Epithelial inclusion cyst of the equine digital flexor tendon sheath: diagnosis by ultrasonography and magnetic resonance and successful treatment by tenoscopy

Epitheliale inclusiecyste in de sesamschede bij een paard: diagnose met behulp van echografie en magnetische resonantie en succesvolle therapie via tenoscopie

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ABSTRACT

A six-year-old warmblood horse was presented with a longstanding frontlimb lameness with mild digital flexor tenosynovitis and swelling of the distomedial pastern. Ultrasonography and magnetic resonance revealed a dense mass lesion in the distal aspect of the digital flexor tendon sheath, with a partial lamellar architecture, absence of internal vascularization and adjacent smooth pressure osteolysis of the middle phalanx. After surgical excision, histopathology confirmed an epithelial inclusion cyst. Epithelial inclusion cysts, also known as keratinizing or follicular cysts, are expansile benign mass-like lesions of aberrant epidermal tissue. In the horse, they are known to occur in cutaneous and several non-cutaneous tissues. In the digital flexor tendon sheath, they have rarely been described. Given their often chronic presentation in this location, they may appear as an atypical dense mass on imaging, uncommon for cystic lesions. Complete tenoscopic removal, even for larger masses, is achievable and considered curative with good prognosis for return.

SAMENVATTING

Een zesjarige warmbloed werd aangeboden met langdurige voorbeenclaudicatie met milde tenosynovitis van de sesamschede en een zwelling van het distomediale aspect van de kootholte. Via echografie en magnetische resonantie werd een dense massa aangetoond in het distale aspect van de sesamschede, gekenmerkt door een partiële lamellaire vorm, afwezige interne vascularisatie en een aanliggende druk-geïnduceerde osteolyse van het kroonbeen. Na chirurgische excisie werd op het histopathologisch onderzoek een epitheliale inclusiecyste vastgesteld. Epitheliale inclusiecysten, ook bekend als gekeratiniseerde of folliculaire cysten, zijn expansiele, goedaardige massa's ten gevolge van aberrant epidermaal weefsel. Bij het paard komen ze vaak voor in de huid en in verschillende niet-cutane weefsels, maar in de sesamschede werden zij nog maar zelden beschreven. Ten gevolge van hun vaak chronisch voorkomen op deze locatie, kunnen zij zich op medische beeldvorming uiten als een atypisch dense massa, ongewoon voor cysteuze letsels. Volledige tenoscopische excisie is zelfs voor grote massa's mogelijk en wordt als curatief beschouwd met een goede prognose voor herstel.

INTRODUCTION

Epidermal inclusion cysts, also known as epidermoid, keratinizing or follicular cysts, are considered benign, mass-like lesions, originating from aberrant embryological epidermal tissue remnants or faulty epidermal inclusions secondary to trauma (Grant, 2016). They have been found in the skin, eyes, ovaries, esophagus, colon, nasal and paranasal cavities, mandibula, cranium and central nervous system of the horse (Scott et al., 1977; Camus et al., 1996; Hillyer et al., 2003; Peters et al., 2003; Brünott et al., 2007; Mc-

