Equine Hoof Canker – A clinical trial of topical cisplatin chemotherapy

Apprich, V., Dr. med. vet. [a], Licka, T., Dr. med. vet., MRCVS[a,b]

[a] Equine Clinic, Large Animal Surgery and Orthopaedics, University of Veterinary Medicine, A-1210 Vienna, Austria; telephone: 0043 1 25077 5501; fax: 0043 1 25077 5590; email: theresia.licka@vetmeduni.ac.at

[b] Department of Veterinary Clinical Studies, The Roslin Institute, Royal (Dick) School of Veterinary Studies, University of Edinburgh, Roslin, Midlothian EH 259 RG, United Kingdom

Abstract

The aim of this clinical trial was to document the results of a new and promising therapy for equine hoof canker. Ten horses were treated from May 2011 to October 2012 at the Equine Clinic of the University of Veterinary Medicine, Vienna with topical cisplatin chemotherapy on the basis of a previously reported detection of bovine papillomaviral DNA in canker lesions (Brandt and others, 2010). Therapy included surgical debridement of canker lesions prior to start of chemotherapy. Two to six days after debridement, at the time of healthy granulation in the absence of any tissue suspicious of canker, cisplatin chemotherapy was started using a topical formulation within a foot bandage. All horses were topically treated once every other day for 10 treatments under strict precautions. During topical cisplatin chemotherapy no recurrence of canker tissue was seen until full keratinisation had occurred. Treated hooves were kept bandaged until superficially keratinised or shod with treatment plates for discharge of horses, respectively. Mean hospitalisation time was 32.1 days and only one horse developed a recurrence 13 months after discharge. Coinciding with the reported detection of sarcoid-inducing bovine papillomaviral DNA in canker, the apparent success of topical cisplatin chemotherapy underlines this similarity.

Introduction

Equine hoof canker (Pododermatitis chronica verrucosa s. migrans) is a destructive hypertrophic pododermatitis of the frog, hoof wall and adjacent structures in equids. The disease is diagnosed by its typical clinical appearance: filamentous or cauliflower-like proliferation of the hoof matrix with foul smell and white cheesy exsudate. It is a sporadic chronic disorder, and at later stages it compromises the use and welfare of horses. The disease often shortens lifetime of affected animals, as therapy is often insufficient (Wilson and others; 1989, Stashak, 2002; Dietz, 2006; Knottenbelt, 2009). It is likely that infection and an underlying defect in horn production are involved (Knottenbelt, 2009), but several attempts to identify causative agents have been unsuccessful (Turner, 1989, Lacerda Neto and others, 2001, Jongbloets and others, 2005; Brandt and others, 2010). Surgical debridement of canker lesions in combination with a variety of topical formulations are common treatment protocols (Wilson, 1994; Dietz, 2006; Stashak, 2002; O'Grady and Madison, 2004; Fürst and Lischer, 2006), also combined with prednisolone (Oosterlinck and others, 2011). If at all successful, horses which recover often show short to medium term recurrence of the problem.

In a recent study sarcoid-inducing viral DNA and RNA of bovine papillomaviruses of *types 1* and *2* (Brandt and others, 2010) have been detected in 24/24 canker tissue samples as well as in intact skin and peripheral blood mononuclear cells of affected horses, whereas no viral DNA was detected in horses without canker lesions. Also, clinical and histological similarities to equine sarcoids have been observed (Rooney and Robertson, 1996). Cisplatin is one of the most potent chemotherapy agents used in human and veterinary medicine and intralesional cisplatin chemotherapy with and without surgery is a well-documented and successful therapy for equine sarcoids (Hewes and Sullins, 2006; Theon and others, 2007; Tamzali and others, 2011). This paper documents a new and promising therapy for canker with topical cisplatin chemotherapy aimed at a reduction of hospitalisation period and short term recurrence.

Materials and Methods

Ten horses (see Table 1), admitted to the Equine Clinic of the Veterinary University Vienna from May 2011 to October 2012 for treatment of canker, were included in the study (Table 1). The disease was diagnosed by its typical clinical appearance (Figure 1). A total of 19 hooves were affected, 13 front and 9 hind hooves.

