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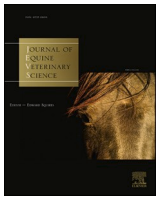

Case Report

Sarcoid within the oral cavity of a horse

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ABSTRACT

Equine sarcoids are common skin tumors that are thought to be caused by cross-species infection by bovine papillomaviruses (BPV). A 16-year-old horse developed a 1cm diameter mandibular gingival mass opposite the right second premolar tooth (406) and a 2cm diameter mass close to the commissure of the lips on the same side of the mouth. The right cheek was diffusely thickened. Histology of the smaller mass revealed a proliferation of mesenchymal cells covered by hyperplastic epithelium that formed thick rete pegs. BPV2 DNA was amplified from the mass. Although the mass had been incompletely excised, there was no recurrence after 5 months. The histological features and detection of BPV2 DNA is consistent with a diagnosis of equine sarcoid. Sarcoids have not previously been reported in the oral cavity of horses. It is hypothesized that trauma to the mouth may have been important for sarcoid development. Additionally, different BPV types may have variable ability to infect the gingiva. While rare, sarcoids are a differential for an oral mass in a horse.

1. Introduction

Equine sarcoids are common skin tumors that can be locally invasive, but do not metastasize [1]. It has previously been thought that sarcoids usually recur after surgical excision [1]. However, more recent studies reported less than half of sarcoids recurred, even after incomplete excision [2,3] and up to half of sarcoids may spontaneously resolve without treatment [4,5]. The increasing evidence of spontaneous resolution suggests that, at least a proportion of sarcoids, may be better considered a hyperplastic process rather than a true neoplasm. Sarcoids frequently develop in areas of the skin that are predisposed to trauma. The skin around the head is a frequent site of development and sarcoids of the haired skin of the lips are not uncommon [6]. However, equine sarcoids have not previously been reported to develop within the oral cavity.

Sarcoids are thought to be caused by bovine papillomavirus (BPV) types within the *deltapapillomavirus* genus including BPV1, 2, and 13. There are significant geographical differences in the predominant BPV type associated with sarcoids with BPV1 detected in most sarcoids in Europe and Australia, but BPV2 more commonly detected in equine sarcoids in North America and New Zealand [7–10]. While BPVs are recognized to be important in the development of sarcoids, the epidemiology of infection is unclear and BPV DNA has been detected in normal equine skin and some non-sarcoid lesions of horses [11,12].

Both histology and PCR to amplify BPV DNA can be helpful in making a diagnosis of equine sarcoid [6]. However, while sarcoids have some histological features that are considered suggestive of this diagnosis, definitive differentiation from other types of soft tissue sarcoma can be problematic [6]. Likewise, the detection of BPV DNA in some non-sarcoid lesions suggests that a lesion cannot be definitively diagnosed as a sarcoid based solely on PCR results [11]. Currently, the detection of BPV DNA within a skin lesion that contains histological features of a sarcoid allows the highest degree of confidence in a diagnosis of equine sarcoid.

We report a horse with a gingival mass that was histologically consistent with an equine sarcoid. A diagnosis of sarcoid was supported by the amplification of BPV2 DNA from the lesion. The is the first time that an equine sarcoid has been reported within the mouth.

2. Case report

2.1. Case presentation

A 16-year-old bay thoroughbred gelding was observed to have moderate diffuse thickening of the upper right cheek during a routine dental procedure. No further investigation was performed as the horse

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did not show signs of discomfort due to the thickening. Seven months later, a 2 cm diameter mass was observed close to the commissure of the lips on the right side of the mouth. Examination at this time also revealed a 1 cm mass on the right mandibular buccal gingiva opposite the right second premolar tooth (tooth 406 using the Modified Triadan System). Palpation of the cheek revealed that the right cheek was thicker than the left cheek. The horse was not showing signs of discomfort or dysphagia. Both the oral and the lip masses were roughly spherical, raised pale lesions (Figs. 1 and 2). The surface of the oral mass was smooth and had the same appearance as normal oral mucosa. The oral mass was surgically excised with the horse standing and sedated using 6 mg detomidine and 6 mg butorphanol IV with submucosal lignocaine infiltration at the site. Despite the location, excision of the mass was uncomplicated, and the surgical wound was left un-sutured to heal by secondary intention. The removal of the oral mass was done primarily to allow a diagnosis. As the mass on the lip was thought to be the same lesion type, samples were not taken from this mass.

2.2. Diagnosis and molecular investigation

Examination of the oral mass revealed a proliferation of spindle-shaped mesenchymal cells arranged in whorls and interlacing bundles within the submucosa (Fig. 3). Mesenchymal cells underlying the mucosa were often arranged perpendicular to the surface resulting in a 'picket fence' appearance. The epithelium overlying the mesenchymal cells was moderately hyperplastic and formed thick rete pegs of epithelium that extended deeply within the proliferating spindle cells (Fig. 4). The mesenchymal cells extended to tissue margins and the mass was considered incompletely excised. The histological diagnosis was an equine sarcoid.

