Pferdeheilkunde 28 (2012) 6 (November/Dezember) 642-649

Use of a parathyroid hormone peptide (PTH_{1-34})-enriched fibrin hydrogel for the treatment of subchondral cystic lesions in 15 horses

Michelle A. Jackson[1], Stephanie Ohlerth[2], Martin Kummer[1], Regula Bettschart[3], John Watson[4], Celine L. Manera[1], Brigitte von Rechenberg[5], Jörg Auer[1] and Anton Fürst[1]

Equine Department[1], Section of Diagnostic Imaging[2], Section of Anaesthesia[3], Vetsuisse Faculty, University of Zurich, Switzerland, Kuros Biosurgery AG, Zurich, Switzerland[4] and Musculoskeletal Research Unit, Equine Department, Vetsuisse Faculty, University of Zurich, Switzerland[5]

Summary

Various treatment methods have been used for the management of subchondral cystic lesions (SCLs) in horses. Filling the defect with parathyroid hormone fragment peptide 1-34 (PTH_{1-34}) in a fibrin matrix represents a relatively new approach that requires further investigation. For this reason fifteen horses with clinical and radiographic evidence of a total of sixteen SCLs (one horse bilaterally affected) were treated surgically with debridement of the cystic contents and injection of PTH_{1-34} in a fibrin hydrogel into the cyst cavity. Objectives of the study were to determine the clinical and radiographic outcome of SCLs treated locally with PTH_{1-34} and to identify factors that may predict outcome. Clinical and radiographic follow-up examinations were carried out at two, four, six and 12 months postoperatively and a telephone inquiry was carried out five to seven years later. The mean age of the horses was 4.9 years. Six SCLs were in the medial condyle of the femur, three in the distal metacarpus, three in the proximal sesamoid bone, two in the first phalanx, one in the patella and one in the calcaneus. Treatment was considered successful in 11 of the 15 cases (73%) because the horses were sound and returned to full work. In the remaining patients, there was improvement in one and no change in three others after treatment. Based on the outcome of this study, PTH_{1-34} in a fibrin matrix administered directly into the cyst after surgical debridement appears to be a promising treatment option for treating SCLs at various anatomic sites in horses.

Keywords: horse / subchondral cystic lesions (SCLs) / surgical curettage / Parathyroid hormone peptide (PTH_{1-34}) / fibrin hydrogel / orthopedics

---

Der Einsatz von Fibrin Hydrogel angereichert mit Parathyroidhormon Peptid (PTH_{1-34}) für die Behandlung von subchondralen Knochenzysten in 15 Pferde

Verschiedene Behandlungsmethoden werden für die Therapie von subchondralen Knochenzysten beim Pferd (SKZ) mit unterschiedlichem Erfolg eingesetzt. In dieser Arbeit werden fünfzehn Pferde mit insgesamt 16 SKZ beschrieben, die mit einem Parathyroidhormon Peptid Fragment 1-34 (PTH_{1-34}) angereichert in einer Fibrin-Hydrogel behandelt wurden. Der Zysteninhalt wurde kürettiert, gespült, getrocknet und anschliessend mit PTH_{1-34} in einem Fibrin-Hydrogel angereichert, gefüllt. Ziel der prospektiven Studie war es, den klinischen und radiologischen Verlauf der SKZ nach der Behandlung mit PTH_{1-34} angereichert im Fibrin-Hydrogel nach 2, 4, 6, 12 und mehr Monaten zu beschreiben. Zudem wurden wichtige Faktoren identifiziert, die für die Prognose von SKZ von Bedeutung sind. Das durchschnittliche Alter der Pferde betrug 4.9 Jahre. Sechs SKZ waren im medialen Femurkondylus, drei im distalen Metakarpus, zwei im lateralen und eine im medialen Gleichbein, eine im proximalen und eine im distalen Fesselbein, eine in der Patella und eine im Kalkaneus. Elf von fünfzehn Pferde (73%) konnten erfolgreich behandelt werden und in ihrer ursprünglichen Aktivität eingesetzt werden. Von den restlichen vier Patienten zeigte ein Pferd eine Besserung der Lahmheit, blieb aber leichtgradig lahm, während bei den übrigen drei Pferden die Lahmheit unverändert blieb. Neben der klinischen Heilung, zeigten viele Pferde auch eine vollständige radiologische Heilung. Die direkte Applikation von PTH_{1-34} in einer Fibrinmatrix in die chirurgisch kürettierte Zystenhöhle scheint aufgrund dieser Resultate eine aussichtsvolle Therapiemöglichkeit von SKZ an verschiedenen anatomischen Stellen beim Pferd zu sein.

