Synovial sepsis of unknown origin in the adult Thoroughbred racehorse

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Keywords: Horse, Haematogenous, Arthritis, Tenosynovitis, Bursitis

Summary word count: 296

Main text word count: 4338

Declarations: None

Authorship: All authors contributed to study design. Data collection, analysis and draft preparation of manuscript was performed by C Byrne. The final manuscript was prepared and approved by all authors.

Sources of funding: None

Competing interests: None

Ethical animal research: No ethical review was performed for this retrospective study of clinical records.

Owner informed consent: Explicit owner consent was not stated for participation in this retrospective review of clinical records.

Acknowledgements: The authors thank Dr A. Begg and Dr K. Todhunter for their assistance in reviewing the microbiological aspects of the study.

Data accessibility statement: N/A due to timescale of original submission.

Masked for review: Line 92 "Randwick Equine Centre"

Summary

Background

Synovial sepsis of unknown origin is a rare cause of lameness in the adult horse and a haematogenous pathogenesis has been proposed in previous cases.

Objectives

To describe the features and outcome of synovial sepsis of unknown origin in adult Thoroughbred racehorses.

Study Design

Retrospective series of cases admitted between 2005 and 2015.

Methods

Hospital records were reviewed to identify adult horses diagnosed with synovial sepsis of unknown origin. Presentation, clinicopathological, microbiological and diagnostic imaging findings were recorded. Treatment methods, surgical findings, complications and long-term outcome were evaluated.

Results

Eleven cases were identified over the study period. Diagnosis was established from clinical examination and clinicopathologic findings, which were comparable to other aetiologies of synovial sepsis. Affected structures included synovial joints, tendon sheaths and bursae. Concurrent osteochondritis dissecans or articular cartilage lesions were evident during arthroscopic surgery in 3 cases. Significant intrasynovial haemorrhage was not identified. Microbial culture of synovial fluid or synovial biopsy was positive in 6/11 of cases, with all isolates being Gram-positive cocci. Of the 6

positive microbial cultures, all isolates demonstrated *in vitro* sensitivity to a cephalosporin antimicrobial agent. A concurrent remote wound was present in a single case. No other potential origins of bacteraemia were identified. Treatment methods included endoscopic surgery, standing multi-needle lavage, intravenous regional limb perfusion, intrasynovial medication and/ or systemic antimicrobial administration. All horses survived to hospital discharge. For the 6/11 cases that raced following synovial sepsis, the median period for return to racing was 221 days.

Main Limitations

A small study population, which was retrospectively reviewed.

Conclusions

Synovial sepsis of unknown origin is rare in the adult Thoroughbred racehorse and can affect a range of synovial structures. A concurrent potential source of bacteraemia is rarely identified. With appropriate management the prognosis to return to racing is fair.

Introduction

Synovial sepsis is a frequently encountered and significant problem in the horse [1,2]. Bacterial inoculation and colonisation of the synovial cavity and the subsequent stimulation of inflammatory and degenerative cytokine mediators can result in substantial irreversible damage to the synovium and articular cartilage [3].

In adult horses the most frequent causes of synovial sepsis are penetrating trauma and iatrogenic contamination by intrasynovial injection or surgical procedures [1,3–11]. Haematogenous localisation of bacteria to multiple synovial structures is common and well documented in foals [5,12,13].

Limited reports of haematogenous synovial infection in adult horses involved the development of synovial sepsis with a concurrent remote focus of microbial infection, which was suspected to have acted as an origin of bacteraemia [14–16]. Synovial sepsis of unknown origin is sporadically identified in adult horses and typically involves a single synovial structure [3]. The designation idiopathic synovial sepsis has been used to describe cases with an unidentified route or causative agent. However, the term synovial sepsis of unknown origin is utilised in this study as it more accurately describes cases with an established synovial microbial isolate but where the route of sepsis is unestablished. When the cause of synovial sepsis is unknown there is reported to be a reduced likelihood of survival [17]. These cases typically present without an obvious origin of bacteraemia, though a haematogenous route is often implicated [1,6,18–22]. There is limited information characterising synovial sepsis of unknown origin in adult Thoroughbred racehorses, including the pathogenesis, treatment and prognosis for future racing. The objectives of this retrospective case series were to describe the presentation, clinicopathological

features, surgical findings, treatment and long-term outcome of synovial sepsis of unknown origin in adult Thoroughbred racehorses.