On day of hospitalisation affected hooves were trimmed, thoroughly cleaned and kept in disinfectant bandages until surgery, which was between 1 and 4 days later. Using a tourniquet, affected epidermal and dermal tissues were surgically debrided under regional anaesthesia. Two to six days later, if healthy granulation tissue in the absence of any tissue suspicious of canker, topical cisplatin chemotherapy was started. This included 10 applications of cisplatin paste (5ml Cisplatin injection solution (1mg/ml), 5g EucillinB crème, Metronidazole-saccharose (125g) qs fiat pasta) on the surgical wounds every other day. Treated hooves were bandaged until superficially keratinised or shod with a treatment plate. During chemotherapy including 2 days after the last cisplatin application horses were kept in isolation from other horses and unauthorized persons. Bandages were changed in a dedicated treatment stable under strict precautions to prevent skin and eye contact of treating personnel with cisplatin.

Results

All horses showed typical clinical signs of canker. In two horses small areas of tissue suspicious of canker had to be removed after surgical debridement prior to the beginning of cisplatin chemotherapy. In two horses some suspicious tissue had to be removed after the 5th cisplatin treatment. Due to bleeding the treatment interval was three days on one of these occasions. Wounds healed without complications (Figure 1). Mean hospitalisation for each cisplatin treatment was 32.1 days (26 – 39 days) (Table 1). Four horses were shod with a treatment plate, because surgical wounds were not fully keratinized at the time of discharge. Horse 5 was hospitalised longer

on special request of owners who could not manage to change treatment plates at home. Follow up-information was obtained for all horses between 0 and 14 months and one horse developed a recurrence 13 months after discharge (Table 1).

Discussion

The lack of a causative and successful therapy of equine hoof canker often leads to euthanasia of affected animals (Wilson and others; 1989, Stashak, 2002; Dietz, 2006; Knottenbelt, 2009).

Canker therapy has been described as very time-consuming, requiring several months or more (Dietz, 2006; Fürst and Lischer, 2006; Knottenbelt, 2009). This could be markedly reduced with the described topical cisplatin chemotherapy. After debridement, hypertrophic growth was easily controlled in this study, which is in contrast to our own previous experience as well as previous reports (Knottenbelt, 2009). During the follow-up period a low incidence of short to medium term recurrence was noted in this study, although high recurrence rates, commonly within 12 months, are described with established treatments (Oosterlinck and others, 2011). The horse that developed a recurrence 13 months after discharge from clinic had undergone quite radical and intensive treatments before the start of cisplatin chemotherapy and all its hooves were severely affected. This agrees with reports, describing a reduced prognosis for extensive lesions for which adequate treatment was delayed both for canker (Wilson, 1994; Stashak, 2002; Oosterlinck and others, 2011) and sarcoids (Hewes and Sullins, 2006; Theon and others, 2007; Tamzali and others, 2011). In contrast to other cancer treatments, topical cisplatin chemotherapy appears to be cost-effective with reduced hospitalisation time and reduced short to medium term recurrence rates. As such, repeated treatments may also be feasible in horses with recurring canker lesions.

No local or systemic side effects of cisplatin were noticed in treated horses; however, health and safety guidelines required strict precautionary measures to protect treating personnel from skin or eye contact. This made this therapy viable only in a hospital setting.

In addition to clinical and histological similarities and the reported detection of bovine papillomaviral DNA in canker, the apparent success of topical cisplatin chemotherapy also underlines the similarity to equine sarcoids.

Acknowledgements

We gratefully acknowledge the support offered by the inner-university research funding program "Profillinien", Profile line 2 – Infection and Prevention.

References

BRANDT, S., SCHOSTER, A., TOBER, R., KAINZBAUER, C., BURGSTALLER, J.P., HARALAMBUS, R., STEINBORN, R., HINTERHOFER, C., STANEK, C. (2010) Consistent detection of bovine papillomavirus in lesions, intact skin and peripheral blood mononuclear cells of horses affected by hoof canker. *Equine Vet. J.* **43**, 202-209

DIETZ, O. (2006) Hufkrankheiten. In: *Handbuch Pferdepraxis*. Eds: O. Dietz and B. Huskamp, Enke, Stuttgart. pp 980-983

FÜRST, A.E., LISCHER, C.J. (2006) Degenerative and neoplastic diseases of the foot. In: *Equine Surgery*, 3rd edn., Eds: J.A.AUER and J.A. STICK, Saunders Elsevier, St Louis. pp1196-1199

HEWES, C.A., SULLINS, K.E. (2006) Use of cisplatin-containing biodegradable beads for treatment of cutaneous neoplasia in equidae: 59 cases (2000-2004). *J. Am. vet. med. Assoc.* **229**, 1617-1622

