white to red-gray pus. External abscesses most often occur in the ventral neck (**Figure 1**), chest, forelimbs, hindlimbs, and abdomen. On palpation, hypertrophied lymph nodes in the neck, legs, and abdomen were evident. The pathogens are located mainly in the cervical lymph nodes (**Table 1**), the most common pathway of entry is through damaged surfaces of the oral mucosa or through

Figure 1.
Ventral neck swellings with enlarged lymph nodes >2 cm.

Anatomical region	Number of samples	%
Base of neck	09	31.03
Jaw	01	03.44
Thoracic cavity	05	17.24
Anterior member	05	17.24
Abdominal cavity	03	10.34
Mammary gland	02	06.90
Posterior member	03	10.34
Testicle	01	03.44
Total	29	100

Table 1.
Distribution of external subcutaneous abscesses in guinea pigs.

the upper respiratory tract [6], spreading to all the superficial ganglia of the body distributed anatomically. Reason for which abscesses are observed in the thoracic, abdominal and limb regions.

In advanced cases, the abscess drains naturally without any treatment and control, causing its rapid spread in the shed, even worse if biosafety protocols are not followed. The chronic infection can compromise other organs close to the abscess, as a control measure it is recommended to eliminate guinea pigs with abscess in the body [1] and quarantine in the shed. Acute cases with non-caseated abscesses <1 cm in diameter can be surgically drained, eliminating the abscess with a frequency of 24 hours/3 days accompanied by powdered penicillin, where a recovery rate of 80% of treated guinea pigs has been observed (Pinares, unpublished data).

It has been shown that lymphadenitis also affects the internal organs of the guinea pig. In decreasing order, the most affected organs are the small intestine, liver, spleen, and kidneys, and the least affected is the cecum (**Table 2**).

The pathogens have a greater tropism for the lymph nodes, during the infection they probably invade the blood and lymphatic circulation, producing septicemia and contaminating the main organs. Other complications include pneumonia, generalized lymphadenitis, sepsis, focal hepatitis, otitis media, pleuritis, peri- and myocarditis, nephritis, mastitis, metritis, and arthritis with necrosis and hemorrhage [2]. During necropsy, macroscopic lesions were observed in the lymph nodes and petechial lesions in the liver, heart, and kidney with micro abscesses (**Figure 2**).

Región anatómica	Number of samples	%
Liver	04	28.57
Spleen	02	14.28
Small intestine	05	35.71
Blind	01	07.14
Kidney	02	14.28
Total	14	100

Table 2.
Distribution of micro abscesses in internal organs of guinea pigs.

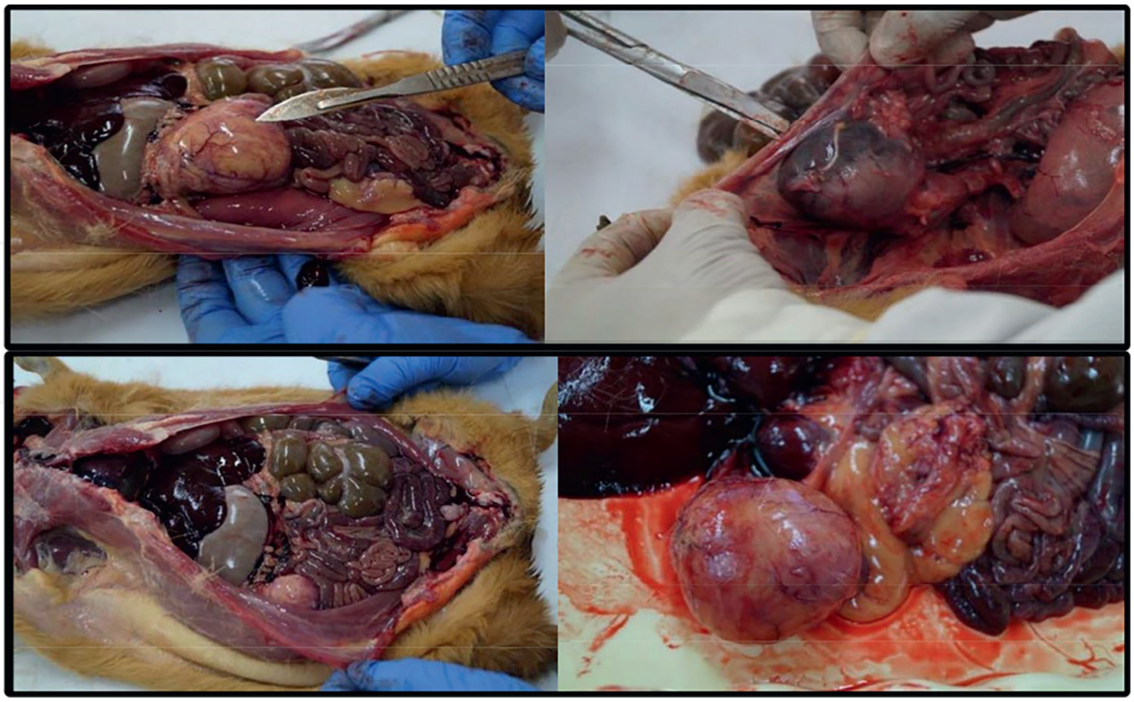

Figure 2.
Autopsy findings, major organs congested with micro abscesses and generalized septicemia.