Schlüsselwörter: Pferd / subchondrale Knochenzysten (SKZ) / chirurgische Kürettage / Parathyroidhormone Peptid (PTH_{1-34}) / Fibrin Hydrogel / Orthopädie

Introduction

Subchondral cystic lesions (SCLs) are defined as radiolucent areas of bone and they usually contain fibrous connective tissue and serous synovial-like fluid. Depending on their stage of development, SCLs may be well demarcated from the surrounding tissue by a sclerotic rim (*Fürst* et al. 2007). In horses, SCLs occur most commonly in the distal femur, followed by the phalanges (*Sherlock* and *Mair* 2011) including the distal and proximal sesamoid bones, carpal bones, third metacarpal and metatarsal bones, tibia, radius and talus (*von Rechenberg* et al. 1998). The cysts are often found beneath the weight-bearing surface of the joint and most communicate with the joint (*McIlwraith* 1982). Proposed mechanisms for development of SCLs include osteochondrosis (*Trotter* 1981, *McIlwraith* 1982), articular trauma (*Kold* et al. 1986, *Ray* et al. 1996, *Kümmerle* et al. 2008, *Hendrix* et al. 2010), infection (*Garcia-Lopez* and *Kirker-Head* 2004) and osteolytic activity with an increase in the concentrations of inflammatory mediators such as prostaglandin E2 (PGE2) and interleukin-1 (IL-1) and -6 (IL-6) (*von Rechenberg* et al. 2001). Subchondral cystic lesions can be treated conservatively with stall rest, controlled exercise and systemic or intra-articular medications (*Wallis* et al. 2008), which include hyaluronan, corticosteroids, polysulphated glycosaminoglycans and benzopyrones (*Jackson* et al. 2008). Methylprednisolone acetate has been

used successfully for the treatment of unicameral bone cysts in humans (*Scaglietti* et al. 1982), and corticosteroids have been investigated for treatment of SCLs in horses (*Vandekeybus* et al. 1999). In a recent study, injection of corticosteroids into the fibrous tissue lining of SCLs in the medial femoral condyle with the aid of an arthroscope had a success rate of 67%, regardless of the age of the horse (*Wallis* et al. 2008). When conservative treatment fails and the lameness persists, surgical curettage of the cyst is recommended (*Bertone* and *McIlwraith* 1986, *Kold* et al. 1986, *Jackson* et al. 2000, *Story* and *Bramlage* 2004, *Smith* et al. 2005). Surgical management includes debridement of the cyst, followed in some cases by filling of the lesion with cancellous bone grafts (*Jakkson* et al. 2000), chondrocytes and insulin-like growth factor (IGF I) (*Nixon* 2002), tricalcium phosphate granules (*Fürst* et al. 1997), mesenchymal stem cells (*Kraus* and *Kirker-Head* 2006), or multiple osteochondral autografts in the form of a mosaic plasty (*Bodo* et al. 2004, *Janicek* et al. 2010). The results of those treatments vary and the reported success rates range from 64 to 82% in young horses (*White* et al. 1986, Howard et al. 1995). In older horses with an SCL in the medial femoral condyle, the prognosis after surgical debridement is worse than in younger horses (*Smith* et al. 2005).

Parathyroid hormone (PTH) is a peptide hormone secreted by the parathyroid gland and composed of 84 amino acids. The main known function of this hormone is to increase serum concentrations of calcium. When PTH is present in low concentrations, it stimulates new bone formation in the endocortical region (*Dempster* et al. 1993, *Oxlund* et al. 1993). The exact mechanism is not clear, but is thought to be the stimulation of osteoblast proliferation (*Rubin* and *Bilezikian* 2003). In previous experiments, locally applied PTH_{1-34} cross-linked to a hydrogel in a fibrin base induced and enhanced localized new bone formation (*Kemper* 2003). The use of PTH_{1-34} in a fibrin hydrogel to treat an SCL in the proximal phalanx of a warmblood filly led to complete healing without complications (*Fürst* et al. 2007). Two horses with a type Ia fracture of the proximal phalanx and concurrent SCL were treated with internal fixation using lag screws and curettage of the cyst via a transcortical approach, followed by filling of the cavity with PTH_{1-34} in a fibrin hydrogel (*Kümmerle* et al. 2008). Both returned to their previous level of activity (*Kümmerle* et al. 2008).

The purpose of this study was to describe the treatment of a series of SCLs at different anatomic sites using PTH_{1-34} in a fibrin matrix and to investigate factors that may affect the outcome.

Material and methods

Case selection

Horses referred to the Equine Hospital, University of Zurich, Switzerland, from December 2003 to May 2005 because of lameness attributable to an SCL were included in the study. Only horses that had no history of surgical treatment before referral and had follow-up examinations for a minimum of 12 months postoperatively were included. The breed, age and sex of the horse, results of clinical, radiographic and orthopaedic examinations, which included duration and degree of lameness (0-5 scale, *Ross* und *Dyson* 2011), palpation of the affected limb, flexion tests and nerve blocks, and the surgical technique and results of follow-up examinations were recorded.

Radiographic assessment

A minimum of two views of the affected joint and the corresponding contralateral joint were taken at the time of presentation, and two views were obtained immediately after surgery and two, four, six and 12 months postoperatively. All radiographic images were reviewed by the same radiologist (S.O.). The number, density and approximate size of the cyst relative to the limb were evaluated on the radiographs. The density of the cyst relative to the density of the normal surrounding bone was determined subjectively using the following scoring system: low (0-30% of the density of the surrounding bone), mild (31-60% of the density of the surrounding bone), moderate (61-90% of the density of the surrounding bone) and high (density similar to that of the surrounding bone, >90%). The approximate size of the cyst relative to the bone was determined subjectively and the size of cysts was compared in a series of related radiographs (before and after surgery and at the different follow up times).

