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NOTE

Surgery

# Regional antibiotic perfusion through the lateral saphenous vein in two horses with septic calcaneal osteitis

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**ABSTRACT.** In this case report, two horses with chronic refractory infections in the tuber calcanei were successfully managed via intravenous antibiotic regional limb perfusion through the lateral saphenous vein after failure of conventional treatment approaches, including surgery and intravenous regional limb perfusion using the cranial branch of the medial saphenous vein. Surgical delay in these cases may have allowed the development of chronic infection, which prevented the conventional regional perfusion from working effectively. The spatial difference of the vessels relative to the tuber calcanei possibly contributed to the treatment outcome in these horses. This report describes a novel approach for regional antimicrobial perfusion to the equine plantar hock region using the lateral saphenous vein.

**KEYWORDS:** antibiotic, calcaneal osteitis, horse, lateral saphenous vein, regional limb perfusion

Management of septic calcaneal osteitis is difficult due to several synovial structures, including the calcaneal bursae, tarsal sheath, and tarsocrural joint, in the vicinity of the tuber calcanei; these synovial structures may also have concurrent synovial sepsis related to the inciting cause [17, 21, 22]. Treating a calcaneal bursae infection and septic calcaneus osteitis requires a multimodal approach, including systemic and local antimicrobial use and surgical intervention [6, 13, 17, 22, 30]. Although surgical intervention is the mainstay treatment [24], the extensive ligament attachment on the tuber calcanei may complicate debridement of all infected bone and soft tissue [17]. Consequently, aggressive debridement of the calcaneus should be performed with caution alongside nonsurgical options [1, 8, 19].

Intravenous regional limb perfusion (IVRLP) is a nonsurgical option in the management of septic synovial structures and osteomyelitis [11, 25, 26]. Many studies suggest the effectiveness of IVRLP for septic synovial structures and bone tissues. Still, various techniques for IVRLP complicate interpretation of the treatment outcomes, and there is no general methodology recommended to achieve maximum effect in clinical settings [2, 5, 26]. Regional antibiotic perfusion through the cranial branch of the medial saphenous vein (MSV) is an accepted treatment for horses with synovial infection in the hock region [13, 22, 27]. A previous report did not examine whether the therapeutic antibiotic concentration can be achieved in the plantar hock region following IVRLP through the conventional technique using the cranial branch of the MSV [27]. Theoretically, any peripheral vessel can be used for IVRLP when regional isolation from systemic circulation is possible via tourniquet placement [2, 5]. In this case report, we describe the treatment outcome of IVRLP using the lateral saphenous vein (LSV) as an alternative to the conventional venous route in two horses with chronic refractory septic calcaneal osteitis.

A 1-year-old Thoroughbred filly weighing 377 kg (case 1) was referred to the Hidaka Horse Breeders' Association on day 1 with a history of puncture wounds over the tuber calcanei one week before referral. The horse showed non-weight bearing lameness (Grade 5/5, American Association of Equine Practitioner (AAEP) Lameness Scale) on the left hindlimb, with two small, healed scars, slightly plantarolateral and plantaromedial to the proximal end of the tuber calcanei. Around the wounds was a localized swelling surrounding the proximal end of the tuber calcanei. Pain was elicited on palpation around the insertional portion of the common calcaneal tendon to the proximal end of the tuber calcanei. The referring veterinarian confirmed no radiographic abnormalities of the calcaneal region. Hematologic examination revealed a white blood cell count of $9.6 \times 10^3$ cells/μL and serum amyloid A concentration of 428 μg/mL (Table 1). Ultrasonography revealed small amounts of anechoic synovial fluid accumulation in the intertendinous calcaneal bursa. A small volume of turbid synovial fluid with fibrin clots was aspirated under ultrasound-guided synoviocentesis of the intertendinous calcaneal bursa. Cytologic smear and microbiological examination of the synovial fluid showed predominantly polymorphonuclear cells (>80%) and negative cultures. Biochemical analysis of the synovial fluid was not performed, as the volume of the retrieved