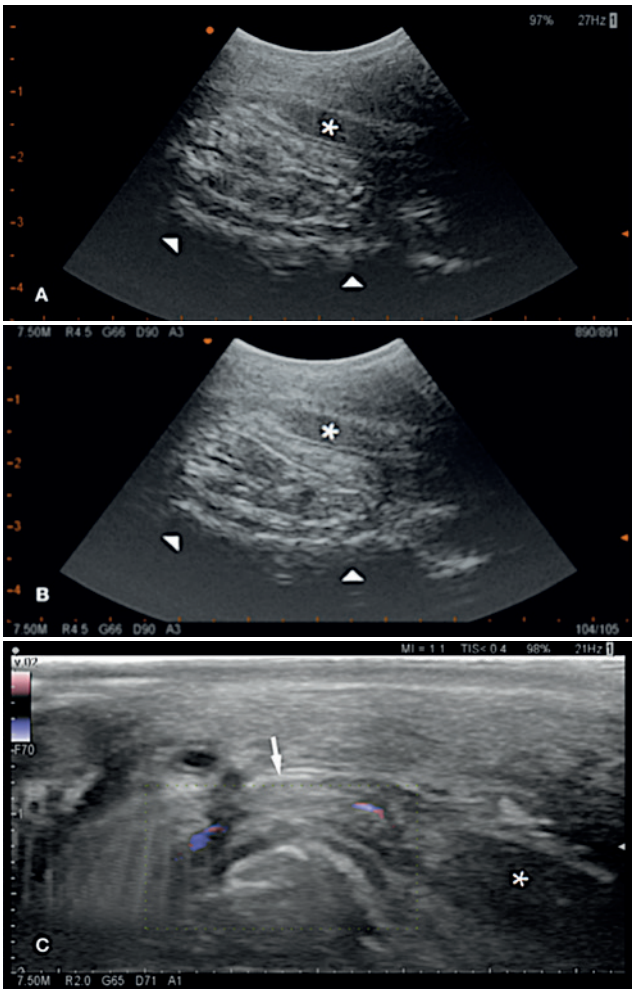

Figure 1. A. and B. Transverse B-mode and C. color Doppler ultrasonographic images of the epithelial inclusion cyst of the digital flexor tendon sheath at the level of the pastern (medial is to the left, asterisk: medial lobe of the deep digital flexor tendon). There is a heterogeneous, mainly dense hyperechoic appearance with multiple hyperechoic reflectors (A), some hypoechoic, ill-defined cavities (B) and only peripheral vascularization (C). Note the smooth concave defect of the middle phalanx, consistent with pressure osteolysis (A-B, arrowheads) and the partial lamellated or target-like appearance (C, arrow).

Gavin and Zachary, 2011; Gunnarsdottir et al., 2014). They are also known to occur in the distal limb, even intraosseously (Headley et al., 2009); in one case report, their presence has been described in the digital flexor tendon sheath (Sanz et al., 2006).

This case report focuses in detail on the appearance of epidermal inclusion cysts on the initial ultrasonographic and magnetic resonance examination, their surgical treatment and follow-up, and the clinical and magnetic resonance findings, in order to facilitate future diagnosis and treatment.

CASE HISTORY AND CLINICAL FINDINGS

A six-year-old warmblood gelding was presented at the clinic for a chronic right frontlimb lameness of a three-year duration. Radiographs taken by field veterinarians, on several occasions prior to presentation, showed no major abnormalities. On general clinical examination, only a mild distension of the digital tendon sheath and a mild, relatively hard, non-painful swelling of the distomedial aspect of the pastern were found. The horse showed a moderate to marked lameness (AAEP grade 3.5-4/5) in the trot on hard and soft surfaces, more pronounced on the inside leg and with a shortening of the caudal phase of the stride. A distal digital nerve block was performed approximately at mid-height of the pastern, abolishing the lameness completely.

DIAGNOSIS

Ultrasonography (Aloka Prosound F75, Hitachi, Ohio, USA) of the palmar pastern, using both microconvex (10-3.75MHz, 20mm radius, 70° field-of-view) and linear (13.3-4.4MHz, 36mm footprint) transducers, revealed a firm, smoothly marginated, mainly hyperechoic, rounded mass lesion (approximately 35mm diameter) between the palmaromedial margin of the middle phalanx and the dorsal border of the medial lobe of the deep digital flexor tendon (Figure 1). Some internal, ill-defined, non-compressible, hypoechoic areas as well as a partially lamellated or target-like appearance were noticed. The distal margin of the mass lesion could not be completely visualized. On color Doppler examination, only mild, peripheral vascularization was found without internal vascularization of the mass itself. No significant changes were seen in the surrounding structures, except for a mild digital flexor tendon sheath distension without major synovial proliferation and a smooth, concave defect in the palmaromedial middle phalanx consistent with secondary pressure osteolysis. The origin of this mass lesion was hard to determine and a subsequent magnetic resonance examination was performed.

On standing low-field magnetic resonance (0.27T, Hallmarq, UK) of the foot and pastern, the mass lesion measured approximately 38x39x20mm and extended the entire palmaromedial margin of the middle phalanx to the proximomedial border of the distal sesamoid bone (Figures 2, 3 and 4). There was a significant mass effect with dorsodistal displacement of the collateral sesamoidean ligament and palmar displacement of the medial lobe of the deep digital flexor tendon and the medial aspect of the distal digital annular ligament. The margins of the mass were rounded, smooth and well-defined. The internal structure showed a heterogeneous, mostly T1-weighted (T1w) hyperintense and T2-weighted (T2w) hypointense signal with some T1w hypointense and T2w hyperintense internal, serpentine striations, as well as one larger, more defined T1w hypointense, T2w hyperintense rounded cavity (10mm diameter). Also on the fluid-sensitive short tau inversion recovery (STIR) sequences, this small cavity showed a hyperintense fluid

