Iranian Veterinary Surgery Association

IRANIAN JOURNAL OF VETERINARY SURGERY

Journal homepage: www.ivsajournals.com

Clinical Report

Cutaneo-Muscular Necrosis of Cervical and Pectoral Region following Intramuscular Injection of Flunixin Meglumine in an Arabian Stallion

Shahram Maleki[1*], Amir Zakian[1], Ali Valizadeh[2], Abbas Raisi[1]

[1] *Department of Clinical Sciences, Faculty of Veterinary Medicine, Lorestan University, Khorramabad, Iran.*

[2] *Graduated Student of Veterinary Medicine, Faculty of Veterinary Medicine, Lorestan University, Khorramabad, Iran.*

Received: 2 May 2019
Accepted: 28 September 2019
Online: 26 October 2019

Keywords:

Cutaneo-muscular necrosis;

Flunixin meglumine;

Horse;

Wound.

Abstract

Case description- A five-year-old Arabian stallion weighing approximately 300 kg with large infected chronic torn wound on the neck and pectoral region 5 days after IM injection of flunixin meglumine with history of anorexia, depression and lack of response to antibacterial treatment referred to the Veterinary Teaching Hospital of Lorestan University.

Clinical findings- The clinical symptoms observed during the examination were hematuria and watery diarrhea with very large skin laceration in the affected area. External examination revealed the infectious cervical and pectoral muscles and necrosed skin with purulent discharge and odorous smell. Skin and surrounding tissues were warm, edematous and swelled.

Treatment and outcomes- Surgical treatment started with physical debridement and maggot therapy using *Lucilia* (*Phaenicia*) *sericata*. Then medical treatment continued with intravenous fluid therapy, antimicrobial and anti-inflammatory drugs (NSAID) along with topical treatment.

Clinical relevance- The present case demonstrates the serious complications that can occur following non-sterile IM injections and/or as a consequence of flunixin meglumine IM administration. An aggressive pharmacological and surgical therapy is very essential in similar cases. In conclusion, successful management of the cutaneo-muscular necrosis depends upon the condition of wound and selection of proper antibacterial drugs along with early surgical intervention.

* Correspondence to: Shahram Maleki, Assistant Professor, Department of Clinical Sciences, Faculty of Veterinary Medicine, Lorestan University, Khorramabad, Iran. E-mail: maleki.sh@lu.ac.ir

DOI: 10.22034/ivsa.2019.183999.1184

1. Introduction

Wounds account for a large portion of the caseload of an equine practitioner.[1] The US Department of Agriculture found that skin wounds are the most common medical condition affecting horses.[2] This is also reported by UK horse owners.[3] Similarly, equine veterinarians in New Zealand and Australia have reported that 25% of their caseload is wound-related.[4] Infectious diseases of the muscular system can be bacterial, viral, fungal or parasitic.[5,6] Bacterial myositis in horses can be caused by a variety of *Clostridium* spp.[7] Myositis, myonecrosis or cellulitis may occur following intramuscular (IM) injection of some drugs included NSAIDs, vitamins, menbutone, and synthetic prostaglandins.[8,9] Successful management of equine wounds relies on knowledge of the stages of wound healing, factors that can alter those stages, how healing stages can be manipulated, and adherence to the principles of wound healing. Challenges that complicate wound management include the inability to immobilize and/or confine equine patients and maintain a clean environment during the critical initial stages of healing.[10] The primary objective for the medical management of wounds is preventing infection and creating an optimum environment for wound healing with the reestablishment of an epithelial cover and recovery of tissue integrity, strength, and function.[11] To select the optimal approach to manage a wound, a full clinical assessment of the patient and a careful examination of the wound are required. The decision to close or not to close a wound should be adapted to each wound and circumstance. Moreover, the veterinarian must recognize that the wound healing process in horses differs from that observed in other mammalian species. Second-intention healing of deep wounds occurs faster in ponies and equines than other mammals. This difference can be largely attributed to a more pronounced and faster wound contraction in ponies and equines than other mammals. Therefore, attempts to improve second-intention wound healing in clinical practice should be directed to the stimulation of wound contraction.[3,11,12]

This report describes a cutaneo-myonecrosis of cervical and pectoral regions of an Arabian stallion following non-sterile injection of flunixin meglumine with emphasize on the optimal protocol approach to managing and successful treatment of the massive chronic torn wounds.