3. Etiology of lymphadenitis

The etiology was identified according to sex (**Table 3**) by cultures (colony type), Gram stain (+ or -) and by microscopy identification (morphological characteristics, cocci and bacilli).

Through microbiological analysis it was determined that the causal agent is Streptococcus sp. followed by Staphylococcus sp. and less frequently Corynebacterium sp. (**Figures 3** and **4**).

Our findings were similar to 91.9% beta-hemolytic Streptococcus sp., 45.9% Staphylococcus sp., and 21.31% Klebsiella sp. reported in Cusco by Angulo-Tisoc et al. (2021). On the other hand, in Ayacucho the most frequent pathogens isolated were Streptococcus sp. (100%), Staphylococcus sp. (90%), Corynebacterium sp. (20%) and Salmonella sp. (20%) [5]. In the chronic phase of lymphadenitis, they are associated with several bacterial species described in other animal species, although in another study only Staphylococcus sp. [7].

Etilology	n	Total (%)	Female (%)	Male (%)
Streptococcus sp.	30	61.77	50.00	11.77
Staphylococcus sp.	09	26.47	20.58	05.89
Corynebacterium sp.	04	11.76	08.82	02.94

n: Number of samples (included female and male).

Table 3.
Identification of the causal agents of lymphadenitis in guinea pigs.

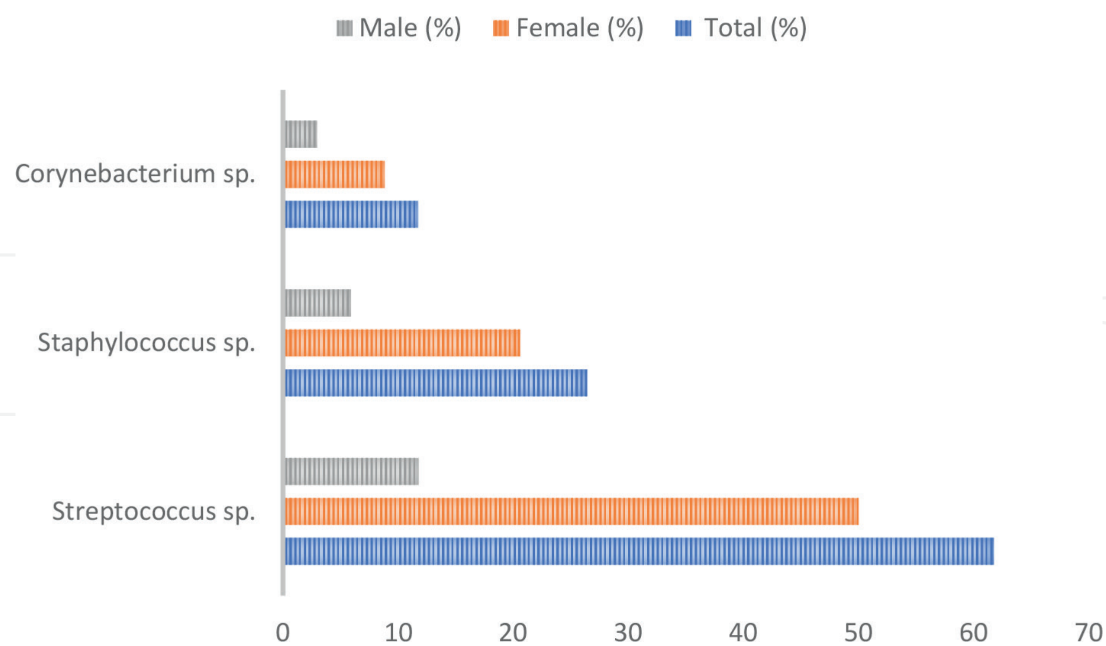

Figure 3.
Frequent pathogens isolated from lymphadenitis in guinea pigs.

