Case studies: Exclusion of non-classical vesicular disease

ANDREW MJ MCFADDEN, THOMAS RAWDON, KELLY BUCKLE, MARY VAN ANDEL
Ministry For Primary Industries, PO Box 2526, Wellington

Introduction

New Zealand would be significantly impacted if an incursion of foot-and-mouth disease (FMD) was to occur (Forbes and van Halderen 2014). The impact will vary depending on a number of factors including the size and geographic limits of the outbreak i.e. North vs. South Island. However, impacts would also vary with extrinsic factors such as the timing of international markets reopening. Forbes and van Halderen (2014) carried out scenario modelling for a specific set of conditions, described as a small, medium and large outbreak. For the large outbreak scenario the effect on GDP in first year after was determined to have a real effect of -7.8%, measured nominally as -13.8 Billion dollars. The scale of any outbreak occurring will be heavily influenced by the speed of detection and response.

A previous report has described the process of investigation and exclusion of FMD in domestic animals in New Zealand (Mcfadden 2011). These included methods of describing skin or mucosal lesions (distribution, consistency, colour, shape and size) and assessing clinical features associated with fever and pain during clinical examination of affected animals. In addition, in this report the need to carry out an epidemiological investigation was emphasised. The epidemiological part of the investigation includes analysis of differences in prevalence of disease by stratum (age and management group) and examination of production records, particularly in lactating dairy cattle where milk production is a sensitive indicator of disease.

Given the importance of FMD and the consequences of making a false negative diagnosis the threshold for the Ministry for Primary Industries (MPI) to carry out an investigation is very low. Those disease differentials that don’t necessary fit the descriptions of classic disease entities can be problematic during the process of clinical exclusion of FMD. This paper seeks to describe a series of case studies where FMD was a differential diagnosis, and yet not classic in its clinical appearance.

Aetiological agents for foot-and-mouth disease

The aetiological agents for differential diagnoses for FMD can be broken down into three main categories: infectious agents, environmental (including traumatic or physical injury) and host factors. The endemic infectious differentials for FMD have been described in a number of reports and publications and include: malignant catarrhal fever (MCF), bovine viral diarrhoea (BVD), infectious bovine rhinotracheitis, papular stomatitis and actinobacillosis (‘woody tongue’). However, these can sometimes present in different ways.
Traumatic injury can sometimes present as a differential to FMD and have been referred to as OMAGOD lesions (Ovine mouth and gum obscure disease; Black et al. 2004). A high prevalence of animals can sometimes be affected because the inciting cause of these lesions often relates to failure of specific equipment that a number of animals are exposed to e.g. drench gun injuries, feed with an abrasive element to it, or the interaction between the environment and animal behaviour. Thus, presentation of lesions and the high prevalence affected can often give the appearance of the syndrome being caused by an infectious agent.

Environmental agents can produce a wide array of different lesions relating to a direct physical effect, e.g. photosensitivity, through a local toxic effect on the oral mucosa or from a systemic effect of an ingested toxin. The numerous potential inciting causes can make diagnosis of a specific agent extremely difficult and often environmental toxins are assumed because infectious disease has been excluded from clinical and epidemiological findings. In other instances hypersensitivity reactions from the host to a pathogen or toxin can result in unusual lesions.

Another factor that is important to consider regarding non-classical differential diagnoses for FMD, is the variation of lesions by species. Exclusion of FMD based on clinical and epidemiological findings in non-bovine species can be very challenging. False positive diagnoses of FMD in sheep without laboratory diagnosis occurred in the 2001 FMD outbreak in the UK (Manlet et al. 2011). Recently a Ministry for Primary Industries project has examined the clinical effect of FMD in red deer. This species proved very resistant to infection and the clinical lesions produced from infection were very mild (Kittelberger et al. 2015).

Infectious agents

**Cow with oral and nasal lesions:** A veterinarian observed a dry cow with granulomatous swellings occluding the nostrils, small (5mm) ulcerations on the hard palate and firm, swollen submandibular lymph nodes (Figure 1). The cow was mouth breathing and coughing but was not pyrexic (38.9°C) and the remainder of the mouth and tongue were clinically normal, as were the feet, udder and vulva. The cow had received a single antibiotic treatment for suspected woody tongue (actinobacillosis) four months earlier. The remainder of the mob of eighty heifers and dry cows were healthy.

Serum was collected prior to the cow being processed for pet food. The head was collected and submitted for post mortem at New Zealand Veterinary Pathology, where samples were collected for histology. An antigen ELISA test for BVD and a molecular assay for MCF were both negative. Post mortem identified multiple granulomas, some with small white to pale yellow centers, affecting the palatine tonsils, surface of the turbinates and along the lymphatic chain extending from the commissure of the lips to the submandibular lymph nodes. Histology confirmed multifocal granulomatous inflammation and fibrosis consistent with actinobacillosis. Cutaneous presentations of actinobacillosis, including those on the nares, are seen infrequently.
Environmental

Bulls at a slaughter plant: The affected animals were in a mob of rising two-year-old bulls presented at the yards of a slaughter plant. Approximately 80% of a 38 cattle mob was reported to have erosive lesions around the coronary band.

