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Review

Epizootic Lymphangitis - A Major Fungal Disease of Equines

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Abstract

Epizootic lymphangitis caused by Histoplasma capsulatum variety Farciminosum is a debilitating disease that incurs considerable economic losses and affects the welfare of carthorses. The mode of transmission of epizootic lymphangitis includes transmission by direct or indirect contact of Histoplasma capsulatum var. farciminosum with traumatized skin, by biting flies, by ticks, or by inhalation of fungus. Horse epizootic lymphangitis disease manifests in three different forms: cutaneous, ophthalmic, and respiratory. The most prevalent type is cutaneous, resulting in lymphangitis and chronic, suppurative, ulcerating pyogranulomatous dermatitis. Epizootic lymphangitis is diagnosed based on clinical findings, animal history, and laboratory confirmation. In contrast, illness control requires culling diseased horses, the adoption of hygiene measures (e.g., washing and disinfection), and pest control. Treatment of epizootic lymphangitis is necessary to prevent the infection from spreading. Vaccination and proper wound care with iodine, sodium iodide intravenous injection, and amphotericin B injections should be used to control this disease. As a result, the current mini-review outlines epizootic lymphangitis as a significant horse illness, with a strong focus on disease prevention and control.

Keywords: Control, Epizootic Lymphangitis, Equines, Prevention.

Introduction

Equines play an important role in the transport of farm products, fodder, firewood, agricultural inputs, construction, and waste materials (Wilson, 1995). Horses are still the sole, easily available, and reasonably priced means of transportation for both passengers and goods in many locations. In certain regions, croplands are prepared using draft power from horses (Bazezew *et al*., 2014). In addition to inadequate husbandry, these horses are vulnerable to diseases caused by bacteria, viruses, fungi, and parasites. It has been shown that equine histoplasmosis (EH), often referred to as epizootic lymphangitis (EL), is a priority disease that has a significant economic impact and a high rate of morbidity and mortality (Ameni and Siyoum, 2002).

One of the infectious diseases that pose significant financial and welfare implications for horses, particularly carthorses, is epizootic lymphangitis (Teixeira *et al*., 2016). It is brought on by Histoplasma capsulatum var. faciminosum (HCF), a dimorphic fungus that starts as mold in the soil and changes into yeast when it parasitizes the tissues of mammals. While HCF is an equine pathogen, Histoplasma capsulatum var. capsulatum (HCC) is responsible for the majority of human infections (Ameni and Siyoum, 2002). Epizootic lymphangitis is a chronic, infectious disease that affects horses and other Equidae animals. Clinically, it manifests as lymphangitis and spreading, suppurative, ulcerating pyogranulomatous dermatitis (Ameni, 2006).

The organisms may have originated from the earth, animal exudates from the nose and eyes, or skin sores. Direct touch with diseased animals or interaction with living things like bedding, grooming products, cutlery, or leashes can spread fungal spores. When flies feed on lesions and exudates, they can also mechanically transmit the skin form (Al-Ani, 1999). From a few weeks to six months is the incubation period (Abdisa, 2017; Kamal *et al*., 2016). After first invading the skin, the organism travels to the local lymph nodes via lymphatic vessels, and in more severe cases, it even affects the internal organs. The skin overlaying lymph arteries and nodes shows signs of persistent suppurating lesions and nodules. Vistrial involvement and hematogenous dissemination (yeast cells present intracellularly or extracellularly, particularly in macrophages) may develop, disrupting the animals' overall health (Scantlebury *et al*., 2015).

Numerous therapies have been attempted most of them unsuccessful. Treatment for the illness is rarely effective (Hadush *et al*., 2008). It has been reported that parenteral iodides and amphotericin B are efficacious (Scantlebury and Reed, 2009). The efficacy of treatment using intravenous sodium iodide delivery, oral potassium iodide administration, and surgical lesion excision is restricted due to the potential for clinical symptoms to reappear months later. Moreover, it has been documented that the organism is sensitive to clotrimazole, nystatin, and amphotericin B in vitro. Nonetheless, treatment for epizootic lymphangitis is prohibited in the majority of places, making ill animals unfit for adoption (Ameni and Terefe, 2004).

