CASE REPORT

Clostridial Cellulitis in the Horse: A Report of Five Cases

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Summary

Five horses with fatal clostridial cellulitis are described. The characteristic findings were the rapid development of a crepitant swelling with an associated toxemia, which in four cases followed intramuscular injections. The clinical features, diagnostic techniques and pathogenesis are discussed. The importance of an early diagnosis is emphasized.

Key words: *Clostridium,* cellulitis, myositis, horse.

Résumé

Rapport de cinq cas de cellulite équine à clostridies

Cet article rapporte cinq cas de cellulite équine mortelle, due à des clostridies. Les observations caractéristiques se traduisaient par le développement rapide d'une tuméfaction crépitante qui s'accompagnait d'une toxémie, laquelle résultait d'injections intramusculaires, dans quatre cas. Les auteurs commentent les signes cliniques, les moyens de diagnostic et la pathogénèse de cette cellulite, en insistant sur l'importance d'un diagnostic précoce.

Mots clés: *Clostridium,* cellulite, myosite, cheval.

Introduction

Clostridial cellulitis of horses is a rapidly progressive, fatal disease which has been infrequently reported. It is characterized by a rapidly enlarging, localized swelling with subcutaneous emphysema, toxemia (1,2,3,4,5,6,7,8,9) and, in most cases, death (3,4,5,6,7,8,9). The disease usually develops as a sequel to an intramuscular injection (1,2,3,4,5,9) but penetrating wounds have been incriminated (7) and occasionally the disease may be idiopathic (6,8). *Clostridium perfringens* (2,5,7,9), *C. septicum* (1,3,4,9) and *C. chauvoei* (1,6,8) have been the reported etiologic agents. Early laboratory diagnosis can be established by immunofluorescence of aspirates from the swellings (1,2,5,9). Other diagnostic tests include anaerobic and aerobic culture and guinea pig inoculation (3,6,7,8,9,10).

The purpose of this paper is to report five cases of clostridial cellulitis in the horse, to emphasize the importance of early recognition and to discuss methods of diagnosis.

Case Reports

Case No. 1

A seven year old Standardbred mare was referred to the Ontario Veterinary College (OVC) with a swelling over the left cervical region. The mare had been injected intramuscularly 48 hours previously with ivermectin.[1] Thirty-six hours postinjection the mare showed signs of abdominal pain and was treated with procaine penicillin G[2] intramuscularly and intravenous flunixin meglumine.[3]

On presentation the mare was depressed, sweating profusely and continuously pawing the ground. The left cervical region had marked crepitant swelling which extended from the ramus of the mandible to the shoulder. The mare did not resent palpation of the area. Rectal temperature was 39.5°C, heart rate was 84/min and respiratory rate was 36/min. The visible mucous membranes were congested, dry and the capillary refill time was three seconds. Dehydration was estimated at 10% body weight. The hematocrit was 0.66 L/L and the total protein was 60 g/L. No bowel sounds could be auscultated. Rectal examination and gastric intubation revealed no abnormalities other than a gas distended large bowel.

A hematological examination revealed a normal leukocyte count (5.7 x 10^9/L) with a mild neutropenia (1.59 x 10^9/L) and mild toxic changes. The results of further diagnostic tests are summarized in Table I.

A sample of subcutaneous fluid was aspirated from the cervical swelling. Cytological evaluation showed large numbers of spore forming Gram-positive bacilli which were identified by immunofluorescence as *Clostridium septicum* and *C. novyi.*

Treatment instituted included intravenous potassium penicillin[4] (20 million units), flunixin meglumine[5] (1.5 g), prednisolone sodium succinate[6] (500 mg), meperidine hydroch-

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[1]Eqvalan, Merck Sharpe and Dohme Canada Ltd., Mississauga, Ontario.
[2]Pen Aqueous, Armitage Carroll Ltd., London, Ontario.
[3]Banamine, Schering Canada Inc., Pointe Claire, Quebec.
[4]Penicillin G Potassium, Ayerst Laboratories, Montreal, Quebec.
[5]Banamine, Schering Canada Inc., Pointe Claire, Quebec.
[6]Solu-Delta-Cortef, The Upjohn Co., Don Mills, Ontario.