2. Case Description

A five-year-old Arabian stallion weighing 300 kg was referred to the Veterinary Teaching Hospital of Lorestan University, for diagnosis and treatment of a large infected chronic torn wound on the neck and pectoral regions. The animal had a history of loose appetite and depression last week. Owner claimed IM injection of 6 ml flunixin meglumine with a non-sterile needle and without disinfection of the injection site led to form a little painful lump in the neck of the horse 5 days later, which gradually grew up in the cervical and pectoral regions. Then, based on local veterinarian diagnosis, the horse received penicillin-streptomycin (Pen & Strep, Norbrook Co., Northern Ireland) 20 mg/kg BW, IM, SID and flunixin meglumine (Flumax M 5%, Rooyan Darou Co., Semnan, Iran) 10 mg/kg BW, IV, SID for 7 days. After above-mentioned treatment, ceftiofur sodium (Accent, Merkatorpharma Co., USA) 1 gr, IM, SID and ceftriaxone (Exir Pharmaceutical Co., Iran) 2 gr, IM, SID administered for 7 and 5 days, respectively. In 21 day, skin at the neck and pectoral areas were torn and discharged a lot of pus, subsequently, treatment with penicillin-streptomycin and flunixin meglumine were continued as described above for 7 consecutive days. Since the treatment was not successful and the horse condition deteriorated with a severe weight loss in the past 20 days, it was referred to the Veterinary Teaching Hospital (Figure 1a and b).

3. Clinical Findings

The clinical symptoms observed during the examination were hematuria, anorexia, and watery diarrhea. The

stallion had a body condition score of 4 based on the modified 9-point Henneke scale[13] and lameness score of 2 in the hind limbs based on the modified 5-point Obel scale.[14] Upon examining the affected area, a very large skin laceration, along with infection in the regions of the neck and chest were seen. External examination revealed the infectious cervical and pectoral muscles and dead skin with pus discharge and odorous smell. Skin and surrounding tissues were warm, edematous and swelled. The main vital signs of the horse were moderate tachycardia (60 beats/min), mild hyperthermia (rectal temperature was 38.7° C), capillary refill time was 5 sec, and mucous membranes were pale. Hematology analyses were performed together with blood parasite test examination before and after treatment (Table 1). The results of urinalysis revealed hematuria (more than 10 and less than 50 RBC/µl), proteinuria (trace, less than 30 mg/dl) and glucosuria (trace, 50 mg/dl). After centrifugation and cytological sediment examination, the presence of RBC in the urine sample approved.

Table 1. Results of hematology analyses of a stallion with cutaneo-muscular necrosis before and 70 days after treatment

Analyte (Unit)	Before	After	Reference Interval[28]
RBC ($\times10^{12}$/L)	7.3	11.2	6.8-12.9
HGB (g/L)	145	150	110-190
HCT (L/L)	0.50	0.37	0.32-0.53
MCV (fL)	39	42	37-59
MCH (Pg)	14.2	15.9	12.3-19.7
MCHC (g/L)	33.6	33.7	31.0-38.6
WBC ($\times10^{9}$/L)	20.7	12.2	5.4-14.2
Neutrophils ($\times10^{9}$/L)	5.23	4.11	2.3-8.5
Lymphocytes ($\times10^{9}$/L)	15.67	7.23	1.5-77