Surgical technique and aftercare

In six cases, the SCLs were debrided via an extraarticular transosseous approach. A Siremobil Iso-C three-dimensional fluoroscope (Siemens, Medical Solutions, Henkestrasse 127, 81052 Erlangen, Germany) was used to visualise the cysts and monitor the direction of the instruments. First, a 3.2-mm hole was drilled into the cyst, which was then enlarged to 4.5 or 5.5 mm. A decrease in pressure on the drill was felt by the surgeon upon penetration of the cyst, which was confirmed by fluoroscopy. Straight and angled arthroscopic curettes were then used to remove as much of the contents and lining of the cysts as possible. Lavage with sterile lactated Ringer's solution was carried out to remove all remnants of the contents and lining of the cystic cavity. Finally, the two syringes of parathyroid fragment peptide 1-34 (PTH_{1-34}) (Kuros Biosurgery AG, Zurich, Switzerland) in fibrinogen and thrombin were concurrently mixed and injected via the drill hole into the surgically prepared cystic cavity using an 18gauge needle. Clotting of the hydrogel took place within 1 to 3 minutes and was verified by gently tapping the material with a blunt metallic arthroscopic probe through the drill hole.

The remaining ten SCLs were debrided arthroscopically under continuous irrigation with lactated Ringer's solution. After localization of the small opening to the joint (Fig.1a), each SCL was curetted under arthroscopic control until all fibrous, cartilaginous and necrotic bone tissue and the lining of the cavity were removed (Fig.1b). Irrigation was then discontinued and joint expansion was maintained using gas insufflation with carbon dioxide at a pressure of 60-80 mmHg. All fluid including blood was removed. Finally, PTH 1-34 in fibrin was injected as described above (Fig.1c).

Postoperative care included four weeks of stall rest followed by turnout in a small 5-6 x 5-6 meter paddock for four weeks. Access to pasture was not allowed during this time. Hand walking was advised for the following 2 months. The horses were

treated with phenylbutazone (1 mg/kg per os) every 12 hours for the first three days postoperatively followed by the same dose every 24 hours for another ten days. The follow-up examinations, which included a complete lameness examination and radiography of the surgical site, were carried out two, four, six and 12 months after surgery. The same scoring system was used for all evaluations pre- and postoperatively.

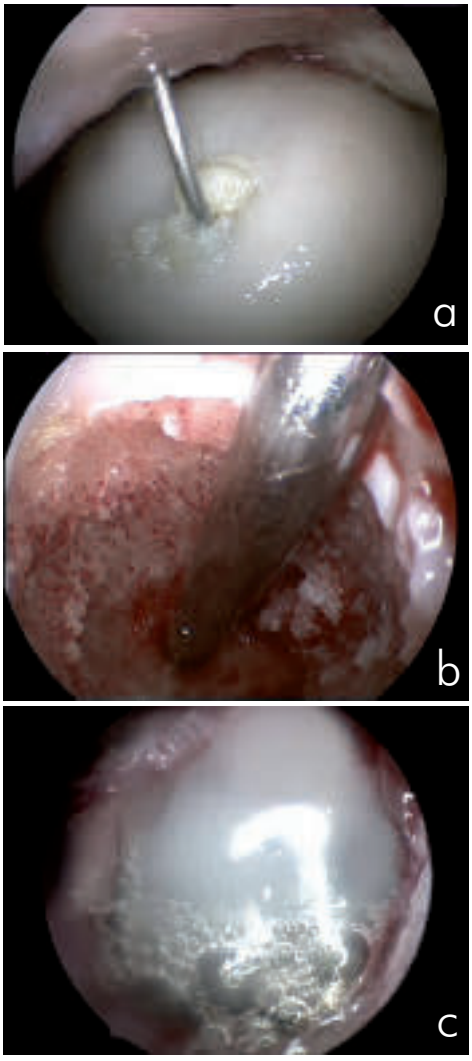

Fig.1a Case 6: Intraoperative view of the small opening of the SCL to the medial femorotibial joint. **b** The cyst cavity after arthroscopic debridement. **c** The cyst has been filled with PTH1-34 in fibrin, and clotting of the hydrogel occurred within 1 to 3 minutes.

Outcome variables

The outcome was considered successful when the horse was sound and able to be used normally in its intended athletic discipline. In all other instances the outcome was considered unsuccessful. A telephone inquiry was performed five to seven years later.

Results

Signalment, results of clinical and radiographic examinations, type of operation, amount of PTH1-34 in fibrin and outcome are summarized in Tables 1 and 2.