Materials and Methods

Case Selection/ Inclusion criteria

Medical records were searched retrospectively to identify Thoroughbred racehorses (two-year-olds or older) with synovial sepsis admitted to Randwick Equine Centre over a 10-year period, from 2005 to 2015.

Hospital records of the cases were reviewed to remove cases with known causes of synovial sepsis from the study. Exclusion criteria included historical evidence of a wound to the affected structure, surgery of the affected structure within the previous year, a peri-synovial septic focus and/or synoviocentesis in the 30 days preceding synovial sepsis. A diagnosis of synovial sepsis required synovial fluid analysis demonstrating a nucleated cell count ≥30.0 $x10^9$ cells/L, neutrophil differential percentage ≥80% and total protein (TP) ≥40 g/L or one of these parameters in addition to a positive microbiological culture of synovial fluid or synovial biopsy.

Presentation

Recent exercise history and duration from presentation and referral to diagnosis of synovial sepsis were collated. In addition, data collected included age, gender, affected limb and synovial structure(s). Clinical findings at presentation included rectal temperature, degree of lameness using the AAEP grading scale [23] and the presence, location and degree (subjectively rated as none, mild, moderate or marked) of synovial effusion.

Clinical Pathology

Synovial fluid samples were evaluated for total nucleated cell count, neutrophil differential percentage, red blood cell count, total protein content and presence of bacteria on cytological examination. Synovial fluid or surgical biopsy samples were collected and submitted in Cooked Meat Medium[a] for aerobic and anaerobic microbial culture. When acquired, samples for peripheral blood culture were submitted for aerobic and anaerobic microbial culture. Microorganisms isolated were examined for morphology and Gram stain. Microbial isolates were identified to a species level using a combination of mass spectrometry (VITEK MS)[b], automated (VITEK 2)[b] and manual (API 20 Strep)[b] biochemical methods as required. Any samples with a positive microbial culture were submitted for antimicrobial susceptibility testing. Haematological and biochemical parameters assessed on venous blood samples included the white cell count, neutrophil differential percentage, total serum protein content and fibrinogen.

Diagnostic Imaging

Radiographic, ultrasonographic and scintigraphic findings of the affected regions were reviewed and classified as either related to synovial sepsis or from a different primary disease process.

Treatment

Pre-referral treatments were noted. Any procedures undertaken prior to admission were recorded including synoviocentesis, intrasynovial antimicrobial medication and standing multi-needle lavage.

Hospital treatment was categorised as arthroscopic, tenoscopic or bursoscopic surgery under general anaesthesia, standing multi-needle lavage, intravenous regional limb perfusion (IVRLP), intrasynovial antimicrobial administration or other.

For each case the frequency of the procedure was recorded and where relevant, the antimicrobial agent utilised was recorded. The duration of treatment was documented for each systemic antimicrobial utilised. Complications occurring during hospitalisation were also documented.

Outcome

Short term outcomes included the duration of hospitalisation, survival to hospital discharge, treatment recommendations after discharge and hospital re-admissions related to synovial sepsis. Long term outcome was determined by review of medical and race records (Racing NSW: www.racingnsw.com.au). Follow-up was performed until October 2017, when all horses completed their racing careers. All horses had a follow up period of at least 2 years following hospital admission. Outcome data collected included number of starts, placings and earnings for each case after the episode of synovial sepsis. The time from hospital admission to return to racing was recorded. The racing careers of horses exported from Australia were followed until exportation.

Where available, dates and reasons for retirement from racing or euthanasia were recorded from medical or Stud Book (Australian Stud Book: www.studbook.org.au) records. Reasons were classified as either lameness related to the synovial sepsis of unknown origin, lameness unrelated to synovial sepsis, other medical or musculoskeletal conditions or retirement to breeding. Where relevant, the date of euthanasia was recorded.

