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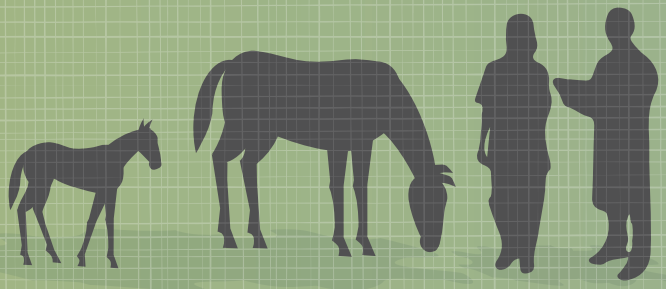
Championing the Equine Vet

60th Handbook of Presentations



ONCOLOGY, CAN WE ADVANCE OUR TREATMENT OF CASES?

Chair: Victoria South

8.30

Diagnostics in suspected neoplasia – let's all biopsy

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Introduction

When investigating cases of suspected neoplasia in horses there are various ancillary diagnostic tests available that can be used to help reach an accurate and early diagnosis. This in turn will guide decision making regarding the most appropriate treatment options and help to determine the prognosis for a particular case.

The foundation of any investigation in cases of suspected neoplasia should be a thorough clinical examination and consideration of the signalment and clinical history. Appropriate selection of ancillary diagnostic tests will then depend on the possible differential diagnoses following this initial examination.

What additional diagnostic tests should I use?

Selection of appropriate ancillary diagnostic tests is generally done on a case-by-case basis. In some cases, general haematology and biochemistry may be indicated as part of the work-up, particularly if there are signs of systemic illness. Basic and advanced imaging (ultrasonography, radiography, endoscopy, CT, MRI) can sometimes be helpful to further determine if a lesion is neoplastic or non-neoplastic, although it does not generally lead to a definitive diagnosis. There is limited availability of tumour biomarkers in equine oncology; however, certain tests can be helpful in selected cases.

Cytological examination of fine needle aspirates (FNA), peritoneal fluid, pleural fluid or impression smears can be helpful in the diagnosis of certain tumours; however, many equine tumours exfoliate cells poorly on FNA or within body cavities and biopsy is often required for further investigation.

Biopsy of a suspected neoplastic lesion for histopathological examination is often the most helpful diagnostic test as in many cases it will give an accurate diagnosis, or at least narrow down a list of possible differential diagnoses.

How do I take a good biopsy sample?

Biopsy samples can be excisional or incisional and factors influencing the type of biopsy to take include the size of the lesion, equipment available and suspected diagnosis. Submission of excisional biopsies of a lesion and surrounding tissue has the advantage of allowing the pathologist to assess all areas of the lesion as well as how a neoplasm is interacting with normal tissue, which can increase the likelihood of reaching a definitive diagnosis. It also allows for the assessment of surgical margins. Excisional biopsies are more readily achieved with cutaneous lesions, that are often of a smaller size.

In some cases, it can be more challenging to clinically differentiate neoplastic and non-neoplastic lesions (e.g. chronic inflammatory lesions) or different types of tumours. Incisional biopsies are therefore sometimes preferred to try to reach a diagnosis prior to planning surgical and/or medical treatment. Types of incisional biopsies include punch biopsies, wedge biopsies, trucut biopsies and endoscopic biopsies and selection of the most appropriate type of biopsy will depend on the suspected diagnosis, location of the lesion (e.g. cutaneous/subcutaneous vs. in a body cavity/internal organ) and the depth of the lesion (e.g. within skin/subcutis).