4. Treatment and Outcome

Based on the characteristics of the wound and physical status of the horse we decided to use surgical treatment including physical debridement for local skin cleansing and irrigation with 5.0% aqueous solution of povidone-iodine (Behsa Pharmaceutical Co., Arak, Iran) under pressure and gentle curettage along with passive drainage by sterile gas saturated 10% povidone-iodine for 2 days. Hereafter wound washed with normal saline solution and maggot debridement therapy (MDT) performed using live, sterile maggots of green bottle fly, *Lucilia* (*Phaenicia*) *sericata* for two days. To recover kidney and liver performance, elimination of diarrhea and hematuria, disposal previous drug residues and maintain the internal electrolyte balance of the body parenteral fluid therapy started via isotonic polyionic solutions (Ringer's and lactated Ringer's) 6 liters for three consecutive days accompanied by slow infusion of Aminoven 10%, (Fresenius Kabi Co., Austria), 2 ml/kg, IV, SID and probiotic powder (Bio-Equine, BioDEP, Zist Takhmir Co., Iran), 0.02 gr/kg, WF, SID, 6 days. Thereupon, in order to topical treating, wound was cleansed daily with normal saline solution and 25% zinc oxide (Daroopakhsh Pharmaceutical Co., Iran) and 0.2% nitrofurazone (Iran Najo Pharmaceutical Co., Iran) ointments were used on the marginal skin of the wound area and depth of the muscles, BID, for the first month, respectively. Along with topical treatment to reduce the damage to the under treatment region the diet was placed at a height of 50 cm above the ground level and the affected area was bandaged after topical treatment during the first month (Figure 1e). Then, a mixture of 1% phenytoin sodium (Daroopakhsh Pharmaceutical Co., Iran) and 1% silver sulphadiazine (Iran Najo Pharmaceutical Co., Iran) combination applied topically, BID, for the second month of the treatment period (Figure 1c and d). After elimination of hematuria, diarrhea and the return of appetite to the normal state, treatment continued with administration of penicillin G benzathine, (AFA Chemie Pharmaceutical Co., Iran), 60000 IU/kg, IM, SID, for 7 days; flunixin meglumine, (Flumax M 5%, Rooyan Darou Co., Semnan, Iran) at a dose rate of 1.1 mg/kg, IV, SID, for 3 days; Metronidazole 500 mg, (Pars Daroo Co., Iran), 15 mg/kg, PO, BID, for 5 days; Theranekron, (Richter Pharma ag., Wels, Austria), 0.03 mg/kg, SC, QWK, for 1 month, and vitamin B complex, (B Coject, Iran), 0.5 ml/kg, IM, SID for 5 days, and topical treatment was continued with replaced mixture

of 1% phenytoin sodium and 1% silver sulphadiazine, SID for 70 days. After 70 days, the wound was completely healed, but the scarring remained (Figure 1f, g, and h). Seventy-five days after treatment, all deteriorated hematological and urine parameters were within the reference ranges (Table 1) and no sign of infection and anemia was noted.

Figure 1. Timeline of wound appearance changing and healing process of cutaneo-muscular necrosis in cervical and pectoral region of Arabian stallion. Wound appearance before treatment (a), after mechanical debridement (b), at day 15 and after topical treatment with mixture of 25% zinc oxide and nitrofrozan 0.2% (c), at day 30 after topical treatment with combination of 1% phenytoin sodium and 1% silver sulphadiazine (d), to reduce the damage to the under treatment region the diet was placed at a height of 50 cm above the ground level and the affected area was bandaged after daily topical treatment during the first month (e), notice to decrease the depth and width of necrotic pectoral muscle after 15 days, at day 45 depth of muscle partially filled with new muscular tissue and epithelial tissue is growing and covering the damaged area (f), after 60 (g) and at the end of treatment duration (h) the affected area completely healed and a small scar remained.