TABLE I
LABORATORY DATA FROM A HORSE WITH CLOSTRIDIAL CELLULITIS (CASE NO. 1)

Test	On Admission	4 Hours Later	Normal Values
Hematocrit (L/L)	0.66	0.70	0.29-0.53
TP (g/L)	60	—	57-74
pH	7.31	7.20	7.27-7.55
pCO_2 (mm Hg)	47.5	40.0	47
HCO_3 - (mm Hg)	23.2	15.1	29
Base Excess (mEq/L)	-3.2	-14.8	+/-2
Na (mmol/L)	140.5	—	134-142
K (mmol/L)	3.27	—	2.1 -4.2
Cl (mmol/L)	98.9	—	94-106
Creatinine (mmol/L)	299	—	70-140
SGOT (μ/L)	680	—	200-400
CPK (μ/L)	9600	—	50-250
Fibrinogen (g/L)	2.2	—	1.6 -2.9

loride[7] (1 g), two doses of xylaxine[8] (100 mg) one hour apart and 36 litres lactated Ringers solution.

The mare continued to deteriorate and the crepitant swelling progressed to involve the head, larynx, left cervical area and left scapular region. The heart rate increased to 92/min and her hematocrit rose to 0.70 L/L. The visible mucous membranes became purple and four hours after admission the mare died.

Postmortem examination revealed marked edema, hemorrhage and emphysema in the subcutis and muscles of the face, larynx, neck, left shoulder and medial aspect of the left forelimb. No anaerobic bacteria were cultured from affected muscle.

On histopathological evaluation, focal and generalized areas of muscle degeneration and necrosis were evident in striated muscle tissues. Extensive areas of myofiber fragmentation were surrounded by an acute inflammatory infiltrate consisting primarily of degenerate neutrophils. In some areas dilated spaces existed between muscle fiber bundles. Blood vessels in necrotic tissues were dilated and congested. Interstitial spaces contained proteinaceous edema and hemorrhage.

Case No. 2

A seven year old Quarter horse mare which had been injected in the left gluteal muscles with a synthetic prostaglandin[9] was referred to the OVC with anorexia, abdominal pain and swelling which developed at the injection site. Intramuscular procaine penicillin[10] and intravenous phenylbutazone[11] were administered prior to presentation.

On admission the mare appeared extremely depressed, sweated profusely and walked stiffly. The mare pawed the ground and shifted her weight continuously. Numerous subcutaneous crepitant swellings were present which extended from the left hip to the neck region (Figure 1). Rec-

