An Orf Outbreak in a Herd of Boer Cross Goats

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Summary:

A goat herd outbreak of skin lesions characterized by scabby, papillomatous dermatitis on the lips and extending into the buccal cavity was investigated. Initial clinical signs in the first animal affected included acute submandibular edema with swollen mandibular lymph nodes. Necrotic areas were observed on the buccal mucosa. Lesions characteristic of orf developed on the muzzle. Over the next seven days, all but one in the group of 38 doe, doeling and wether goats developed similar lesions. A group of 15 buck kids housed separately was initially unaffected, but two developed mild lesions later.

This herd of Boer cross goats had no prior history of orf. Lesions in adult animals were similar in severity and duration to those in the younger animals. Orf virus was found in samples of scab material analyzed using PCR and electron microscopy. All cases resolved spontaneously.

Orf is an epitheliotropic parapoxvirus that infects sheep and goats. Virulence factors have been identified through research directed at the immunomodulatory characteristics of the virus. Autogenous or commercial vaccines are available, but are fully virulent virus. Orf is zoonotic to humans, typically causing single target lesions on distal extremities, with rare more serious lymphadenopathies described. Control is directed at strategic vaccination, and limiting infectious material buildup in the environment associated with lambing or kidding.

Key Words

Orf, contagious ecthyma, Boer goats, parapoxvirus, zoonosis, strawberry footrot

Case Presentation

In August 2002, the owner of a small herd of dairy/Boer cross goats located in central New York noticed subcutaneous swelling in the submandibular region of Karusha, a 5 year old doe. Within 5 days, papular eruptions appeared along Karusha's lip margins and in the mucosa of her buccal cavity. Within this time frame, the owner noticed similar submandibular swelling in several other does, which also exhibited progression to papular eruptions on the lips. The Ambulatory Service at Cornell University College of Veterinary Medicine visited the farm 12 days after initial signs in Karusha. At that time, all but one goat in the doe herd exhibited some degree of the above-described pattern of lesions. Lesions ranged in severity from mild lip scabs to severe papillomatous to necrotic areas of the oral mucocutaneous junction, the pinnae, and teats. None of the goats appeared systemically ill.

The herd of goats consisted of 35 does and doelings, 3 pet wethers (one is an Angora) and 15 buck kids. The does, doelings, and wethers were group housed in a wooden shed at night, and turned out to pasture during the day. Pasture was divided such that the herd rotated through meadow pasture as well as a wooded parcel where browsing in rough brush occurred. The bucks were maintained on separate pasture with no contact with the doe/doeling group.

Gastrointestinal parasitism historically had been problematic on this farm. Goats showing clinical signs such as weakness and pale mucous membranes were routinely dewormed with oral ivermectin. Fecal flotation is done routinely to monitor parasite load.

One of the 6 month-old buck kids was added to the herd in June 2002 as a breeding buck from a Boer herd of over 220 animals, also located in central New York. The buck source herd is endemic with orf. The breeding buck had a presumed case of orf that resolved 5 months prior to arrival on the farm.

Due to the progression of clinical signs and rapid spread through the doe/doeling group, infectious, toxic and metabolic causes were considered in the differential diagnosis. With submandibular swelling in the goat, differential diagnoses that must be considered include; hypoproteinemia due to malnutrition or secondary to liver or kidney disease, Johne's disease (*Mycobacterium paratuburculosis*), gastrointestinal parasitism (haemonchosis), and liver flukes (fascioliasis); anaphylactic reactions due to insect stings or bites and drug reactions.

As the skin lesions progressed through the papular, vesicular and pustular stages, the differential list was expanded to include the following viral diseases: sheep and goat pox (Capripox family)*, foot and mouth disease*, bluetongue, papillomatosis, peste des petits ruminants*, and vesicular stomatitis (*indicates reportable diseases within the United States). As most of the above viral diseases are exotic to the U.S., orf was considered the most likely pathogen. The clinical pattern ranging from papular/pustular to papillomatous lesions with scabbing strongly suggested an orf outbreak in a naïve herd of animals.

Although the farm had no prior history of orf, the source of the current infection was unclear. Several possibilities were entertained, as this was not a closed herd. Eight goats, does and buck kids, were shown at the Tioga Country Fair, July 9-13, 2002. Despite the health certificate requirement for show goats to attend, one owner at the fair

cautioned all participants to quarantine their goats after the show due to concerns that orf may have been present. Goats at this fair are housed in unsanitized wooden pens. The 8 goats taken to the fair were not quarantined upon return to the farm on July 13. Another possible route of introduction was one of the wethers; an Angora that was sheared in June by a neighbor who comes in contact with other sheep and goats. The third major possibility was that the owner of the farm had visited a known infected farm 6 days prior to initial signs in Karusha. She handled an infected goat and had not changed attire before coming into contact with her own goats. Karusha was not one of the goats taken to the County Fair. The outbreak progressed through all animals within the doe/doeling group, whereas only two animals in the buck kid group were observed with mild scabbing around the muzzle, suggesting that something within the doe herd had contributed to a more severe presentation.

