HORSES AND OTHER EQUIDS

Arthritis, panuveitis and hyperaesthesia associated with *Borrelia afzelii* infection in a warmblood gelding

Sophia Sommerauer,[1] Klaas-Ole Blohm ,[2] Joachim Spergser,[3] Heinz Hans Florian Buchner[1]

[1]Department for Companion Animals and Horses, Equine Clinic, University of Veterinary Medicine Vienna, Vienna, Austria
[2]Department for Companion Animals and Horses, Ophthalmology Unit, University of Veterinary Medicine Vienna, Vienna, Austria
[3]Institute of Bacteriology, Mycology and Hygiene, University of Veterinary Medicine Vienna, Vienna, Austria

Correspondence to
Dr Sophia Sommerauer; sophia.sommerauer@vetmeduni.ac.at

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SUMMARY

A 13-year-old warmblood gelding presented with a history of lameness, muscle atrophy and weight loss of 3 months. The horse demonstrated extensive hyperaesthesia over the left dorsal trunk, marked effusion of several joints, laryngitis and a dampened mental attitude. Synovial fluid analysis revealed arthritis of the left tarsocrural joint, being PCR-positive for *Borrelia afzelii* DNA. Subsequently, mild anterior uveitis of the right and severe panuveitis of the left eye with *B. afzelii* PCR-positive aqueous and vitreous humour, respectively, were diagnosed. Treatment included arthroscopy of the left tarsocrural joint, oral doxycycline administration for 6 weeks, ophthalmic and systemic anti-inflammatory therapy and left intravitreal preservative-free gentamicin (4 mg) injection. After initial improvement, the gelding's clinical signs deteriorated resulting in peracute recumbency and sudden death 12 months later. Lyme borreliosis should be considered as differential diagnosis in complex cases of equine lameness, particularly when accompanied by hyperaesthesia and bilateral uveitis.

BACKGROUND

Lyme borreliosis is a vector-borne, infectious disease caused by at least three genospecies of the *Borrelia* (*B*) *burgdorferi* sensu-lato (s.l.) complex. Transmission of spirochetes requires a prolonged attachment and feeding (>24 hours) of infected adult ixodid ticks or nymphs. Successful infection may result in direct or haematogenous dissemination of the organism to connective tissue or other organs.[1] While almost all Lyme disease cases in the USA are caused by *B. burgdorferi* sensu stricto, in Europe the genospecies *Borrelia afzelii* and *Borrelia garinii* are additionally involved in cases of equine Lyme borreliosis.[2]

Arthritis and uveitis associated with *B. burgdorferi* infection in horses have been described for over 20 years, but the exact pathogenesis of clinical manifestation is still unknown and clinical signs are often not well documented.[3 4]Serologic studies in north-eastern America revealed an apparent seroprevalence of *B. burgdorferi* s.l. in 45% of horses.[5] Although the seroprevalence in various locations in central Europe were found to be lower, between 16.8% and 29%, respectively, the presence of serum antibodies was never associated with any signs of clinical disease.[6–9] The detection of borrelial organisms in previous case reports was accomplished by a variety of methods such as culture, dark field microscopy or silver staining, immunofluorescence assays and PCR.[6] However, the experimental infection of ponies with *B. burgdorferi* also failed to produce any clinical signs, while the persistence of infection was confirmed for several months.[10] Therefore, it is imperative to distinguish between latent infection and Lyme disease. Consequently, the clinical relevance of Lyme borreliosis in horses remains speculative and controversial in equine practice.

Clinical signs attributed to Lyme disease in horses are highly variable: arthritis, muscle atrophy, hyperaesthesia, laryngeal dysfunction and uveitis have been described.[3] Ataxia and encephalitis are less commonly reported. It was speculated that the more frequent occurrence of neuroborreliosis in Europe compared to the USA is attributed to the different causative *B. burgdorferi* genospecies.[2] In general, pseudolymphoma, neurologic disease and uveitis were found to be the three confirmed disease entities in equine borreliosis.[11] Recommended treatment options include antimicrobial therapy with intravenous tetracycline, oral doxycycline or intramuscular ceftiofur as well as supportive anti-inflammatory therapy.[3]

To the authors' knowledge, all previously reported cases were subjected to euthanasia due to the severity and progression of clinical signs despite treatment. This case of equine Lyme borreliosis was managed and documented over a follow-up period of 12 months.