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**Table 1.** Hematological examination of case 1

| Hematological parameters | Day 1 | Day 6 |
|---|---|---|
| White blood cell count ($\times 10^3$ cells/μL) | 9.6 | 6.5 |
| Percentage of neutrophils (%) | 68 | 61.4 |
| Total protein concentration (g/dL) | 6.9 | 5.9 |
| A/G ratio | 1.23 | 1.11 |
| Serum amyloid A (μg/mL) | 428 | <2.5 |

synovial fluid was insufficient. The differential diagnoses for the case included septic peribursal cellulitis and soft tissue injuries; however, a presumptive diagnosis of septic calcaneal bursitis was made based on the inciting cause of the disease, clinical evaluation, and cytological and diagnostic imaging findings.

For first-line therapy, medical treatment was provided with 2.2 mg/kg body weight (bwt) of ceftiofur sodium (Excenel; Zoetis Japan, Tokyo, Japan) s.i.d. i.v., 6.6 mg/kg bwt of gentamicin sulfate (Gentamax$^{TM}$ 100 injection; Ceva Animal Health Pty Ltd., Glenorie, Australia) s.i.d. i.v., and 4.4 mg/kg bwt of phenylbutazone (Equi-phar phenylbutazone injection; Sparhawk Laboratories, Inc., Lenexa, KS, USA) s.i.d. i.v. Regional therapy with intrabursal injection of 1 g of amikacin sulfate (Amikacin sulfate injection; Fuji Pharma Co., Ltd., Toyama, Japan) at the synoviocentesis was performed. The first-line therapy failed to improve any clinical signs. The horse was re-evaluated on day 6, at which the horse showed non-weight bearing lameness (Grade 5) on the same limb but had all hematologic parameters within the normal reference range (Table 1). Ultrasonography revealed small amounts of synovial fluid in the intertendinous calcaneal bursa and a dome-shaped bone defect at the proximal aspect of the tuber calcanei where the gastrocnemius tendon was inserted. Gastrocnemius tendon injury at the insertional part of the tendon onto the proximal end of the tuber calcanei was noted adjacent to the bone defect and extended proximally for about one inch (Fig. 1A). Radiographic projections of the left hock revealed an osteolytic lesion at the plantarolateral aspect of the proximal apophysis of the tuber calcanei (Fig. 1B and 1C). A final diagnosis of septic calcaneal osteitis and concurrent persistent septic calcaneal bursitis was made based on the emerging osteolytic lesions in the tuber calcanei and persistence of clinical signs.

The need for surgical intervention was discussed with the horse owner; eventually, 1-day surgery was scheduled for day 8. Before surgery, the horse was treated with the same parenteral antibiotics and NSAIDs as the first-line therapy. IVRLP with 1 g of ceftiofur sodium (60 mL final volume) through the cranial branch of the MSV, with two tourniquets applied to proximal and distal aspects of the hock, under standing sedation was administered on day 7.

Bursoscopy for the calcaneal bursa was performed under general anesthesia, according to previous reports [12, 19]. During surgery, a small amount of fibrin was deposited in the intertendinous calcaneal bursa with adhesion formation between the superficial digital flexor tendon (SDFT) and bursal wall. Still, the gastrocnemius calcaneal bursa had no gross abnormalities. Osseous defects detected on radiography at the proximal end of the tuber calcanei could not be visualized at the time of surgery; thus debridement of the bone was not performed. A thorough investigation of the calcaneal bursae was followed by copious lavage of the calcaneal bursae with isotonic fluid. After surgery, 1 g of amikacin sulfate was injected directly into the osteolytic lesion under ultrasonographic guidance.

The systemic medication regimen was continued postoperatively. Intravenous regional perfusion through the cranial branch of the MSV was conducted with either 1 g of amikacin sulfate in 10% dimethylsulfoxide (DMSO) solution (60 mL final volume) or a combination of 1 g of amikacin sulfate and 1 g of ceftiofur sodium (60 mL final volume) at 24–48-hr intervals for five rounds. Each round of IVRLP was performed with two tourniquets applied to the same positions. Due to concerns of nephrotoxicity and gastrointestinal disturbances from the frequent use of antibiotics, gentamicin and ceftiofur were removed from the daily parenteral medication when IVRLP was performed with corresponding antibiotics on the same day.