Diagnostic Tests

Samples of the scab material were collected from the lips of affected animals on the farm. Additional samples were collected from other area herds known to have soremouth, including the buck source herd and the known infected herd the owner visited shortly before the outbreak. All samples were sent to a laboratory at Texas A & M University for polymerase chain reaction (PCR) analysis and electron microscopy.

Using primers for an orf virus envelope gene, PCR amplification and gel electrophoresis were used to determine the presence of viral DNA. The presence of the orf virus was confirmed with electron microscopy, which showed characteristic morphology.

After confirmation of the presence of virus, the viral interferon resistance gene (vaccinia E3L IFN resistance gene homologue) was isolated and sequenced from the orf isolate from this outbreak and the infected herd the owner came in contact with using PCR amplification (1). The PCR products were then compared to each other for homology as an indicator of relatedness among the isolates. The strain found on this farm was more similar to a strain from San Angelo, Texas than to the strain isolated from the infected herd the owner came in contact with. As this is an experimental model currently under review for publication, results must be interpreted cautiously (2).

Etiology

Orf is caused by a parapoxvirus closely related to pseudocowpox, bovine papular stomatitis virus, Ausdyk virus of camels, and species-specific parapoxviruses of deer, squirrels, and seals. Like other parapoxviruses, it is a 135 kbp double-stranded DNA virus. Morphologically, the virions are ovoid in shape and approximately 260nm X 160nm in size. As with other parapoxviruses, orf virus requires regenerating epithelium to replicate (3). Usual lesion distribution in natural infection is confined to the muzzle, teats and feet. Unusual distributions have been reported on other areas of the head, neck, chest and flanks (4).

Cutaneous lesions caused by orf usually are noticed as papules initially. A central vesicle forms in the papule, which enlarges and becomes a pustule. The surface, a thin epithelial remnant, is fragile and ruptures shortly after formation. Within 2 to 14 days, the pustule ruptures and a large scab is formed due to extensive serum exudation. Within 28 to 42 days, the scab dries out and is shed (5). The uncomplicated skin lesion heals

with no scarring (6, 7). The scab contains a high titer of virus, and once shed, contributes to environmental viral contamination that has been linked to outbreaks in subsequent years on the same premises (6).

Histologically, papillomatous lesions have been described as having focal proliferation of basal and prickle cell layers. Ballooning degeneration was seen in the cytoplasm of superficial epithelial cells, many of which contained eosinophilic intracytoplasmic inclusions (8).

Viral infectivity has been shown to be resistant to organic solvents and desiccation. Heating infectious material to 58-60°C for 30 minutes has reportedly destroyed infectivity (6). These control measures are not practical or possible in eliminating environmental contamination as a source of new infection in endemic farms.

Reinfection with orf is common, although the clinical disease is shorter in duration and signs are milder in subsequent infections. Infection induces a short-lived immunity, thought to involve both humoral and cell-mediated mechanisms, discussed below.

Current research on the orf virus as the type virus for the parapoxvirus family has focused on immune-modulatory genes within the parapoxvirus genome. Four putative virulence factors have been identified (9). Ovine vascular endothelial growth factor (OVEGF) homologue, ovine interleukin-10 homologue, vaccinia E3L interferon resistant gene homologue, and granulocyte-monocyte colony stimulating factor (GM-CSF) inhibitory factor (GIF), are all soluble proteins synthesized early in the course of infection.

The OVEGF homologue acts locally to induce angiogenesis in a concentration-dependent manner. It also induces vascular permeability, which leads to serum exudation, contributing to a large scab once the pustular stage ruptures. Naïve sheep have been inoculated with VEGF knockout virions, resulting in a much milder infection with decreased morbidity and lack of a papillomatous reaction. Interestingly, the viral VEGF homologue is more similar to ovine than human VEGF, suggesting a co-evolution (9, 10).

The ovine interleukin-10 (IL-10) homologue is an anti-inflammatory factor that inhibits or down-regulates production of the pro-inflammatory mediators tumor necrosis factor α (TNF-α) and IL-8 by macrophages and interferon γ (IFN-γ) by lymphocytes (9, 11).

An IFN resistance gene homologue, similar to the vaccinia E3L gene has been demonstrated as a highly conserved gene in all of the parapoxviruses. This factor binds to double stranded RNA (dsRNA), a by-product of viral replication. Normally, dsRNA triggers the PKR kinase pathway in an infected cell with the result of cell lysis through apoptotic pathways. Binding of dsRNA inhibits the natural signaling within an infected cell to prevent premature lysis of the cell, giving the virus adequate time to replicate (11).