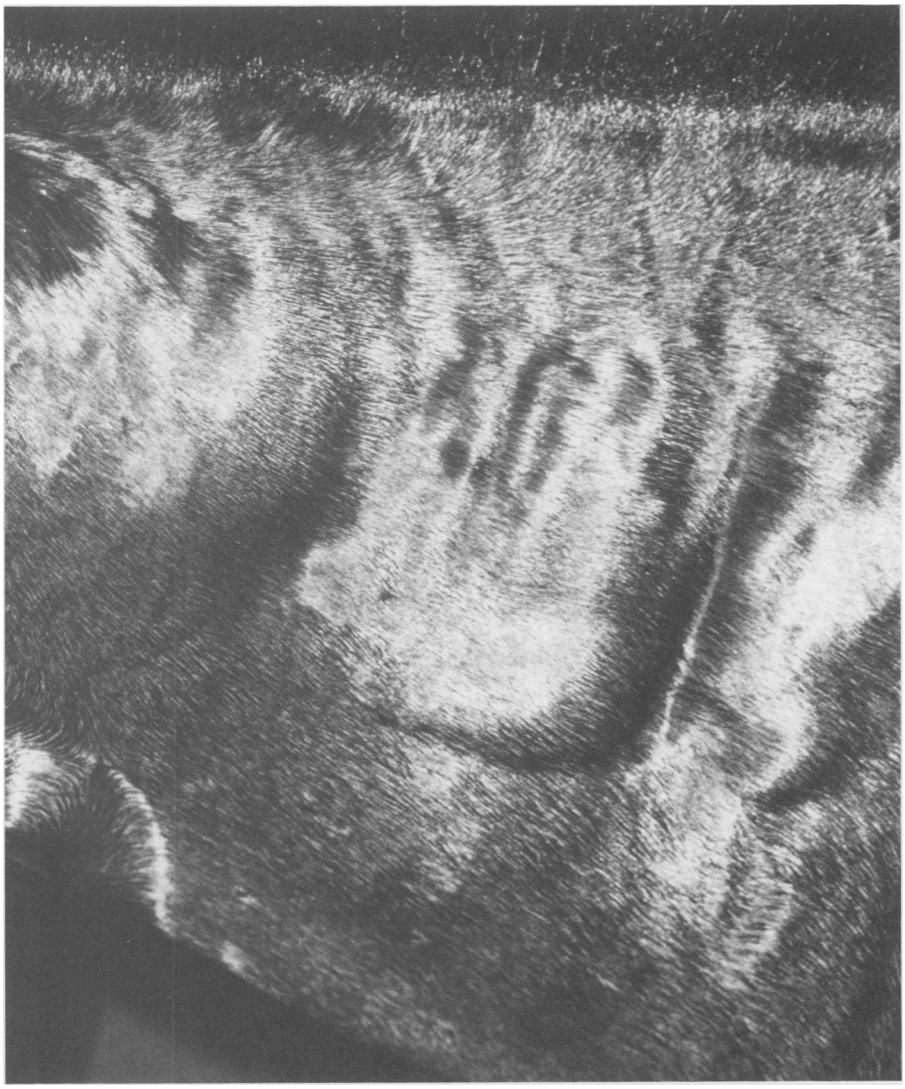

FIGURE 1. Marked emphysema in the cervical area of a horse with clostridial cellulitis (Case no. 2).

[7]Demerol, Winthrop Laboratories, Aurora, Ontario.
[8]Rompun, Haver-Lockhart, Mississauga, Ontario.
[9]Synchrocept (prostalene) solution, Syntex Inc., Mississauga, Ontario.
[10]Pen Aqueous, Armitage Carroll Ltd., London, Ontario.
[11]Butazone, Rogar/STB, London, Ontario.