A clinical examination of cattle in the mob showed there were a range of lesions; however, generally the affected cattle had ulcerations extending proximal to the coronary band and on other parts of the leg (Figure 2). Most of the lesions were observed to be on the caudal surface of the leg. No oral lesions were present in any of the affected cattle, nor did any cattle present with a fever. Clinically the lesions observed were likely caused by trauma rather than an infectious aetiology. We hypothesised that sexual riding behaviour of the bulls was responsible for the lesions observed.
Case studies: Exclusion of non-classical vesicular disease

Horses with lip lesions: A horse at an agricultural college presented with lesions of approximately 2–6mm in diameter located on the outer lip area (Figure 3). One other horse in the group appeared to have a single healed gum lesion. Over the following four weeks a further two cases with similar lesions were identified from the 25 horses on the farm. The college had been the subject of an exotic disease investigation in 1998 as a result of mouth lesions in resident horses. The clinical presentation at the time was more dramatic than that in the present case, with oral papules, erosions and ulcers affecting the mucosa of the lower and upper jaw and tongue, although horses remained otherwise healthy with little or no rise in temperature. The syndrome was termed: 'Balclutha horse syndrome'. Exotic vesicular diseases were excluded although no firm aetiology was established (Anonymous 1998).

Blood samples were collected from the four affected and nine in-contact horses and submitted to IDC Wallaceville for exclusion of vesicular stomatitis virus, and for herpes virus serology. Molecular assays for vesicular stomatitis virus were carried out on acute cases at IDC with negative results, and virus neutralisation tests (VNT) for antibodies to both Indiana and New Jersey serotypes were carried out on acute and convalescent sera at the Australian Animal Health Laboratory, Geelong, again with all negative results.

There was no indication of rising titres to any of the herpes viruses that could explain the lesions observed. Biopsies were collected from the first and a subsequent case. In the first case, moderate, acute, ulcerative and erosive dermatitis with cellulitis and myositis, was seen. Findings were considered indicative of trauma. The predominant bacteria were gram negative, filamentous, and elongate, suggestive of the anaerobe *Fusobacterium necrophorum*. Histology carried out on gum lesions on a further horse identified mild non-specific dermatitis and cellulitis. There were no viral inclusions visible, nor intracellular oedema or pathology suggestive of a viral aetiology. During the

Figure 2. Areas of bruising occurring above the claws and interdigital areas (Photos provided courtesy of Michael Lintott, Carlyle Veterinary Clinic)
1998 investigation a single EHV2 virus was isolated from a buffy coat sample which at the time was considered an incidental finding (Anonymous 1998). The findings of this investigation support previous conclusions and found no evidence for the involvement of a herpes virus in the presented lesions.

Figure 3. Erosive lesions of the lip in multiple horses at an Agricultural College (Photos provided courtesy of Pamela Doig from Vets@ Balclutha Ltd)

High prevalence disease outbreak: An investigation was carried out on a 397-cow dairy herd that had healing oral erosive lesions (Figure 4) in 80 percent of the herd. None of the affected cows were systemically ill and there was no decrease in milk production. Lesions were predominantly erosions. A single intact vesicle was identified on the muzzles of two cows during the investigation (Figure 3), as well as several ruptured vesicles on the muzzles of other cows. A selection of 34 affected cattle were examined in detail. Erosions were generally circular in shape, and averaged 20mm in diameter (range 5–60mm). Twenty-one percent (7/34) of the cows had one oral lesion, 44 percent (15/34) had two, and 29 percent (10/34) had three or more lesions. No infectious aetiological agent for any exotic infectious vesicular disease or any endemic cause of vesicular disease was detected using virus isolation, polymerase chain reaction (PCR), electron microscopy (EM) or serological tests. The investigation is described in detail by McFadden et al. (2007).
Sheep with coronary band and interdigital lesions: Six of 504 lambs were affected with mild focal to severe extensive proliferative and ulcerated coronary band and interdigital lesions (Figure 5). Examination of sheep from the affected mob showed a high prevalence of small, proliferative nose and lip lesions consistent with those caused by ovine parapox virus (orf). These lambs had been run through fresh gravel multiple times in the week preceding this event. Gravel can cause coronary damage (excoriations), allowing viral entry and secondary bacterial infection.

On histopathology, lesions were consistent with ovine parapoxvirus and secondary bacterial infection. The history of exposure to gravelled areas and the pathogenesis of viral entry via coronary lesions (excoriations) explains the unusual and severe distribution of lesions on the coronary band and interdigital region of these animals. Foot and mouth disease in sheep can be subclinical or may present with very mild lesions which may be easily overlooked, therefore lack of systemic clinical illness in these sheep was not a helpful differentiating factor.
Case studies: Exclusion of non-classical vesicular disease

**Hypersensitivity host reaction**

Recently imported alpaca with mouth lesions: An alpaca imported from Australia six weeks was reported to MPI with unusual mouth lesions (Figure 6). The affected animal was in good health, but had concurrent heavy infestation with demodex mites, a common condition in alpacas. Biopsies of oral mucosa were collected and the histopathogy performed on tissue showed there were large numbers of eosinophils present. The hypothesized aetiology of these lesions was demodicosis leading to a hyper immune reaction in this animal. No demodex mites were identified on histopathology examinations of the lesions, but mites were previously identified from skin examination of the animal. There is no indication of infectious disease as a cause of the lesions in this case.

*Figure 5. Proliferative and ulcerative lesions of the interdigital and coronary band areas of multiple sheep presented for slaughter*
Case studies: Exclusion of non-classical vesicular disease

Discussion

Building on previous MPI case reports where infectious aetiologies have been investigated, this paper lays out the complexities of excluding exotic vesicular disease in species and under conditions with non-classical presentations. The paper works to refine knowledge of endemic syndromes to build knowledge in an important area of exotic disease investigation, where the threshold for investigation must be low to ensure our passive surveillance systems retain high sensitivity.
References


**McFadden AMJ.** Clinical and epidemiological investigation to exclude foot-and-mouth disease in cattle. *Surveillance* 38 (1), 2011

Case studies: Exclusion of non-classical vesicular disease