

Skin and Lymph Node Pathogens in Small Ruminants: *C. pseudotuberculosis* compared with *Staphylococcus aureus*

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ABSTRACT

Small ruminants (sheep and goats) are prone to a wide range of bacterial pathogens which become localized to the skin, lymph nodes and deeper tissues. The most important ones include *Corynebacterium pseudotuberculosis*, the causative organism of caseous lymphadenitis (CLA) and *Staphylococcus aureus*, a ubiquitous opportunistic pathogen, which causes skin infections, lymph node abscessation, and mastitis. Although both are Gram-positive and can result in the development of abscession, *C. pseudotuberculosis* is a chronic granulomatous infection that is often characterized by chronic infection and loss of economy, whereas *S. aureus* is an acute suppurative infection usually accompanied by virulence factors like enterotoxin production and antibiotic resistance. This paper summarizes the pathogen biology, clinical disease, epidemiology, molecular virulence, host immune interactions, diagnostic features, challenges of treatment and control of disease, and provides similarities and critical differences in the importance of disease management in small ruminant populations.

Keywords: *Corynebacterium pseudotuberculosis*, *Staphylococcus aureus*, Lymph nodes, Small ruminants, caseous lymphadenitis

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Introduction

The skin and lymphatic tissue bacterial infections in the small ruminants contribute significantly to the morbidity of the small ruminants across the world resulting in abscess, decreased production, condemnation of carcasses, and welfare issues [1]. *Corynebacterium pseudotuberculosis* and *Staphylococcus aureus* are two common pathogens that are often identified as a result of lesions. They have many differences in the pathogenesis and clinical manifestations, as well as in host interactions and control strategies, although both of them are Gram-positive organisms that can induce purulent lesions [2].

Corynebacterium pseudotuberculosis

Microbiology and Taxonomy

C. pseudotuberculosis is an anaerobic and rod shaped Gram positive bacterium. Isolates in small ruminants are the biovar ovis, nitrate negative and adapted to sheep and goats. The organism has a complex cell envelope containing mycolic acids and can generate long term lesions of granuloma [3].

Clinical Disease of Caseous Lymphadenitis

Caseous lymphadenitis (CLA) is the hallmark disease brought about by *C. pseudotuberculosis* in small ruminants and is a chronic pyogranulomatous disease, which is described as a thick-walled abscess of both the superficial and internal lymph nodes and organs. These granulomatous lesions can be seen to have onion rings on cross-section, that is, repeated necrosis and fibrous encapsulation of the lesion [4]. The clinical manifestations are:

- Superficial cervical, submandibular and prescapular lymph node external abscesses.
- Internal lesions of mediastinal lymph nodes, lungs, liver, and kidneys-usually subclinical until severe.
- The loss of major production is brought about by reproductive performance and loss of weight gain.
- Lesions may be life-long and chronic in case they are not removed [5].

Pathogenesis and Virulence Factors

The important determinants of virulence are the toxin phospholipase D causes vascular permeability that assists the bacteria to multiply via lymphatics. Bacteria with mycolic acids on their cell envelope are able to survive by evading phagocytic lysosome killing [6]. It has an Iron acquisition systems (FagA-FagD) which contributes towards the survival of bacteria in environments with nutrient limitations by the hosts. All these contribute to the ability of the organism in terms of causing chronic granulomatous inflammation and not acute suppuration [7].

Immune Response

The infected tissues form pyogranulomas with concentric fibrin and inflammatory cell layers. It has been demonstrated that there are massive IL-1b and NF-Kb-signaling at the lesions of CLA, which demonstrates the presence of a strong pro inflammatory environment required to support the formation and maintenance of granulomas [8].

Transmission and Epidemiology

C. pseudotuberculosis causes CLA known to be highly contagious in flocks all over the world. It occurs mostly in cases of skin wounding, shearing injuries and environmental fomites, the organism is able to survive in soil and bedding [9].

Staphylococcus aureus

Microbiology and Ecology

Staphylococcus aureus is a Gram-positive coccus, it is a normal flora of the skin and mucous membranes. It is an opportunistic pathogen, which can invade the tissues in case of the destruction of the skin barrier [10].

Small Ruminant Disease Manifestations

S. aureus can cause variety of disease in small ruminants that include the infection of the skin and abscesses after the abrasion or trauma. Suppuration of lymph nodes adjacent to skin lesion may occur in case of Staphylococcal infection [11]. Morel's disease cause disease in young sheep that leads to abscesses of the mandibular lymph nodes. Most importantly, *S. aureus* is a major cause of mastitis in sheep and goats that affects the economy in a major way through the reduction of milk yield and quality [12].

Virulence Factors and Pathogenesis

Different virulence factors such as enterotoxins and hemolysins effects tissues and systemic system. Host immune system are disrupted through protein A and coagulase. *S. aureus* normally produces acute suppurative inflammation and more superficial lesions compared to *C. pseudotuberculosis* and may spread by lymphatic or blood in certain circumstances [13].

Antibiotic Resistance

Methicillin resistant *S. aureus* strains have also been reported in small ruminants, which can be a significant problem in the treatment and public health because of the potential of transmitting zoonotically through milk and direct contact [14].

Pathological Comparison

C. pseudotuberculosis and *S. aureus* have a marked difference in the nature and progression of lesions in the skin and lymph nodes of small ruminants, pathologically. *C. pseudotuberculosis* has a tendency to cause chronic granulomatous inflammation leading to well encapsulated abscesses that present thick fibrous walls and laminated, caseous (cheese-like) interiors. These lesions grow gradually and are frequently permanent during the life of the animal, which represents the resistance of the organism to intracellular survival and clearance by the immune system [15]. Although the lesions of staphylococcal could comprise the lymph nodes as a result of the skin infections, they are often more localized and are more responsive to medications as compared to those associated with *C. pseudotuberculosis*. Therefore, the pathological characteristic of *C. pseudotuberculosis* is a chronic course of the disease with the development of granulomas, and *S. aureus* infections are characterized by acute pyogenic processes and tissue destruction as shown in figure 1[16].