Temporal amelioration of the lameness was observed after surgery, and the lameness grade was recorded as Grades 4 and 3 on days 9 and 10, respectively. However, gradual deterioration into non-weight-bearing lameness (Grade 5) was observed by day 15. Repeated diagnostic imaging demonstrated no remarkable changes in ultrasonographic findings and progressive enlargement of the radiolucent area without a sclerotic rim margin on the tuber calcanei (Fig. 2A and 2B). Careful re-evaluation of the horse showed a persistent local infection in the tuber calcanei. After deliberations with the horse owner, conservative medical therapy was continued instead of a second surgery.

Systemic medication was switched to trimethoprim-sulfamethoxazole (DAIPHEN Tablets; Tsuruhara Pharmaceutical Co., Ltd., Osaka, Japan, 15 mg/kg bwt b.i.d. p.o.) on day 16 and continued for another 14 days. The LSV was used as an alternate route of IVRLP instead of the cranial branch of the MSV because of the following reasons: the LSV follows distally along the caudolateral aspect of the gastrocnemius muscle to the proximal hock, giving rise to the direct perforating branch to the tuber calcanei, where the spatial location of the LSV relative to the tuber calcanei seemed appropriate to perfuse the plantar hock region [3] effectively.

This novel attempt for IVRLP was introduced on day 16 and repeated at 24–48-hr intervals. The technique for the novel IVRLP was as follows: After appropriate sedation, a small, tightly rolled gauze was applied to the lateral groove cranial to the common calcaneal tendon to act as a pressure device approximately 10 cm above the proximal end of the tuber calcanei. This was followed by placement of a 10-cm wide rubber tourniquet over the rolled gauze. A second rubber tube tourniquet was applied at the proximal third of the metatarsus to isolate the hock region from systemic circulation. We did not exsanguinate the distal limb. After visualization of the small palpable LSV at the lateral groove cranial to the common calcaneal tendon, the area was aseptically prepared. A 21-gauze butterfly catheter was introduced into the LSV (Fig. 3). Once the catheter was placed, antibiotics (1 g of amikacin sulfate in 10%

