

Case Report

An atypical case of recurrent cellulitis/lymphangitis in a Dutch Warmblood horse treated by surgical intervention

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Summary

The case reported here describes an atypical presentation of cellulitis/lymphangitis in an 8-year-old Dutch Warmblood mare. The horse was presented with a history of recurrent episodes of cellulitis/lymphangitis and the presence of fluctuating cyst-like lesions on the left hindlimb. These lesions appeared to be interconnected lymphangiectasias. Surgical debridement followed by primary wound closure and local drainage was performed under general anaesthesia. Twelve months post surgery, no recurrence of cellulitis/lymphangitis had occurred and the mare had returned to her former use as a dressage horse.

Introduction

In horses, septic inflammation of subcutaneous tissue and vascular structures leading to insufficient lymphatic drainage and development of chronic lymphoedema is a frustrating condition. A painful and generalised limb swelling due to accumulation of fluid with high protein concentration and subsequent formation of interstitial oedema are the clinical symptoms in the acute phase. After recurrent episodes and as a more long-term effect, fibrotic changes in the affected limbs with persistent limb swelling and limb deformation (elephantiasis) can develop that may lead to loss of functionality of the affected limb with a negative effect on athletic performance (Adam and Southwood 2007; Fjordbakk *et al.* 2008).

The syndrome in horses is generally caused by pastern dermatitis or other small skin lesions that become infected secondarily by *Staphylococcus* spp. and/or *Streptococcus* spp. (Risberg *et al.* 2005; Adam and Southwood 2007; Fjordbakk *et al.* 2008). Whether a primary cellulitis develops with secondary inflammatory response in the lymphatic and/or vascular vessels or the reverse occurs, is often difficult to determine, as the inflammatory response mostly takes place concurrently in both types of tissues (Risberg *et al.* 2005; Adam and Southwood 2007; Fjordbakk *et al.* 2008). Treatment consists of broad spectrum antimicrobials, nonsteroidal anti-inflammatory agents, and ultrasound-guided surgical drainage of fluid accumulations (Fjordbakk *et al.* 2008).

A primary nonseptic disease of the skin and its lymphatic system in the distal limb has been described in draught horses (de Cock *et al.* 2003, 2006; Ferraro 2003; van Brantegem *et al.* 2007). In Shires and Clydesdales, it has been reported that elastin degradation of the lymphatic wall seems to play a central role. A failure of elastic fibres to support the skin and its lymphatics appropriately is

proposed as a possible contributing factor for chronic progressive lymphoedema of the limb in these breeds of horses (de Cock *et al.* 2003, 2006; Ferraro 2003; van Brantegem *et al.* 2007).

Other diseases related to the lymphatic system are lymphangioma/lymphangiosarcoma and development of lymphangiectasia. Cutaneous lymphangioma has been described as a solitary mass on the limb, thigh or inguinal region of horses without the typical signs of progressive lymphoedema (Turk *et al.* 1979; Gehlen and Wohlsein 2000; Junginger *et al.* 2010). Lymphangiectasias in horses have been described in the intestinal wall of foals and horses with clinical signs of colic and diarrhoea (Milne *et al.* 1994; Campbell-Beggs *et al.* 1995). To the authors' knowledge, the occurrence of lymphangiectasias in the limbs of horses, either as a primary developmental disorder or as a secondary feature to progressive lymphoedema due to recurrent attacks of cellulitis/lymphangitis has not been reported before. This report describes the presentation and surgical treatment of an atypical case of recurrent, chronic cellulitis/lymphangitis in the hindlimb of a Dutch Warmblood horse, in which lymphangiectasias had developed during the course of the disease.