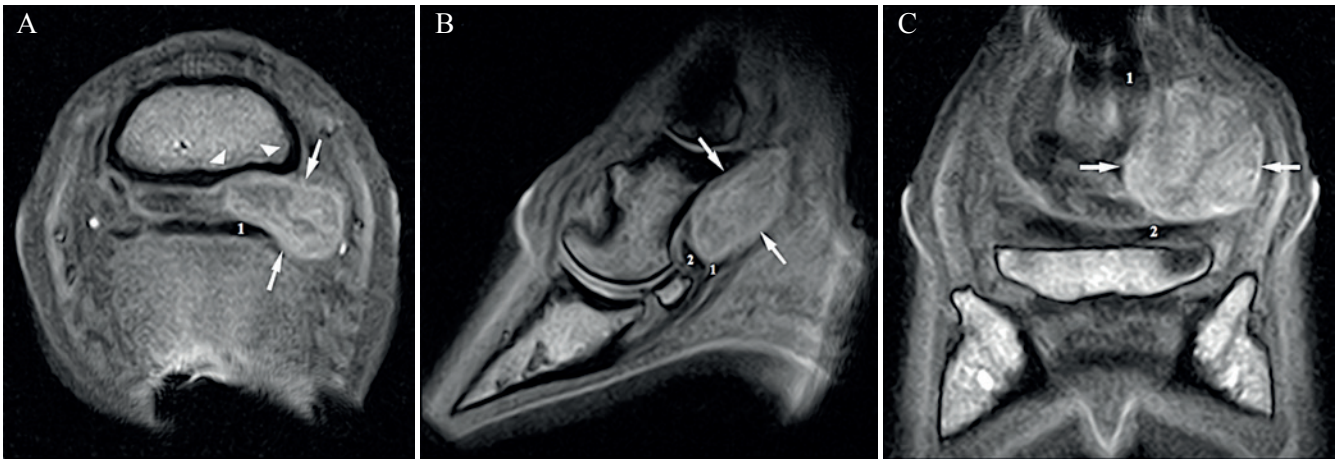

Figure 2. A. T1w GRE 3D HR transverse, B. sagittal and C. frontal MRI images of the epithelial inclusion cyst (A-C, arrows) of the distal aspect of the digital tendon sheath, showing expansile growth with displacement of the adjacent medial lobe of the deep digital flexor tendon (A-C, 1) and collateral sesamoidean ligament (B-C, 2) and pressure osteolysis of the middle phalanx (A, arrowheads).

signal, while the remainder of the mass was predominantely hypointense. On T2*oW sequences, a heterogeneous hyper- to hypointense signal was noted with some discrete striated signal voids, compatible with faint magnetic susceptibility artefacts. Near its proximal margin, the mass lesion showed a partially target-like appearance, with lamellated alternating T1w and T2w hypo- and hyperintense concentric rings. The concave defect in the palmar cortex of the middle phalanx was confirmed, as well as a similar defect in the adjacent fibrocartilage of the distal aspect of the palmar middle scutum. The trabecular bone of the middle phalanx did not show abnormal signal change in any sequence. There was moderate distension of the digital flexor tendon sheath and podotrochlear bursa. The MRI appearance of this expansile non-aggressive mass lesion indicated a mainly dense, fibrous to mildly mucous nature, with a small (proteinaceous) fluid-filled cavity and a partially lamellated or target-like appearance. The origin seemed to be the distomedial recess of the digital flexor tendon sheath, although involvement of the proximomedial recess of the podotrochlear bursa could not be excluded.