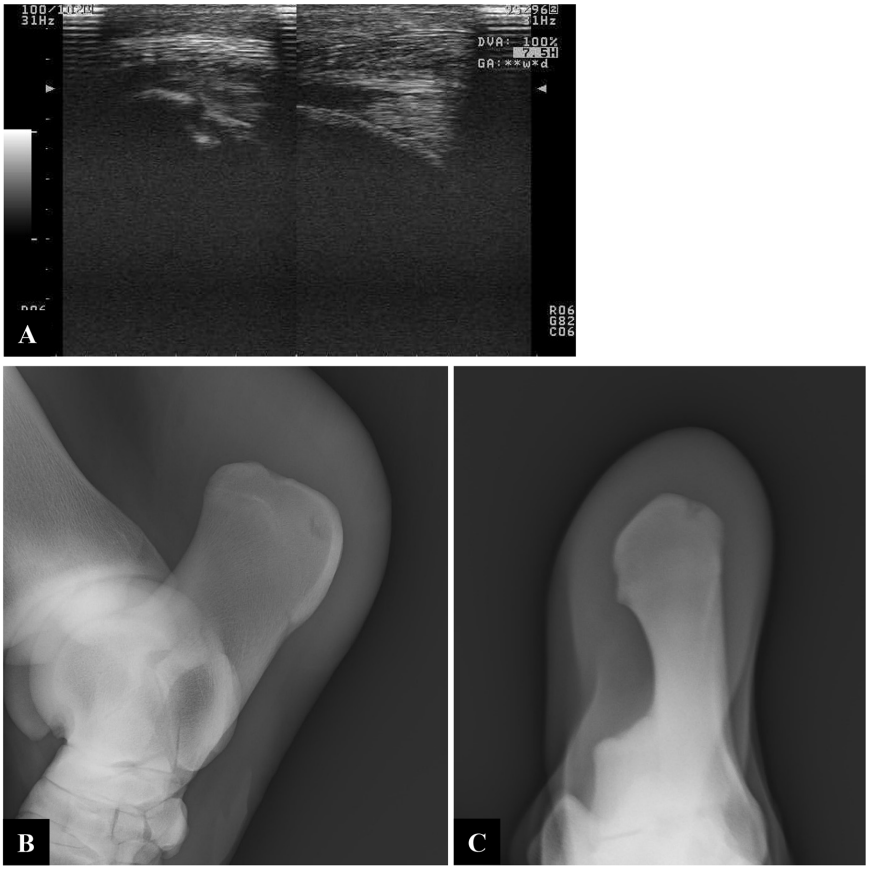


**Fig. 1.** Diagnostic imaging of case 1 on re-evaluation after failure of the first-line therapy. (**A**) Ultrasonography detected dome-shaped bone concavity at the proximal end of the tuber calcanei onto which the gastrocnemius tendon was inserted. Concurrent gastrocnemius tendon injury extending proximally for about one inch was also noted adjacent to the bone defect. Image obtained on plantaroproximal aspect of the point of the hock, angled dorso-distally along to longitudinal plane of the common calcaneal tendon. Right of the image is proximal to the point of the hock. (**B**) Plantarolateral-dorsomedial oblique, and (**C**) flexed plantaroproximal-plantarodistal oblique skyline projections of the left hock showed an osteolytic lesion at the plantarolateral aspect of the proximal apophysis of the tuber calcanei.

DMSO solution and 1 g of ceftiofur sodium in a separate syringe, 50 mL total volume) were slowly administered. The tourniquets were maintained in position for 20 min.

Lameness was significantly improved soon after introduction of IVRLP treatment through the LSV. On day 19, after the second treatment of IVRLP through the LSV, the lameness was slightly perceived at walk but moderately observed at trot (Grade 3–4). The horse appeared more comfortable and ambulated actively within the stall, characteristics not observed during the previous medication period. Lameness progressively improved until day 22. We performed four rounds of IVRLP through the LSV. On day 24, after the final round of IVRLP through the LSV, the lameness was recorded as Grade 1–2. The horse was kept under observation without treatment.

Only slight gait abnormalities were observed while walking and trotting on some occasions during a follow-up examination on day 29. Repeated radiography revealed no progression of the bone lysis and sharp delineation with sclerotic rim margin, indicating the local infection in the tuber calcanei was controlled (Fig. 4A and 4B) [16]. Ultrasonography demonstrated a residual hypoechoic lesion in the gastrocnemius tendon; therefore, we instructed that the horse be kept in the stall for another month before resuming light exercise. On repeated on-farm ambulatory examination 3 months post-injury, the horse had undergone controlled exercise, including hand-walking and paddock turnout, without clinical signs. Radiographic views demonstrated residual osteolytic lesions without evidence of bone remodeling (Fig. 4C and 4D). The owner of the horse did not provide consent to perform ultrasonography after the horses clinical improvement; therefore, the lesion in the gastrocnemius tendon could not be evaluated.

The horse owner was contacted three years later. They reported that the progression of resuming exercise was satisfactory after the last follow-up three months post-injury, and no abnormalities were observed. However, mild lameness of the same limb relapsed when the horse started to trot under saddle six months post-injury. It was eventually decided that the horse be withdrawn from future athleticism.

A 1-year-old Thoroughbred colt weighing 410 kg (case 2) with an unknown history was claimed to have observable right hindlimb lameness at trot (Grade 3) on day 1. There was subcutaneous swelling over the proximal end of the right tuber calcanei, with no resistance against palpation of the proximal calcaneal region. The referring veterinarian administered NSAIDs to control suspected inflammation of the proximal calcaneal region. The next day, the horse showed obvious lameness at walk (Grade 4), with an elevated