Quarantines and the killing of diseased animals are two ways to prevent or completely eradicate epizootic lymphangitis (CFSPH, 2019). Vaccines that are heat-attenuated and formulated with aluminum hydroxide adsorbed have been used extensively, seemingly with good results (Radostits *et al*., 2000). In nations where it is common, epizootic lymphangitis is extremely important due to the disease's long-term, crippling effects on the health and welfare of affected animals as well as its socioeconomic effects on the owners of the animals, who are completely dependent on the animals for their livelihood and the support of their families (Timoney, 2015).

In Ethiopia, the diagnosis of epizootic lymphangitis is currently made via microscopic analysis to look for HCF yeast cells in pus in addition to clinical signs. Due to their low specificity and sensitivity, these traditional diagnostic techniques are not appropriate for the identification of asymptomatic carriers, even though they are helpful for routine case management in endemic areas. Therefore, comprehending the molecular epidemiology of the illness depends critically on the assessment of PCR-based diagnostic procedures to quickly identify HCF directly from equine clinical specimens (Scantlebury *et al*., 2016). As a result, the current mini-review describes epizootic lymphangitis, a significant horse illness, with a focus on disease prevention and control.

Epizootic Lymphangitis

A fungal disease primarily affecting horses and other equines, epizootic lymphangitis causes severe illness and substantial morbidity in affected populations of horses, mules, and, to a lesser extent, donkeys (Scantlebury and Reed, 2009). Pseudoglanders, or pseudofarcy, were other names for the illness. Equine histoplasmosis, farciminosis,

African farcy, equine blastomycosis, and equine cryptococcosis are more synonyms. Clinically, it is defined as a suppurative inflammation of the skin, lymph nodes, and cutaneous lymphatic vessels that spreads (Negesse *et al*., 2012). This condition affects the epidermis, lymph vessels, and lymph nodes in the neck and legs of horses and other equines. It is a chronic infectious granulomatous illness (OIE, 2008). One of Ethiopia's most common equine illnesses with serious veterinary and economic repercussions is epizootic lymphangitis (Ameni and Siyoum, 2002).

Etiology

Epizootic lymphangitis is caused by infection with a saprophytic mycelium (mold) in the environment and a dimorphic fungus called Histoplasma capsulatum, yeast found in animal tissues. It belongs to the order Onygenales and the family Ajellomycetaceae. We call it Ajellomycescapsulatus during its teleomorph stage. The majority of cases of histoplasmosis, particularly in the Americas, are caused by Histoplasma capsulatum var. capsulatum. The other two subspecies of Histoplasma capsulatum are found in Africa and have mostly been linked to human cases of epizootic lymphangitis and Histoplasma capsulatum var. duboisii. Histoplasma farciminosum, Cryptococcus farciminosis, Zymonemafarciminosa, and Saccharomyces farciminosus are a few of the previously used names for Histoplasma capsulatum var. farciminosum (CFSPH, 2019).

Species Affected

Mules, horses, and donkeys are the primary animals affected by epizootic lymphangitis. Camels, cattle, and dogs have also been found to have Histoplasma capsulatum var. farsiminosum, while mice, guinea pigs, and rabbits have all been experimentally infected (CFSPH, 2019). The most susceptible are horses younger than six years old (Radostits *et al*., 2007).

Geographic Distribution

During the late 19th and early 20th centuries, epizootic lymphangitis was common throughout Europe; nevertheless, it was eliminated by routine surveillance and slaughter programs (CSA, 2017). At the moment, it is widespread in many tropical and subtropical nations in Africa, the Middle East, Russia, and Asia (Ameni, 2006). Seasonal dusty winds in endemic areas in some parts of the world expose horses to dust and spore inhalation, which can result in pneumonia (Jubb *et al*., 2006). The geographic location and the animal's age have an impact on the infection rate of epizootic lymphangitis (Radostits *et al*., 2007). The disease was once significantly more common than it is now, having been brought to several European nations, where it was eventually declared exterminated by enacting laws requiring its killing (Scantlebury and Reed, 2009).