Fifteen horses with a total of 16 SCLs (one horse was affected bilaterally) met the inclusion criteria. There were 10 warmblood horses, two arabian horses, one quarter horse, one thoroughbred and one pinto horse. The mean age was 4.9 years (range, 2 months–10 years), and there were nine mares, four geldings and two stallions. The median degree of lameness was 3 (range, 1-5), and cyst density before treatment was low in all the horses. Of the 16 SCLs, six were in the medial condyle of the distal femur (one horse had bilateral lesions), three in the distal metacarpus, three in the proximal sesamoid bones, two in the proximal phalanx, one in the patella and one in the calcaneus.

Radiographs showed communication between the joint and SCL in ten cases and no communication in five (3 SCLs in the proximal sesamoid bones, 1 in the proximal phalanx and 1 in the patella). Most of the SCLs with joint communication were treated arthroscopically, whereas the SCLs without joint communication were treated via an extraarticular transosseous approach. After curettage, 0.2 to 2.5 ml PTH_{1-34} in a fibrin hydrogel was placed into the cavity using a volume that depended on the size of the cyst (Table 1).

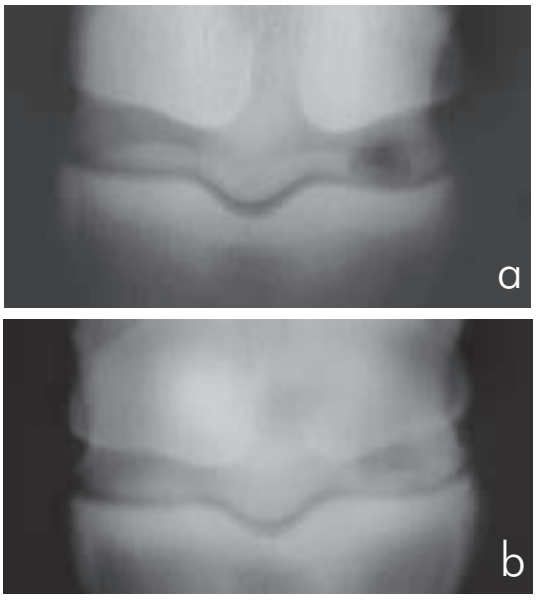

Fig. 2a Case 1: Dorsopalmar radiographic view of an SCL after surgical debridement in the distal third of the metacarpal bone. **b** Dorsopalmar radiographic view of the same SCL shown in (a) 12 months postoperatively, at which time a high cyst density was recorded.

The outcome of treatment was deemed successful in 11 of the 15 horses (73%), which included three SCLs located in the medial condyle of the femur, three in the proximal sesamoid bone, two in the distal metacarpus, one in the first phalanx, one in the patella and one in the calcaneus. These horses returned to their previous level of activity without recurrence of lameness. In all cases with a successful outcome, radiographic density of the cyst content was greater two to six months postoperatively than preoperatively. At 12 months, density of the defect was high in five cases (Figs. 2a and 2b), moderate in another five (Figs. 3a and 3b) and mild in one case. In nine cases the cystic lesion appeared smaller, in one case the size was unchanged and in one it appeared larger. None of the horses with a successful outcome developed

Table 1 Details listing breed, age, location of the 16 SCLs, radiographic findings and surgical approach in 15 horses reported in the study

			Radiographic Findings				
Horse	Signalment	Localization	Lameness grade	Joint communication	Cyst density	Surgical approach	PTH_{1-34} injected (ml)
1	WB, 10 years, mare	Distal third metacarpal bone, right	3	Yes	Low	Articular	1.5
2	WB, 1 year, mare	Proximal aspect of the proximal phalanx, front left	3	No	Low	Extraarticular	1.5
3	Pinto, 3 years, mare	Patella, left	2	No	Low	Extraarticular	1.5
4	TB, 3 years, mare	Proximal sesamoid bone, lateral, front right	2	No	Low	Extraarticular	2
5	WB, 10 years. stallion	Distal aspect of the proximal phalanx, hind right	3	Yes	Low	Extraarticular	1
6	QH, 4 years, mare	Distal medial condyle of the femur right and leftt	3/5 (right)	Yes	Low	Bilateral Articular	Right: 2 Left: 2
7	WB, 3 years, stallion	Distal third metacarpal bone, right	3	Yes	Low	Articular	0.5
8	WB, 3 years, mare	Proximal sesamoid bone, lateral, front left	3	No	Low	Extraarticular	2
9	WB, 3 years, mare	Distal medial condyle femur right	3	Yes	Low	Articular	5
10	Arabian, 10 years, gelding	Distal medial condyle femur right	2	Yes	Low	Articular	2.5
11	WB, 2 months, mare	Distal medial condyle femur right	3	Yes	Low	Articular	4
12	WB, 2 months, gelding	Distal medial condyle femur right	1	Yes	Low	Articular	2
13	Arabian, 5 years, gelding	Distal third metacarpal bone, left	1	Yes	Low	Articular	0.15
14	WB, 9 years, gelding	Calcaneus, right	1	Yes	Low	Articular	1
15	WB, 6 years, mare	Proximal sesamoid bone, medial, hind right	3	No	Low	Extraarticular	1

Table 2 Clinical outcome and radiographic findings at 12 months, and outcome of telephone inquiry five to seven years later in 15 horses