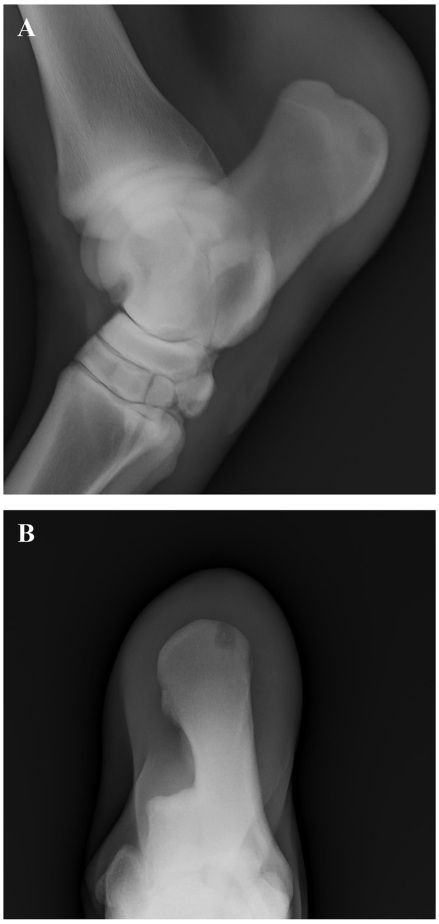


**Fig. 2.** Diagnostic imaging of case 1 after surgery, before proceeding to intravenous regional perfusion through the lateral saphenous vein. Enlargement of the radiolucent area without a sclerotic rim margin on the tuber calcanei was noted on (**A**) plantarolateral-dorsomedial oblique and (**B**) flexed plantaroproximal-plantarodistal oblique skyline projections of the left hock. The horse showed severe non-weight bearing lameness.

**Fig. 3.** Twenty-one-gauge butterfly catheter was introduced and securely placed in the lateral saphenous vein in case 1 horse.

body temperature (39.1°C) and mild pain elicited by palpation to the medial aspect of the proximal end of the tuber calcanei. Ultrasonography revealed increased thickness of the subcutis over the proximal end of the tuber calcanei and accumulation of anechoic synovial fluid in the intertendinous calcaneal bursa, with no abnormality in the tendon structures. No detectable bone abnormalities were observed on radiography (Fig. 5A). A tentative diagnosis of septic peribursal cellulitis of the calcaneal region and associated secondary inflammation of the calcaneal bursa was made based on clinical assessments of the horse.

After diagnosis of the infection, the referring veterinarian initiated treatment with antibiotics (cefalotin sodium 20 mg/kg bwt i.v. b.i.d. and gentamicin sulfate 6.6 mg/kg bwt i.v. s.i.d), anti-inflammatory medications (phenylbutazone 2.2 mg/kg bwt i.v. b.i.d.), and IVRLP through the cranial branch of the MSV (600 mg of amikacin sulfate; 40 mL total volume), as with case 1. The horse responded well to the initial treatment and had Grade 2–3 lameness on day 5. However, a rapid progression of lameness was observed on day 10, necessitating a repeated detailed examination.

The horse showed severe lameness (Grade 4) with considerable pain elicited upon deep palpation of the proximal aspect of the tuber calcanei. Diagnostic radiography revealed two radiolucent foci on the calcaneal apophysis; one was located at the proximal aspect and another at the plantaromedial aspect (Fig. 5B). Calcaneal bursitis of the intertendinous calcaneal bursa with fluid accumulation and fibrin deposition was confirmed on ultrasonography on day 13. Upon considering the emerging radiographic findings and progression of clinical signs, septic calcaneal osteitis with calcaneal bursitis was the most likely diagnosis.

Cephalosporin antibiotic was changed on day 10 to 2.2 mg/kg bwt of ceftiofur sodium i.v. b.i.d. without any change in the other medications. Intravenous regional limb perfusion through the cranial branch of the MSV was performed with 600 mg of amikacin sulfate on day 10. After ultrasonographic diagnosis of calcaneal bursitis on day 13, the horse underwent one-day bursoscopic surgery under general anesthesia. During surgery, a small amount of fibrin clot that was detected by ultrasonography before surgery was found in the intertendinous calcaneal bursa. No other gross abnormalities were observed in the intertendinous and gastrocnemius


**Fig. 4.** Follow-up radiographs for case 1 taken 5 weeks (A, B) and 3 months (C, D) post-injury. (**A, B**) Bone lytic lesion had ceased to expand alongside sharp delineation with sclerotic rim margin during four rounds of intravenous regional limb perfusion through the lateral saphenous vein. The horse showed only slight gait abnormalities at follow-up examination on day 29. (**C, D**) Radiographic views obtained 3 months post-injury demonstrated residual osteolytic lesions without evidence of bone remodeling. The horse showed no evidence of lameness.