CASE PRESENTATION

A 13-year-old warmblood gelding presented with a history of lameness, muscle atrophy and weight loss of 3 months duration (figure 1). A serologic analysis (ELISA) targeting *B. burgdorferi* antibodies, requested by the attending veterinarian, was positive at a titre of 1:256, whereas antibody titres>1:12 were deemed positive by the testing laboratory (IDEXX Europa B.V.Hoofddorp, Netherlands). There was no history of injury or arthrocentesis of any joints in the preceding months, after the symptoms had developed.

On initial examination, the gelding had a body condition score of 2/5 based on the Carroll and Huntington system,[12] was of dampened mental attitude and showed reduced appetite with obvious difficulties swallowing. The laryngeal region was very sensitive on palpation. The horse was reluctant to move and showed toe dragging in both hind limbs and a moderate mixed left hind lameness at walk and trot. Extensive hyperaesthesia was present over the left thoracolumbar and sacroiliac regions,

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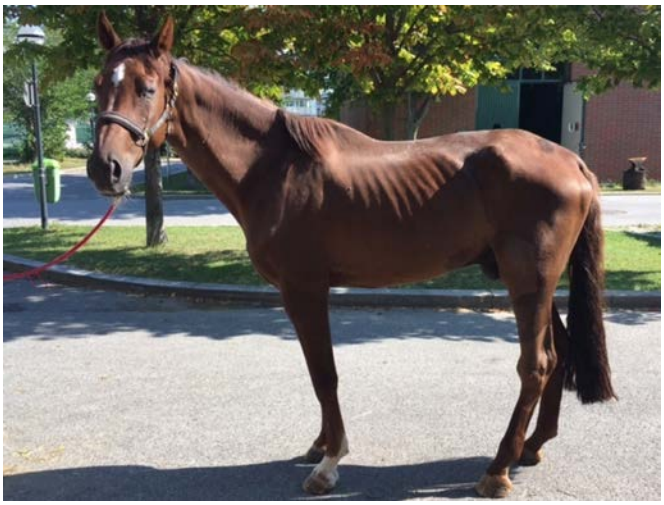

Figure 1 The 13-year-old warmblood gelding presenting with weight-loss and effusion of several joints.

and the coxofemoral joint was extremely painful on palpation. Multiple joints were markedly effused, predominantly both stifle and tarsocrural joints, and left-sided gluteal muscle atrophy was apparent. Furthermore, the horse was slightly weak on tail pulling to the left without other neurological abnormalities at this point.

INVESTIGATIONS

Haematology and blood biochemistry yielded mild leucocytosis (10.09×10^9 cells/L, reference range $5–10\times10^9$ cells/L) with a relative neutrophilia (92%, reference range 45%–70%) and moderately increased serum amyloid A (SAA) levels (556.5 mg/L, reference range <10 mg/L). Upper airway endoscopy and two tissue samples from the arytenoid cartilages and epiglottis revealed a chronic, purulent laryngitis with epithelial hyperplasia. Histopathological evaluation of the tissue samples showed abundant lymphocytes and plasma cells with follicular orientation, and sparse neutrophilic cells. Ultrasonography of the lungs and the abdomen and the rectal examination were within normal limits.

Radiography of both hocks and stifles did not show significant osseous changes. However, ultrasonography of the left tarsocrural joint showed severe capsule thickening and hyperechoic proliferations within the joint. The capsule of the left femoropatellar joint was unremarkable and the synovial fluid appeared homogenously anechoic. Arthrocentesis of both joints was performed and cytology of the left tarsocrural joint revealed a total cell count of 8.1×10^9 cells/L (reference range $<1.5\times10^9$ cells/L) of which 92% were neutrophils and a total protein of 22 g/L (reference range <25 g/L). Although the nucleated cell count was only mildly elevated, the presumptive diagnosis of a chronic septic arthritis of the left tarsocrural joint was made based on the presence of more than 90% neutrophils.[13] Simultaneously to arthrocentesis, 5 mL of 2% mepivacaine (Mepinaest, Gebro Pharma GmbH, Fieberbrunn, Austria) was administered to the left tarsocrural joint and resulted in a 90% improvement of the left hind lameness. While synovial cytology of the left femoropatellar joint was within normal limits, both samples tested positive for *B. burgdorferi* s.l. DNA employing a PCR targeting the gene for the flagellar protein P41. *B. afzelii* was identified and further specified by sequencing the amplicon. Appropriate negative and positive controls were included in all PCR analyses. No bacterial growth was observed after culturing the samples on standard agar plates. Synovial fluid was additionally cultured in BSK-H (commercially available Barbour-Stoenner-Kelly medium, Sigma-Aldrich, Vienna) medium supplemented with 6% rabbit serum (B8291, Sigma-Aldrich, Vienna) incubated at 33°C under microaerobic conditions. The cultures were examined weekly for spirochetes by dark field microscopy. No growth was detected during an incubation period of 8 weeks.