Punch biopsies are easy to obtain and can be appropriate for some superficial skin tumours that often extend to the epidermal junction (e.g. squamous cell carcinomas, melanomas); however, their relatively small size and superficial nature means they can miss lesions deeper in the dermis and may not always be fully representative. Incisional wedge biopsies generally allow for histopathological examination of larger areas of tissue, including areas of the neoplasm and ideally also regions in which neoplastic cells interact with normal tissue. Trucut biopsies only sample small areas of tissue but can be helpful when suspected neoplasms are within body cavities or internal organs, or are located in subcutaneous or muscle tissue. A combination of biopsy types, or obtaining biopsies from multiple areas of a lesion should also sometimes be considered, and can be helpful in increasing the certainty of a histopathological diagnosis in some cases.

How do I get the most from my biopsy sample?

To ensure you get the most from your biopsy sample it is important to handle the tissue carefully to avoid crush artefact interfering with histopathological interpretation and tissue should be immediately placed into an appropriate volume of fixative (usually 10% formalin). If assessment of surgical margins is required, try to avoid slicing into the sample prior to fixation, or if a sample is very large only cut into it away from the areas of the margins. Ensure that appropriate clinical information is submitted along with the biopsy sample to allow for the most accurate interpretation of the histopathological findings.

8.45

An update on sarcoids – novel intralesional treatments

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Introduction

Sarcoids continue to present a clinical challenge, and the vast number of potential treatments reflects that there is no one treatment suitable for every case. Tigilanol tiglate is licensed for the treatment of mast cell tumours in dogs, and intralesional tigilanol tiglate has been described for the treatment of a single sarcoid (and a squamous cell carcinoma) [1]. A relatively simple treatment to administer, it has a number of potential advantages over other intralesional treatments. It is described as a 'tumour agnostic' drug, making it potentially suitable for any tumour type, and its administration leads to an acute inflammatory response at the treatment site with immune cell recruitment and disruption of the tumour vasculature. Intralesional administration leads to the rapid onset of haemorrhagic necrosis of the tumour, subsequent sloughing of the lesion with full re-epithelialisation of the defect and a good functional outcome [1]. Compared with cisplatin and carboplatin, there are fewer concerns for the health and safety of those administering the drug and handling the horse after treatment, and its method of action should allow for successful treatment of any lesion with sufficient tumour bulk to facilitate accurate intralesional injection.

Materials and methods

Fourteen horses and 18 sarcoids received intralesional tigilanol tiglate for the treatment of sarcoids at Cambridge Equine Hospital, University of Cambridge. Of these, five sarcoids had received other treatments prior to referral, including radiotherapy, laser surgical resection, intralesional treatment (mitomycin C and cisplatin), and electrochemotherapy (with cisplatin). Intralesional tigilanol tiglate injections were administered according to the previously described protocol, using a carefully calculated dose per volume of the tumour to achieve the reported 35% v/v of tumour [1] but increasing the dose up to a maximum of 4 mg if required to achieve this v/v administration. Twelve horses were treated under routine standing sedation following the administration of mepivacaine to provide sufficient local anaesthesia. Two horses were treated under general anaesthesia to facilitate treatment due to the temperament of the horses and the location of the lesions (one lesion was located on the medial aspect of the right ear, and one was located on the palmar aspect of the right carpus, **Figs 1** and **2**). Total dose administered in one treatment ranged from 0.4 mg to 4 mg of tigilanol tiglate. All horses were maintained on i.v. flunixin meglumine for a minimum of 24 hours following treatment, and on oral flunixin meglumine or phenylbutazone for ongoing analgesia as required. Follow-up treatments were administered if the initial treatment did not lead to regression of the lesion. All owners agreed to long-term follow-up of the cases via WhatsApp photographic updates.

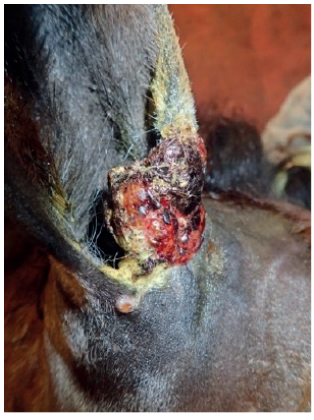

Fig 1: Lesion on the medial aspect of the right ear immediately prior to treatment. This lesion had previously undergone laser surgical resection and radiotherapy, but had recurred.