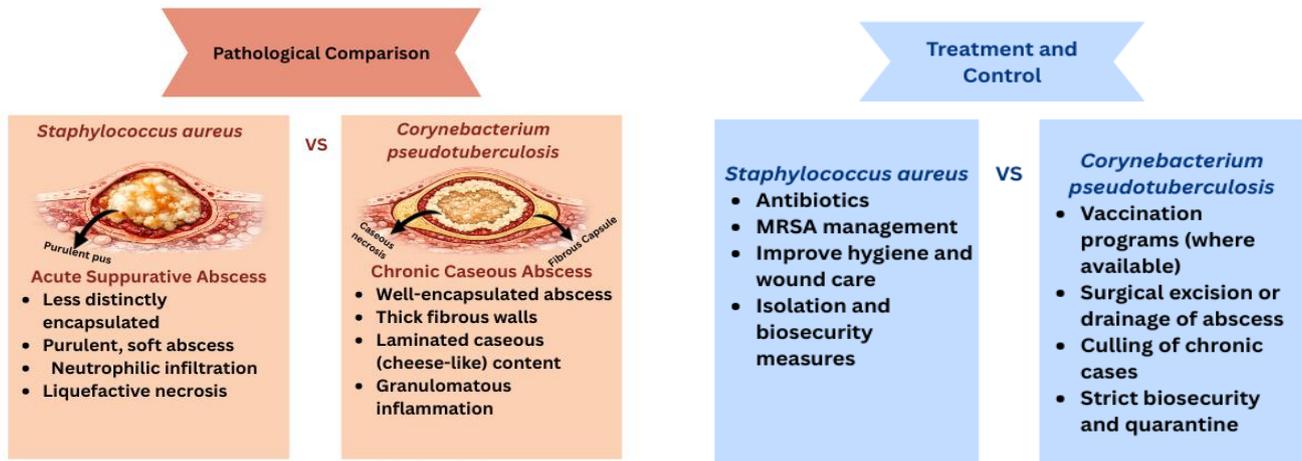


Fig. 1: Pathological comparison of *C. pseudotuberculosis* and *S. aureus*

Diagnosis

Small ruminants infected with *C. pseudotuberculosis* and *S. aureus* infections are diagnosed using a combination of both clinical and laboratory. The animals with *C. pseudotuberculosis* are clinically characterized by well-encased firm abscesses that affect superficial lymph nodes such as prescapular, submandibular or prefemoral ones, and in certain instances, internal abscess signs are evident as either weight loss or respiratory distress. In cases of mastitis, purulent material of abscesses or milk should be cultured using bacteria through bacteriological culture and biochemical identification should be performed. Molecular diagnostics methods are more accurate and specific, PCR of *pld* (phospholipase D) gene is mostly used to confirm that the organism is *C. pseudotuberculosis* [17]. The amplification of species-specific genes such as *nuc* (thermonuclease gene) and *mecA* (methicillin resistance gene) can help identify *S. aureus* and identify methicillin-resistant strains (MRSA). Also, serological tests, in particular enzyme-linked immunosorbent assays (ELISA) are especially useful in identifying antibodies to *C. pseudotuberculosis* at flock level, which would assist in epidemiology monitoring and early diagnosis of subclinical carriers [18].

Public Health and Zoonotic implications

Both pathogens are zoonotic *C. pseudotuberculosis* through direct contact with abscess contents and *S. aureus*, especially MRSA, through direct contact and contaminated milk. Both animal and human health are safe through ensuring that milk is pasteurized and biosecurity practices are taken to ensure safety [19].

Treatment and Control

Systemic antibiotic treatment of *C. pseudotuberculosis* infections is not usually effective as the thick fibrous capsule containing CLA abscesses inhibits drug penetration and bacteria survive as part of granulomatous tissue. Therefore, the main treatment still is surgical drainage or excision of abscesses, accompanied by appropriate disposal of contaminated material and disinfection of the environment. The important control measures include culling chronically infected animals and taking of stringent biosecurity actions in form of quarantine of new additions, wound management, and sanitation of shearing equipment [20]. Conversely, the *S. aureus* infections tend to respond better to the antimicrobial intervention under the guidance of culture and susceptibility tests; but the rise of MRSA strains has forced more attention on the antimicrobial drug choice and the responsible use of the drugs to avoid the development of resistance. The management practices that are important in the control of *S. aureus* include better hygiene, prevention of skin trauma, appropriate milking routines to reduce cases of mastitis, isolation of infected animals, and the application of antimicrobial stewardship principles in order to limit the occurrence of the resistant strains [21].

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Fig. 2: treatment and control of both bacteria (*C. pseudotuberculosis* and *S. aureus*) and how it control.

Conclusions

Both the *C. pseudotuberculosis* and the *Staphylococcus aureus* are serious bacterial pathogens of small ruminants which have different pathobiological profiles. *C. pseudotuberculosis* causes chronic granulomatous disease (CLA) with huge losses in production and management difficulties, *S. aureus* is causing acute suppurative infections frequently complicated by antibiotic resistance. The necessary control requires combined measures, such as proper diagnosis, specific treatment, vaccination in case of need, and strict management to minimize prevalence and financial effects.

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