In conclusion, clinical symptoms combined with laboratory testing led to the diagnosis of Lyme borreliosis.

TREATMENT

Arthroscopy of the left tarsocrural joint revealed synovial hyperaemia, villous hypertrophy and cartilage degeneration, consistent with arthritis. The horse was treated with intravenous flunixin meglumine at a dose of 1.1 mg/kg two times per day (Niglumine, Henry Schein Animal Health, Austria) and intramuscular methadone at a dose of 0.1 mg/kg as needed (Methadon, Streuli Pharma AG, Uznach, Switzerland). Based on the *B. afzelii*-positive PCR results, oral doxycycline (Vibramycin, Pfizer, Austria) was administered at a dose of 10 mg/kg two times per day for a total of 6 weeks. The antimicrobial treatment was suspended for 7 days after the first 3 weeks to trigger the activation of bacterial cyst forms, and then continued for another 3 weeks. Additionally, omeprazole (Equinor, Pro Zoon Pharma GmbH, Wels, Austria) was given orally at the gastroprotective dose of 1 mg/kg once daily. This treatment improved the horse's appetite by gradually reducing laryngeal inflammation as dysphagia was attributed to the painful laryngitis and not considered a neurological sign. There was an obvious regression of synovial distension of the tarsocrural joint and with adjunctive physiotherapy the left hind lameness was considerably diminished to an inconsistent, mild degree 3 weeks post-surgery. Hyperaesthesia was no longer present and a repeated synovial fluid sample of the left tarsocrural joint 4 weeks after initial testing was PCR-negative for *B. burgdorferi* s.l.

After 19 days of initiating systemic treatment, left-sided ocular discomfort with seromucoid discharge, blepharospasm, conjunctival hyperaemia and chemosis became apparent (figure 2). Ophthalmic examination revealed deep-stromal perilimbal

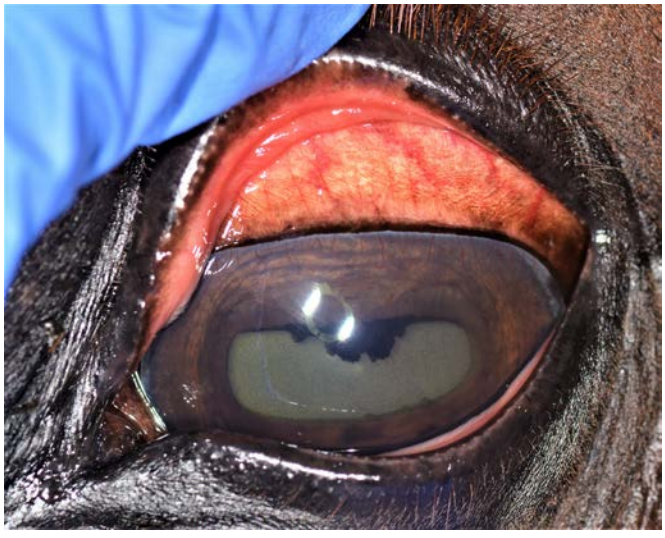

Figure 2 Left eye showing conjunctival hyperaemia and chemosis, deep-stromal perilimbal corneal neovascularisation, miosis and aqueous flare (perceptible in pupillary aperture).

corneal neovascularisation, corneal oedema and keratic precipitates in the left eye (oculus sinister - OS). Additional findings were photophobia, aqueous flare, miosis, vitreal opacification, and a yellow tapetal reflex. The right eye (oculus dexter - OD) showed no obvious signs of discomfort; however, trace flare was identified by slit-lamp biomicroscopy. The intraocular pressure was 14 and 21 mm Hg, respectively, in the left and right eye. Menace response, pupillary, dazzle reflexes and fluorescein staining were bilaterally within normal limits. Direct ophthalmoscopy of OD was unremarkable. These clinical signs were consistent with severe chronic-active panuveitis (OS) and mild acute anterior uveitis (OD).