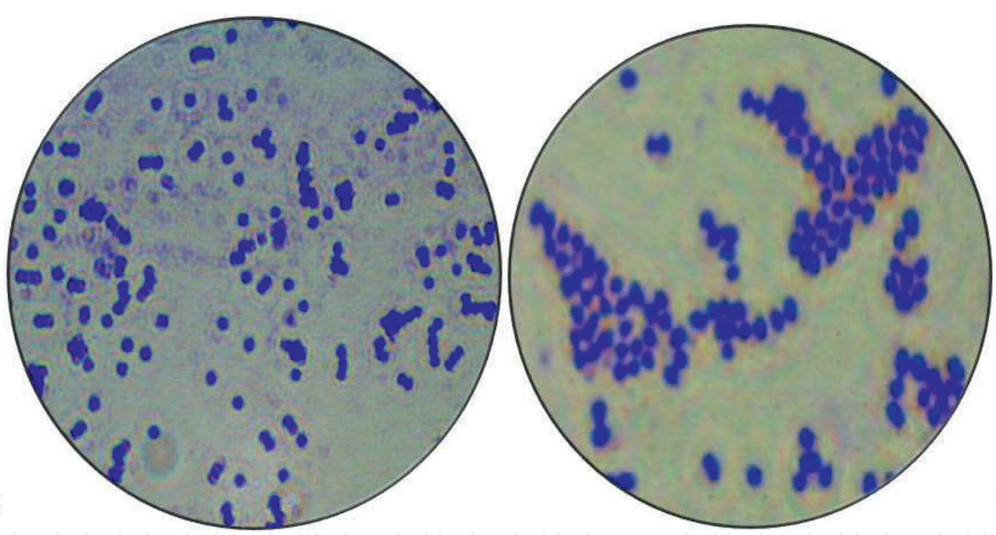

Figure 4.
Streptococcus sp. (left) and staphylococcus sp. (right) isolates from lymphadenitis in guinea pigs.

4. Cases of antibiotic resistance

The in vitro antibiotic susceptibility test was performed as described in the manual of procedures for the antimicrobial sensitivity test by the disc diffusion method. The inhibition halos were measured with a ruler and expressed in millimeters (mm). In our study, four non-traditional antibiotics were tested in this species, which were found to be sensitive (**Table 4**).

Gentamicin shows greater sensitivity consistent with other studies [4, 7], although it has not been verified with animals. Antimicrobial resistance against cervical lymphadenitis in guinea pigs has not been well studied in our region, there are only studies

Antibiotic	Initials	Sensitivity	Inhibition halo (mm)
Bacitracin	BA10	≥08	40
Polymyxin B	PB300	≥12	40
Vancomycin	VA30	≥17	39
Gentamicin	GM10	≥15	38

Initials: BA10 (Bacitracin at 10 μg), PB300 (Polymyxin B at 300 μg), VA30 Vancomycin at 30 μg), and GM10 (Gentamicin at 10 μg).

Table 4.
Pharmacological sensitivity and inhibition halos.

on the treatment of ulcerative pododermatitis in guinea pigs caused by *Staphylococcus aureus*, where gentamicin was used subcutaneously at a dose of 6 mg/kg p.v. every 24 hours for a minimum of 21 days, reducing lesions, the number of bacteria and inflammatory cells [8].

Estupiñán et al. evaluated various antibiotics gentamicin, streptomycin, enrofloxacin, tetracycline, cephalotin, amoxicillin+clavulanic acid, chloramphenicol, sulfamethoxazole+trimethoprim, penicillin and ampicillin. In Ecuador these authors suggest that resistance had not yet developed despite owners administering orally or in the feed enrofloxacin, chloramphenicol, and oxytetracycline [7].

Therefore, resistance depends on the correct use of the dose and the specificity of the drug, traditionally conditioned by the owner or the veterinarian who omits sensitivity tests. In this regard, [7] suggest that, although a bacterium may demonstrate sensitivity in vitro, in vivo there are other factors, such as under dosing, pharmacokinetics, and the presence of fibrous capsules in abscesses and affected organs, that affect the adequate efficacy of the drug.

In this sense, in companion animals, beta-lactam antibiotics (natural penicillins) were administered indiscriminately against the presence of abscesses and pyodermas, generating the greatest resistance. As a second alternative against resistance, the administration of synthetic penicillins: amoxicillin and ampicillin or in combination amoxicillin+clavulanic acid was chosen. Due to the fact that beta- lactams are the only ones that penetrate the abscessed tissues, the use of third-generation cephalosporins, such the ceftiofur, has been suggested with good results in animals. However, in humans some enterococcal isolates are penicillin resistant; most do not produce beta-lactamase as the mechanism of penicillin resistance and should be treated with a combination of vancomycin plus gentamicin [9].