Data Analysis

The relevant clinical, racing and Stud Book data were compiled into a database (Microsoft Office Excel 2016)[c]. The data were assembled into frequency tables,

evaluated graphically and descriptive statistical analysis was performed. Where appropriate, clinical and clinicopathological data were grouped relative to defined normal reference ranges and assembled into frequency tables. For ordinal and discrete numerical data, analysis included calculation of the median and range. Analysis of continuous data included calculation of the median, mean and range. Where distribution of data resulted in similar values for measures of central tendency, only the mean was reported.

Results

Presentation

Eleven adult Thoroughbred horses were diagnosed with synovial sepsis of unknown origin from 2005 to 2015. The median age at presentation was 2 years (range 2-6 years). There were 5 fillies/mares, 2 colts/stallions and 4 geldings. At the time of presentation 7/11 horses were unraced. A forelimb was involved in 4/11 and hindlimb in 7/11 cases. A summary of case details is presented in Table 1.

The femoropatellar joint accounted for 3/11 cases and the digital flexor tendon sheath and metacarpo/metatarsophalangeal joint accounted for 2 cases each. The remaining 4 cases involved the antebrachiocarpal joint, tarsocrural joint, bicipital bursa and tarsal sheath. A lameness grade was not available for 1 horse, though all other cases demonstrated a grade 3/5 or greater lameness during at least one examination. The median lameness grade at initial presentation was grade 4/5 (range 0-5/5). Rectal temperature was recorded in all horses during at least one initial examination. At presentation the mean rectal temperature was 38.7 ^{o}C (range 37.8 to 40.4^{o}C). Pyrexia was identified in 7/11 cases (rectal temperature >38.5^{o}C). Degree of synovial effusion was recorded in 9 cases, ranging from no effusion to

marked effusion, with 8/9 horses having moderate or marked effusion at presentation.

A diagnosis of synovial sepsis was achieved prior to referral in 2/11 cases. The mean duration from presentation to diagnosis was 2 days (median 1 day, range 1-4 days). No horses had a history of synoviocentesis or medication of the affected synovial structure prior to presentation. Case 5 presented as a 2-year-old and had yearling sale radiological records indicative of previous surgery of the affected femoropatellar joint but no other horses had historical evidence of surgery of the affected synovial structure. A single case had clinical signs of a potential concurrent remote site of infection with a wound on the ipsilateral hoof coronary band. At the time of presentation 9/11 horses were in training or pre-training, with 1 horse undergoing paddock rest and the status not reported in a single case. Four horses had performed trot/canter work in the previous 24 hours and 1 horse had not worked for the preceding 48 hours. In the remaining cases details of recent exercise was not available.

Clinical Pathology

In all cases synoviocentesis and synovial fluid analysis was performed on the affected structures. Arthrocentesis was performed in multiple stifle compartments in case 1 (femoropatellar and lateral femorotibial joints) and case 5 (femoropatellar, medial femorotibial and lateral femorotibial joints). In these cases, the synovial compartment with the greatest elevation of synovial parameters was included in further analysis. Synovial fluid analysis findings are presented in Table 1. The mean nucleated cell count was 82.0 $x10^9$ cells/L (median 71.0 $x10^9$ cells/L and range of 12.4- 166.0 $x10^9$ cells/L). Neutrophil differential percentage was performed in all

cases with a mean of 90% (median 94% and range of 80-96%). Total protein content was evaluated in all samples, with a mean of 48 g/L (range of 39-60 g/L). One sample was noted as grossly haemorrhagic. A red blood cell count was performed in 9 cases, with a mean of 0.04 $x10^{12}$ cells/L (range 0 – 0.08 $x10^{12}$ cells/L).

Gram stain cytology was performed in 10/11 cases. Gram-positive cocci were identified in a single sample, however, in the remaining preparations no micro-organisms were observed. Aerobic culture was positive in 6/11 cases. All isolates were Gram-positive cocci with antimicrobial susceptibility patterns shown in Table 2. Three horses received antimicrobial therapy prior to referral and in 2/3 cases synovial fluid culture was positive. A synovial tissue sample was submitted for microbiological culture in a single case but no growth occurred.