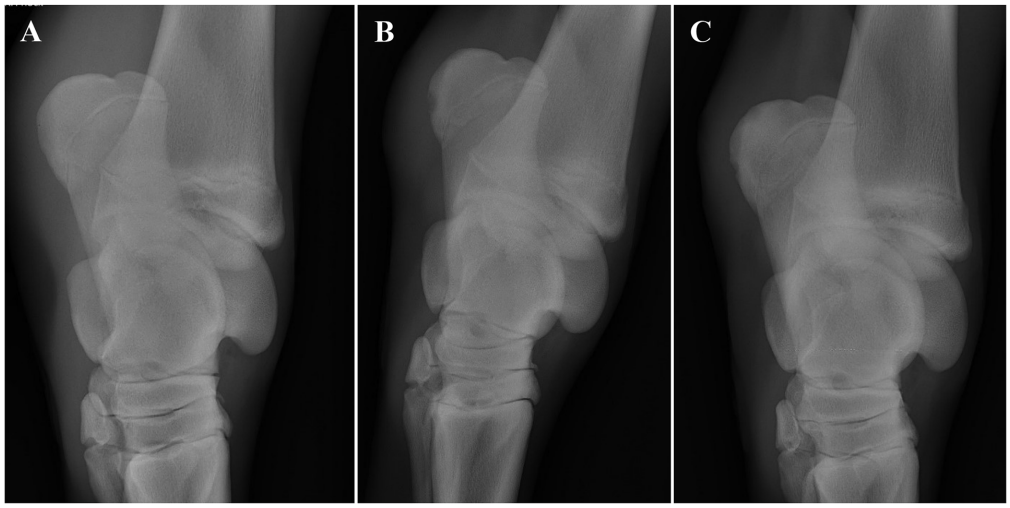


**Fig. 5.** Changes in radiographic findings for case 2. (**A**) No radiographic abnormality was found at initial visit radiograph. (**B**) Two radiolucent foci on the calcaneal apophysis, one located at the proximal aspect and another at the plantaromedial aspect, were noted on re-evaluation on day 10. (**C**) Follow-up radiographs taken 4 weeks postoperatively confirmed no progression of the osteolytic lesion.

calcaneal bursa, or for any tendon structures. As with case 1, osseous defect of the tuber calcanei could not be visualized at the time of surgery, and debridement of the bone was not performed. The same systemic medication was administered following the surgery. No improvement in lameness was observed on the following day; hence, we proceeded to IVRLP through the LSV with 1 g of amikacin sulfate (45 mL total volume) on day 15. This procedure was repeated 48 hr later (day 17) with the same medication.

The lameness progressively improved after initiating IVRLP through LSV, and Grade 1–2 lameness was recorded 1 week postoperatively (day 21). At this point, gentamicin was withdrawn from the systemic medication regimen, and ceftiofur and phenylbutazone were continued for another 10 days. Follow-up radiographs taken 4 weeks postoperatively confirmed no progression of the osteolytic lesion (Fig. 5C). Since lameness had disappeared by that time, the horse was allowed pasture turnout. One year after the initial onset of clinical signs, the horse was in training, with no clinical abnormalities.

In these cases, we observed no clinical benefit after the initial bout of IVRLP in which the conventional MSV was used. However, we observed clinical improvement during the second bout of IVRLP in which the LSV was used. Clinical signs indicated the osseous infection was not controlled during the initial bout of IVRLP. This was visualized on radiography, which showed expansion or emergence of the osteitis lesion, despite treatment (Figs. 2A, 2B and 5A, 5B). After the second bout of IVRLP, the osteitis lesion ceased to expand with delineation of the lesion by sclerotic rim margin; this may indicate that the local infection in the tuber calcanei was controlled [16]. Delayed surgery in both cases contributed to the development of persistent, chronic infection where invading bacteria might have formed a biofilm layer. Consequently, an additional higher concentration of antibiotics was required to treat the refractory infection [4, 11]. Although no quantitative assessment of antibiotic concentration in the plantar hock region was conducted in this case report, the difference in antibiotic concentration achieved in the proximal hock region may explain the deviation between the treatment outcomes of the two IVRLP techniques.