Total DNA was extracted from the tissue block to investigate the presence of BPV DNA in the lesion. To prevent detection of any PVs that may be present incidentally in the surface epithelium, DNA was extracted from an approximately 2 mm diameter sample that was taken from the deep edge of the embedded mass. DNA was also extracted from samples of normal-appearing mandibular buccal gingiva taken from 12 older horses that had died due to diseases unrelated to the oral cavity. DNA was extracted using a NucleoSpin DNA FFPE XS kit (Macherey-Nagel GmbH, Duren, Germany) according to manufacturer's instructions. Specific PCR primers were used to amplify BPV1 and BPV2 DNA from the mass and the non-neoplastic gingival samples as previously described [13]. DNA extracted from equine sarcoids known to contain either BPV1 or BPV2 were used as positive controls and no template DNA was added to the negative controls. The BPV1-specific primers only amplified DNA from the positive control sample. However, the BPV2-specific primers amplified DNA from the oral mass and positive controls, but from none of the 12 samples of normal gingiva. The DNA amplified from the mass was sequenced and found to be identical to sequences of BPV2 contained within GenBank.

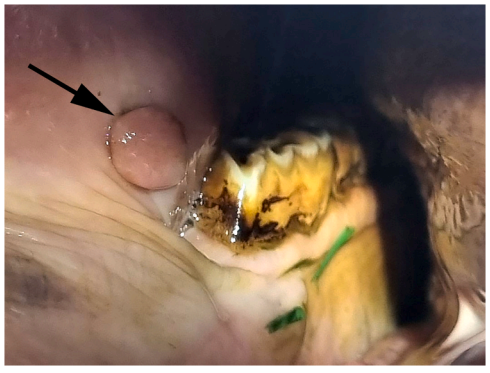

Fig. 1. A raised pale 1cm diameter roughly circular mass was present on the mandibular gingiva close to the premolar teeth.

Fig. 2. The cheek was thought to be thicker on the right side of the mouth than the left and a raised pale mass was visible at the right commissure of the lips.

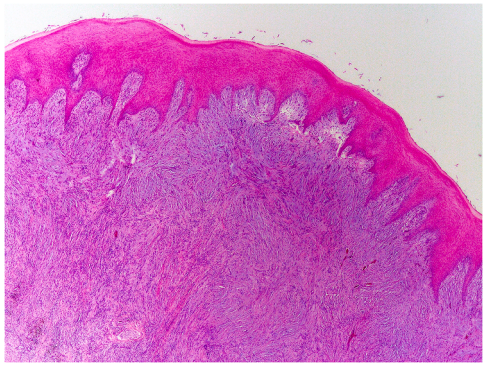

Fig. 3. Photomicrograph of the gingival mass. The mass consists of a proliferation of mesenchymal cells covered by hyperplastic epithelium. HE 40×.

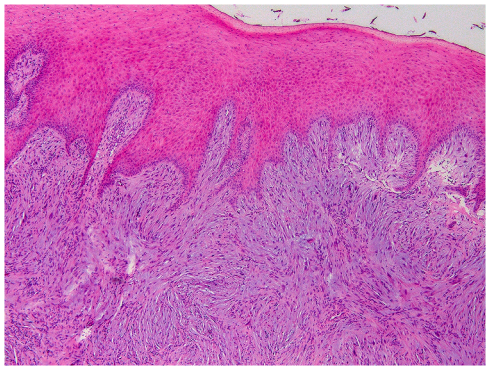

Fig. 4. Photomicrograph of the gingival mass. The hyperplastic epithelium forms thick trabeculae that extend into the underlying population of mesenchymal cells. HE 100×.

2.3. Outcome

No regrowth of the mass was visible when the horse was re-examined five months later. Additionally, the lip mass was no longer detectible, and the right cheek was judged only mildly thicker when compared to the left.

3. Discussion

The oral mass in this horse was histologically consistent with a sarcoid. This diagnosis was supported by the amplification of BPV2 DNA from the mass. While it cannot be excluded that BPV2 was an incidental

infection in this case, the extraction of DNA from a deep area of the mass and the failure to detect BPV DNA within any of 12 samples of normal gingiva make this less likely. Therefore, the findings in this case are consistent with a diagnosis of oral sarcoid. While sarcoids are common neoplasms of the skin of horses, this is the first report of an oral equine sarcoid.