Haematology and biochemistry were performed in 9/11 cases. The white blood cell count was elevated (>10 $x10^{9}$ cells/L, lab reference range 6 - 10 $x10^{9}$ cells/L) in 5/9 cases with a mean count of 11.0 $x10^{9}$ cells/L (range 5.9-16.6 $x10^{9}$ cells/L). The mean total plasma protein was 68 g/L with a range of 63-74 g/L (lab reference range 57-70 g/L). In 10 cases the neutrophil percentage and fibrinogen were also recorded, with means of 74% (range 52-84% and lab reference range 48-68%) and 4 g/L (range 3-5 g/L and lab reference range 0-4 g/L), respectively. Venous blood culture was performed in one case, which was negative.

Diagnostic Imaging

Radiography of the affected region was performed in all cases. Pathology was identified in 3/11 cases. In case 6 markedly increased soft tissue opacity surrounding the affected metacarpophalangeal joint was suspected to be secondary to synovial sepsis. In cases 5 and 7 osteochondritis dissecans lesions were categorised as pre-

existing intra-articular radiographic abnormalities. Case 7 had a large, previously operated osteochondritis dissecans lesion on the lateral trochlear ridge of the femur with a small osteochondrosis lesion on the medial trochlear ridge. A small osteochondral fragment was evident on the craniolateral aspect of the femoropatellar joint.

Ultrasonography was performed in 5/11 cases, with findings attributable to synovial sepsis identified in all ultrasonographic studies [24]. In 3 studies, hyperechoic material consistent with fibrin or pannus formation was identified within the synovial structure. Case 6 demonstrated a grade 4/4 (scale adapted from [25]) lateral suspensory branch core lesion, which extended peripherally and to the distal insertion of the branch with a small, non-articular abaxial avulsion fragment from the lateral proximal sesamoid bone. Scintigraphy was performed in case 9, demonstrating mild generalised increased radiopharmaceutical uptake of the cranioproximal humerus during the bone phase, with ultrasonography revealing effusion of the bicipital bursa and an irregular synovial margin overlying the thecal surface of the proximal tendon of the *biceps brachii* muscle.

Treatment

Six cases received treatment prior to hospital referral, which included systemic (3 cases) and intrasynovial (2 cases) antimicrobial therapy. Case 10 underwent standing multi-needle lavage of the affected tarsocrural joint. Non-steroidal anti-inflammatory therapy was administered prior to referral in 5 cases. Further anti-inflammatory therapies pre-referral included topical dimethyl sulfoxide (case 8) and intravenous dexamethasone (case 9).

Treatment methods and procedures are summarised in Supplementary Item 1. Arthroscopic, tenoscopic or bursoscopic surgery included lavage of the affected synovial structure performed under general anaesthesia in 9/11 cases. Intrasynovial fibrin or pannus formation was noted in 8/9 surgical cases. Evidence of traumatic synovial puncture or foreign material was not evident in any case. Intrasynovial lesions identified during endoscopic surgery include osteochondrosis lesions and articular cartilage wear lines. Further details of endoscopic surgery findings are outlined in Supplementary Item 2. At the end of all procedures, synovial structures were medicated with an antimicrobial medication.

A standing multi-needle lavage was performed in 6/11 cases. In 4 cases this was performed in addition to arthroscopic or tenoscopic lavage. Two cases were treated with 3 sequential multi-needle lavages multi-needle lavage without undergoing endoscopic surgery. At the end of each procedure the synovial structure was medicated with an aminoglycoside antimicrobial agent. Antimicrobial IVRLP was performed using ceftriaxone (1g)[d] in 3/11 cases. Intrasynovial antimicrobial medication (performed on a separate occasion to other procedures) was undertaken in 7/11 horses, with a median of 3 treatments (range 1 to 5).