The fourth putative virulence factor, GIF has been shown to bind GM-CSF and IL-2 in afferent lymph obtained through cannulation of ducts draining infected tissue *in vivo*. Both GM-CSF and IL-2 cause recruitment of macrophages and neutrophils to the site of infection. Epithelial cells normally secrete these pro-inflammatory factors in response to viral infection (1). Binding and inhibiting these factors delays the inflammatory response, giving the virus more time to establish its replication cycle.

Recent work by Lloyd et al. suggests that both humoral and cell-mediated responses are required for elimination of orf infection (12). In his study, lambs depleted of $CD4^+$ cells using monoclonal antibodies were unable to clear the virus. Earlier work showed a specific humoral response to infection, but demonstrated that level of antibody cannot be correlated with protection (6).

Complications of orf virus include persistence of the orf virus and/or secondary bacterial invaders. One ram was reported as having a persistent orf infection of six months duration (13). The most commonly isolated agent associated with orf infection is *Dermatophilus congolensis*, which leads to a severe proliferative lesion at the coronary band (strawberry footrot), but can extend to the axilla and groin (6).

A major concern regarding orf is the zoonotic potential (14). As with other parapoxviruses of domestic animals, transmission to humans can occur. Ecthyma contagiosum, the disease in humans, is similar to the disease in sheep and goats in that a typical skin lesion pattern is observed over time. Initially there is a circular erythematous area that develops a central pallor resembling a target. The central area forms a raised papule that progresses through vesicular and pustular stages before rupture and scab formation. Spontaneous resolution usually occurs with no scarring in 4 to 6 weeks (6). In contrast to the disease in ruminants, lesions in humans usually affect only the distal thoracic limb and are solitary. There are reports in the literature of susceptible individuals developing more serious signs such as malaise, lymphangitis, fever, and regional lymphadenopathy associated with cutaneous lesions (15). Orf is a concern for immunocompromised patients. The primary mode of transmission is through contact of infectious material with abraded skin. Orf has been reportedly transmitted to a human

having no direct contact with infected animals via contact with another human who had been in contact with sheep. Differential diagnosis in humans includes pseudocowpox infection, herpes simplex, molluscum contagiosum, vaccinia, and anthrax (6).

Treatment and Control

Treatment of soremouth in goats and sheep is focused toward preventing secondary bacterial infections while the viral infection resolves. Various anecdotal treatments have been suggested to have some efficacy in resolving clinical signs of viral infection (6). Monitoring for resolution of clinical signs with no additional treatment was elected on this farm. All cases completely resolved.

Losses due to orf usually are due to secondary problems such as toxic mastitis or starvation in kids or lambs unable to nurse due to muzzle lesions, or not allowed to nurse by dams with teat lesions (7). Control of clinical outbreaks of orf is directed at minimizing signs associated with the muzzle lesions in young lambs or kids through vaccination. Commercial live vaccines made from fully virulent, wild-type virus are available. Since orf strain variation exists, it may be more beneficial to make an autogenous vaccine from scab material obtained directly from the farm, as this decreases the likelihood of introducing a new, potentially more pathogenic strain. The vaccine is rubbed into scarified skin in the axilla or pinna to inoculate. These areas are less likely to result in complications associated with muzzle or teat lesions. Vaccination should be done in does 4-6 weeks prior to kidding so that all scabs will be shed prior to the birth of a new group of immunologically naïve animals (3). Vaccinated animals should be kept

in an area separate from the kidding area to reduce environmental viral pool from the shedding scabs.

In orf-free, closed herds, vaccination should not be done, as this will introduce fully virulent orf into a previously unaffected herd. Research should focus on developing an efficacious subunit or killed vaccine that will not contribute to the environmental pool of virus.

Conclusion

This case of orf is classic in clinical presentation and epidemiology, aside from the submandibular swelling. Although the outbreak was worse in the doe/doeling herd than the buck herd, all cases resolved spontaneously without therapy. The source of the introduced virus in this case is not known. The index case was not one of the animals taken to the county fair. If this was the source, she may have been infected from one of the other goats that acted as a mechanical vector for the virus. The 6-day lag time between the owner coming in contact with a known infected animal and initial signs in the first doe supports this as the source. Less homology in nucleotide and amino acid sequence of the strain circulating in this group of goats with the strain affecting the farm argues against this, unless there were multiple strains circulating in the group of goats that the owner came in contact with. Due to the length of time between the other events and development of clinical signs, the other modes of introduction seem less likely.

Rapid spread throughout the doe herd was probably due to browsing of the animals in brush, an environment prone to causing micro trauma on the muzzle, an easy route of inoculation for new infections. Oral dosing with ivermectin when the owner

assumed that the submandibular edema was caused by parasitism may also have contributed to a more rapid spread.

Personal hygiene, quarantine procedures for new acquisitions and for animals returning from shows, protective clothing, and limiting visitor access to livestock, should be recommended at the farm level to prevent introduction of an agent such as orf.

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