Aqueous paracentesis was performed, after ocular surface irrigation with 1% dilute iodine and balanced saline solution, in standing sedation facilitated by 10 µg/kg intravenous detomidine hydrochloride (Equidor, Richter Pharma, Wels, Austria) and 1 mL subcutaneous 2% mepivacaine hydrochloride (Mepinaest purum, Gebro Pharma, Fieberbrunn, Austria) injected bilaterally over each auriculopalpebral branch of the facial nerve. The bulbus was stabilised dorsotemporally with a 0.4% oxybuprocaine hydrochloride (Novain, Agepha Pharma, Senec, Slovakia) soaked cotton-tipped applicator and the anterior chamber was entered translimbally with a 12 mm length 30-gauge needle (1 mL insulin syringe; B. Braun, Melsungen, Germany) to aspirate 0.8 mL from each eye. Both samples yielded negative microagglutination tests including *Leptospira* serovars Bratislava, Canicola, Grippotyphosa, Hardjo, Icterohaemorrhagiae, Javanica, Pomona and Pyrogenes. Subsequently performed ELISAs for *Leptospira* serovars Bratislava and Grippotyphosa were negative in both eyes. Bilateral aqueous humour PCR was positive for *B. afzelii* DNA in the right eye, whereas no *B. afzelii* DNA was detected in the left eye. Topical diclofenac-sodium (four times per day: OS; two times per day: OD; Voltaren Ophtha ABAK, Thea Pharma, Vienna, Austria) and atropine hydrochloride 1% eye drops (initially two times per day, then given to effect: OS; custom-made) were added to existing treatment regime which resulted in bilateral decrease in inflammation and resolution of apparent left-sided ocular discomfort.

OUTCOME AND FOLLOW-UP

After 10 weeks of the first presentation, the gelding's clinical appearance had continued to improve with normal demeanour, only mild left hind limb lameness and absent synovial effusions. The SAA concentration was again markedly elevated (994.9 mg/L) without significant clinical manifestation, except moderate, predominantly posterior uveitis OS, which was appreciated better since anterior uveitis had improved. Dorsotemporal pars plana vitreocentesis of the left eye was conducted in standing sedation as mentioned above with additional retrobulbar regional anaesthesia using 8 mL of 2% mepivacaine injected via 0.7×75 mm 22-gauge spinal needle (BD, Eysins, Switzerland). A 1 mL sample of liquified vitreous was obtained with a 0.9×40 mm 20-gauge needle through 2 mL syringe aspiration (B. Braun, Melsungen, Germany). Immediate injection of 0.1 mL preservative-free, gentamicin (Refobacin 40 mg/mL, Merck GmbH, Vienna, Austria) via 1 mL syringe (B. Braun, Melsungen, Germany) was performed utilising the same intravitreal 20-gauge needle consistently angled toward the optic nerve head. Bilateral aqueous paracentesis and unilateral vitreocentesis in the sedated horse were performed by an experienced ophthalmologist without complications. Vitreous humour tested positive for *B. afzelii* DNA (PCR). The residual sample was used for cultivation in modified Kelly-Pettenkofer (MKP) medium without antibiotics at 33°C as described.[14] Weekly, the culture was subcultivated and controlled for growth of *Borrelia* by dark field microscopy for 16 weeks. Although no living spirochetes were detected, the amplicon sequences of *B. afzelii* DNA in both joints and ocular samples were identical. Diffuse cellular infiltrate and fibrin accumulation were discernible in the anterior vitreous by slit-lamp (figure 3) and ultrasound examination (figure 4). Strikingly, these exudative opacities regressed within 24 hours following gentamicin injection. SAA levels declined while features of chronic-inactive posterior uveitis remained