All cases received systemic antimicrobial therapy, with a mean duration of 17 days (range 9-34 days). Procaine penicillin G (22 000 iu/kg bwt i.m. q12h, Propercillin)[e] and gentamicin sulphate (6.6 mg/kg bwt i.v. q24h, Gentam)[e] were used in 10 horses. A single case was treated with ceftiofur (4 mg/kg bwt i.v. q12h, Accent)[f] and gentamicin (6.6 mg/kg bwt i.v. q24h,Gentam)[e]. Six horses were treated with a course of trimethoprim potentiated sulfadimidine (30 mg/kg bwt p.o. q12h, Sulprim)[e] after the primary parenteral antimicrobial agents were discontinued. The decision to continue antimicrobial therapy was based on clinical progression following treatment,

277 which included sequential synoviocentesis and synovial fluid analysis in some cases.
278 Phenylbutazone was administered on a decreasing regime determined by clinician
279 assessment of clinical progression, with a mean duration of 9 days (median 4 days
280 and range 1 -37 days).

281 Complications occurred during hospitalisation of 3 cases, including jugular
282 thrombophlebitis, a procaine penicillin hyperexcitability reaction and a foot abscess
283 (in a different limb to the primary synovial sepsis).

284 Outcome

285 All horses were discharged from the hospital, with a mean hospitalisation period of
286 13 days (range 5-17 days). Three horses developed recurrent sepsis of the affected
287 synovial structure and a further case developed sepsis of other synovial structures.
288 Case 9 was re-admitted 29 days after discharge with recurrence of right forelimb
289 lameness. Further investigation included scintigraphy which demonstrated increased
290 radiopharmaceutical uptake in the intermediate tubercle of the right humerus during
291 the bone phase, which was suspected to represent persistence of local infection. A
292 course of systemic antimicrobials was administered based on previous culture and
293 susceptibility testing. Case 10 was re-admitted to the hospital at 40 days following
294 discharge with a recurrence of tarsocrural joint sepsis. Further treatment included a
295 second arthroscopic lavage procedure, 3 standing multi-needle lavages, 4 IVRLPs,
296 intrasynovial antimicrobial medication and systemic antimicrobial therapy. The horse
297 subsequently returned to training before commencing a breeding career. Case 1 was
298 euthanased one year following hospital discharge due to recurrence of the original
299 femoropatellar joint sepsis. Case 2 was originally treated for hindlimb digital flexor
300 tendon sheath sepsis but was readmitted to the hospital 14 days after discharge,

with bilateral forelimb metacarpophalangeal joint sepsis. An aggressive septic process was demonstrated radiographically and arthroscopically, with evidence of osteomyelitis, cartilage degeneration and marked pannus formation. Treatment with bilateral metacarpophalangeal joint arthroscopic lavage, repeated standing multi-needle lavage and local and regional antimicrobials did not produce a clinical improvement, resulting in euthanasia.

A total of 6/11 horses raced following synovial sepsis. The mean time to return to racing was 237 days (median 221 days and range 107- 429 days). Five horses had five or more race starts post-synovial sepsis. Mean earnings from racing post-synovial sepsis was $63182 (median $1125 and range $0 -$635500). One horse was retired from training for lameness unrelated to synovial sepsis and 2 for respiratory abnormalities. Four horses left race training to commence a breeding career. The reason for retirement for 2 geldings following five or more race starts was not known. Case 6 was euthanased due to respiratory disease and case 3 was euthanased for unknown reasons after a career as a broodmare. Therefore, a total of four horses were reported as deceased in the follow-up period of at least two years following admission.

Discussion

This study presents data from 11 cases of synovial sepsis of unknown origin in adult Thoroughbred racehorses admitted over a 10-year period. Most horses were in training at the time of presentation and a range of synovial structures were affected. No clear aetiologies of sepsis were identified, therefore, a haematogenous pathogenesis was suspected. All bacterial isolates were Gram-positive cocci though no obvious origins of bacteraemia were evident. Treatment with methods typical for the management of synovial sepsis resulted in a fair prognosis for return to racing.