		Radiographic Findings at 12 Months			Five to seven years later
Horse	Outcome	Cyst Density	Cyst Size	OA	Tel inquiry
1	Lame (1/5)	High	Larger	Severe	Pleasure horse
2	Sound	High	Smaller	No	Sound
3	Sound	Moderate	Smaller	No	Sound
4	Sound	High	Smaller	No	Sound
5	Lame (2/5)	Low	Larger	No	Pleasure horse
6	Euthanasia	Right: Low Left: Moderate	Right: Unchanged Left: Larger	Mild	Euthanasia after 1 year
7	Sound	Moderate	Smaller	No	Sound
8	Sound	Moderate	Smaller	No	Sound
9	Sound	Moderate	Smaller	No	Sound for 4 years, then navicular bone fracture hind left, conservative treatment
10	Lame (2/5)	Low	Unchanged	Mild	Lost to follow up
11	Sound	High	Smaller	No	Sound
12	Sound	High	Smaller	No	Sound
13	Sound	Moderate	Smaller	No	Sound
14	Sound	Mild	Smaller	No	Sound for 5 years, then sold
15	Sound	High	Smaller	No	Sound for 4 years, then euthanasia because of colic

osteoarthrosis (OA) of the affected joint. Eight of the 11 horses with a successful outcome horses were ≤ 3 years old.

In one horse (Case 1), the outcome was not considered successful although the lameness improved after treatment. On admission, the horse had a large SCL in the distal third metacarpal bone and OA of the adjacent metacarpophalangeal joint. Twelve months after surgery, the cyst appeared healed radiographically and had a high density. However, the horse remained slightly lame (1/5) and could be used only for pleasure riding. Three horses with a total of four SCLs had an unsuccessful outcome: Case 10 had an SCL in the medial femoral condyle and OA of the stifle joint. Previous treatment consisted of several intraarticular injections of corticosteroids. The horse was still lame after surgical treatment, and radiographically the cyst remained unchanged in size and density. Case 5 had an SCL in the distal aspect of the first phalanx with an associated fissure fracture into the proximal interphalangeal joint. Treatment consisted of internal fixation with lag screws and debridement of the cyst. The horse developed an implant infection, which required removal of the screws after healing of the fissure. After 12 months, the cyst appeared larger radiographically and the horse had a grade 2/5 lameness. The third unsuccessful outcome occurred in Case 6, which had large SCLs in both distal femoral condyles, mild OA of both stifle joints and a grade 3/5 right hind limb lameness. Both cysts were treated during the same surgical intervention. The horse showed initial improvement, but after 12 months still had a grade 3/5 right hind limb lameness, and both SCLs were still clearly visible radiographically. Furthermore, the right femorotibial joint had signs of severe OA. The owner elected to have the horse euthanased.

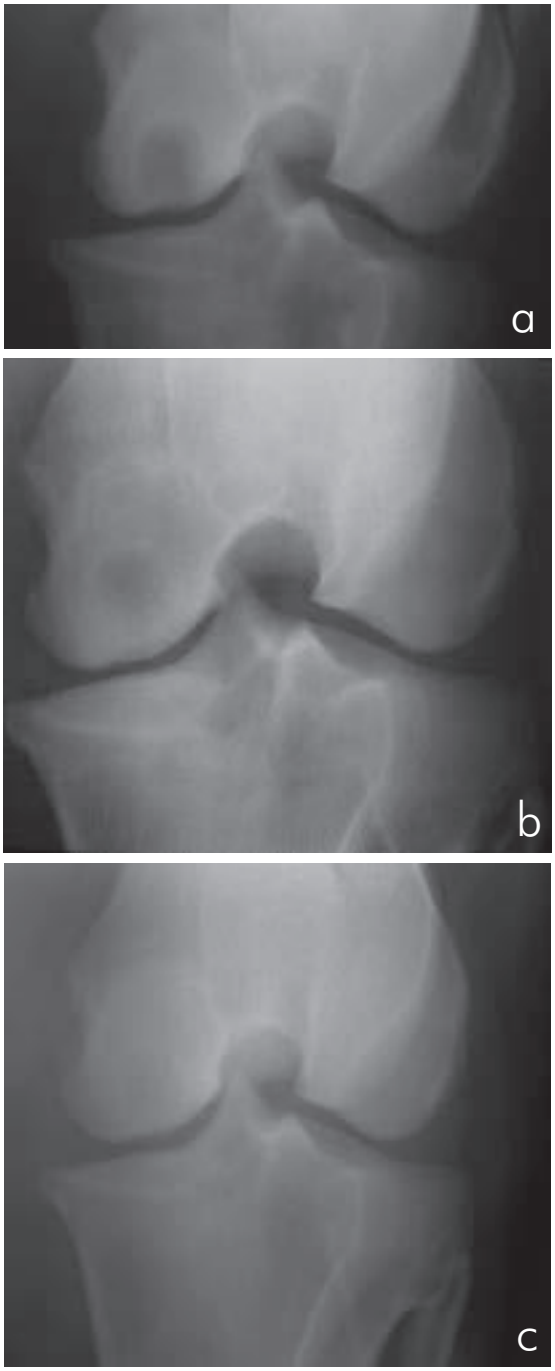

Fig. 3a Case 9: Caudocranial radiographic view of the right femorotibial joint after surgical debridement of an SCL in the medial femoral condyle. **b** The same radiographic view of the femorotibial joint 12 months postoperatively showing moderate cyst density. **c** The same radiographic view 18 months postoperatively showing high cyst density.