Case details

History

An 8-year-old Dutch Warmblood mare used for dressage (545 kg bwt) was admitted to the Veterinary Teaching Hospital of Utrecht University, The Netherlands. The horse had a history of pastern dermatitis and recurrent (at least 4) episodes of the classical form of septic cellulitis/lymphangitis with lymphoedema of the left hindlimb over a period of 4 months. The horse had repeatedly been treated with trimethoprim-sulphadiazine (Sulfatrim¹, 30 mg/kg bwt *per os* b.i.d. for 3–10 days), dexamethasone (Dexadron², 0.055 mg/kg bwt *i.v.*, single dose) and meloxicam (Metacam³, 0.6 mg/kg bwt *per os* s.i.d. for 3–10 days). Each medical therapy episode resulted in a partial resorption of the oedema and reduction of limb swelling, but after the fourth treatment, several 'cyst-like' swellings became apparent that did not disappear with treatment. Six days before admittance, a new episode of cellulitis/lymphangitis had started with a lameness of Grade 1/5 (AAEP scale). The referring veterinarian had started treatment immediately again with trimethoprim-sulfadiazine, as described above, dexamethasone and meloxicam. On admission the horse was still on trimethoprim-sulphadiazine and meloxicam.

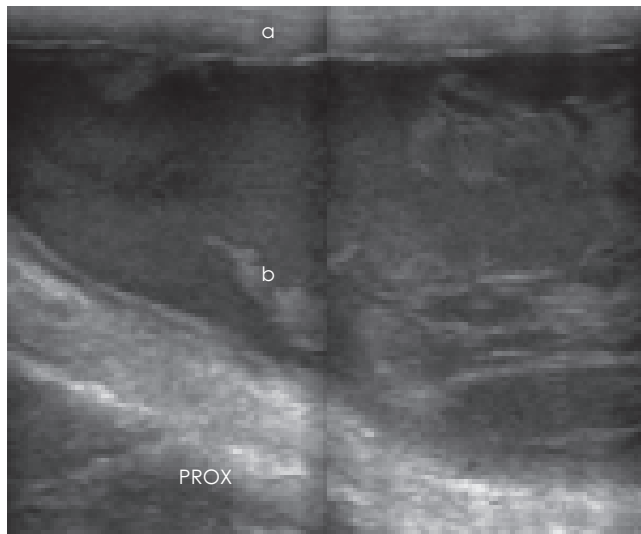


Fig 2: Ultrasonographic appearance of the proximal swelling. It is lined by a thick capsule (a) and filled with fluid interspersed with fibrin-like tissue (b).

Clinical examination

Upon admission to the hospital, the left hindlimb was still oedematous from the pastern up to the tibia. The horse showed a 1/5 lameness of the left hindlimb (AAEP scale) and abducted this limb during locomotion. Physical examination did not yield any significant findings other than changes in the left hindlimb. On the lateral aspect of the limb 4 swellings were visible, 2 at the level of the tarsus and 2 located along the metatarsus (**Fig 1**). On palpation, the swellings were fluctuating, there was no increased temperature of the limb and no pain response could be evoked by firm palpation. There were some scars due to previous episodes of pastern dermatitis but there was no active dermatitis at the time of admission.

Diagnostic imaging

Ultrasonography

Upon ultrasonographic examination, the swellings were found to be filled with fluid interspersed with fibrin-like material. The hyperechoic material in the fluid seemed to settle distally. The 2 proximal cavities contained more hyperechoic fluid and somewhat less fibrinous-like tissue, compared to the 2 distal cavities. There was a clear connection between the 2 proximal cavities but no connection could be discerned between the distal 2 swellings. All 4 swellings were surrounded by a thick capsule (**Fig 2**).

Radiography

Native radiographs of the tarsus and metatarsus did not show any abnormalities other than the soft tissue swelling on the lateral aspect. Contrast radiography was performed by injection of contrast agent (Xenetix⁴, 350 mg/ml, 20 ml) into the proximal cavity. The contrast radiographs showed that all swellings were connected through small ducts (**Fig 3**).

Bacteriology and histopathology

Under ultrasonographic guidance a centesis of the proximal swelling and a punch biopsy of the skin-subcutis-capsule



Fig 1: Presentation of the swellings (marked with an asterisk) at the lateral aspect of the limb, lateral and frontal view. The 2 proximal swellings are clearly visible; the sutures (arrows) are placed over the biopsy site. The 2 distal swellings are smaller than the 2 proximal swellings.



Fig 3: Anterior-posterior radiograph of the left hindlimb. Contrast fluid (marked by asterisks) shows the connection between the cavities.