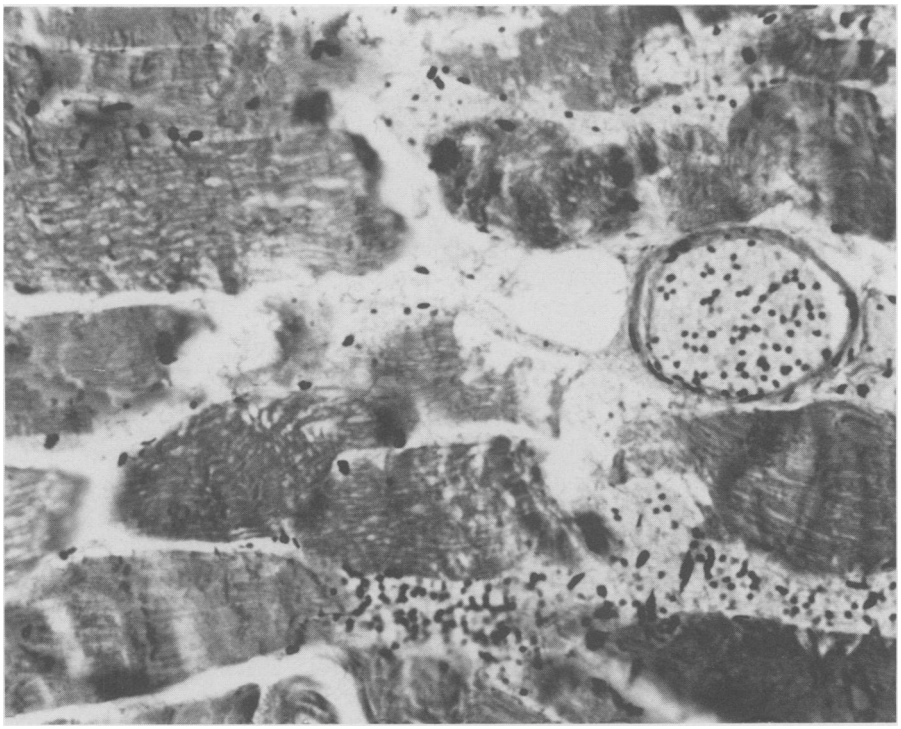

FIGURE 2. Early degeneration, hypercontraction, vacuolation and fragmentation of muscle fibres from a horse with clostridial cellulitis. *Clostridia* (arrows) from a horse with clostridial cellulitis (Case no. 2).

tal temperature was 38.1°C, heart rate was 72/min and respiratory rate was 28/min. The visible mucous membranes were congested, dry and capillary refill time was three seconds. The mare was approximately 10% dehydrated the hematocrit was 0.58 L/L and the total serum protein was 55 g/L. No bowel sounds could be auscultated and rectal examination revealed a mild impaction of the pelvic flexure. A venous blood-gas analysis indicated a metabolic acidosis, pH 7.27, PCO_2 38 mm Hg, bicarbonate 20 mEq/L, with base excess -9 mEq/L.

The mare was treated intravenously with potassium penicillin[12] (30 million units), flunixin meglumine[13] (2.5 g), sodium bicarbonate (1680 mEq) and 23 litres of lactated Ringers solution. A deep incision was made over the left gluteal region and debridement was performed. No pain was present during this local treatment. The area was flushed with hydrogen peroxide, povidone iodine[14] and 5 million units of potassium penicillin[15] in 500 mL of saline. The mare progressively deteriorated and died four hours after presentation.

On postmortem examination extensive crepitant swelling was present over the left gluteal, flank and shoulder regions. Marked edema and hemorrhage were present (Figure 2). The muscles surrounding the hip incision had a cream-colored necrotic core of muscle tissue with a cooked appearance and a faintly sweet smell. Large numbers of *Clostridium chauvoei* were identified by immunofluorescence and large numbers of *C. perfringens* were cultured anaerobically. *Escherichia coli* was recovered from subcutaneous edema fluid but not from muscle tissue.

The histological appearance of the affected muscle (Figure 2) resembled that described previously in case no. 1 and, in addition, foci of bacilli were present (Figure 3).

Case No. 3

A six year old gelding was presented to the OVC three days after sustaining a pitchfork wound in the left rump. Treatment had included intramuscular penicillin dihydrostreptomycin,[16]