Results

Rapid onset of haemorrhagic necrosis was observed in all treated lesions (**Fig 3**). All horses were noted to be quiet for 24–36 hours after treatment. All but one lesion developed significant local swelling and oedema, and three horses required i.v. dexamethasone to provide additional anti-inflammatory effects due to the magnitude of the associated swelling and discomfort. One lesion did not respond to a first treatment, and the owners declined further intervention. Five horses and six sarcoids received more than one treatment with tigilanol tiglate. Of these, five sarcoids had received various treatments prior to referral, and one was a naïve periocular lesion. Two horses developed local lymph node abscessation following treatment, both of which resolved with supportive care. One horse developed jugular vein thrombophlebitis (the treated lesion was distant to the jugular vein). One horse that underwent surgical resection before injecting tigilanol tiglate into the margins developed a very wide slough ventral to the lesion that required more significant wound care over a prolonged period, although healing was complete and a good functional outcome was achieved (**Figs 4–6**). One horse is still having ongoing treatment, but appears to be responding well to date. In those horses where

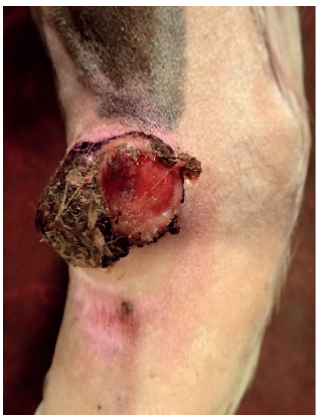

Fig 2: Lesion on the palmarolateral aspect of the right carpus immediately prior to treatment.

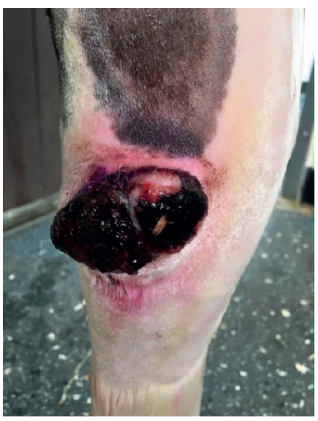

Fig 3: The same lesion as Figure 2, showing haemorrhagic necrosis 4 hours after intralesional tigilanol tiglate administration.

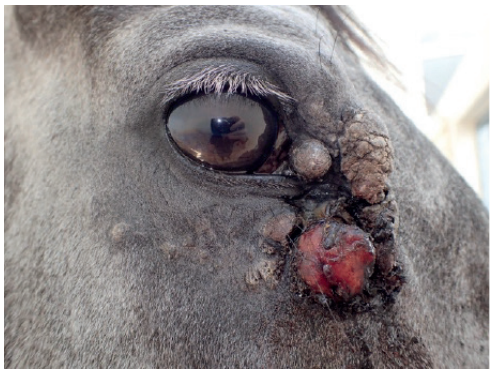

Fig 4: Complex periocular lesions immediately prior to treatment.

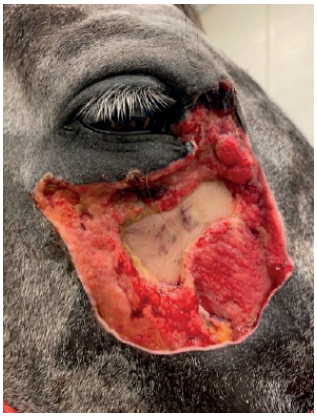

Fig 5: The same horse as Figure 4, following wide slough ventral to the lesion.