Regarding regional perfusion, locally administered antimicrobials diffuse preferentially into the adjacent, highly vascularized, and more dependent compartments through the venous system [10, 18, 25, 27, 32]. Many studies have achieved clinically relevant antibiotic concentration in specific sites via IVRLP with various techniques [2, 23]. The use of proximal vessels for IVRLP with a single, proximal tourniquet was rational to achieve a high concentration of the antibiotics in the distal limb [15]. In contrast, a double tourniquet placed proximal and distal to the target compartment was required to achieve those concentrations in the proximal compartments [15, 20, 28]. A recent study [10] revealed the possible role of gravity in sufficient vascular perfusion and distribution of the perfusate into adjacent soft tissue in the distal limbs of horses under the IVRLP procedure. Therefore, in addition to the IVRLP technique, reviewing the spatial orientation and vascularization of the tissue of interest relative to the site of infusion when IVRLP is performed is meaningful.

The cranial branch of the MSV is widely used in IVRLP for hindlimb infections because of its accessibility and larger diameter [14]. The cranial branch of the MSV runs distally, along with the craniomedial aspect of the tibia, to the dorsal flexor aspect of the hock [3, 9, 29]; therefore, the dominant drainage region of this vein may be a dorsal plane of the hock. The access of the cranial branch of the MSV to the plantar hock region is through the perforating tarsal vessel that traverses the vascular canal formed by the central, third, and fourth tarsal bones at the distal hock [9, 29]. In contrast, the LSV follows distally along the caudolateral aspect of the gastrocnemius muscle to the proximal hock, where it ends via anastomoses with the caudal branch of the MSV [3, 29]. The LSV gives rise to direct perforating branch to the proximal tuber calcanei before its end at the proximal hock [29], and it is likely a dominant draining vein of the calcaneal region. Given the anatomical plane of the hock and the spatial relationship of the vessels to the tuber calcanei, we used the LSV for the second series of bouts of IVRLP. A direct perforating branch of the LSV to the tuber calcanei [29] could make direct access to the tuber calcanei possible when the LSV is used for IVRLP. Furthermore, the osteitis lesions in these cases were in the proximal aspect of the tuber calcanei, where treatment efficiency may have been enhanced with the use of the LSV for IVRLP; the proximal location of the LSV relative to the osteitis lesion could facilitate the antibiotic diffusion, depending on gravity.

In both cases, obvious clinical improvement was observed for refractory septic calcaneal osteitis that was unresponsive to conventional IVRLP through the MSV, after the same procedure was done through the LSV. In case 1, the horse could not return to athletics due to recurrent lameness of the same limb six months after treatment completion. Although the horse had a concurrent tendon injury, we could not attribute the recurrent lameness to tendon lesion as the lesion was not evaluated after treatment completion. In contrast, case 2 had no tendinous lesions, and the horse resumed training without abnormality. This is in accordance with previous reports identified tendon lesions as negative predictors of future athleticism [7, 13, 31].

A limitation of our case reports is that surgery was delayed in both cases, complicating the patient outcomes. In addition, prolonged use of parenteral antibiotics may cause complicated interpretations of the treatment outcomes. However, although there are slight differences in the antibiotics used in treatment processes for our case reports, apparent clinical improvement after IVRLP through the LSV may encourage the use of the LSV in cases with plantar hock infection. The LSV was insufficiently large for easy access, but no difficulty was encountered except for the hard pressure required for drug administration. To our knowledge, these are the first case reports demonstrating the use of LSV as a regional route of antibiotic administration for IVRLP in horses. We believe IVRLP using the LSV is a simple and non-invasive alternative approach for treating plantar hock infection in horses.

POTENTIAL CONFLICTS OF INTEREST. The authors have nothing to disclose.

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