Discussion

The treatment of SCLs with PTH_{1-34} in a fibrin hydrogel administered directly into the cyst after surgical curettage was considered successful in 11 of the 16 cysts (69%), with 11 of 15 horses (73%) becoming sound and returning to full work. The use of PTH_{1-34} in a fibrin hydrogel for the treatment of SCLs in the phalanges of three horses has previously been reported (*Fürst* et al. 2007, *Kummerle* et al. 2008). Here we describe a larger series of SCLs at different anatomic locations.

Removal of the fibrous content and lining of the cyst is probably critical to ensure filling of the defect with bone tissue. Residual cystic tissue is considered a contributing factor in recurrence of the lesions because of the production of local inflammatory mediators and matrix-degrading enzymes (*von Rechenberg* et al. 2000). In our patients, debridement of the cysts was achieved using straight and angled arthroscopic curettes via an articular or extraarticular transosseus approach, depending on the location of the cyst. Although arthroscopy is the approach of choice for debridement of bone cysts because it minimises the risk of postoperative complications (*Trotter* and *McIlwraith* 1996), we had a better outcome in patients that had undergone the extraarticular approach, probably because this caused less damage to the articular cartilage covering the cyst (*Fürst* et al. 2007). The disadvantage of the extraarticular approach is that complete removal of the cyst contents cannot be verified.

It has been shown that when administered systemically, intermittently and at lower dosages, PTH induces bone formation, mostly in cancellous bone (*Dempster* et al. 1993). Local treatment with PTH_{1-34} was therefore based on the hypothesis that it induces new bone formation and accelerates bone healing. To achieve this, PTH_{1-34} was incorporated into a hydrogel with a natural base (fibrin), to produce a clot within the cyst cavity, thus filling it. This was expected to facilitate filling of the cyst with bone tissue and prevent compression of synovial fluid against the underlying compromised subchon-

dral bone during weight bearing, which may cause bone resorption and enlargement of the cystic lesions (*Trotter* and *McIlwraith* 1996, *Schmalzried* et al. 1997). In human medicine, hydrogels have been used as carriers of various growth factors (*Cascone* et al. 1995).

Monitoring of healing of the SCLs was based on three variables (cyst density, approximate size of the cyst relative to the limb, degree of lameness) in an attempt to maximise the reliability of the findings of our study. The radiographic healing of SCLs was based on cyst size and cyst density. In all cases with a favourable outcome, there was reduction in the size of the cyst and in 10 of 11 cases the density had increased by 12 months after surgery. Because none of the horses that became sound underwent arthroscopy for a second time, healing of the cartilage could not be assessed directly. However, because all cysts were near a weight-bearing surface of a joint and the horses remained sound for several years after surgery, we assumed that healing of cartilage was good. To assess healing of subchondral cysts objectively, studies that include follow-up arthroscopic examination of the affected joint and histological examination of the tissue filling the defect as well as of the articular cartilage covering the defects are needed.

The most common location of the SCLs in the present study was the medial femoral condyle, and five horses with a total of six SCLs at that location were treated. Three horses less than three years old became sound and two that were older than three years and had radiographic signs of OA in the affected joint before surgery remained lame. This was in general agreement with the findings of *Smith* et al. (2005) who found that horses older than three years have a worse prognosis than younger horses with subchondral cysts.

Three horses had an SCL in the distal metacarpus. Subchondral cysts at these locations occur predominantly in the forelimbs, and are rarely bilateral (*Nixon* 1990). Two horses (3 and 5 years) returned to their intended use and one, which was older then 3 years old and showed OA of the affected joint, remained slightly lame. Similar results had been reported in an earlier study of 15 horses with SCLs of the third metacarpal bone, where 80% became sound after surgery (*Hogan* et al. 1997).

Three horses had SCLs in the proximal sesamoid bones. In our patients, the cysts were debrided via a transosseus approach, and all three horses returned to their intended use. In another study treatment of lesions at the axial aspect of the sesamoid bone allowed four of five horses, all without evidence of sepsis, to return to their previous use (*Dabareiner* et al. 2001). However, in all these cases the cysts were debrided arthroscopically.

The lack of uniformity of our sample of patients with respect to age, history of OA and related treatments and location and size of the cysts is a limitation of the study. Subchondral cystic lesions at different anatomic locations can be expected to differ with respect to clinical manifestation and response to treatment, and this may explain, at least in part, the variation in outcome. However, the presence of OA in the affected joint and the age of the horse (older than 3 years) appeared to influence negatively the healing of SCLs at different anatomic locations. A transosseus approach, which helps to preserve the articular cartilage over the cyst, appears to contribute to a positive outcome.