JONGBLOETS, A.M.C.,SLOET VAN OLDRUITENBORGH-OOSTERBAAN, M.M., MEEUS, P.J.H.M., BACK, W. (2005) Straalkanker: een (auto-)immuungemedieerdeaandoening? *Tijdschr. Diergeneeskd*. **130**, 106-109

KNOTTENBELT, D.C. (2009) Injuries and diseases of the hoof. In: *Pascoe's Principles and Practice of Equine Dermatology.* Eds: Knottenbelt, D.C., Saunders, Elsvier pp 370-371

LACERDA NETO, J.C., MARTINS FILHO, L.P., ALESSI, A.C., FERRAZ, G.C., MARQUES, J.A., VALADAO, C.A.A. (2001) Observacoes clinicas, anatomopatologicas etratamento de seis casos de dermovilite exudativa vegetante cronica (cancro da ranhilha) de equinos. *Arq. Bras. med. vet. Zootec*. **53,** 93-102

O'GRADY, S.E., MADISON, J.B. (2004) How to treat equine canker. *Proc. Am. Ass. equine Practnrs.* **50**, 202-205

OOSTERLINCK, M., DENEUT, K., DUMOULIN, M., GASTHUYS, F., PILLE, F. (2011) Retrospective study on 30 horses with chronic proliferative pododermatitis (canker). *Equine Vet. J.* **23**, 466-471

ROONEY, J.R., ROBERTSON, J.L. (1996) Canker. In: *Equine Pathology*, Eds: J.R. ROONEY and J.L. ROBERTSON, Iowa State University Press, Ames. pp 195-196

STASHAK, T.S. (2002) The foot. In: *Adam's Lameness in Horses*. Ed: T.S. Stashak, Lippincott Williams and Wilkins, Philadelphia. pp. 718-719

TAMZALI, Y., BORDE, L., ROLS, M.P., GOLZIO, M., LYAZRHI, F., TEISSIE, J. (2012) Successful treatment of equine sarcoids with cisplatin electrochemotherapy: A retrospective study of 48 cases. *Equine Vet. J.* **44**, 214-220

THEON, A.P., WILSON, W.D., MAGDESIAN, K.G., PUSTERLA, N., SNYDER, J.R., GALUPPO, L.D. (2007) Long-term outcome associated with intratumoral chemotherapy with cisplatin for cutaneous tumors in equidae: 573 cases (1995-2004). *J. Am. vet. med. Assoc.* **230**, 1506-1513

TURNER, T.A. (1989) Treatment of equine canker. *Proc. Am. Ass. equine Practrns*. **34,** 1721-1723

WILSON, D.G., MAYS, M.B.C., COLAHAN, P.T. O'Grady and Madison(1989) Treatment of canker in horses. *J. Am. vet. med. Assoc.* **194**, 1721-1723

WILSON, D.G. (1994) Topical Metronidazole in the Treatment of Equine Canker. *Proc. Am. Ass. equine Practrns*. **40**, 49-50

153

Table 1

Animals	**Breed**	**Gender**	**Age** (years)	**Hooves affected**	**Hospitalisation** (days)	**Follow Up** (months)	**Recurrence**
Horse 1	Warmblood	Gelding	16	2 front hooves, 2 hind hooves	32* 34*	14	yes
Horse 2	Standardbred	Mare	17	1 front hoof	32	11	no
Horse 3	Draft Horse	Mare	12	1 front hoof	39	8	no
Horse 4	Warmblood	Gelding	19	2 front hooves, 1 hind hoof	34	3	no
Horse 5	Standardbred	Mare	24	2 front hooves	29 (26)**	2	no
Horse 6	Haflinger	Mare	16	1 front hoof	31	2	no
Horse 7	Warmblood	Gelding	9	1 hind hoof	35	1	no
Horse 8	Warmblood	Gelding	16	1 front hoof	26	1	no
Horse 9	Kladruber	Gelding	8	1 front hoof, 2 hind hooves	26	0	no
Horse 10	Standardbred	Mare	12	2 front hooves	still in clinic	0	no
Mean Values	-	-	14,9	-	32,1	4,2	-