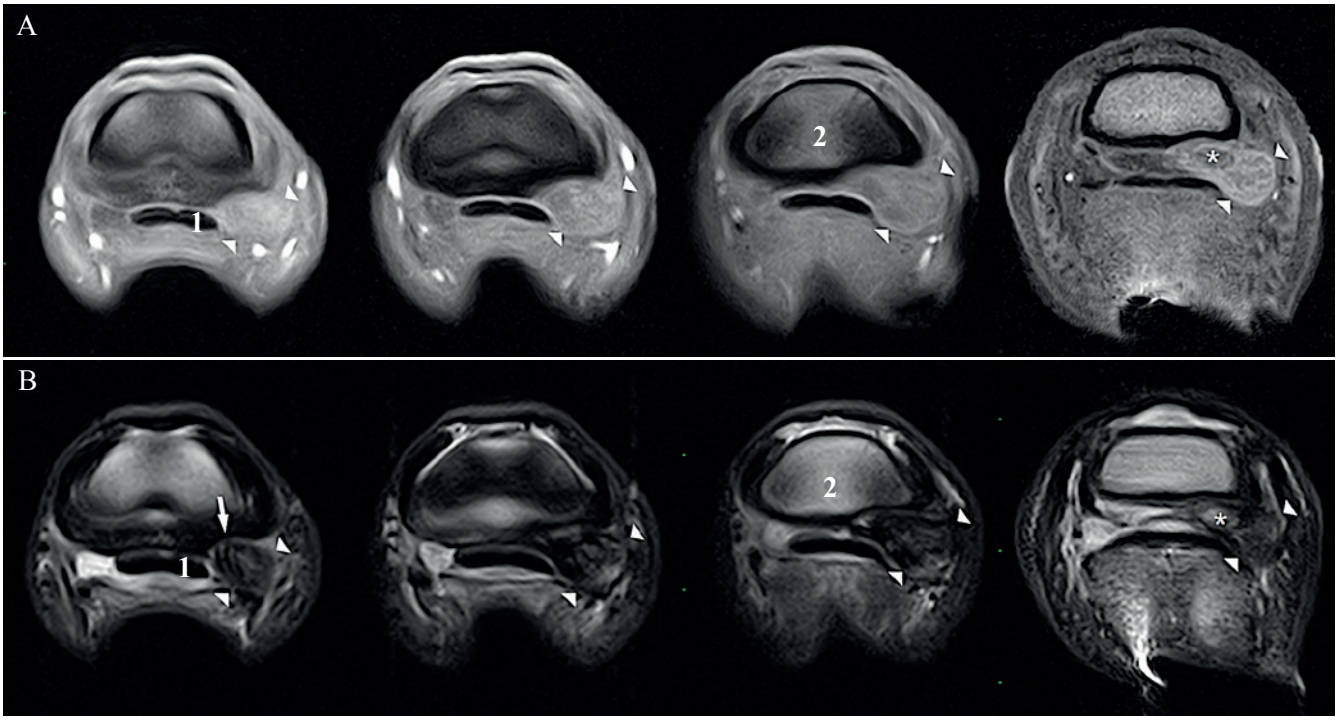

Figure 3. A. T1w GRE 3D/HR and B. T2w FSE subsequent transverse images (left-to-right = proximal-to-distal, medial is to the right) showing the mainly dense appearance of the epithelial inclusion cyst (arrowheads), with a partially lamellated aspect (arrow) and one small T1w hypointense and T2w hyperintense cystic cavity (asterisk). 1 - Medial lobe of the deep digital flexor tendon, 2 - middle phalanx.

TREATMENT AND OUTCOME

Prior to surgery, the horse was premedicated with acepromazine (0.04mg/kg IV, Placivet, Kela, Belgium) and detomidine (20µg/kg IV, Detonervin, Le Vet, the Netherlands). General anesthesia was induced with ketamine (2.2mg/kg IV, Ketamidor, Ecuphar, Belgium) and diazepam (0.08mg/kg IV, Valium 10mg/2ml, NV Roche SA, Belgium) and maintained with isoflurane (IsoFlo, Zoetis, New Jersey, USA) in a constant oxygen flow. The mass lesion was removed through tenoscopy of the digital tendon sheath (McIlwraith et al., 2014a). The mass lesion showed a firm nature, with multiple lamellar layers of thick fibrous material (Figure 5A), as well as some thin peripheral fibrous strands adhering to the surrounding synovial lining and adjacent deep digital flexor paratenon. The collateral sesamoidean ligament was partially opened, to exclude involvement of the proximal recess of the podotrochlear bursa and the palmar recess of the distal interphalangeal joint (McIlwraith et al., 2014b). Complete removal was achieved. No lesions were detected in adjacent structures. After exuberant lavage of the sheath and closure of the skin, a supportive zinc-lined bandage was put in place and the patient recovered uneventfully. After four days, postoperative antibiotics (22.000 IU/kg sodium benzyl-penicillin IV, Penicilline, Kela, Belgium and 6.6mg/kg gentamycin IV,