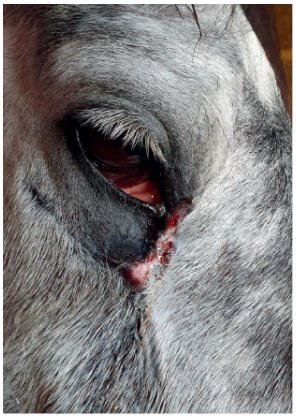

Fig 6: The same horse as Figures 4 and 5, almost completely healed with a good functional outcome.

the lesion resolved, a good functional and cosmetic outcome was achieved, even after multiple treatments (**Figs 7** and **8**). However, one lesion has recurred approximately 11 months after an apparently successful treatment.

Summary

In total, 13 of 16 sarcoids were successfully treated with tigilanol tiglate. One lesion showed recurrence at approximately 11 months, one lesion did not respond to a single treatment and did not receive any further follow-up, and one lesion continues to show a promising response to a third treatment but has not yet fully regressed. These data include five sarcoids which had received multiple other treatments that had proven unsuccessful. Four of these lesions have now resolved.

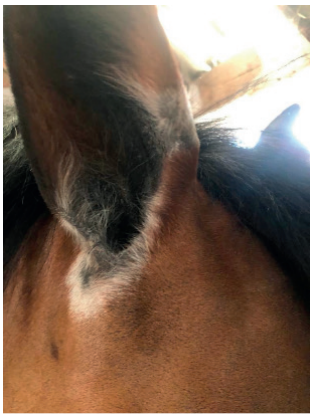

Fig 7: The same horse as Figure 1, after five rounds of treatment with tigilanol tiglate. Note that much of the leucotricia and alopecia was already present following previous unsuccessful treatment with laser surgical excision and radiotherapy.

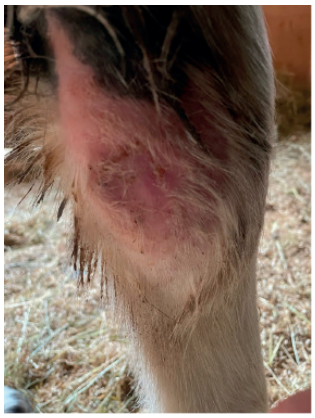

Fig 8: The same horse as Figures 2 and 3, showing a good functional and cosmetic outcome after four rounds of treatment with tigilanol tiglate.

Fig 9: A naïve lesion before and 30 days after treatment, showing a typical outcome of a straightforward case.

Tigilanol tiglate appears to be a promising treatment for lesions that are suitable for intralesional injection, and appears to be safe and practical for potential use outside a hospital setting (**Fig 9**). However, persistence and repeated treatments may be required for more complicated lesions, and there may be side effects associated with treatment. Further work is required to better understand its utility for the treatment of naïve and previously treated sarcoids.

Reference

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9.00

Evaluation and treatment options in melanoma cases

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This lecture will evaluate the current literature and treatment protocols for melanomas in the equine patient. Potential new therapies include the use of autologous cancer vaccines, which have been shown to be safe (1.6% rate of adverse events) although their efficacy has not been fully reviewed [1]. Further topical treatments including betulinic acid and NVX-207 will be discussed, although their use in clinical cases will likely still be limited due to a paucity of clinical research [2].

The use of electrochemotherapy [3] shows promise in a number of neoplastic processes although case numbers in most research papers are too small to draw complete conclusions.

Although very limited research is available relating to the use of xenogeneic tyrosinase DNA vaccination, its use is increasing within the equine population and some research has been undertaken. Tyrosinase is overexpressed within equine melanoma cells and therefore the vaccination has a theoretically appropriate action in the horse [4]. Lembcke *et al.* showed that there is an immunological response to the vaccination consistent with that seen in other animals, although they do not discuss its efficacy as a treatment protocol [5]. Anecdotal evidence shows that many melanomas appear to stall in their growth; however, a prospective study is required to analyse its true effect. Potential positive outcomes will be discussed as well as adverse reactions associated with the vaccination.

Although often deemed a benign tumour, melanomas frequently lead to euthanasia of the horse. Therefore, it is important to consider the most appropriate treatment and review what limited research is currently available to guide the treatment protocol.

References

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