Origins of bacteraemia

Haematogenous synovial sepsis has multifactorial pathogenesis, requiring a state of bacteraemia, which permits the invasion of pathogens into a synovial structure [26]. The horses in this study were considered immunocompetent, therefore, a transient, subclinical bacteraemia is suspected. In the present study sepsis involved a single synovial structure, except in case 2; an unusual case of simultaneous sepsis of multiple distant structures in an adult horse. Synovial sepsis was generally monomicrobial and all isolates were Gram-positive cocci. *Staphylococcus aureus* has been reported as the most common isolate from equine synovial sepsis [27] and coagulase positive *Staphylococcus spp.* accounted for 3/6 of positive cultures in the present study. However, a range of other pathogens, including Enterobacteriaceae, have been isolated from cases of suspected haematogenous synovial sepsis [1,16,26]. The source of bacteraemia is likely to vary between cases of haematogenous synovial sepsis.

Previously implicated origins of bacteraemia in adult equine synovial sepsis include a subsolar abscess, septic peritonitis, intra-arterial catheters, infective endocarditis and distant traumatic and surgical wounds [1,14–16,26]. S*taphylococcal spp.* are the most common isolates from traumatic and surgical wounds [28]. A wound remote to the site of synovial sepsis was evident in a single case of the present study. The gastrointestinal tract has also been proposed as an origin of bacteraemia in cases of haematogenous synovial sepsis [26]. Bacteraemia has been associated with intestinal disease in the adult horse including enterocolitis [29] and small intestinal lesions requiring resection [30]. However, severe gastrointestinal disease was not identified in the present study. In humans and horses intense exercise results in reductions in splanchnic blood flow [31,32], which may result in localised intestinal

ischaemia, metabolic injury and damage to the intestinal barrier [33]. An inflammatory response is also stimulated by intense exercise [31], which may contribute to changes in intestinal integrity [34]. Endotoxaemia due to increased intestinal barrier permeability during strenuous exercise has been recognised in human athletes and Thoroughbred racehorses [35,36]. The potential for bacterial translocation from the gastrointestinal tract during exercise has also been proposed [37]. Gram-positive cocci, consistent with the synovial isolates from the present study, were occasionally identified in a study of bacteraemia in horses with diarrhoea [29]. Other commensal organisms of the gastrointestinal tract have been isolated in synovial sepsis of suspected haematogenous origin [26]. Bacteraemia has been reported in equine and human patients following dental extraction [38–40]. Dental procedures were not evident in the historical findings of this retrospective study.

In human patients bacteraemia is often of unknown origin, though intravenous catheters are frequently implicated [41]. Ramzan [14] described a case of haematogenous septic digital flexor tendon sheath tenosynovitis in an adult Thoroughbred with infective endocarditis, suspected to be secondary to jugular thrombophlebitis. Similarly, Barr et al. [42] reported haematogenous microbial inoculation following catheterisation of the dorsal metatarsal artery, leading to destructive lesions in the proximal sesamoid bones. No cardiovascular abnormalities were reported at presentation in the current study, though a single case developed jugular thrombophlebitis following admission. Specific assessment for evidence of septic cardiovascular disease, in combination with blood culture, may corroborate the association of lesions such as thrombophlebitis with haematogenous synovial sepsis.

Mechanisms of synovial invasion

The vascular supplies of synovial structures are an important consideration in the mechanism of synovial sepsis of haematogenous origin. The major vascular supply to the synovial cavity is within the synovium [43]. This partially fenestrated capillary network [44] is suspected to be the site of entry in synovial sepsis of haematogenous origin (S type) in foals [45] and the adult horse, particularly if vasculitis is present. Synovitis due to pre-existing intra-synovial or peri-synovial pathology may act as a predisposing factor for microbial invasion through this capillary network, into a synovial structure [46–48]. Case 6 of the present study demonstrated a lateral suspensory ligament branch insertional avulsion injury and there was no evidence that this acted as a primary septic focus. Exercise may have a role in this mechanism by exacerbating local inflammation. Recent exercise has been described in previous reports of suspected haematogenous synovial sepsis [14,16,19] and 9/11 of horses in the present study were in training or pre-training. Intra-articular haemorrhage from the synovium has been associated with exercise [49,50] and could theoretically predispose to bacterial colonisation. However, significant haemorrhage was not a feature of cases in the present study. A small number of vessels penetrate from subchondral bone plate into the overlying calcified cartilage [51]. These channels can be exposed from the articular surface [52]. The pre-existing lesions affecting articular cartilage in the current study are common in this population and no cases had evidence septic processes affecting adjacent bone. This method of microbial entry is considered unlikely.

