

Why clinicians should consider tumour staging and grading in horses

For many of us, the time may come that our doctor asks us to sit down because they have to tell us the bad news that: 'Yes, it is cancer'. We hope that, after the initial shock and grief, we will tackle the important questions with our doctor. What are the treatment options? Can we hope for a complete cure? Or will treatment be only palliative? And how much time will it give us? To this discussion we all will bring our personal attitudes, ranging from 'I will do anything to beat this cancer' to 'I have always said I'd rather spend my last 3 months with my family than my last year in and out of hospital'.

Owners of a horse with a penile squamous cell carcinoma (SCC) go through much the same emotional process when having to decide on treatment. As veterinarians we want to give the best advice on treatment options and prognosis. Because penile tumours occur more often in aged horses, owners may be reluctant to choose a more invasive treatment that may entail more discomfort for their horse, such as an *en bloc* resection with removal of the inguinal lymph nodes. In contrast, less invasive treatments have a higher incidence of recurrence. In studies describing the results of partial phallectomy using Williams' technique, recurrence rates of 19–26% have been found [1,2]. As veterinarians we should try to provide objective information on the advantages and disadvantages of the different treatment options for the individual patient.

When we want to accurately predict tumour behaviour, staging and grading of the tumour may prove useful. The TNM (tumour, node, metastasis) classification system is used widely in human oncology. This system will help veterinarians examining all items that are important for the prognosis and for the proper choice of treatment [3].

The T for tumour includes the size of the tumour and possible invasion of adjacent structures. Invasion is a very important factor in penile SCC because once the tumour cells have invaded the *corpus cavernosum* or *corpus spongiosum*, further spread is easy. Careful palpation of the penis to identify firm thickening is important in this context [1]. In man, ultrasonography of penile tumours has proved useful to identify invasion of the tumour into the *corpus cavernosum*. With practice, this may prove to be a valuable diagnostic tool for veterinarians too [3].

The N for (lymph) node is a challenging item in the examination of a horse with penile SCC. First, most older horses have fat deposits in the inguinal area, making it difficult to identify the lymph nodes on palpation. Second, balanoposthitis will often accompany SCC so the lymph node may be enlarged without the presence of metastases. In the study of van den Top *et al.* enlarged lymph nodes were found in a relatively high proportion of cases, while metastases were confirmed in only 32% of these animals [4]. Third, absence of palpable lymph node enlargement does not rule out metastasis: in the same study 36% of cases with unremarkable lymph nodes had 'occult' metastasis confirmed histologically after surgery or at *post mortem* histological examination [4]. When the lymph nodes can be identified by palpation or ultrasound examination, a fine needle aspiration biopsy (FNAB) of the lymph node may confirm metastasis of SCC. Unfortunately, FNAB cannot exclude metastasis to the lymph node: in man up to 29% false negatives have been reported. After the lymph nodes in the inguinal area, the lymph nodes in the abdomen (medial iliac) are the next station for the SCC, so palpation *per rectum* of these lymph nodes is routine.

The M in the TNM classification is for distant metastasis. Fortunately, it seems that penile SCC of the horse is not very quick to metastasise, so distant metastases are rarely present at presentation. Extrapolating from other species, metastasis to the lungs could be expected, but in horses this seems to be very rare. For this reason, radiography of the thorax is usually reserved for those horses with (a strong suspicion of) metastases in the lymph nodes [3]. While distant metastases are rare, they do occur and it is good to keep in mind that penile SCC can spread in two ways. The first is the 'normal' pathway for SCC: to lymph node and lung. The second is to the *corpus cavernosum* or *c. spongiosum*, followed by spreading through the circulation. Therefore, clinicians should beware of any sign of distant metastasis, especially after recurrence of SCC. Three out of six cases that

suffered recurrence in the study of Mair *et al.* had metastasis to the abdomen [1]. In the material of van den Top *et al.* there was one horse with recurrence of SCC after *en bloc* resection, which had metastasis in the prescapular lymph node confirmed with FNAB [4].

Recent work included in this issue of *Equine Veterinary Journal* has shown that it is important to add G for grade to the TNM classification. In the study of van den Top *et al.* penile epithelial tumours are graded as penile intraepithelial neoplasia (PIN) lesion, papilloma, SCC G1, SCC G2 and SCC G3 [5]. The PIN and papilloma are often considered 'pre-malignant'. The malignant tumours are divided into: G1 – well differentiated SCC; G2 – moderately differentiated SCC; and G3 – undifferentiated SCC. In the work of van den Top *et al.* a positive correlation between a higher grade and the incidence of metastasis is shown [2,5]. Horses with a G1 SCC have metastases in 0–3% of cases, for G2 this is 25% and for G3 it is as high as 45% and a striking influence of the grade on survival was shown [5]. All horses with PIN as the primary lesion survived. Eight per cent of horses with papilloma died of the disease, 26.1 and 26.3% of horses with G1 and G2 SCC respectively died, and 63% of horses with G3 SCC died.

To grade the tumour, a representative biopsy of the tumour has to be examined. Taking an incisional biopsy may seem a big step to an owner, but the facts discussed above show that it is very important for decision making. For a G1 SCC the less invasive Williams' technique may be curative. With the higher grades, metastases may already be present so an *en bloc* resection (or partial phallectomy and sheath ablation) may be more suitable [6]. Even when metastases in the regional lymph nodes are present the success rate of these surgical techniques may be as high as 86–100% [2,6].

Another reason to choose one of these more invasive techniques may be the additional presence of PIN lesions or papillomas on parts of the penis and prepuce that cannot be removed with Williams' technique. In these cases, the aim is to remove all the epithelium that is prone to developing these tumours and so to exclude the need for follow-up treatments for new tumours [2].

When we have staged and graded a penile tumour in this way, we are well equipped to explain all the pros and cons of the different treatment options to the owner. Thus we may help the owner to decide which treatment is most suitable for their horse.

J. M. Ensink

Department of Equine Sciences, Faculty of Veterinary Medicine,
Utrecht University, The Netherlands.

References

1. Mair, T.S., Walmsley, J.P. and Phillips, T.J. (2000) Surgical treatment of 45 horses affected by squamous cell carcinoma of the penis and prepuce. *Equine Vet. J.* **32**, 406–410.
2. Van den Top, J.G.B., de Heer, N., Klein, W.R. and Ensink, J.M. (2008) Penile and preputial squamous cell carcinoma in the horse: a retrospective study of treatment of 77 cases. *Equine Vet. J.* **40**, 533–537.
3. Van den Top, J.G.B., Ensink, J.M., Gröne, A., Klein, W.R., Barneveld, A. and van Weeren, P.R. (2010) Penile and preputial tumours in the horse: literature review and proposal of a standardised approach. *Equine Vet. J.* **42**, 746–758.
4. Van den Top, J.G.B., de Heer, N., Klein, W.R. and Ensink, J.M. (2008) Penile and preputial tumours in the horse: a retrospective study of 114 affected horses. *Equine Vet. J.* **40**, 528–532.
5. Van den Top, J.G.B., Harkema, L., Lange, C., Ensink, J.M., van de Lest, C.H.A., Barneveld, A., van Weeren, P.R., Gröne, A. and Martens, A. (2014) Expression of p53, Ki67, EcPV2- and EcPV3 DNA, and viral genes in relation to metastasis and outcome in equine penile and preputial squamous cell carcinoma. *Equine Vet. J.* **47**, 188–195.
6. Doles, J., Williams, J.W. and Yarbrough, T.B. (2001) Penile amputation and sheath ablation in the horse. *Vet. Surg.* **30**, 327–331.