Severe acute inflammatory reaction (SAIR) of the fetlock joint after intraarticular hyaluronate injection in a horse

J. M. Kuemmerle¹, H. Uhlig², J. Koffer³
¹Vienna University of Veterinary Medicine, Department of Horses and Small Animals, Clinic of Orthopaedics in Large Animals, Vienna, Austria
²Bayer Austria, Bayer Health Care, Animal Health, Vienna, Austria

Summary
Hyaluronate (HA) was administered by intra-articular injection to a 13-year-old Haflinger mare for treatment of metacarpophalangeal osteoarthritis. Ten hours after the injection, a severe inflammatory reaction developed in the treated joint. While awaiting results of synovial fluid analysis, treatment for iatrogenic infectious arthritis was initiated, but the analysis did not confirm sepsis. Clinical signs improved significantly following systemic non-steroidal anti-inflammatory medication and the horse was discharged three days later. Following an intravenous hyaluronate injection, four days after discharge, the synovitis recurred. Synovial fluid analysis did not show any abnormalities, but the clinical signs were severe. The severe acute inflammatory reaction required systemic non-steroidal anti-inflammatory and intra-articular corticosteroid treatment in order to resolve the problem.

Keywords
Horse, SAIR, joint, arthritis, hyaluronate

Case history
A 13-year-old Haflinger mare was diagnosed with osteoarthritis of the left metacarpophalangeal (MCP) joint on the basis of a orthopaedic examination, which included intra-articular (i.a.) anaesthesia. Radiographs in latero-medial projection revealed mild osteophyte formation present at the proximodorsal aspect of the proximal phalanx. There was also ultrasonographic evidence of articular cartilage damage at the medial aspect of the metacarpal condyle. A therapeutic i.a. injection of sodium HA (Hyonate®) and a glucocorticoid was performed. Three months later, the horse was readmitted for investigation of mild lameness and was administered another injection of the same joint.

Clinical course
Ten hours after i.a. injection, the mare was severely lame in the left front limb. The rectal temperature was 38.4°C. She was moderately lame at the walk and there was severe effusion and periarticular swelling of the left MCP joint, which was painful on palpation. Arthrocentesis revealed turbid synovial fluid with moderate viscosity. A synovial fluid sample was obtained for laboratory analysis. The initial treatment of suspected iatrogenic septic arthritis consisted of joint lavage under sedation, using 1.2 mm needles with 500 ml of sterile 0.9% NaCl solution followed by i.a. administration of neomycin and bacitracin. The limb was bandaged following lavage. Systemic antibiotics was initiated with penicillin G sodium (30 000 IU/kg i.v. TID) and gentamicin (6.6 mg/kg i.v. SID). A non-steroidal anti-inflammatory drug (NSAID) therapy was initiated with flunixin meglumine (1.1 mg/kg i.v. BID). The laboratory analysis of the synovial fluid indicated a white blood cell count of 850/µl with 67% neutrophils and 33% mononuclear cells. Systemic antibiotic and NSAID therapy was continued for three days and in addition, an ointment containing the anticoagulatory agent hirudoid, dimethylsulfoxide and flumethasone, was applied to the fetlock region. The lameness gradually decreased and, after three days, the horse was sound at the walk, the periarticular swelling had resolved and the synovial effusion was classified as mild to moderate. The mare received 40 mg HA (Hyonate®) i.v. and was discharged from the hospital. Four days later the horse was readmitted with a severe front left limb lameness, se-

Clinical findings
Abnormalities were not detected on the initial clinical examination. At the trot, lameness on the left forelimb was graded 1/5. There was mild effusion of the left MCP joint but it was not painful on palpation. On the second occasion, diagnostic anaesthesia and diagnostic imaging were not performed.

Employed an aseptic technique, 20 mg HA (Hyonate®) was injected into the palmar MCP joint pouch using a 21 G (0.9 x 40 mm) needle. Arthrocentesis revealed a pale yellow and clear synovial fluid, seen in the cone of the needle immediately following insertion.