Some intrasynovial structures have additional vascular supplies [53]. Within the digital flexor tendon sheath the deep digital flexor tendon is supplied primarily by the mesotenon vascular network [54]. Kidd et al [55] described cases of septic tendonitis without evidence of pre-existing tendon disruption that were suspected to

have a haematogenous origin. Features of this disease mirror those of synovial sepsis of unknown origin, including an association with exercise, predominance of Gram-positive cocci isolates and an absence of obvious origin of bacteraemia. This may reflect a shared mechanism of haematogenous microbial inoculation facilitated by localised inflammation or vasculitis.

The range of synovial structures in the current study is consistent with those reported in studies of multi-aetiology synovial sepsis [5,17]. In a previous study 58% of cases of synovial sepsis of unknown origin involved the tarsocrural joint [1] but the present study does not reproduce this predominance. Nonetheless, relatively high-motion joints and tendon sheaths appear to be over represented. Case 9 of the present study was diagnosed with septic bicipital bursitis, which was rare in studies of multi-aetiology synovial sepsis [1,5]. There have been numerous case reports of idiopathic or haematogenous septic bicipital bursitis in the adult horse [16,21,22,47,48]. No significant predisposing pathology was identified on bursoscopy of the horse in this study, which differs to previous reports [16,21,48]. Synovial sepsis of unknown or haematogenous origin should be considered as a differential diagnosis in adult horses with lameness originating from this region.

Treatment and outcome

Third generation cephalosporin antimicrobials remain above minimum inhibitory concentrations of common pathogens in synovial fluid and subcutaneous tissue for 24 hours following IVRLP. However, these agents are rated as highly important by the Australian Strategic and Technical Advisory Group on Antimicrobial Resistance [56–58] and should be reserved for cases with suitable culture and susceptibility testing or exceptional cases with clinical indications [59]. Culture and susceptibility

findings from the present study suggest that third-generation cephalosporin antimicrobial agents may be valuable in cases of synovial sepsis of unknown origin, especially when isolates demonstrate resistance to other antimicrobial agents.

Return to athletic function following synovial sepsis has been reported to range from 54- 92% for mixed equine populations [4,5,20,60]. In the present study 55% of horses returned to racing, which is slightly greater than the 36% of Thoroughbreds reported by Schneider et al. [1]. Milner et al. [17] reported that only 63% cases from a mixed breed population with synovial sepsis of unknown origin survived to hospital discharge, compared to 88% of horses with a wound. The authors suggested that a wound results in earlier identification of pathology and reduces accumulation of synovial fluid inflammatory mediators and microbial pathogens by permitting drainage. In the present study referral and diagnosis were generally rapidly achieved despite the lack of an obvious cause of synovial sepsis. This may reflect the management of the Thoroughbred racehorse population in the present study, where horses are regularly examined for lameness.

Limitations and conclusions

The retrospective design of this study introduces some limitations in the availability of historical and clinical features that could offer further information on the pathophysiology of synovial sepsis of unknown origin. The infrequent nature of cases resulted in a small study population, which limited the use of some analytical methods. It is often not possible to exclude all other possible aetiologies of synovial sepsis in a clinical context. For example, it is possible that minor local pathology prior to synovial sepsis was managed routinely by stable staff and may not have been reported at presentation. Nonetheless, evidence of penetration or foreign material is

relatively frequently recognised surgically in contaminated synovial structures following traumatic inoculation, but was not identified in any case in the present series [3,5,17,61]. A prospective multi-centre study, would minimise some of these limitations and allow further characterisation of the risk factors, pathophysiology and prognosis for synovial sepsis of unknown origin when a haematogenous route is suspected.

In conclusion, synovial sepsis of unknown origin is uncommon in the adult Thoroughbred racehorse and can affect a range of synovial structures. A haematogenous origin is suspected in these cases though an origin of bacteraemia is rarely identified. With appropriate management the prognosis for return to racing is fair.