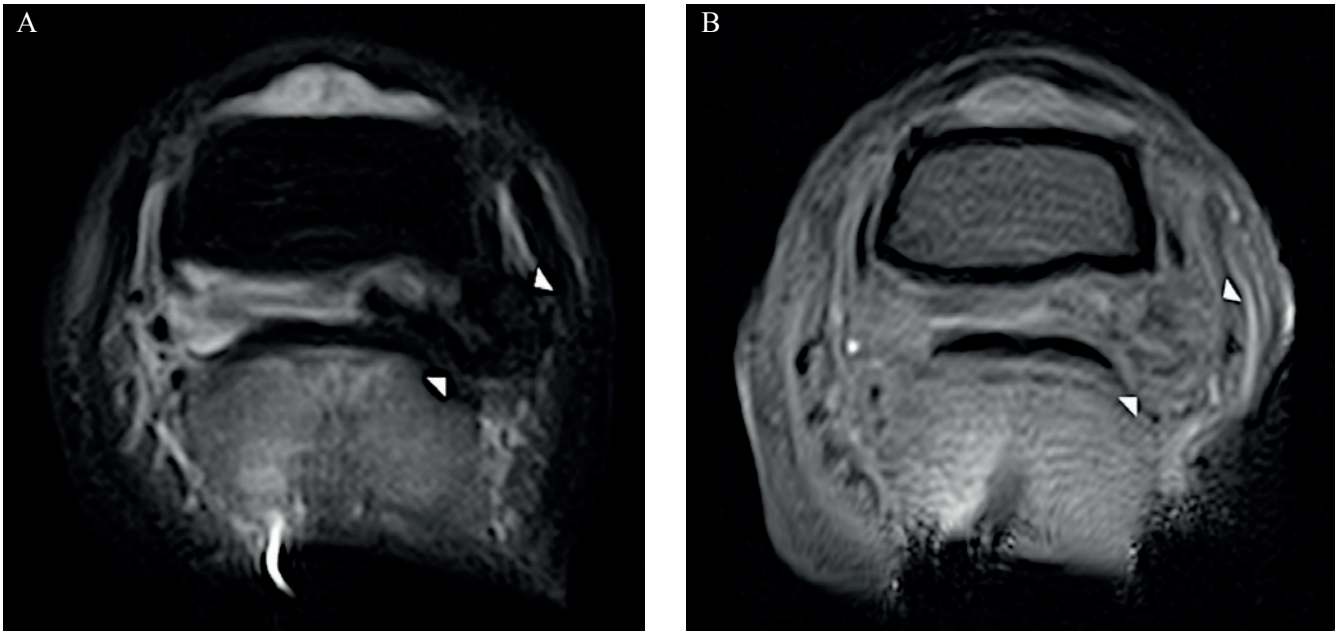

Figure 4. A. STIR FSE and B. T2*oW transverse images showing a heterogeneous, mainly dense appearance of the epithelial inclusion cyst (arrowheads), with only small, ill-defined, fluid signal areas.