Conclusions

Despite the limitations of the study, the following conclusions can be drawn from our results. Regardless of anatomic location, the filling of SCLs with PTH_{1-34}-enriched fibrin hydrogel after surgical debridement is a viable treatment that produces clinical and radiographic outcomes comparable to those of other therapeutic methods. The prognosis appears to be favourable when an extraarticular transosseus approach is used, when the affected joint does not present OA and when the patients are not older than three years. Further studies using larger patient samples are needed to substantiate these findings.

Conflict of interest statement

None of the authors of this paper has a financial or personal relationship with other people or organisations that could inappropriately influence or bias the content of this paper.

References

Bertone A. L. and *McIlwraith C. W.* (1986) Subchondral osseous cystic lesions of the elbow of horses: conservative versus surgical treatment. Journal of the American Vet. Med. Assoc. 189, 540-546

Bodo G., Hangody L., Modis L. and *Hurtig M.* (2004) Autologous osteochondral grafting (Mosaic arthroplasty) for treatment of subchondral cystic lesions in the equine stifle and fetlock joints. Vet. Surg. 33, 588-596

Cascone M. G., Sim B. and *Downes S.* (1995) Blends of synthetic and natural polymers as drug delivery systems for growth hormone. Biomaterials 16, 569-574

Dabareiner R. M., Watkins J. P., Carter J. K., Honnas C. M. and *Eastman T.* (2001) Osteitis of the axial border of the proximal sesamoid bones in horses: eight cases (1993-1999). Journal of the American Vet. Med. Assoc. 219, 82-86

Dempster D. W., Cosman F., Parisien M., Shen V. and *Lindsay R.* (1993) Anabolic actions of parathyroid hormone on bone. Endocrine Reviews 14, 690-709

Fürst A. E., Kaegi B., von Rechenberg B. and *Auer J. A.* (1997) Die Behandlung von 5 Pferden mit subchondralen zystoiden Defekten im Fesselbein. Pferdeheilkunde 13, 147-161

Fürst A., Derungs S., von Rechenberg B., Auer J. A., Schense J. and *Watson J.* (2007) Use of a parathyroid hormone (PTH1-34) enriched hydrogel for the treatment of a subchondral cystic lesion in the proximal interphalangeal joint of a warmblood filly: A case report. Journal of the American Vet. Med. Assoc. 54, 107-112

Garcia-Lopez J. M. and *Kirker-Head C. A.* (2004) Occult subchondral osseous cyst-like lesions of the equine tarsocrural joint. Vet. Surg. 33, 557-564

Hendrix S. M., Baxter G. M., McIlwraith C. W., Hendrickson D. A., Goodrich L. R., Frisbie D. D. and *Trotter G. W.* (2012) Concurrent or sequential development of medial meniscal and subchondral cystic lesions within the medial femorotibial joint in horses (1996-2006). Equine Vet. J. 42, 5-9

Hogan P. M., McIlwraith C. W., Honnas C. M., Watkins J. P. and *Bramlage L. R.* (1997) Surgical trteatment of subchondral cystic lesions of the third metacarpal bone results in 15 horses (1986-1994). Equine Vet. J. 29, 477-482

Howard R. D., McIlwraith C. W. and *Trotter G. W.* (1995) Arthroscopic surgery for subchondral cystic lesions of the medial femoral condyle in horses: 41 cases (1988-1991). Journal of the American Vet. Med. Assoc. 206, 842-850

Jackson M. A., Fricker C., Kümmerle J. and *Fürst A.* (2008) Die Behandlung von subchondralen zystoiden Defekten beim Pferd mit Benzopyron: eine retrospektive Analyse. Wien. Tierärztl. Mschr. 95, 158-165

Jackson W. A., Stick J. A., Arnoczky S. P. and *Nickels F. A.* (2000) The effect of compacted cancellous bone grafting on the healing of subchondral bone defects of the medial femoral condyle in horses. Vet. Surg. 29, 8-16

Janicek J. C., Cook J. L., Wilson D. A. and *Ketzner K. M.* (2010) Multiple osteochondral autografts for treatment of a medial trochlear ridge subchondral cystic lesion in the equine tarsus. Vet. Surg. 39, 95-100

Kemper M. (2003) Screeningversuch zur Optimierung synthetischer und fibriner Hydrogele als dreidimensionale Trägersubstanz für Bone Morphogenetic Protein, Transforming Growth Factor Beta und Parathormon zur Beschleunigung der Knochenheilung. Muskuloskeletal Research Unit., diss. University of Zurich, 95

Kold S. E., Hickman J. and *Melsen F.* (1986) An experimental study of the healing process of equine chondral and osteochondral defects. Equine Vet. J. 18, 18-24

Kraus K. H. and *Kirker-Head C.* (2006) Mesenchymal stem cells and bone regeneration. Vet. Surg. 35, 232-242

Kuemmerle J. M., Auer J. A., Rademacher N., Lischer C., Bettschart-Wolfensberger R. and *Fürst A.* (2008) Short incomplete fractures of the proximal phalanx in ten horses not used for racing. Vet. Surg. 37, 193-200

