Clinical Commentary

Corynebacterium pseudotuberculosis infection in horses: An emerging disease associated with climate change?

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Infection caused by Corynebacterium pseudotuberculosis in horses assumes many forms. The most common clinical expression of the disease, characterised by external abscesses in the pectoral or ventral abdomen, is often called ‘pigeon fever’, due to the swelling of the horse’s pectoral region resembling a pigeon’s breast (Fig 1), or ‘dryland distemper’, reflecting its prevalence in arid regions of the Western US. Two other clinical forms of the disease are internal organ involvement including hepatic, renal (Fig 2) or splenic abscesses, and infection of the limbs, termed ‘ulcerative lymphangitis’. In this issue, Gonzalez et al. (2008) present an interesting case report of a breeding stallion with internal infection involving the right testis and epididymis. This horse had a history of a pectoral abscess 1.5 years prior to presentation for internal infection, and while internal infection was suspected at the initial work-up, localisation of the infection was challenging.

Deep i.m. abscesses in horses caused by Corynebacterium pseudotuberculosis were first reported in San Mateo County, California, in 1915 (Hall and Fisher 1915). Since that time, disorders caused by this bacterium have been among the most frequent infectious diseases in the Western USA, particularly in California. Unprecedented epidemics in 2002 and 2003 affected thousands of horses in Colorado, New Mexico, Utah, Wyoming and Kentuckk, all states historically low in prevalence (Foley et al. 2004). In 2005, hundreds of horses were affected in Ramona, California (near San Diego), leading to speculation that a new strain of bacteria had emerged (Conaughton 2005).

High environmental temperatures and drought conditions preceded all reported outbreaks. This was also the case when the stallion in the case report by Gonzalez et al. (2008) first exhibited a pectoral abscess, as well as when it presented for internal infection (Anon 2003). In 2005 and 2007, outbreaks of Corynebacterium pseudotuberculosis infection were once again reported in Oregon and adjacent Idaho (Anon 2007) suggesting that these states should now be considered endemic for this soil-dwelling bacterium. Once disease becomes endemic to a region (such as California or Texas), infections tend to occur as sporadic cases with a prevalence of 5–10%. However, outbreaks involving hundreds to thousands
of horses can occur in areas where large numbers of naïve horses are exposed.

The perceived increase in number of infections in recent years could be no more than reporting bias, or instead environmental factors facilitating infection or host factors such as greater herd susceptibility. There is no overt reason to suspect a change in the probability of cases coming to the attention of equine health professionals. Consideration of environmental factors includes a diversity of conditions that may promote soil survival of the bacteria (e.g. dry soil with faecal contamination favours survival), or insect populations that vector disease (particularly house fly [Musca domestica], stable fly [Stomoxys calcitrans] and horn fly [Haematobia irritans] populations). Disease incidence is seasonal, with highest number of cases occurring during the dry months of the year, which are late summer and autumn in southwestern USA, (although cases may be seen all year). Horses with internal infection are more frequently seen 1–2 months following the peak number of cases with external abscesses (Pratt et al. 2005). In the case considered here, a pectoral abscess was treated in autumn, and internal infection was noted in March. It is unclear whether this was recrudescence of the original infection or re-infection. While most horses have a single lifetime episode, a few have recurrent or persistent infections (>1 year), suggesting immune compromise (Aleman et al. 1996).

Inferences about transmission may come from geographic analyses. In one spatial study, the disease appeared to be transmitted throughout a 4.3–6.5 km distance in a period spanning 7–56 days. Such a rapid spread strongly suggests that disease transmission occurs through horse-to-horse contact, or from infected to susceptible horses via insects, other vectors or contaminated soil (Doerr et al. 1999). The portal of entry is thought to be through dermal abrasions or wounds or mucous membranes. Many insects, particularly flies, vector disease to horses, and studies have shown that house, stable and horn flies can all act as vectors of pigeon fever (Spier et al. 2004). Epidemiological models incorporating ongoing global climate change project increases in such vector-borne diseases. Fly generation times are inversely correlated with environmental temperatures. To take one example, house fly populations are projected to double in this century (Goulson et al. 2005), which could significantly increase the rate of spread and incidence of diseases such as pigeon fever.