5. Clinical Relevance

Flunixin meglumine is used in equine medicine in the prevention of endotoxic shock, in the management of colic patients, musculoskeletal injuries, and ocular diseases.[15-18] Intramuscular administration of flunixin is not advisable due to the side-effects of muscle soreness, as well as the possibility of severe complications (abscess, myositis). Intramuscular injection of flunixin meglumine is most commonly associated with clostridial myonecrosis, but it is unknown if this is because of the properties of the drug, or simply because this drug is more commonly injected intramuscularly than others.[17] Clostridial myositis subsequent to intramuscular flunixin meglumine, as well as hemolytic anemia, hepatopathy, osteitis and transient hypertrophic cardiomyopathy in horse has been reported in the scientific literature.[19]

The present case demonstrates the serious complications that can occur following IM injections. It seems this horse developed clostridia myositis with diarrhea and hematuria subsequent to the IM injection of flunixin meglumine and/or nonsterile injection. According to literature, most previously reported cases of clostridial myositis in horses developed after the IM administration of non-antibiotic medication.[8,9] The treatment protocol of the stallion was performed according to the reported protocols for treatment of acute myonecrosis in horses.[7] An aggressive pharmacological and surgical therapy is essential in the treatment of presumptive cases of myonecrosis. Surgical fenestration and/or debridement of necrotic tissues is essential in the treatment of myonecrosis. It provides oxygenation, reduces swelling, and makes it possible to clean the affected areas and to administer topical treatment. Systemic administration of antibiotics is warranted when the degree of infection exceeds the efforts of local control of the bioburden and signs of local soft tissue infection or systemic infection are apparent.[20] Muscle wounds typically respond very well to antimicrobial therapy, needing only a short course of treatment. Open drainage of muscle wounds, which is not difficult at most sites, speeds resolution of infection particularly with IM abscesses. Clostridial myonecrosis can rapidly cause severe systemic illness but with aggressive surgical debridement and aeration, local and systemic antibiotic therapy often resolve infection within days.[21] In the current case, we don't start

treatment with antimicrobial drugs, because owner claimed inappropriate use of different antibiotics for consecutive days which had led to the destruction of the cecal microbial flora, distrusting of the normal digestive condition, hematuria, and glomerular damage.

Because the indication for systemic antibiotic therapy is not always clear, antimicrobial drugs are often administered empirically, as a routine adjunct to the management of open wounds or when the wound is at high risk of infection, such as with puncture wounds, devitalized tissues, open fractures, or has entered a body cavity.[2] High doses of penicillin and metronidazole are recommended for treating deep fascial cellulitis, septic myositis, or pyonecrotic processes associated with Clostridium spp.[20] Antibiotic treatment of clostridial infection is typically required for weeks and discontinuation is based on the health of the affected tissues and negative culture results.[12,20] The duration of treatment of any wound infection is primarily dictated by the patient's response to therapy. The benchmarks that indicate a positive response include resolution of systemic signs of inflammation, continued improvement in comfort and function, reduction and ultimately resolution of the localized signs of inflammation and purulent discharge, negative culture result, and a normal rate of wound healing. Administration of antimicrobial drugs should not be continued once there is clinical and microbiologic evidence that an infection has been eliminated.[22,23]

We used MDT for the first time in the treatment of cutaneo-muscular necrosis of horse which had acceptable and positive results in improving the condition of the infected wound as they prefer necrotic tissues over healthy for feeding. Also, medicinal maggot larvae with secretion of digestive enzymes including carboxypeptidase, leucine aminopeptidase, collagenase, and serine proteases breakdown the dead tissue, liquidize it and ingest the resulting material and digest wound matrix which lead to degradation of extracellular matrix components laminin, fibronectin and collagen stimulate of healing and tissue debridement.[24]