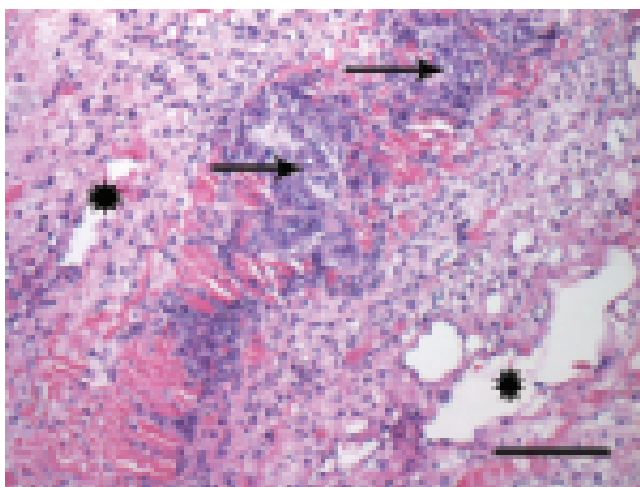


Fig 4: Skin biopsy, deep dermis. Vascular proliferation (arrows) is associated with perivascular infiltration of lymphocytes, plasma cells and histiocytes, and lymphangiectasia (asterisks) embedded in intradermal oedema. Haematoxylin and eosin stain, scale bar 200 μ m.

complex were performed; the latter material was immediately fixed in 10% neutral buffered formalin. The samples were submitted for bacteriological and histopathological examination. Bacterial culture of the fluid was negative. Standard haematoxylin and eosin (HE) stained slides revealed mild chronic dermatitis associated with severe, active, chronic panniculitis (**Fig 4**) in the deepest layers of the biopsy. Extensive lymphangiectasias filled with serum and a perivascular inflammation with granulocytes, lymphocytes and plasma cells were present. Additional Gram, Ziehl-Neelsen and periodic acid Schiff (PAS) staining could not confirm the presence of Gram-positive bacteria, acid-fast bacteria or fungi/parasites respectively.

Diagnosis and presurgical considerations

A chronic cellulitis/lymphangitis with development of lymphangiectasias was diagnosed. The owner opted for treatment, to preserve the horse for dressage purposes. Considering the chronic character and recurrence of the cellulitis/lymphangitis and the lack of response to previous medical treatments, we felt that part of the therapy should focus on the treatment of the lymphangiectasias. The lymphangiectasias were considered a likely contributing factor for the recurrent lymphoedema, although it was the recurrent lymphoedema itself that principally limited the horse for athletic function. In the first instance, we decided to continue medical treatment with NSAIDs (meloxicam 0.6 mg/kg bwt per os s.i.d. for 3 days) and trimethoprim-sulphadiazine (30 mg/kg bwt per os b.i.d. for 2 weeks) as the horse had passed through a recurrence of the lymphoedema just 6 days before and a low-grade infection could possibly still be present despite the negative results from the bacteriological and histological examination, a situation similar to septic synovial cavities (Pille *et al.* 2004; Steel 2008). The treatment with meloxicam was discontinued after 3 days because the horse showed only a subtle lameness and did not show other signs of discomfort at that or on the following days. During the 2 weeks of medical treatment, human literature with regard to treatment modalities of lymphangiectasias was reviewed. Reported procedures include electrodesiccation, laser therapy, sclerotherapy, cryotherapy and surgical excision followed by daily compression through bandaging (Landthaler *et al.* 1990; Ahmed *et al.* 1998; Meisler *et al.* 2003; Fraunfelder 2009). Surgical excision followed by limb bandaging post operatively was deemed a feasible option, but the owner was notified that this case was a very atypical case, and so therefore a well-based prognosis of the proposed surgical intervention could not be given. The owner gave permission to operate on the horse, mentioning that in case of insufficient improvement the horse would have to be subjected to euthanasia.