Mode of Transmission

The inhalation of HCF, biting flies, ticks, or direct or indirect contact with injured skin are among the ways that epizootic lymphangitis is spread. Open wounds allow HCF to enter the body (Timoney, 2015). Indirect contact with contaminated items, such as such as dressings for wounds, leashes, feeding and watering utensils, and grooming tools, can also result in the transmission of illness (Jubb *et al*., 2006). The majority of animal infections are believed to result from skin breaches, although Histoplasma capsulatum var. farciminosum can also infect mucosal membranes, such as the nasal mucosa or conjunctiva, and inhalation is assumed to be the mode of infection in certain cases affecting the respiratory tract. It has been reported that stallions and mares can mate. Histoplasma capsulatum var. farciminosum can spread on grooming or harness equipment. It also seems that biting flies, such as those belonging to the genera Musca and Stomoxys, are a mechanical means of transmission. Flies may have a significant role in eye contamination. Ticks may potentially be involved in the development of epizootic lymphangitis in mules, as evidenced by a study that linked tick bites to the condition (CFSPH, 2019).

Clinical Signs

Although epizootic lymphangitis can affect a wide range of organs and tissues, the respiratory system, underlying bones and joints, conjunctiva, and/or skin and lymphatics are the most commonly affected organs in equids. Large lesions can be fatal, particularly if the animal is in poor condition and veterinary care is either limited or nonexistent, or if the respiratory tract is impacted (CFSPH, 2019). The disease mostly causes discomfort and debilitation. The illness manifests itself in three ways. Ocular, respiratory, and cutaneous (skin) are the three types. Epizootic

lymphangitis most commonly affects the skin and lymphatic system. It can appear anywhere the organism is injected into a wound; however, it most frequently affects the face, neck, chest wall, and limbs (CFSPH, 2019).

The most prevalent type of the illness is the cutaneous form, which is also the name of the disease. A lymphatic vessel's initial lesion is an open, granulomatous wound that tends to ulcerate or alternate between periods of closure and discharge for a few weeks before healing and leaving behind residual scar tissue (Ameni, 2007). The illness develops slowly, taking anywhere from a week to months to fully develop. Lymphangitis and persistent, suppurative, ulcerating pyogranulomatous dermatitis are the disease's clinical hallmarks. Animals who have severe symptoms develop anorexia, degenerate physically, and, in cases where joint involvement occurs, become lame (Scantlebury and Reed, 2009).

The organism enters the eye, most likely by biting flies, causing the ocular form of the disease (Radostitis *et al*., 2007). It is rarely noticed in large quantities and is not easily generalized (Scantlebury and Reed, 2009). An initial sign of infection is a fluctuating swelling of the eyelids and a watery ocular discharge that can be unilateral or bilateral. The result is the development of button-like growths and papules on the nictitating membranes and conjunctivae. A granulomatous reaction may develop as a result of the infection spreading to the per-orbital tissues. Myiasis, panopthalmitis, and corneal ulcers are among the secondary consequences of the disease's ocular manifestation (Timoney, 2015).

Inhalation of the organism, either as spores from the surroundings or by the spread of infection from the nares' exterior mucous membranes or the nasolacrimal duct, is assumed to be the cause of respiratory cases. Nodules can be found in the vicinity of the nose's mucocutaneous junction, and they are frequently observed to migrate from the nasal passages into the trachea and lung parenchyma after death (Scantlebury and Reed, 2009). The hematological results show that there is neutrophilia, leukocytosis, and an increase in erythrocyte sedimentation rates (Ameni *et al*., 2006). The lesions are typically located close to the outside nares. The lungs could also sustain this damage. A thick, mucopurulent nasal discharge appears in affected animals, and dyspnea may occur. Progression of weakness, coughing, and loss of body condition are signs of advanced cases (Timoney, 2015).