* 2 separate treatment cycles for front hooves and hind hooves, respectively

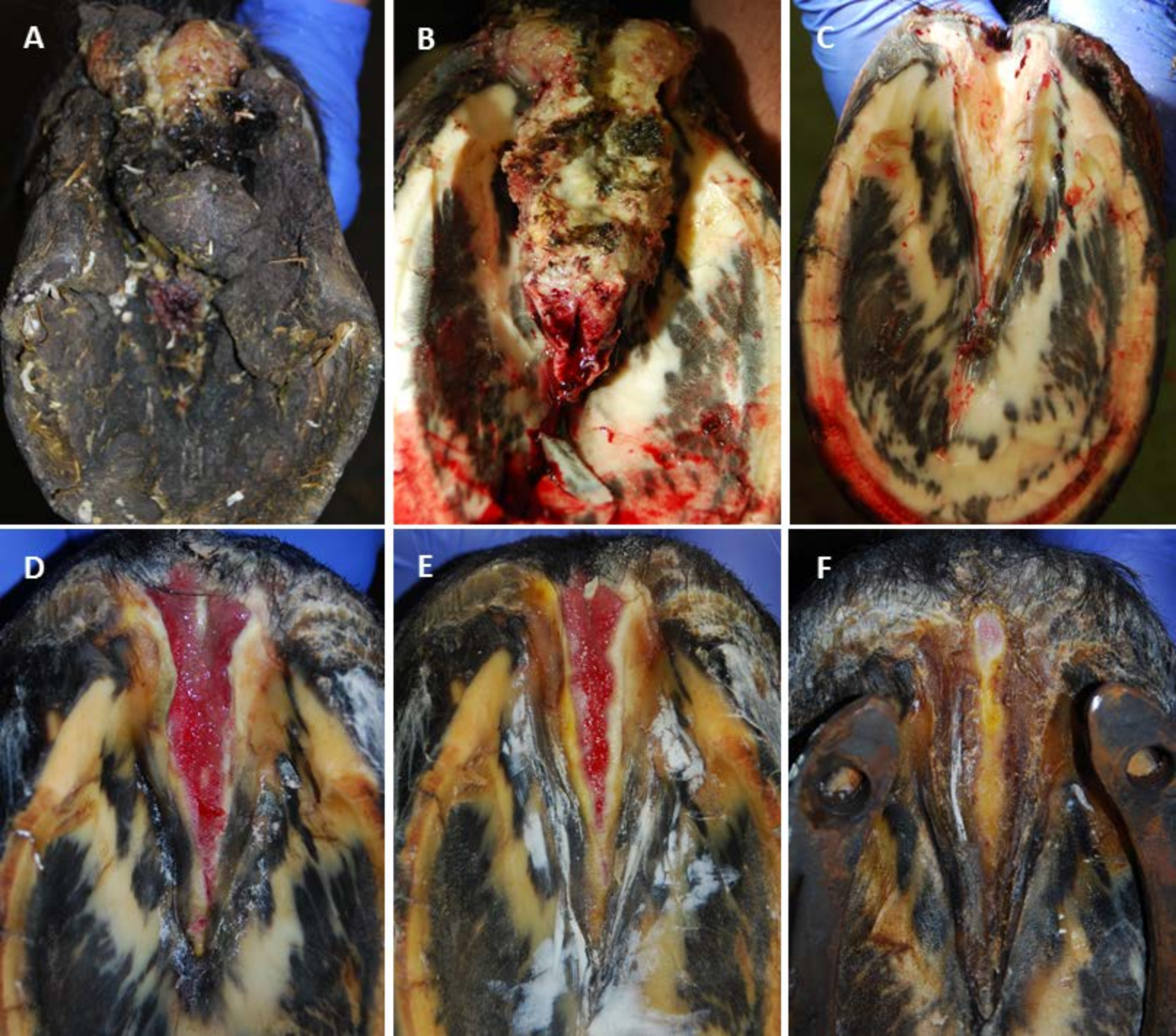
154 ** on request of owners (the number of days in parentheses indicates longer hospitalisation due to management problems at home)

Table and Figure Legends:

Table 1: Details of patient horses included in the clinical trial of topical cisplatin chemotherapy from May 2011 to October 2012

Figure 1: Progress of topical cisplatin chemotherapy of the left front hoof of horse 5; typical white cheesy exudate and cauliflower-like proliferation of the matrix of the frog without adequate keratinisation of the epidermis before (A) and after superficial trimming and disinfection of the hoof (B), after surgical debridement of the frog (C), at the day of the 8th cisplatin chemotherapy with good keratinisation of the surgical wound from the sides (D), two days after the end of cisplatin chemotherapy with progressing keratinisation (E), and after shoeing with a treatment plate (F)

167


A
B
C
D
E
F