Surgery

Preoperatively, meloxicam (0.6 mg/kg bwt i.v.) and sodium ampicillin (Ampi-dry⁵, 10 mg/kg bwt i.v.), were administered. The horse was sedated with detomidine (Domosedan⁶, 0.015 mg/kg bwt i.v.) and methadone (Methadon HCl⁷, 0.1 mg/kg bwt i.v.). Induction of general anaesthesia was performed with midazolam (Midazolam⁸, 0.06 mg/kg bwt i.v.) and ketamine (Narketan⁹, 2.4 mg/kg bwt i.v.), and anaesthesia was maintained with isoflurane¹⁰ in 100% oxygen and detomidine constant rate infusion (0.01 mg/kg bwt/h). The horse was positioned in right lateral recumbency. After routine surgical preparation, a proximodistal incision with a length of 8 cm was made through the skin, subcutis and capsule of the proximal swelling, which appeared to be filled with haemorrhagic fluid. The inner lining consisted of endothelium-like tissue, surrounded by chronic interstitial inflammation. The encapsulating tissue was resected as much as possible without damaging the overlying skin and connective tissue. The same procedure was performed with the remaining 3 swellings but with smaller incisions of approximately 3–5 cm. Care was taken not to connect the separate skin incisions by keeping a bridge of intact skin between the incisions. The ducts between the swellings were blindly curetted underneath the intact skin bridges. The connections between the proximal second and the

proximal third and between the proximal third and most distal swelling were only marginal. In the most distal incision a closed suction-drain system (Porto Vac)¹¹ was placed, after which the incisions were closed in 2 or 3 layers. All deep layers were closed with USP 1 polyglactin 910 (Vicryl)¹² in a simple continuous pattern. The skin was closed with interrupted far-near-near-far sutures of USP 1 polydioxanone (PDS)¹². A 3 layer Robert Jones full limb bandage was applied and recovery was uneventful. Tissue samples were fixed in 10% neutral buffered formalin and submitted for histopathology.

Post operative care

At the end of surgery, a single dose of procaine penicillin (Depocilline¹³, 10.5×10^6 iu i.m.) was administered. Oral trimethoprim-sulphadiazine was continued for 2 weeks and the horse received meloxicam *per os* for 12 days at the doses mentioned earlier. Bandage changes were performed on a regular basis. During the first 10 days post operatively, the horse was sensitive at the operation site. Fluid was evacuated from the suction-drain reservoir 4 times a day. The drain was removed on the third day after surgery. The proximal wound showed a fluctuating swelling, indicative of formation of a seroma. The seroma was aspirated on the third and fifth day after surgery and the aspiration fluid was clear and serum-like. Bacteriology of the fluid was negative. Ten days post operatively, the proximal wound started to drain through the sutures, which resolved spontaneously after 7 days without further intervention. The wounds healed by primary intention, after which the skin sutures were removed at Day 14 post surgery. After removal of the bandages 3 weeks post operatively, the limb became oedematous. Hand walking was started at that moment and 4 weeks post operatively most of the oedema had been resorbed again. The horse was discharged with the advice to hand walk the horse for 15 min 2-3 times daily during the first month after discharge. The second month the horse was turned out in a paddock and the third month regular exercise was started.

Histopathology

The results of the histopathological examination were similar to the results of the diagnostic punch biopsy. The HE stained tissue was characterised by very active proliferating fibro-angioblastic tissue with extensive neovascularisation perpendicular to the surface of the cavity, and mild perivascular lymphoplasmacellular infiltration with some neutrophils.

The overall picture was of a granulomatous inflammation with very active proliferative angioblastic tissue.

Follow-up

Five months after surgery, a routine check-up revealed that the horse was sound. Only very marginal swelling was present at the incision sites (Fig 5). One year later the horse was doing well and the owner reported no new episodes of lymphangitis. The horse was sound and returned to its intended use.

Discussion

To our knowledge, the specific changes of chronic ongoing cellulitis/lymphangitis as described in this case have not been reported before. The 4 fluctuating swellings had the aspect of severely dilated lymph vessels surrounded by an active



Fig 5: The left hindlimb 18 months after surgery, oblique and frontal view. Small scars with very marginal swelling at the surgical sites (arrows) are visible.

chronic inflammation. Similar histopathological changes have been described before in cases of chronic lymph stasis (Rockson 2001; de Cock *et al.* 2003) and in cases of lymphangioma (Junginger *et al.* 2010). However, based on the history, clinical signs and follow-up, lymphangioma could be excluded from the list of differential diagnoses in this case and therefore the present findings were interpreted as a case of severe chronic cellulitis/lymphangitis with secondary development of lymphangiectasia.