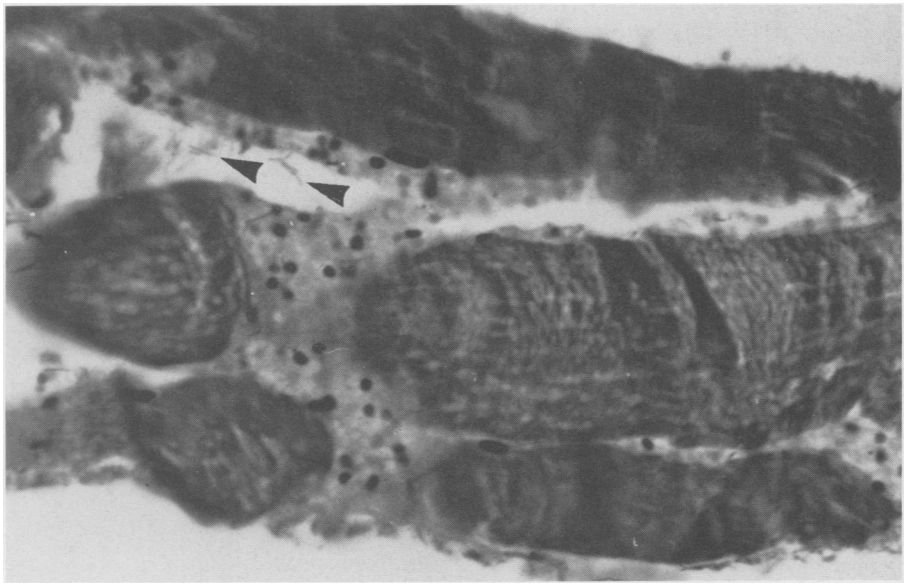

FIGURE 3. Two adjacent myofibers in hypercontraction surrounded by edema fluid in which are suspended pyknotic nuclei, red blood cells and Edema, hemmorhage and pyknotic nuclei are evident and veins are congested and degenerate (Case no. 2).

[12]Penicillin G Potassium, Ayerst Laboratories, Montreal, Quebec.
[13]Banamine, Schering Canada Inc., Pointe Claire, Quebec.
[14]Betadyne Solution, The Purdue Frederick Co., Montreal, Quebec.
[15]Penicillin G Potassium, Ayerst Laboratories, Montreal, Quebec.
[16]Pen di Strep, Rogar/STB, London, Ontario.

furosemide[17] and 1500 I.U. tetanus antitoxin.[18]

On admission the gelding was depressed and extremely painful over the left hindlimb. Swelling involved the entire hindleg and rump and focal crepitus was present dorsally around six distinct puncture wounds. The rectal temperature was 40°C. The heart rate was 92/min and the respiratory rate was 40/min. No bowel sounds could be auscultated. Hematology revealed a hematocrit of 0.50 L/L and a normal white blood cell count (10.2 x 10^9/L) with evidence of a stress response.

Treatment consisted of a local magnesium sulphate compress, intramuscular penicillin (6 million units) with dihydrostreptomycin[19] (7.5 g) and phenylbutazone[20] (2 g) intravenously. The gelding became recumbent, was unable to rise and died within six hours of admission.

Postmortem examination revealed extensive edema and hemorrhage in the subcutis of the entire left hindlimb and extending to the prepuce and left lateral abdominal wall. Massive muscle necrosis, edema and emphysema were present in the area of the six, 3 cm deep, wounds.

Large numbers of *Clostridium chauvoei* and *C. septicum* were identified by immunofluorescence on muscle smears. The histological findings were similar to case no. 1.

Case No. 4

A yearling colt was treated for colic with unknown preparations and two days later developed a crepitant swelling over the left cervical area. The cold exhibited signs of abdominal pain, the heart rate was 120/min and signs of shock were present. The colt died soon after examination.

Postmortem examination at the OVC revealed widespread hemorrhage, edema and emphysema in the subcutis and muscle of the cervical, pectoral and ventrolateral thoracic regions. Muscle tissue was soft, red to black in color and had a strong butyric odor. *Clostridium septicum* in large numbers were identified by immunofluorescence on muscle smears.

Histological findings were similar to case no. 1 and, in addition, numerous bacilli were seen in the necrotic tissue.

Case No. 5

A seven year old Standardbred mare in late pregnancy was examined because of anorexia. The mare's teeth were rasped and vitamin B complex administered intramuscularly into the cervical area. Two days later the horse had signs of abdominal pain and a swelling was present over the injection site. Rectal temperature was 39.2°C and heart rate was 80/min. Treatment consisted of dioctyl sodium sulfosuccinate,[21] mineral oil and warm water by stomach tube. Three days postinjection there was an extensive crepitant swelling covering the head, neck, pectorals and forelimbs. The heart rate had risen by then to 100/min. Treatment consisted of intramuscular penicillin-dihydrostreptomycin[22] and a dexamethasone-trichlormethiazide[23] combination. The mare died that day.

Postmortem examination at the OVC revealed marked edema, hemorrhage and emphysema, in the muscles and subcutaneous tissues of the head, neck, chest and upper forelimbs. Immunofluorescent staining was negative for *Clostridia* and anaerobic culture was negative. A small number of *E. coli* were isolated aerobically. Inoculation of a guinea pig with affected muscle tissue resulted in death and *C. septicum* was isolated. No bacteria were detected when the vitamin B complex solution was cultured aerobically and anaerobically and examined microscopically. Histopathological examination of muscle tissue showed similar findings to those in case no 1.