Corynebacterium pseudotuberculosis produces various extracellular exotoxins that play a role in virulence. Of these the most studied is phospholipase D (PLD), which contributes to tissue pathology, and host recognition of PLD can be used diagnostically. Phospholipases are enzymes that share the ability to hydrolyse one or more ester linkages in glycerophospholipids. PLD causes hydrolysis and degradation of sphingomyelin in endothelial cell membranes, increasing vascular permeability and thereby facilitating the spread and persistence of the bacterium in the host. Notably, the bacterial PLD is similar to that of the brown recluse spider, an observation consistent with the reliable expressions of pain and oedema at the sites of infection (Coyle and Lipsky 1990; McNamara et al. 1994). In the stallion considered here, effects of the PLD toxin, in addition to compression from the abscess, could have reduced blood supply to the testis that was documented by Doppler ultrasound and histopathology.

The synergistic activity of C. pseudotuberculosis exotoxins with the exotoxins of Rhodococcus equi in lysing red blood cells in agar forms the basis for the synergistic haemolysis inhibition (SHI) test (Knight 1978), presently the most useful serological test available to detect IgG antibody to C. pseudotuberculosis in horses with internal infections. In the stallion studied by Gonzalez et al. (2008), serology might have been helpful at the first visit to confirm internal infection from this bacterium and the need for long-term antimicrobials, which, in conjunction with unilateral castration, led to the successful outcome in this case.

Some controversy exists over the use of antimicrobials for infection, however. The use of antimicrobials for external abscesses is not necessary in most horses and may prolong the time to resolution (Aleman et al. 1996). At the same time, antimicrobials are clearly indicated for horses with ulcerative lymphangitis or internal abscesses. Antimicrobial therapy may therefore be justified when signs of systemic illness, such as fever, depression and anorexia, or extensive cellulitis are present. Horses with deep intramuscular abscesses that are lanced and draining through healthy tissue may also benefit from antimicrobial therapy.

Corynebacterium pseudotuberculosis is susceptible in vitro to many antimicrobials commonly used in horses, including penicillin G, macrolides, tetracyclines, cephalosporins, chloramphenicol, fluoroquinolones and rifampicin (Foley et al. 2004). Several factors should be considered when choosing an antimicrobial. The intracellular location of the organism, the presence of exudates and a thick abscess capsule, and the duration of therapy are important, as are the cost of the drug and the convenience of administration. Despite in vitro susceptibility, the nature of the bacterium and the copious exudate render certain antimicrobials ineffective for some cases. Trimethoprim-sulpha (5 mg/kg bwt based on the trimethoprim fraction, twice daily per os) or procaine penicillin (20,000 u/kg bwt twice daily i.m.) are effective for external abscesses especially on the ventral midline. Rifampicin (2.5–5 mg/kg bwt twice daily per os) in combination with cefiofur (2.5–5 mg/kg bwt twice daily i.v. or i.m.) appears highly effective for treatment of internal abscesses. Internal abscesses have reportedly responded to procaine penicillin (dose as above), trimethoprim-sulpha (dose as above) and potassium penicillin (20,000–40,000 u/kg bwt 4 times daily i.v.) (Pratt et al. 2005).

Horses with ulcerative lymphangitis or cellulitis should be treated early and aggressively with antimicrobials to reduce the risk of residual lameness or limb swelling. Typically, i.v. antimicrobials (cefiofur or penicillin G), either alone or in combination with rifampicin (orally) are used until lameness and swelling improves, and then therapy with orally administered antimicrobials such as trimethoprim sulphonamethoxazole or rifampin are continued to prevent
relapse. The time to resolution reported in one study was approximately 35 days (Aleman et al. 1996). Physical therapy, including hydrotherapy, hand walking and wraps, as well as NSAIDs for pain management, are also recommended.

For prevention of disease, until a protective bacterin or toxoid is developed for horses, the best that we can suggest to horse owners in endemic areas is that they practice good sanitation and fly control, and avoid unnecessary environmental contamination from diseased horses. Oil-based fly repellents provide longer-lasting protection than aqueous products. Presently, there is no evidence that diseased horses within a stable should be quarantined, other than paying strict attention to insect control. The feed-through products containing insect growth regulators such as cyromazine (Solitude Insect Growth Regulator)\(^1\), which inhibits formation of chitin, are safer than organophosphate products, and may reduce the incidence of disease by controlling vector populations. Proper sanitation, disposal of contaminated bedding and disinfection may reduce the incidence of new cases. Proper wound care is also important to prevent infection from a contaminated environment.

Clearly, more attention should be directed toward the epidemiology, immunology and pathophysiology of this disease. It is my hope that further epidemics will not be required before this bacterium commands the respect it deserves. An efficacious bacterin/toxoid for horses that serves to prevent disease is now within the reach of veterinary researchers, and is likely to be the best hope for managing this environmentally resilient pathogen in the future.

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Manufacturer’s address

\(^{1}\)Pfizer Animal Health, New York, USA.

References