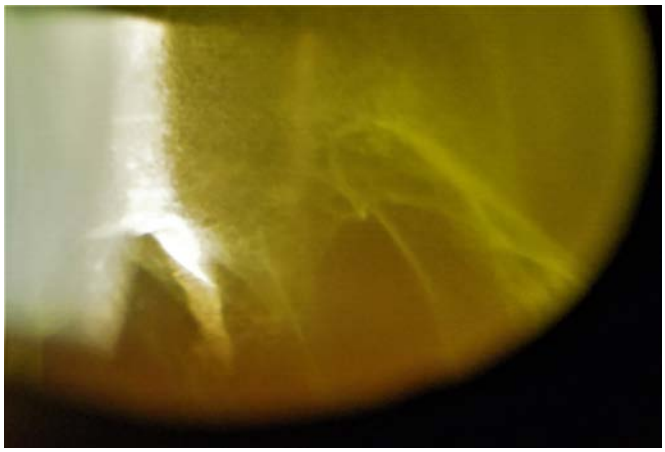

Figure 3 Slit-lamp biomicroscopy of the anterior vitreous in the left eye highlighting retrolental cellular infiltration and fibrin strands extending throughout the degenerated vitreus.

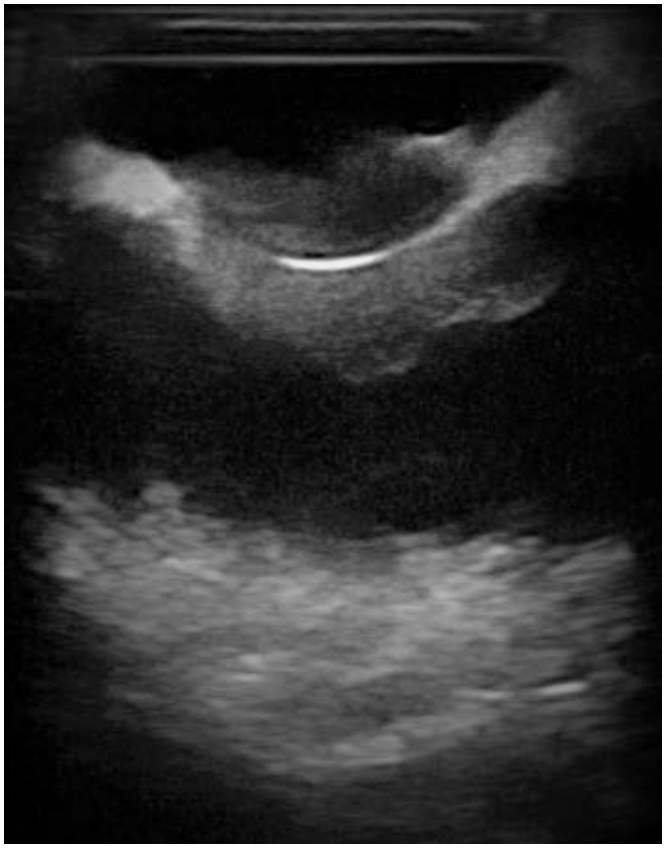

Figure 4 Ocular ultrasound of the left eye demonstrating hyperechoic diffuse cellular infiltration and inflammatory exudate in the anterior vitreous.

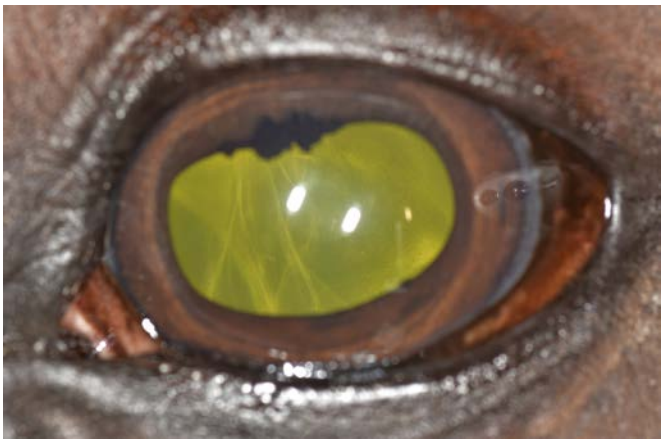

Figure 5 Bright yellow tapetal reflex in the left eye turned to green, consolidated cyclitic membranes persisted without cellular infiltrate and pupil eventually dilated.

(figure 5). Flunixin meglumine and topical atropine were tapered and maintenance therapy with preservative-free diclofenac (two times per day: OS) was prescribed.