Discussion

All five cases seen at OVC were fatal. Successful treatment of clostridial cellulitis requires early recognition, local debridement, local and parenteral penicillin and supportive therapy such as intravenous fluid administration. Four cases have been reported where recovery occurred following the early institution of such treatments (1,2,9).

Recognition of clostridial cellulitis necessitates knowledge of the clinical features, supplemented by appropriate diagnostic tests. Initially, our cases presented with a rapidly developing, hot, painful swelling within 48 hours of injection or injury. As the swellings enlarged crepitus developed, localized pain appeared to decrease and all the horses became depressed with elevated heart and respiratory rates. Profuse sweating and marked dehydration became evident. The dehydration became extremely difficult to correct and was probably due to fluid sequestration in necrotic muscle mass, increased vascular permeability caused by clostridial toxins (11) and progressive shock. Death soon followed. It is interesting that all cases had signs of severe abdominal pain, which became evident late in the course of the disease. While clinically and at postmortem no gastrointestinal abnormalities were present, the sweating, pawing, treading, lack of bowel sounds and increased respiratory and heart rates all clinically resembled features of abdominal pain. These clinical findings are cited in two other cases of clostridial cellulitis (3,4). Clostridial cellulitis in man is associated with severe pain originating from the periphery of the wound (10).

Diagnosis can readily be achieved using Gram stains and immunofluorescent staining on a subcutaneous fluid apirate taken from the swelling. Postmortem diagnosis can be made on a large sample of muscle tissue obtained soon after death and stored at 50°C during transport to the diagnostic laboratory (12,13). Laboratory diagnostic procedures include Gram stain and immunofluorescent staining on impression smears and aerobic and

[17]Lasix, Hoechst Canada Inc., Toronto, Ontario.
[18]Tetanus Antitoxin, Colorado Serum Co., Denver, Colorado.
[19]Pen di Strep, Rogar/STB, London, Ontario.
[20]Butazone, Rogar/STB, London, Ontario.
[21]Dioctol, Rogar/STB, London, Ontario.
[22]Pen di Strep, Rogar/STB, London, Ontario.
[23]Naquasone, Schering Canada Inc., Pointe Claire, Quebec.

anaerobic culture. Guinea pig inoculation has been a standard diagnostic procedure but it can produce misleading results (10), due to the ability of *C. septicum* to invade tissues after death and multiply more rapidly than any primary pathogen present. Slower growing primary pathogens would not be detected using this technique. For these reasons, in our case no. 5 the *C. septicum*, isolated using guinea pig inoculation, may not have been the primary pathogen. The ideal diagnostic technique is to isolate large numbers of the causative *Clostridia* from a sample taken before or soon after death.

The origin of the *Clostridia* involved in these cases is open to speculation. The spores could have originated from two sources. They could have been introduced, either in the drug product or with the needle, or they could have been endogenous in the muscle. It is unlikely that the spores were present in the drug product because several horses received injections from each of the drug vials but only one horse became ill on each occasion. In addition, no bacteria were isolated from the drug used in case no. 5. It is possible since *Clostridia* are present in soil and feces (13) that the infection was introduced by a penetrating wound or contaminated needle in all these cases.

It has not been established whether dormant clostridial species are present in equine muscle. In healthy cattle *C. novyi* spores are found in the liver and *C. chauvoei* spores have been found in spleen and liver tissue (14,15). It appears that spleen, liver and muscle are seeded by spores from the intestine which remain dormant until tissue necrosis occurs (11). *Clostridium novyi* has been isolated from the livers of three horses which died from infectious necrotic hepatitis (17,18,19). Activation of dormant *C. chauvoei* spores in bovine muscle can be achieved by injecting a necrotizing solution intramuscularly (16). It is also possible that, in horses, intramuscular injection of an irritating drug produces a similar effect. The five cases described were fatal clostridial infections, four of which followed intramuscular injections. Aseptic injection technique is currently the most practical prevention available.

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