

Case Report Rapport de cas

Anthrax vaccine associated deaths in miniature horses

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Abstract – During a widespread anthrax outbreak in Canada, miniature horses were vaccinated using a live spore anthrax vaccine. Several of these horses died from an apparent immune-mediated vasculitis temporally associated with this vaccination. During the course of the outbreak, other miniature horses from different regions with a similar vaccination history, clinical signs, and necropsy findings were found.

Résumé – **Vaccin contre l'anthrax associé à la mort de chevaux miniatures.** Durant une vaste éclosion d'anthrax au Canada, des chevaux miniatures ont été vaccinés en utilisant un vaccin à base de spores viables d'anthrax. Plusieurs chevaux sont morts d'une vasculite d'origine immunologique associée temporellement avec cette vaccination. Pendant l'éclosion, on a trouvé d'autres chevaux miniatures de régions différentes présentant une anamnèse de vaccination, de signes cliniques et de résultats d'autopsie semblables.

(Traduit par Isabelle Vallières)

Can Vet J 2015;56:359–360

Beginning June 26, 2006 and continuing until September 21, 2006, an anthrax outbreak took place in Saskatchewan, Canada (1). This outbreak was larger in the number of animals and number of premises involved than is typical in the sporadic anthrax incidences seen in Saskatchewan (1). During this time, 804 animals died on 153 individual premises (1). Most of these deaths were of cattle, with smaller numbers of farmed bison, sheep, cervids, horses, pigs, and goats. As a result of this outbreak, quarantine and mandatory anthrax vaccination of animals on affected premises were instituted (1). Vaccination of susceptible animals, including horses, was recommended for all animals within the outbreak area which comprised a large portion of central and eastern Saskatchewan (2).

Case description

On July 26, a group of 12 miniature horses was vaccinated against anthrax using a Sterne 34F avirulent live spore vaccine. Animals were vaccinated subcutaneously in the mid portion of the neck. The owner reported that all the horses were stiff and sore 4 to 5 d later. On August 3, a local veterinarian was called to examine the animals. Four horses (1 filly, 2 mares, and 1 stallion) exhibited anorexia, listlessness, muscle tremors, and a temperature of 41°C. They were given injectable penicillin, but

the product used or amount given was not specified. Following this treatment there was no noticeable improvement. The next day, all 4 horses died. Because of concern that these animals may have died of anthrax, 3 carcasses (filly, pregnant mare, and stallion) were submitted to Prairie Diagnostic Services (PDS) for necropsy while the fourth was necropsied in the field.

Prior to necropsy, presence of *Bacillus anthracis* in the 3 submitted horses was ruled out by direct examination of blood. Necropsy findings were similar in nature in all horses, but varied in severity. The jejunum and ileum had extensive areas of petechial hemorrhage on the serosa. The gastric wall was markedly thickened (up to 1.5 cm). The kidneys had petechial hemorrhages beneath the capsule, and streaks of dark red throughout the cortices. Urine in the bladder was uniformly dark. Histologically, there were multifocal areas of necrosis within the renal cortices which varied from confluent areas of cortical infarction to acute proximal tubular necrosis. Abundant intratubular hemorrhage, and protein and cellular casts were present. Areas of necrosis were also present in the wall of the intestine and the adrenal glands. There was fibrinoid necrosis of small arterioles in many of these areas. Classical features of anthrax infection such as marked splenic congestion and enlargement were not present in any animals.

Discussion

Based on their location and shape, the areas of necrosis in the renal cortex correspond to infarction as a result of damage to small caliber arteries, such as the interlobular arteries, rather than obstruction of large caliber arcuate arteries which produce the classic wedge-shaped renal infarcts (3). No evidence of embolism was seen, but necrotizing vasculitis was present in these small caliber arteries. In areas with no evidence of renal infarction, the lesions were of renal proximal tubular necrosis. Renal proximal tubules are at an increased risk of ischemic

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Table 1. Deaths in miniature horses following anthrax vaccination during an anthrax outbreak in Saskatchewan, Canada in 2006

Farm number	Number vaccinated for anthrax	Number dead	Number necropsied	Seen by a veterinarian
1	12	4	4	Yes ^a
2	4	2	1	Yes
3	20	1	0	Yes

^a Current case.

damage due to their higher requirement for oxygen, and thus, decreased blood flow is likely the cause of these lesions as well (4).

Fibrinoid necrosis of arteries with subsequent thrombosis and hypoxia or infarction was present in all 4 cases. To rule out infectious causes of vasculitis, bacterial culture of multiple tissues and immunohistochemistry for equine viral arteritis were performed, but were negative. Over the summer, other miniature horses from different regions within Saskatchewan with a similar vaccination history and clinical signs were reported anecdotally, and 1 other miniature horse was necropsied at PDS with similar findings (Table 1).

Apart from being miniature horses, the only common factor among the cases was anthrax vaccination. As no infectious cause for the vasculitis was found, type 3 hypersensitivity reaction (antigen-antibody complex deposition) seemed likely. We attempted to demonstrate this using immunohistochemistry for IgM and C3 in areas with vasculitis. There was specific positive granular staining for IgM in areas of vasculitis, but we were unable to demonstrate C3, as adequate staining of control tissues was not effective. The presence of IgM in the lesions is compatible with small vessel hypersensitivity vasculitis (5).

The only anthrax vaccine available for use in animals in Canada is based on Sterne 34F avirulent live spores. This strain lacks the pX02 plasmid and does not produce a capsule. The vaccine is licensed for use in cattle, pigs, goats, sheep, and horses, but has not been tested in miniature horses. The American Association of Equine Practitioners recommendations for anthrax vaccination include the statement: "Adverse reactions to the vaccine have been reported in young, and miniature, horses. Local swelling may occur at the injection site, most of which resolves within a few days" (6). No further information is available, nor have reactions of the type reported here been described in the scientific literature. Reversion to virulence following vaccination with this vaccine has been reported in llamas (*Lama glama*) and vaccination is not recommended in that species (7).

Anthrax vaccination has been used widely in humans, primarily military personnel, in recent years. Mandatory vaccination of United States military personnel was begun in 2002 and millions of doses have been administered. The human vaccines are derived from the Sterne strain of *B. anthracis*, but contain only cellular products, and not live spores, as in the animal vaccine. Reports of reactions to these vaccines are very rare. A single case of lymphocytic vasculitis following vaccination has

been reported. Clinical signs began 6 d following vaccination and were limited to the skin (8).

Why these miniature horses reacted in this way to the vaccination is not clear. The problem could theoretically be with the animals or the vaccine. These particular horses may have a relatively small genetic base, as the number of miniature horses in Saskatchewan is unknown. Genetic predispositions to vascular reactions to antigens has been previously reported in related horses (9). A problem with individual vials or lots of vaccine is possible, but not likely, as the cases were spread over 153 individual premises and a large number of doses was given over the course of the outbreak, but reactions only occurred in miniature horses. In addition, the miniature horses from the additional farms (Table 1) that also died following anthrax vaccination were vaccinated by different individuals and are located in different rural municipalities. It should be noted, however, that it is possible that the death of the miniature horse in Farm 3 was unrelated to anthrax vaccination as no necropsy was performed.

Anthrax is widespread and outbreaks are common. In 2012, outbreaks were reported in 67 countries and in all continents except Antarctica (10). The most common response to outbreaks is vaccination of susceptible animals with the live Sterne vaccine (2,11–13). Given the serious nature of the reaction in miniature horses, lack of understanding of the nature of the reaction, and lack of an alternate vaccine available for use in these animals, care should be taken to determine whether vaccination of these animals is reasonable.

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