Following discharge, the gelding gained weight and training was slowly resumed. Two months after intravitreal treatment, OS topical medications were discontinued and a board-certified ambulatory ophthalmologist (PG) detected no evidence of uveitis, lens or retinal alterations in either eye. After a total time of 5 months signs of right-sided uveitis, laryngeal swelling and mild weight loss reoccurred. As transport could not be arranged by the owner, the gelding was treated by a general practitioner with intramuscular cefquinome injections for 14 days and prednisolone acetate in both eyes. According to the owner, the horse responded well to this treatment. A telephone follow-up 6 months later, however revealed that the gelding had subsequently suffered from behavioural changes, such as ongoing lethargy alternated with excitatory episodes and had recently been found recumbent in an agonal state in the pasture, resulting in the horse's death 12 months after the initial onset of clinical signs. A post-mortem examination was not performed.

DISCUSSION

Equine Lyme disease was consistently associated with lameness and synovial effusion in literature.[4 15 16] This horse was presented with a variety of clinical signs and a recently confirmed seropositivity for *B. burgdorferi* s.l. Numerous serologic tests with varying sensitivities and specificities are available and reference values depend on the designated testing laboratory.[11] In this case, an antibody titre of 1:256 was considered significant, based on the reference value of antibody titres>1:12 being positive (IDEXX Europa B.V.Hoofddorp, Netherlands). Positive serologic testing only indicates the presence of antibodies at the time of sampling and there is no correlation between serologic tests and the level of infection.[11] Additionally, the seropositivity from a single sample cannot constitute a basis for the diagnosis of an active infection as it does not indicate differentiation between past and present exposure. However, *B. afzelii* DNA was detected at several body sites of this horse: the left tarsocrural joint, the left femoropatellar joint, aqueous humour OD and vitreous humour OS.[6] Although *B. afzelii* was detected in synovial structures before, this is, to the authors' knowledge the first case of *Borrelia* induced presumed septic arthritis in a horse.[16] Despite the presence of marked effusion of multiple joints, an increased percentage of neutrophilic granulocytes (92%), suggestive of septic arthritis, was only found in the tarsocrural joint. The ultrasonographic evaluation appeared to have a higher diagnostic value compared with other imaging techniques, such as radiography, to diagnose arthritis.[17]There was no history of injury or synoviocentesis of the affected joint within 3 months prior to initial presentation. While septic arthritis in horses is most commonly a result of penetrating traumatic injuries or iatrogenic following intrasynovial injections, idiopathic synovial sepsis typically also involving one joint has recently been described.[13 18 19] In a case series involving 11 horses, the diagnosis of synovial sepsis was based on an elevated nucleated cell count, total protein and a neutrophil differential percentage of ≥80%, whereas the culture of a causative organism was successful in only 6 patients.[19] In our patient, *B. afzelii* DNA was detected in the tarsocrural joint via PCR analysis although synovial culture yielded a negative result. Based on the synovial fluid analysis and the high percentage of neutrophilic granulocytes, the arthritis was probably septic or immune mediated, but almost certainly related to the detected *Borrelia* DNA. Although synovial sepsis through haematogenous infection has been described,[20] other sources of septic foci such as the pleural and abdominal cavity were ruled out by rectal and ultrasonographic examination. According to those normal findings, abdominal fluid analysis was not indicated. The culture of spirochetes was often unrewarding in previous reports and *B. burgdorferi* has not been reliably cultivated from synovial fluid, even when grown in a specific medium.[3 21 22]

On the one hand, the reported muscle atrophy may be related to the horse's history of left hind lameness for several months; on the other hand, muscle wasting as well as hyperaesthesia may be explained by the reported lymphocytic-histiocytic and plasmacytic inflammation of the deep dermis, muscle and the panniculus during spirochetal invasion.[3] While laryngitis is most commonly a clinical signs of viral or bacterial upper airway infections,[23] it may, in this case, have been a result of borrelial dissemination as the inflammatory tissue showed the same histopathological pattern as previously described during spirochetal invasion. Since the sample did not confirm the presence of spirochetal bacteria, an immune-mediated inflammation appears to be a more likely explanation.