¹Hyionate®, Bayer Health Care, Vienna, Austria.
vere synovial effusion and pain on palpation of the MCP joint. Rectal temperature was normal. An ultrasound examination identified gross thickening of the synovial membrane and a moderate quantity of anechoic fluid in the MCP joint. Radiographic changes, other than those described three months previously, were not present. A clear, yellow synovial fluid, with decreased viscosity, was aspirated at arthrocentesis. The white blood cell count of the synovial fluid was 40/µl with 99% mononuclear cells and a total protein of 28 g/l. The culture of the synovial fluid was negative. A diagnosis of acute aseptic arthritis was made, a bandage was applied and NSAID therapy consisting of flunixin meglumine (1.1 mg/kg i.v. BID) followed by phenylbutazone (2.2 mg/kg orally BID) was initiated and continued for seven days. The lameness and local inflammatory signs improved markedly within 24 hours. Additionally, two days later an i.a. injection of 40 mg methylprednisolone acetate was administered. The horse responded well to therapy and one week later was sound at walk and trot. She was discharged from the hospital and the owner was advised to ‘box rest’ her with twice daily walks on the lead rope for one week, and then to start riding again. At the follow-up phone call, six months later, the owner reported that the horse had returned to its normal level of activity (pleasure riding) without any lameness problems nor visible joint effusion.

### Discussion

Hyaluronan (HA) is a linear polysaccharide molecule composed of N-acetyl glucosamine and glucuronic acid. It is responsible for the viscoelastic properties of synovial fluid and is endogenously synthesized by synoviocytes.

Intravenous (i.v.) or intraarticular (i.a.) administration of sodium HA is thought to have a chondroprotective and anti-inflammatory effect in human and equine patients suffering from non-infectious synovitis or osteoarthritis.

There are reports of a severe acute inflammatory reaction (SAIR) as a rare complication after i.a. HA administration in humans (1) but to the authors’ knowledge, the possibility of acute inflammatory reactions following i.a. medication is only sporadically mentioned as reactive synovitis in the equine literature (2).

In human medicine, SAIR, also called ‘pseudoseptic reaction’, is well described and clinically defined by the following characteristics:
1. Severe joint inflammation with significant cellular effusion and pain occurring 2 – 72 hours post injection;
2. It typically occurs after exposure to more than one injection;
3. Absence of infectious agents and calcium pyrophosphate dihydrate crystals in synovial fluid;
4. Often high numbers of mononuclear cells infiltrating the synovial fluid from the surrounding membrane;
5. Typically not self-limiting, requiring anti-inflammatory treatment (3). However, there are no distinct criteria for a clear differentiation of SAIR from mild, transient local reactions.

The horse in this report showed many characteristics of a SAIR. A severe painful joint inflammation with synovial effusion occurred 10 hours after injection. The severe thickening of the synovial membrane as detected ultrasonographically was remarkable. There was a history of previous i.a. HA injection. The synovial culture was negative and calcium pyrophosphate dihydrate crystals were not detected in synovial fluid. The cytological examination revealed 99% mononuclear cells in the second synovial sample. Treatment was required to control the condition.

Septic arthritis is an important differential diagnosis to SAIR. In the case reported herein, septic arthritis was the suspected and initial diagnosis based on the elevated rectal temperature, lameness, local inflammatory signs and turbid synovial fluid. In the early phase of SAIR, even synovial fluid analysis may not allow clear differentiation from septic arthritis. Intra-articular corticoste-

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8 Depo-Medrol™ with Lidocaine, Pharmacia NV/SA, Puurs, Belgium.
piration and i.a. corticosteroids (3). The horse in our case report showed marked improvement after NSAID administration but required i.a. methylprednisolone acetate to become sound.

Often HA products are added to i.a. corticosteroid injections for therapy of osteoarthritis to provide chondroprotection (8). It is speculative as to whether, if in instance, the concurrent injection of corticosteroids would have prevented SAIR. Another way of avoiding SAIR is to avoid i.a. injection altogether, and to administer HA i.v. (9).

This case report demonstrates that SAIR can occur in the horse as a rare complication following i.a. sodium HA injection and this risk should be kept in mind when evaluating joint inflammation following i.a. injection.

References

Correspondence to:
Prof. Dr. Johann Kofler
Vienna University of Veterinary Medicine
Department of Horses and Small Animals
Clinic of Orthopaedics in Large Animals
Veterinaerplatz 1
A-1210 Vienna, Austria
Phone: +43 1 25077 6100, Fax: +43 1 25077 5590
E-mail: Johann.Kofler@vu-wien.ac.at

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