The oral sarcoid did not recur despite being incompletely excised. As sarcoids have previously been thought to frequently recur after excision [1], this could suggest the mass was not a sarcoid. However, there is increasing evidence that many incompletely excised equine sarcoids do not recur [2,3]. Why incompletely excised sarcoids do not recur is uncertain. It is possible that the causative papillomavirus could be excised even if some surrounding fibrosis remains. Alternatively, the difficulties in predicting neoplasm recurrence from surgical margins are becoming well recognized for all neoplasms in veterinary medicine [14]. It is also possible that the body mounts an immune respnse which prevents detectible lesion recurrence. It should also be noted that, although most sarcoids recur within 3-6 months after excision, recurrence can occur up to 18 months after excision [3]. Therefore, although no recurrence had been observed 5 months after excision, surgical cure could not be definitively confirmed in this case.

Surgical excision was used in this case to remove the oral mass as topical therapies cannot be used in the oral cavity. An additional consideration was the fractious nature of the horse which would have made repeated treatments of the oral lesion difficult. While not used in this case, other treatment options could have included cryotherapy, laser cautery, or intralesional injection of a therapeutic such as cisplatin [15].

While it cannot be confirmed that the mass from the lip was also a sarcoid, this appears most likely due to the similar clinical appearance of these masses. The mass from the lip resolved without any treatment. While spontaneous resolution of sarcoids has been previously reported [4,5], the rapid resolution in the presently reported case was unexpected. It is currently unknown whether sarcoids caused by BPV2 are less likely to recur after surgical excision or spontaneous resolve than sarcoids caused by BPV1.

The significance of the thickening of the cheek is difficult to determine. Considering the likely presence of two sarcoids on the same side of the face, the thickening could have been due to a diffuse sarcoid within the cheek tissue. Alternatively, the thickening could have been a reparative process due to an unobserved traumatic injury in this area. It is possible that this traumatic injury then predisposed to the sarcoids in the mouth and on the lips. Histology of the cheek was not performed, although histological differentiation between a diffuse sarcoid and fibrosis would most likely not be possible. The apparent resolution of the thickening of the cheek also does not help determine the nature of the lesion as both a sarcoid and an inflammatory reaction may resolve over time.

It is uncertain how the BPV entered the mouth of the affected horse. Cutaneous sarcoids have been hypothesized to be caused by transmission of BPVs by biting flies [16]. However, transmission by biting flies to the gingiva of the presently described horse is unlikely. Instead, it is possible that a cutaneous BPV2 infection could have entered the mouth from the horse licking itself or other in-contact horses. Alternatively, the sarcoid could have developed after the horse chewed on a fomite that was contaminated by BPV2. Repair of tissue injury is thought to be important in sarcoid development [6]. If the present horse chewed on a contaminated fomite and the fomite caused trauma to the mouth, this could explain the location of the sarcoid adjacent to the premolar teeth and involving the lips.

In the present case, the lesions within the mouth did not result in discomfort or difficulty eating. Therefore, it is possible that some oral sarcoids may develop, but spontaneously resolve without being detected. Oral sarcoids could therefore be more common that currently realized.

Papillomaviruses in humans typically infect either haired skin or the mucus membranes [17]. While this is also true for some PVs that infect the veterinary species, other veterinary PV types appear able to infect a wider range of epithelial surfaces [17]. In cattle, BPV2 cause fibropapillomas of the skin and fibropapillomas of the upper alimentary tract [18]. Therefore, this PV type may similarly be able to infect both haired skin and mucosa of horses. In contrast, BPV1 is rarely present in bovine upper alimentary lesions suggesting this BPV type may be less able to infect non-cutaneous epithelium. As BPV1 is the predominant cause of equine sarcoids in Europe [8], a reduced ability of BPV1 to infect the gingiva may explain why oral sarcoids have not been previously reported. In contrast, as BPV2 causes almost all equine sarcoids in New Zealand [10], oral sarcoids would be expected to occur more frequently in this country. Interestingly, sarcoids in other species are not restricted to the skin with a BPV14-associated oral sarcoid reported in a cat [19] and an ovine PV-associated sarcoid-like lesion reported in the mouth of a pig [20].

4. Conclusion

The histological and molecular findings in this case support a diagnosis of oral sarcoid. While rare, sarcoids are a differential for an oral mass in a horse. The development of sarcoids in the mouth of horses may be dependent on the causative BPV type. Trauma could be important in the development of oral sarcoids.

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Authors' contributions

All authors contributed to the clinical investigation and diagnosis of this case. All authors contributed to the writing of, and have approved, the final manuscript.

Animal Ethics approval

All manipulations reported were done as part of regular veterinary care and no animal ethics is required.

Owner Consent

The owner of the horse agreed for the horse to be treated and for the case details and outcome to be reported in this manuscript.

CRediT authorship contribution statement

John S. Munday: Methodology, Writing – original draft. **Michelle C. Lewis:** Investigation, Methodology, Writing – review & editing. **Margaret H. Leyland:** Investigation, Methodology, Writing – review & editing.

Declaration of competing interest

The authors declare they have no known competing financial interest or personal relationships that could have appeared to influence the work reported in this paper.

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