The dilatations can only have been formed as a consequence of local stasis of lymphatic fluid due to (partial) obstruction of the draining ductules. Partial obstruction of the draining ductules can be caused by direct damage of the wall of these ductules, inflammation of the wall itself, or by compression due to chronic inflammation of the surrounding subcutaneous tissue (cellulitis). Histopathology indicated that both inflammation of the lymphatic duct wall and inflammation of the surrounding subcutaneous tissue (cellulitis) were present and hence probably responsible for the development of lymphangiectasias. In a classical case, ineffective medical treatment of acute lymphangitis will result in diffuse formation of fibrous tissue. It is therefore hypothesised that the atypical presentation in this report may have developed through regional differences in the severity or effects of the inflammatory process in the affected tissues. The cause of these possible regional differences in the inflammatory process could not be determined. Possibly, without surgical intervention and with ongoing repetitive episodes of cellulitis/lymphangitis, this atypical presentation would have evolved further into the ultimate well-known chronic state of elephantiasis.

Surgical intervention is indicated in those cases of lymphangitis in which there is ultrasonographic evidence of cavities filled with (suspected) septic fluid. Treatment then consists of surgical drainage with subsequent wound healing by second intention, combined with medical treatment with antibiotics and NSAIDs (Fjordbakk *et al.* 2008). It is clear that open surgical drainage is the treatment of choice from a general surgical perspective for infected cavities. In our case, however, there was no evidence of a septic process. This theoretically opened the way for surgical intervention followed by primary closure, a more desirable option. However, despite a negative bacterial culture, the persistent presence of very low concentrations of bacteria in the limb could not be excluded and might even be an explanation for the recurrent repetitive episodes of cellulitis/lymphangitis in this horse; we therefore continued antimicrobial therapy for 2 weeks before surgical intervention.

The ultimate reason to decide on surgical therapy was lack of sufficient response to medical intervention, the lymphangiectasia being a likely contributing factor for the recurrent episodes of the lymphoedema, and the wish of the owner to use the horse as a dressage horse. We decided not to remove the swellings with their surrounding tissue 'en bloc' because this would have created such large defects that primary closure would have been impossible. Draining the swellings without removing the endothelial lining also seemed inappropriate, because this might have led to the formation of lymphocutaneous fistulas. Therefore, the approach was taken to incise the lymphangiectasias sharply and to remove the lining of the cavities. Removal of the endothelial lining would prevent continued secretion and lead to elimination of possibly remaining foci of bacterial contamination in the

synovial lining. We decided to leave a bridge of intact skin between the 4 incisions and to curette the connecting ducts blindly under the intact skin bridges to facilitate primary closure and prevent wound dehiscence. In anticipation of possible seroma formation, a closed suction drainage system and pressure bandages were used. These precautions could not completely prevent seroma formation, but the seroma that formed resolved in due course.

In summary, this case report describes an atypical presentation of chronic lymphangitis in the form of development of several lymphangiectasias. Surgical removal of the lining of the cavities and subsequent primary closure after medical antimicrobial and anti-inflammatory treatment and in combination with appropriate post operative care led to full functional recovery.

Authors' declaration of interests

No conflicts of interest have been declared.

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Manufacturers' addresses

- ¹ASTFarma BV, Oudewater, The Netherlands.
- ²Intervet Schering-Plough Animal Health, Wellington, New Zealand.
- ³Boehringer Ingelheim BV, Alkmaar, The Netherlands.
- ⁴Guerbet, Gorinchem, The Netherlands.
- ⁵Dopharma Holding, Raamsdonksveer, The Netherlands.
- ⁶Pfizer Animal Health s.a., Louvain-la-neuve, Belgium.
- ⁷Eurovet Animal Health BV, Bladel, The Netherlands.
- ⁸Sandoz BV, Almere, The Netherlands.
- ⁹Vetoquinol UK Limited, Buckingham, UK.
- ¹⁰Abbott Laboratories Ltd, Maidenhead, Kent, UK.
- ¹¹Howmedica, Toronto, Canada.
- ¹²Ethicon, Johnson & Johnson, Amersfoort, The Netherlands.
- ¹³MSD Animal Health, Intervet, Boxmeer, The Netherlands.

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