Oral doxycycline was the selected treatment to avoid described side effects associated with intravenous tetracycline therapy.[24] A sufficient response to doxycycline treatment was reported in previous cases until clinical signs reoccurred approximately 2 months later when the horses developed severe neurological signs, presumably due to *B. burgdorferi*-induced meningitis.[25] Even though oral doxycycline is highly efficacious in humans,[26] its bioavailability in horses is significantly lower and so is the distribution into cerebrospinal fluid (CSF) and aqueous humour compared with minocycline.[27] A recent study targeting the in vitro susceptibility of *B. burgdorferi* sensu stricto to different antibiotics suggests the superiority of ceftiofur compared with other commonly used antimicrobials.[27] Evidence of a fourth-generation cephalosporins' superiority is lacking. The decision to initiate the cefquinome therapy when symptoms reoccurred was solely made at the general practitioner's discretion without consultation and was thereby not supported by the authors.

Doxycycline was overall found to be less effective, but treatment efficiency can be increased by twice daily administration.[28]Nevertheless, it is questionable if the initial clinical improvement was attributed to bacteriostatic or anti-inflammatory properties of doxycycline.[29 30] It can be assumed that the improvement of the arthritis as well as the negative PCR results for *B. burgdorferi* s.l. on the tarsocrural joint

4 weeks after the commencement of doxcycycline treatment were facilitated by the performed arthroscopy and mechanical removal of inflammatory pannus.

Bilateral uveitis in the present case was noticed after orthopaedic symptoms and commencement of treatment. In contrast to previously reported advanced manifestations of ocular spirochetal infections,[4 31] this gelding exhibited no recognisable visual impairment or blindness which might have been due to the relatively early assessment of uveitis and subsequent treatment. The consecutive detection of identical *B. afzelii* DNA sequences in the tarsocrural and femoropatellar joint, aqueous and vitreous humour of the right and left eye, respectively, is a unique feature of this case and provides evidence of haematogenous dissemination. However, it remains unknown whether the spirochetes directly caused a primary infectious uveitis or if intraocular penetration occurred secondary to immune-mediated or traumatic blood–ocular barrier breakdown. Non-infectious uveitis accompanied by incidentally positive serology appears generally more likely than ocular borreliosis except concomitant systemic signs attributed to equine Lyme disease are present.[32] A recent study tested aqueous and vitreous humour of eyes with and without typical signs of equine recurrent uveitis (ERU) and overall leptospiral DNA was found in 76%, whereas all eyes were PCR negative for *B. burgdorferi* s.l.[33] In Lyme uveitis, *B. burgdorferi* DNA was detected bilaterally in vitreous samples but not in aqueous humour.[31] This observation is in agreement with the laboratory testing of the more severely affected left eye in our patient. Therefore, false-negative aqueous testing should be taken into consideration and vitreocentesis presumably has superior diagnostic value. Systemic inflammatory disease elevated peripheral blood SAA significantly more compared with different types of keratitis and uveitis.[34] The clinical utility of serum SAA to monitor ocular disease is questionable, whereas local aqueous and vitreous SAA production was suggested in particular with infectious bacterial uveitis.[35] Despite abundant studies, compelling research elucidating the pathophysiology of leptospiral-induced ERU is lacking.[36] In our patient, ocular leptospiral infection was ruled out with almost absolute certainty by bilaterally negative aqueous humour microagglutination and ELISA results.

Doxycycline was undetectable in the aqueous and vitreous humour of healthy equine eyes after repeated oral administration.[37] Blood–ocular barrier breakdown might promote diffusion of the antimicrobial; however, intraocular therapeutic concentration after orally administered doxycycline was considered unlikely.[37] It can be speculated whether achieved doxycycline concentrations in the current case induced an ocular anti-inflammatory effect. Similar considerations hold true for the low-dose intravitreal gentamicin (4 mg) injection, which successfully controlled different stages of inflammation in horses with recurrent or persistent uveitis.[38] In a second case series,[39] potential antibiotic properties addressing leptospiral-induced ERU have been suggested. Recent human research proved high susceptibility of *B. afzelii* to gentamicin.[40] Nevertheless, conclusions for equine intravitreal efficacy should be drawn cautiously and low-dose gentamicin's impact on persistent posterior uveitis and ocular infections in horses warrants further investigation. Beneficial immune-modulative or simply mechanical effects are also conceivable.

When posterior uveitis persisted, vitreocentesis combined with preservative-free low-dose gentamicin injection was chosen as an appropriate and cost-effective treatment option, considering the generally guarded prognosis of the gelding. The peri-injectional suppression of uveitis and a positive outcome in 88.1% of eyes with ERU regardless of the type of inflammation served as justifying evidence.[38] A marked improvement was observed the day after this minimally invasive procedure and left-sided vitritis was absent at the 2-month follow-up ophthalmic exam. Although the specific influence is unknown, a contribution of the gentamicin injection to recovery of ocular immunological homoeostasis is suspected.