Manufacturer's addresses

[a] Thermo Fisher Scientific Australia Pty Ltd, Scoresby, Australia

[b] bioMérieux Australia Pty Ltd, Baulkham Hills, Australia

[c] Microsoft Corporation, Redmond, USA

[d] Sandoz Pty Ltd, Macquarie Park, Australia

[e] Troy Laboratories Pty Ltd, Glendenning, Australia

[f] Zamira Life Sciences Pty Ltd, Kenmore, Australia

Supporting Information

Supporting Information 1: Summary information for the treatment procedures, antimicrobial administration and hospitalisation of 11 adult Thoroughbred racehorses with synovial sepsis of unknown origin.

Supporting Information 2: Summary information of surgical findings for 9 adult Thoroughbred racehorses with synovial sepsis of unknown origin managed with endoscopic surgery.

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651 **Table 1:** Summary of case details and synovial fluid analysis findings for 11 cases of synovial sepsis of unknown origin in adult
652 Thoroughbred racehorses. Abbreviations: TB, Thoroughbred, G, Gelding, M, Mare, F, Filly, S, Stallion, C, Colt, R, right, L, left, F,
653 fore, H, hind, NR, not recorded

Case	Signalment	Limb	Synovial Structure	Total Nucleated cell count (x10^9/L)	Neutrophil differential (%)	Protein (g/L)	Microbial culture	Red Blood Cell Count (x10^{12}/L)	Grossly haemorrhagic appearance
1	3 yo TB G	RH	Femoropatellar joint	71.0	95	46	Positive	0.01	No
			Lateral femorotibial joint	38.5	91	51	Negative	0	No
2	4 yo TB M	RH	Digital flexor tendon sheath	166.0	95	40	Positive	0.06	No
3	2 yo TB F	RF	Antebrachiocarpal joint	44.8	80	49	Negative	0.02	No
4	4 yo TB S	LH	Metatarsophalangeal joint	103.5	94	52	Negative	0.06	No
5	2 yo TB F	RH	Femoropatellar joint	57.6	87	44	Negative	0.04	No
			Medial femorotibial joint	7.4	NR	42	NR	NR	No
			Lateral femorotibial joint	8.6	NR	38	NR	NR	No
6	2 yo TB C	LF	Metacarpophalangeal joint	110.8	94	54	Negative	0.08	No
7	2 yo TB F	LH	Femoropatellar joint	50.0	93	46	Negative	0.02	No
8	2 yo TB G	LH	Tarsal sheath	38.7	96	40	Positive	NR	No
9	3 yo TB G	RF	Bicipital bursa	156.0	95	54	Positive	0.08	No
10	2 yo TB F	LH	Tarsocrural joint	12.4	80	39	Positive	NR	No
11	6 yo TB G	LF	Digital flexor tendon sheath	90.8	85	60	Positive	NR	Yes

Table 2: Microbiological findings and antimicrobial susceptibility of isolates from synovial fluid of 6 cases of synovial sepsis of unknown origin in adult Thoroughbred racehorses**.** Abbreviations: NPO, no pathogen observed, NT, not tested, R, resistant, S, susceptible

Case	Gram Stain	Synovial Fluid Culture Isolate	Antimicrobial Susceptibility								
			Ampi/ Amoxycillin	Ceftiofur	Ceftriaxone	Neomycin	Gentamicin	Amikacin	Tetracycline	Enrofloxacin	Trimethoprim / sulpha
1	NPO	Coagulase positive *Staphylococcus sp.*	S	S	NT	S	S	S	R	S	S
2	NPO	Coagulase positive *Staphylococcus sp.*	R	S	NT	R	R	NT	R	S	S
8	NPO	Coagulase positive *Staphylococcus sp.*	R	S	NT	S	S	NT	R	S	R
9	Gram-positive cocci	*Streptococcus dysgalactiae subsp.equisimilis*	S	S	S	R	R	R	R	S	S
10	NPO	*Staphylococcus xylosus*	R	S	NT	S	S	NT	S	S	S
		Streptococcus uberis	S	S	NT	R	R	NT	S	R	S
11	NT	*Streptococcus dysgalactiae subsp equisimilis*	S	S	S	R	R	R	S	R	S