Different factors can influence wound healing and the outcome of treatment; these must be recognized for a clinician to adapt his/her approach and to anticipate the evolution of the wound. Knowledge of these factors is prerequisite to effective client communication.[1] Primary closure refers to closing the wound immediately after cleansing, debriding, establishing proper drainage and immobilization, as needed.[25] If successful, this approach provides the best cosmetic and functional outcomes for the horse because bringing wound edges together covers the defect, protects from further contamination, and decreases the amount of tissue repair needed to re-establish skin function and integrity. Primary closure, however, can sometimes fail due to dehiscence caused by infection. A correct wound evaluation and preparation is, therefore, mandatory before any attempt at primary closure.[1] Repeated debridement and irrigation reduce the bacterial burden and prevent the formation of biofilm.[23] Repeated debridement and irrigation prior to closure, however, are certainly beneficial because wounds in horses are subject to heavy contamination.[26] For wounds with larger tissue defects and in which suturing the wound edges together is not possible, second-intention wound healing management is used. Large open wounds in horses are prone to a number of complications, including infection, prolonging recovery and long wound contraction time. Second-intention wound healing management do so mainly by the slow process of epithelialization; this new epithelial tissue is fragile and susceptible to reinjures which requires proper care and treatment.[27,28]

Finally, a number of important limitations need to be considered. First, this study did not evaluate the use of a sterile sample in wound area for aerobic and non-aerobic microbial culture. We believe the important bacterial agent which can grow in a similar situation is clostridia spp. Second, proper tissue samples from the affected area for histopathological examination and the diagnostic procedure were not prepared. Third, the study did not

investigate liver and kidney function by serum biochemical analysis after admission to Veterinary Teaching Hospital. This limitations means that the study findings need to be interpreted cautiously. To put it in a nutshell, early proper surgical intervention was necessary for the treatment of cutaneo-muscular necrosis and no local or general complication was observed postoperatively.

Conflict of Interests

None.