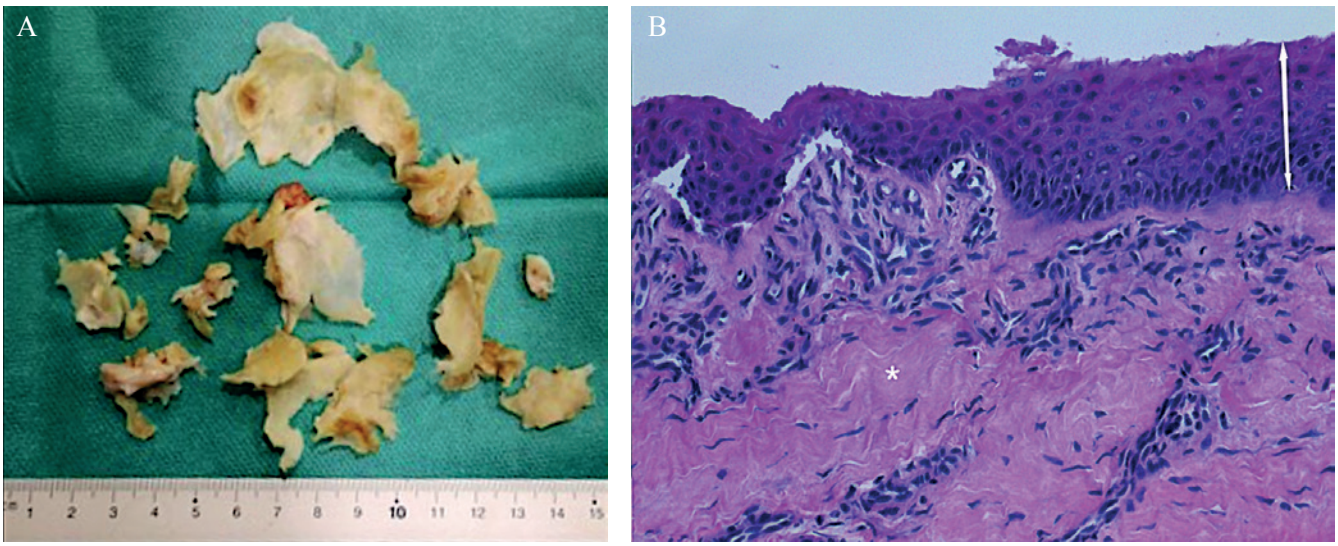

Figure 5. A. Macroscopic and B. microscopic appearance of the epithelial inclusion cyst. A. Note the multiple dense fibrous tissue strands, which were organized and could be peeled off in concentric rings. B. Histopathological examination showed multiple small cavities lined by a well-differentiated stratified keratinized epithelium (double arrow), surrounded by dense, cell-rich, collagenous, connective tissue (asterisk), (HE, 200x).

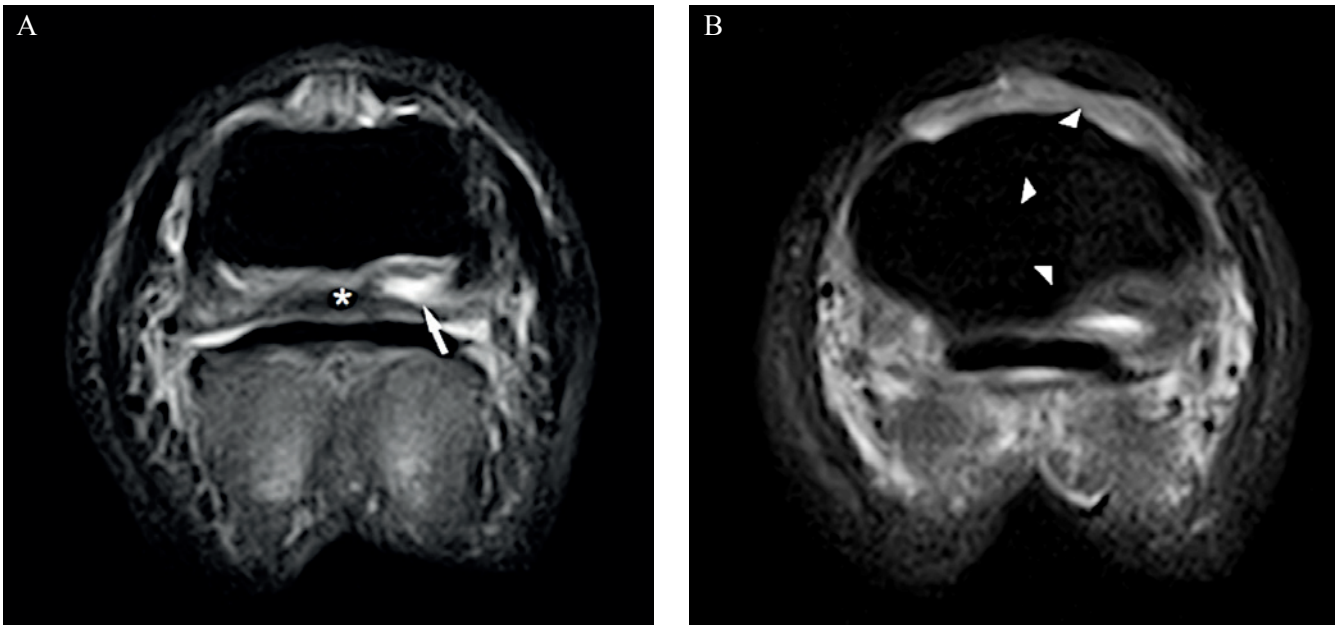

Figure 6. Follow-up STIR FSE transverse images showing complete removal of the mass, with A. realignment of the collateral sesamoidean ligament (asterisk), although a persistent defect to the palmaroproximal recess of the distal interphalangeal joint is still visible (arrow); and B. a faint STIR FSE hyperintensity (arrowheads) of the middle phalangeal trabecular bone, consistent with a mild bone marrow lesion (edema-like).