The recurrence of clinical signs within a 12-month period suggested the persistence of borrelial infection. Persistent *Borrelia* infections were found in humans as a result of round body cyst and biofilm formation, and immune-mediated synovitis has a reported prevalence of 20%, despite supposedly effective treatment.[1 41] In any case, chronic infections are believed to require a longer treatment duration than early infections and horses may be at greater risk for chronic *B. burgdorferi* s.l. infections because initial infection signs such as erythema migrans or pseudolymphoma often go unnoticed.[27] Even horses in which antimicrobial treatment seems to be successful may remain serologically positive without ongoing clinical signs. It remains to be determined if this phenomenon is caused by persistent infections or continued IgG production against the organism after elimination.[3] A deterioration of clinical signs and the onset of neurological symptoms over a course of 5 months to 4 years have been documented in two horses, ultimately resulting in neuro-borreliosis.[2] Further research elucidated that uveitis may predate the occurrence of neurological signs.[32] The present case resulted in a final state of recumbency and sudden death in the pasture, which is why post-mortem examination was not available. A CSF analysis during initial hospitalisation could have indicated borrelial dissemination to the central nervous system, but was not performed due to the absence of neurological signs at that time. Moreover, CSF examination is often unrewarding because spirochetes rather reside in the dura mater and leptomeninges than float freely.[11] In summary, the potential association between the end stage of this horse and persistence of borrelial infection cannot be determined, presenting a limitation of this case report.

Prevention of equine Lyme disease appears to be vital as the described treatment options do not reveal sustainable success, neither in the current case nor in previous reports.[16 21 25 29] Thereby, the reduction of the vector population is recommended. This can be achieved by appropriate pasture management including cutting the grass shorter, avoiding excessive areas of woodlands and thickets and by removal of leaf litters. However, *B. burgdorferi* s.l. may reside in wildlife reservoirs such as mice and deer which complicates environmental spirochete reduction. Furthermore, chemical tick repellents such as permethrin 'spot-on' products only provide protection for a short period of time in horses.[3 11]

A more novel approach which was already established in dogs is the development of an approved equine Lyme vaccine, protecting horses from *B. burgdorferi* s.l. infection. A recent study describes a sufficient humoral immune response in all vaccinated horses following a *B. burgdorferi* outer surface protein A (OspA) vaccination with minimal adverse effects.[42] Although future studies are indicated to assess the protective nature of OspA vaccines, preliminary results are promising for the development of a strategic equine vaccination protocol.

Further investigations regarding predisposing factors for development of serious equine Lyme disease symptoms, while most horses remain asymptomatic, are warranted. Immunodeficiency, time of infection and geographical conditions are potential contributing factors.[21 25] Infection models additionally

suggest that the severity of disease is rather attributed to a self-perpetuating, autoimmune reaction triggered by spirochetal lipoproteins than to the mere presence of the spirochete itself.[16] This pathophysiology would also apply to the clinical course of systemic, orthopaedic and ophthalmic symptoms in our patient.

In summary, the presented case emphasises consideration of Lyme borreliosis as a differential diagnosis in complex equine lameness cases or horses with neurological abnormalities, particularly when effusion of multiple joints, hyperaesthesia and bilateral uveitis are present. Clinical symptomatic cases of equine Lyme borreliosis tend to have a poor long-term prognosis even with various treatment approaches.

Learning points

- *Borrelia burgdorferi* infection in horses is often asymptomatic.
- Equine Lyme borreliosis should be considered as a differential diagnosis in complex lameness cases or horses with neurological abnormalities, particularly when concurrent uveitis is present.
- Bilateral aqueous paracentesis and unilateral pars plana vitreocentesis for diagnostic purposes were performed by an experienced ophthalmologist in standing sedation without complications. Intravitreal low-dose gentamicin (4 mg) injection to address persistent posterior uveitis and ocular infections in horses merits future research.
- Clinically symptomatic cases of Equine Lyme borreliosis tend to have a poor long-term prognosis.
- Further investigations are needed to determine predisposing factors supporting the development of Lyme disease.

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ORCID iD
Klaas-Ole Blohm http://orcid.org/0000-0002-2475-7740

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