McIlwraith C. W. (1982) Subchondral cystic lesions (osteochondrosis) in the horse. Comp. cont. Educ. pract. Vet. 4, 394-404

Nixon A. J. (1990). Osteochondrosis and Osteochondritis dissecans of the Equine Fetlock. Comp. cont. Educ. pract. Vet. 12, 1463-1475

Nixon A. J. (2002). Arthroscopic Techniques for Cartilage Repair. Clinical Techniques in Equine Practice 1, 257-269

Oxlund H., Ejersted C., Andreassen T. T., Torring O. and *Nilsson M. H.* (1993) Parathyroid hormone (1-34) and (1-84) stimulate cortical bone formation both from periosteum and endosteum. Calcif. Tissue Int. 53, 394-399

Ray C. S., Baxter G. M., McIlwraith C. W., Trotter G. W., Powers B. E., Park R. D. and *Steyn P. F.* (1996) Development of subchondral cystic lesions after articular cartilage and subchondral bone damage in young horses. Equine Vet. J. 28, 225-232

Ross M. W. and *Dyson S. J.* (2011) Diagnosis and Management of Lameness in the Horse, 2nd Edition, W.B. Saunders, Philadelphia, p. 72

Rubin M. R. and *Bilezikian J. P.* (2003) The anabolic effects of parathyroid hormone therapy. Clin. Geriatr. Med. 19, 415-432

Scaglietti O., Marchetti P. G. and *Bartolozzi P.* (1982). Final Results Obtained in the Treatment of Bone Cysts with Methylprednisolone Acetate (Depot-Medrol) and a Discussion of Results Achieved in Other Bone Lesions. Clin. Orthop. 165, 33-42

Schmalzried T. P., Akizuki K. H., Fedenko A. N. and *Mirra J.* (1997) The role of access of joint fluid to bone in periarticular osteolysis. The Journal of Bone Joint Surg. (Am) 79, 447-452

Sherlock C. and *Mair T.* (2011) Osseous cyst-like lesions/ subchondral bone cysts of the phalanges. Equine Vet. Educ. 23, 191-204

Smith M. A., Walmsley J. P, Phillips T. J., Pinchbeck G. L., Booth T. M., Greet T. R. C., Richardson D. W., Ross M. W., Schramme M. C., Singer E. R., Smith R. K. and *Clegg P. D.* (2005) Effect of age at presentation on outcome following arthroscopic debridement of subchondral cystic lesions of the medial femoral condyle: 85 horses (1993-2003). Equine Vet. J. 37, 175-180

Story M. R. and *Bramlage L.* (2004) Arthroscopic debridement of subchondral bone cysts in the distal phalanx of 11 horses (1994-2000). Equine Vet. J. 36, 356-360

Trotter G. W. (1981) Ostochondritis dissecans and subchondral cystic lesions and their relationship to ostochondrosis in the horse. Journal of Equine Vet. Sci. 1, 157-162

Trotter G. W. and *McIlwraith C. W.* (1996) Advances in equine arthroscopy. Vet. Clin. North Am. Equine Pract.12, 261-281

Vandekeybus L., Desbrosse F. and *Perrin N.* (1999) Intralesional long acting corticosteroids as a treatment for subchondral cystic lesions in horses. A retrospective study of 22 cases. In: Proc. of the 8th Annual Scientific Meeting of the European College of Veterinary Surgeons, pp. 33-34

von Rechenberg B., McIlwraith C. W. and *Auer J. A.* (1998) Cystic Bone Lesions in Horses and Humans: A Comparative Review. Vet. Comp. Orthop. Traumatol. 11, 8-18

von Rechenberg B., Guenther H., McIlwraith C. W., Leutenegger C., Frisbie D. D., Akens M. K. and *Auer J. A.* (2000) Fibrous tissue of subchondral cystic lesions in horses produce local mediators and neutral metalloproteinases and cause bone resorption in vitro. Vet. Surg. 29, 420-429

von Rechenberg B., Leutenegger C., Zlinsky K., McIlwraith C. W., Akens M. K. and *Auer J. A.* (2001) Upregulation of mRNA of interleukin-1 and -6 in subchondral cystic lesions of four horses. Equine Vet. J. 33, 143-149

Wallis T. W., Goodrich L. R., McIlwraith C. W., Frisbie D. D., Hendrikkson D. A., Trotter D. A., Baxter G. M. and *Kawcak C. E.* (2008) Arthroscopic injection of corticosteroids into the fibrous tissue of subchondral cystic lesions of the medial femoral condyle in horses: A retrospective study of 52 cases (2001-2006). Equine Vet. J. 40, 461-467

White N. A., McIlwraith C. W. and *Allen D.* (1986) Curettage of subchondral bone cysts in medial femoral condyles of the horses. Equine Vet. J. Suppl. 6, 120-124

Dr. Michelle A. Jackson
Equine Department
Vetsuisse Faculty
University of Zurich
Winterthurerstrasse 260
8057 Zurich
Switzerland
mjackson@vetclinics.uzh.ch