References

1. Kamus L, Theoret C. Choosing the best approach to wound management and closure. *Veterinary Clinic of North America Equine Practice,* 2018; 34(3): 499-509.
2. USDA. Equine: Baseline Reference of Equine Health and Management in the United States. Section I: Population Estimates, 2015:73-77.
3. Owen KR, Singer ER, Clegg PD, Ireland JL, Pinchbeck GL. Identification of risk factors for traumatic injury in the general horse population of north-west England, Midlands and north Wales. *Equine Veterinary Journal,* 2012; 44(2): 143–148.
4. Theoret CL, Bolwell CF, Riley CB. A cross-sectional survey on wounds in horses in New Zealand. *New Zealand Veterinary Journal,* 2016; 64: 90–94.
5. Adam EN, Southwood LL. Surgical and traumatic wound infections, cellulitis, and myositis in horses. *Veterinary Clinic of North America Equine Practice,* 2006; 22: 335-361.
6. Crum-Cianflone NF. Bacterial, fungal, parasitic, and viral myositis. *Clinical Microbiological Rev*iew, 2008; 21: 473-494.
7. Farias LD, Azevedo-Mda S, Trost ME, De La Corte FD, Irigoyen LF, De-Vargas AC. Acute myonecrosis in horse caused by *Clostridium novyi* type A. *Brazilian Journal Microbiology,* 2014; 45: 221-224.
8. Peek SF, Semrad SD, Perkins GA. Clostridial myonecrosis in horses (37 cases 1985-2000). *Equine Veterinary Journal,* 2003; 35: 86-92.
9. Rebhun WC, Shin SJ, King JM, Baum KH, Patten V. Malignant edema in horses. *Journal of the American Veterinary Medical Association,* 1985; 187: 732-736.
10. Sedigh HS, Rajabioun M, Razmyar J, Kazemi-Mehrjerdi H. An unusual necrotic myositis by Clostridium perfringens in a German Shepherd dog: A clinical report, bacteriological and molecular identification. *Veterinary Research Forum,* 2015; 6(4): 349-353.
11. Eggleston RB. Equine wound management: Bandages, casts, and external support. *Veterinary Clinic of North America Equine Practice,* 2018; 34(3): 557-574.
12. Theoret CL. Physiology of wound healing. In: *Equine wound management*. Theoret CL, Schumacher J, editors. 3rd edition. Ames (IA): Wiley Blackwell, 2017; 1–13.
13. Henneke DRPG, Kreider JL, Yeates BF. Relationship between condition score, physical measurements and body fat percentage in mares. *Equine Veterinary Journal,* 1983; 15: 371-372.
14. Obel N. Studies on the Histopathology of Acute Laminitis. Almquisst and Wiksells Boktryckeri, 1948.
15. Brooks DE. Equine ophthalmology. In: *Veterinary Ophthalmology*. Gelatt KN. editor, 3rd edition. Lippincott, Williams and Wilkins, Baltimore, 1998; 1053–1116.
16. Turek JJ, Templeton CB, Bottoms GD, Fessler JF. Flunixin meglumine attenuation of endotoxin-induced damage to the cardiopulmonary vasculature endothelium of the pony. *American Journal of Veterinary Research*, 1985; 46: 591–596.
17. Pellegrini-Masini A, Poppeng, RH, Sweeney RW. Disposition of flunixin meglumine injectable preparation administered orally to healthy horses. *Journal of Veterinary Pharmacology and Theraputics*, 2004; 27: 183–186.
18. Clark JO, Clark TP. Analgesia. *Veterinary Clinics of North America: Equine Practice,* 1999; 15: 705–723.
19. Anderson FL, Secombe CJ, Lester GD. Clostridial myonecrosis, haemolytic anaemia, hepatopathy, osteitis and transient hypertrophic cardiomyopathy after intramuscular injection in Thoroughbred gelding. *Australian Veterinary Journal*, 2013; 91: 204-208.
20. Siddiqui AR, Bernstein JM. Chronic wound infection: facts and controversies. *Clinical Dermatology*, 2010; 28: 519–526.
21. Wilson WD. Rational selection of antimicrobials for use in horses. *Proceeding of American Association Equine Practice Annual Convention*, 2001; 47: 75–93.
22. Freeman KD, Southwood LL, Lane J, Lindborg S, Aceto HW. Post-operative infection, pyrexia and

perioperative antimicrobial drug use in surgical colic patients. *Equine Veterinary Journal*, 2012; 44(4): 476–81.

23. Dart AJ, Sole-Guitart A, Stashak TS, Theoret C. Management practices that influence wound infection and healing. In: *Equine wound management*. Theoret CL, Schumacher J, editors. 3rd edition. Ames (IA): Wiley Blackwell, 2017; 47–74.
24. Dholaria S, Dalal P, Shah N. Narkhede R. Maggots debridement therapy [MDT]. *Gujarat Medical Journal*, 2014; 69: 1.
25. Elce YA. Approaches to wound closure. In: *Equine wound management.* Theoret CL, Schumacher J, editors. 3rd edition. Ames (IA): Wiley Blackwell, 2017; 157–72.
26. Dart AJ, Sole-Guitart A, Stashak TS. Selected factors that negatively impact healing. In: *Equine wound management*. Theoret CL, Schumacher J, editors. 3rd edition. Ames (IA): Wiley Blacwell, 2017; 30–46.
27. Carnevali F, Argentieri M, Ippedico G, Alberto Minniti C, Amodio L, Mellano L, Andrew van der Esch S. Managing horse wounds either presenting or not with exuberant granulation tissue using an innovative wound dressing: A retrospective non-controlled study. *Journal of Animal and Veterinary Sciences*, 2014; 1(2): 6-16.
28. Constable P, Hincheliff KW, Done S, Gruenberg W. Veterinary medicine: A textbook of the disease of cattle, horses, sheep, pigs and goats. 13: Diseases of the urinary system. Philadelphia, PA, USA. 11th edn. Saunders Elsevier, 2017.