The ß-lactamases are enzymes that generate resistance to most beta-lactams, including penicillins, first, second, and third-generation cephalosporins, where 25% of the strains of *S. aureus* were resistant to cefoxitin and oxacillin [10], resistance is a public health problem, in Ecuador it has been shown that 6.25% of *S. aureus* in the nasopharynx of guinea pigs are resistant to methicillin, therefore, it may have a potential role in the transmission of resistance to people [11]. For an adequate control and management of cervical lymphadenitis in guinea pigs, we suggest making an adequate diagnosis of the causal etiological agent of the disease, once the agent is identified, determine the antimicrobial susceptibility in vitro to be successful in the treatment. Likewise, disinfection of the sheds should be carried out periodically to prevent cervical lymphadenitis in this species.

5. Conclusions

In Peru, lymphadenitis in guinea pigs has multiple bacterial etiologies, where at least Streptococcus sp. and Staphylococcus sp.; the spread of these pathogens can be controlled by applying biosecurity with extensive disinfection and rest of ponds or cages. In vitro, these pathogens can be highly sensitive to bacitracin, polymyxin, vancomycin, and gentamicin. Resistance to the most widely used antibiotics, such as enrofloxacin, penicillin and oxytetracycline by the same producers, is suspected to be due to use and abuse without considering the specificity or spectrum of their pharmacological action; which causes a relevant public health problem at the regional level. Antimicrobial resistance against lymphadenitis in guinea pigs has not been well studied in our region, so it is suggested to give greater importance and carry out research on the subject.

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Conflict of interest

There is no conflict of interest.

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References

[1] Chauca L. Manual técnico crianza de cuyes. Primera edición. Instituto Nacional de Innovación Agraria. Lima, Perú: INIA; 2018. p. 80

[2] Shomer NH, Holcombe H, Harkness JE. Biology and diseases of guinea pigs. In: Fox JG, Anderson LC, Otto GM, Pritchett-Corning KR, Whary MT, editors. Laboratory Animal Medicine. 3rd Edition. New York: Academic Press; 2015. pp. 247-283

[3] Mescco JR. Sensibilidad farmacológica del agente etiológico de la linfadenitis en cuyes del centro de producción de reproductores Huayllapampa-San Jerónimo, Agencia Agraria Cusco [tesis]. Cusco: Universidad Nacional de San Antonio Abad del Cusco; 2019

[4] Angulo-Tisoc J, Siuce J, Jara LM. Frecuencia de patógenos asociados a linfadenitis cervical en cuyes de centros de crianza familiar-comercial en Cusco, Perú. Revista de Investigaciones Veterinarias del Perú. 2021;**32**(1):e19505. DOI: 10.15381/rivepv32i1.19505

[5] Flores DY. Identificación del agente causal de linfadenitis cervical en cuyes (*Cavia porcellus*) mediante métodos microbiológicos en el centro experimental Pampa del Arco, Ayacucho—2017 [tesis]. Huamanga: Universidad Nacional de San Cristóbal de Huamanga; 2018

[6] Murphy JC, Ackerman JI, Marini RP, Fox JG. Cervical lymphadenitis in Guinea pigs: Infection via intact ocular and nasal mucosa by streptococcus zooepidemicus. Laboratory Animal Science. 1991;**41**(3):251-254

[7] Estupiñán P, Burgos A, Chacha S, Baquero MI, Gómez C, Sánchez X, et al. Linfadenitis en un plantel productor de cuyes. Revista Científica Ecuatoriana. 2018;**5**:1-5. DOI: 10.36331/revista.v5i1.33

[8] Venturo BR, Morales-Cauti S, VenturoBR,Morales-CautiS.Pododermatitis ulcerativa severa infectada con Staphylococcus aureus y Proteus sp en un cuy (*Cavia porcellus*): reporte de caso. Revista de Investigaciones Veterinarias del Perú. 2021;**32**(4):e20925. DOI: 10.15381/rivep.v32i4.20295

[9] Baddour LM, Freeman WK, Suri RM, Wilson WR. Cardiovascular infections. In: Douglas P, Zipes MD, editors. Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine. 11th ed. Vol. 73. Philadelphia: Elsevier; 2018. pp. 1483-1509

[10] Urquizo G, Arce J, Alanoca G. Resistencia Bacteriana por beta lactamasas de epectro extendido: un problema creciente. Revista Médica La Paz. 2018;**24**(2):77-83

[11] Zambrano-Mila M, Rodriguez AS, Rivera-Olivero IA, Salas-Rueda M, Caceres-Orellana MV, de Waard JH, et al. Methicillin resistant Staphylococcus aureus carriage among Guinea pigs raised as livestock in Ecuador. One Health. 2020;**9**:100118. DOI: 10.1016/j.onehlt.2019.100118