Gentaveto-5, VMD, Belgium) were stopped and the bandage was removed. The horse walked comfortably and was discharged twelve days postoperatively. A progressive hand-walking regime was put in place for the next four weeks (from five to twenty minutes, once to twice daily), while kept under an oral non-steroidal (4.4mg/kg decreasing to 2.2mg/kg phenylbutazone, Butagran equi, Dopharma, the Netherlands) and steroidal (0.01mg/kg dexamethasone, ex officina preparation), anti-inflammatory, alternating regime. Small paddock turn-out was allowed. Clinical and imaging follow-up was planned eight weeks postoperatively.

Multiple samples were fixed in a standard, 10%-formalin solution for routine histopathology. Histopathological examination revealed several small cystic cavities, lined by a stratified, well-differentiated, keratinized epithelium, in a cell-rich, collagenous, connective tissue surrounding the synovium, consistent with an epithelial inclusion cyst (Figure 5B). Within the cyst wall, there was marked granulation tissue with metaplastic bone formation and a foreign body reaction.

The horse was re-evaluated eight weeks postoperatively. A mild forelimb lameness persisted (AAEP grade 1.5-2/5), particularly on the inside leg in the trot on a hard surface. A mid-pastern digital nerve block was repeated and showed mild improvement. A subsequent digital tendon sheath intrathecal anesthesia abolished lameness completely.

On follow-up standing MRI examination, complete removal of the cyst lesion was confirmed (Figure 6). A persistent moderate distension of the digital tendon sheath without major synovial proliferation was diagnosed. The trabecular bone of the middle phalanx (adjacent to the concave defect) showed a very faint STIR hyperintensity, without obvious signal change in T1w images, compatible with a mild bone marrow or edema-like lesion.

The digital flexor tendon sheath was infiltrated with a combination of triamcinolone acetonide (10mg, Kenacort-A 10, Bristol, the Netherlands) and sodium hyaluronate (40mg, Ostenil 2%, TRB Chemedica, UK). Additionally, a distal regional limb perfusion with tiludronate disodium (1500mg, Tildren, Audevard, France) was performed (using the lateral palmar digital vein at the level of the fetlock) (Hunter et al., 2015). Hand-walking regime and progressive trot work (five to fifteen minutes, once daily) were continued for another four weeks. Twelve weeks postoperatively, the patient showed no persistent lameness in the trot and started normal breaking-in work.

DISCUSSION

Epidermal inclusion cysts are usually described as slow-growing, benign, cyst-like lesions with an outer fibrous wall, lined with squamous epidermal cells, and an internal fluid-filled cavity of cell and keratin debris (Grant, 2016). Most commonly, their appearance on US and MRI is therefore that of a fluid-filled cavity, with a typical hypoechoic or T1w hypointense/T2w hyperintense center bordered by a thin hyperechoic or T1w hyperintense/T2w hypointense outer rim (Shibata et al., 2003; Huang et al., 2011; Kim et al., 2011; Vanhoenacker et al., 2011). In this case however, the epidermal inclusion cyst showed an