Diagnosis

Depending on a clinical examination of the lesions, microscopic analysis of the yeast form of HCF in pus, serological testing, and skin hypersensitivity testing, epizootic lymphangitis is diagnosed (OIE, 2000). The organism grows slowly; thus, care must be taken to prevent contamination from overgrowing, and culture of the organism is required to confirm the existence of Histoplasma species. To minimize contamination, it is better to cut and sanitize the skin before aspirating a sample from an undisturbed nodule. Additionally, the organism can be seen in stained histological sections of lesions that are either mature or developing (Scantlebury and Reed, 2009). Another diagnostic technique is to inoculate samples into immune-compromised mice (OIE, 2008). Within areas where the disease is prevalent, the mycelial form of HCF is locally used to manufacture histofarcin, a skin test antigen used to diagnose epizootic lymphangitis. The "gold standard" for validating this test should include microscopic and mycological analyses of clinical lesions (Ameni, 2006).

Laboratory Diagnosis: The diagnosis of epizootic lymphangitis is made by laboratory testing, which includes identifying the yeast form of HCF in exudate smears or in histological sections of material from lesions; skin hypersensitivity tests; serological testing (such as fluorescent antibody tests, enzyme-linked immunosorbent assays, and passive hem agglutination tests); and isolating the causative agent by culture (Ameni***et al***., 2006). The organism is present in the tissues as yeast. Giemsa, Diff-Quick, or Gomorimethenamine silver staining are possible options (OIE, 2008).

Treatment

Currently, there is no effective therapy for the condition, so sick horses are abandoned to scavengers outside. Treatment for the condition is rarely effective. One of the causes might be the chronic nature of the lesions combined with their consequences from various microorganisms. Antibiotic resistance in Histoplasma capsulatum var. farciminosum is often lowers (Hadush *et al*., 2008). There is currently no effective treatment for the illness, despite reports of effectiveness with intravenous sodium iodide administration, oral potassium iodide administration, and surgical lesion excision (DACA, 2006). In early cases, inorganic iodides may be utilized; amphotericin B is also

advised as the preferred medication. However, for financial reasons, the local veterinary facility does not offer both treatment choices. Successful therapy depends on early case identification, even in the absence of accessible medications. It is also possible to lance localized nodules, drain the pus, and pack the nodules with an iodine tincture (7%). Epizootic lymphangitis is generally an illness that needs to be reported and is not covered by insurance (CFSPH, 2019).

Control and Prevention

The World Organization for Animal Health (OIE) states that the primary method of controlling epizootic lymphangitis is usually the removal of infection. Only by eliminating diseased equids and enforcing stringent biosecurity protocols can this be accomplished in order to stop the infectious agent from spreading (Scantlebury and Reed, 2009). In addition, as the organism may remain in the environment for a long time, extreme vigilance should be used when grooming or using harness equipment to prevent the spread of epizootic lymphangitis. Contaminated bedding should be burned. The disease is eliminated through the humane killing of diseased horses, the cleaning of contaminated areas, and limiting the movement of animals from contaminated areas (OIE, 2008). Thorough cleaning and disinfection can help stop the organisms from spreading between animals in endemic areas. To avoid transmission on grooming tools or leashes, extra caution should be used. Fly control is anticipated to be beneficial as well. Although some studies indicate both live and inactivated vaccines have been investigated (and maybe utilized) in some endemic regions (e.g., China), they do not currently have a commercial vaccine for epizootic lymphangitis (CFSPH, 2019).

Conclusion and Recommendations

A devastating fungal disease called epizootic lymphangitis primarily affects horses. The dimorphic fungus Histoplasma capsulatum var. farsiminosum is the cause of the sickness. The disease appears in three different forms: respiratory, ocular, and cutaneous (skin). Epizootic lymphangitis must be contained with strict hygiene measures; additionally, grooming or harness equipment must be handled with extreme caution. The disease is eliminated through the humane killing of contaminated horses, the cleaning of contaminated areas, and limiting the movement of horses from contaminated areas.

Based on the above conclusion, the following recommendations are forwarded:

- Public education and horsemanship owners should be made more aware of the value of early epizootic lymphangitis treatment and preventative measures.
- The government should focus on the prevention and control of this illness.
- It is important for owners to know how to use harnesses correctly and to keep healthy horses away from sick ones.

Contribution by Authors

Equal contribution. All authors declared that ‘written informed’ consent was obtained from the approved parties for the publication of this article and accompanying images.

Conflict of Interests

There is no conflict of interest.

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