atypical dense nature with a mainly echoic or T1w hyperintense/T2w hypointense signal and only small focal areas of typical fluid signal, mimicking a fibrous, partially necrotic or mucous, neoplastic mass. This alternative appearance has previously been described in human medicine, where some chronic cases presented as firm masses (Ben Hamouda et al., 2011; Kim et al., 2011) and is retrospectively in agreement with the MRI appearance in a previously published case report by Sanz et al. (2006). The densification on imaging has been postulated to be mainly due to a more proteinaceous or viscous fluid nature (with shortening of T1w and T2w relaxation times) and to an important deposition of layered keratinized debris (Shibata et al., 2003; Hong et al., 2006; Kim et al., 2011). This layered deposition as reported here, often results in a typical target-like or lamellated appearance (Huang et al., 2011; Kim et al., 2011). In the present case, there were no persistent compressible cavities on ultrasonography. However, such cavities are still frequently present in human epithelial inclusion cysts and often even show a typical swirling pattern when moving the internal debris (Kim et al., 2011). During histopathological examination in the horse of the present case, diffuse areas of dense collagenous granulation tissue with only small cavities were confirmed, and additionally, some metaplastic micromineralizations were found, likely corresponding to the faint (para-)magnetic susceptibility artefacts on T2*oW sequences and adding to the general dense appearance. On color Doppler examination, only a mild perilesional, but no internal vascularization was found; an observation common for epidermal inclusion cysts, but uncommon for neoplastic masses (Huang et al., 2011; Kim et al., 2011). On gadolinium-contrast enhanced MRI sequences, this often corresponds to a peripheral rim enhancement (Shibata et al., 2003; Kim et al., 2011), which was unfortunately not performed in this study, nor was dynamic ultrasound due to anatomical and technical restrictions in the distal pastern; therefore, the mild perilesional adhesions diagnosed during tenoscopy were not foreseen. As epithelial inclusion cysts are usually non-painful lesions (Shibata et al., 2003; Pandya and Radke, 2009), the authors attribute the discomfort and lameness in this case predominately to the size and localization of the mass. To which extent the minor perilesional adhesions might have added to the lameness is unknown. Secondly, as epidermal inclusion cysts are slow-growing and non-aggressive lesions, their appearance in the equine digital flexor tendon sheath on initial presentation may thus more often be of an atypical chronic mass-like nature as described here, in correspondence with the previously published case report by Sanz et al. (2006). Combining the appearance on imaging, the clinical presentation and the patient's age, a neoplastic mass seemed less likely in this case. In human medicine, extra-axial epithelial inclusion cysts are usually attributed to previous trauma, even as minor as local injections (Shibata et al., 2003; Vanhoenacker et al., 2011). In the central nervous system or adjacent axial localizations however, both in human and veterinary medicine, a congenital origin due to aberrant embryogenesis has been suggested (Hillyer et al., 2003; Ben Hamouda et al., 2007; Gunnarsdottir et al., 2014). Brünnott et al. (2007) also found similarities between their colonic epithelial inclusion cyst and a genetic predisposition described in the human Gardner's syndrome (Pandya and Radke, 2009), but the authors did not postulate a definitive relationship. Anamnesis in the present case did not include trauma nor prior injection, although a small puncture wound could easily have been missed. In favor of a congenital origin is the patient's young age. The exact origin of the epithelial inclusion cyst in this case, traumatic or congenital, unfortunately remains unelucidated. Definitive preliminary diagnosis of an epithelial inclusion cyst can be made based on aspiration of the internal fluid and/or fine-needle aspirations, although caution is warranted not to disperse cystic tissue (Pandya and Radke, 2009). As the owner agreed, surgery and a complete excisional biopsy were performed immediately, and complete removal was confirmed on follow-up MRI. Unfortunately, persistent digital tenosynovitis and mild bone marrow (edema-like) lesion of the middle phalanx were also encountered. Although epithelial inclusion cysts do not usually cause an inflammatory response in neighboring tissues, it has been described and even postulated as pathognomonic in ruptured cysts in human medicine (Hong et al., 2006). Histopathological examination in the present case had already confirmed some focal pre-existing areas of foreign body reactions. A similar secondary inflammatory response due to inevitable cyst rupture during tenoscopy likely occurred despite thorough lavage. Intrathecal anti-inflammatory treatment performed early postoperatively, as in the previously published case report (Sanz et al., 2006), might have prevented this. As for the minor bone marrow (edema-like) lesion confined to the medial aspect of the middle phalanx, the authors attributed it to the altered mechanical properties in the bone after removal of the large adjacent mass. The authors decided to perform a regional limb perfusion with tiludronate disodium (Hunter et al., 2015). Although in some studies, beneficial effects in cases of bone contusion have been reported (Kamm et al., 2008; Mizobe et al., 2017), its resolution on MRI was not verified; moreover, the authors are uncertain of its contribution to the clinical improvement. Albeit minor complications in the present case, prognosis for full recovery after complete excision remains good (Sanz et al., 2006; Pandya and Radke, 2009). Finally however, it needs to be stated that even after complete removal of all cystic structures, recurrence up to 3% has been reported in human medicine (Pandya and Radke, 2009).

CONCLUSION

In conclusion, although they are only rarely encountered, epithelial inclusion cysts are an important differential diagnosis for mass-like lesions in the equine digital flexor tendon sheath. Often presented as chronic cases, they might predominately show an atypical firm mass appearance, uncommon for cystic lesions. Non-aggressive, expansile characteristics, absence of internal vascularization on US and a lamellated or target-like appearance on MRI, as described here, may aid in future diagnosis. Complete tenoscopic removal, even for larger distal masses, is achievable, although thorough lavage and early postoperative, anti-inflammatory, intrathecal treatment are advised to avoid secondary inflammation due to inevitable surgical cyst rupture.

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