

# Case Report Rapport de cas

## Costochondral junction osteomyelitis in 3 septic foals

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**Abstract** – The costochondral junction constitutes a potential site of infection in septic foals and it could be favored by thoracic trauma. Standard radiographs and ultrasonography are useful tools for diagnosis of this condition and ultrasound-guided needle aspiration could permit the definitive confirmation of infection.

**Résumé** – L'ostéomyélite de la jonction costochondrale chez trois poulains septicémiques. La jonction costochondrale constitue un site potentiel d'infection chez le poulain septicémique et le développement de l'infection pourrait être favorisée par un traumatisme costal. Les radiographies standards et l'échographie sont des aides diagnostiques et l'aspiration à l'aiguille échoguidée pourrait permettre une confirmation définitive de l'infection.

(Traduit par les auteurs)

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### Case descriptions

#### Foal 1

**A** 5-day-old Holsteiner filly was presented to the Veterinary Teaching Hospital (VTH) for diarrhea of 2 days duration and failure of passive transfer. She was born at 318 gestational days from a primiparous mare. Before admission, the foal had received penicillin, amikacin, and a blood transfusion from the dam.

The initial examination revealed a normal rectal temperature [38.5°C; reference range (RR): 37.0°C to 39.0°C] and heart rate [100 beats/min (bpm), RR: 80 to 120 bpm], but a moderate tachypnea (60 breaths/min; RR: 20 to 40 breaths/min). Based on the grade 0–5 Lameness Scale of the American Association of Equine Practitioners, a 3/5 left hindlimb lameness was identified. The entire left hock was swollen and a superficial cutaneous wound was present on the lateral side. The navel was swollen and dry. Biochemical tests revealed a transient hyperglycemia (11.2 mmol/L; RR: 3.4 to 6.2 mmol/L) that was attributed to the stressed condition of the foal. A complete blood (cell) count (CBC) revealed an inflammatory leukocytosis ( $19.3 \times 10^9/L$ ; RR:  $5.5$  to  $12.5 \times 10^9/L$ ), neutrophilia

( $15.6 \times 10^9/L$ ; RR: 2.7 to  $6.7 \times 10^9/L$ ), lymphopenia ( $1.2 \times 10^9/L$ ; RR: 1.5 to  $7.5 \times 10^9/L$ ), monocytosis ( $1.7 \times 10^9/L$ ; RR: 0 to  $0.8 \times 10^9/L$ ) and hyperfibrinogenemia (8 g/L; RR: 2 to 4 g/L). Failure of passive transfer of immunity was confirmed by semi-quantitative analysis of blood IgG by enzyme-linked immunosorbent assay (ELISA) (Snap® Foal™, Idexx Laboratories, Markham, Ontario) with a result of < 4 g/L.

Thoracic radiographs revealed a caudoventral interstitial to alveolar pattern (Figure 1A). Arthrocentesis of the left tibiotarsal joint performed under sedation (xylazine, Rompun; Bayer Health Care, Toronto, Ontario), 0.3 mg/kg body weight (BW), IV yielded fluid that was classified as slightly suppurative based on an elevated leukocyte count ( $1.82 \times 10^9/L$ ; normal value: <  $0.5 \times 10^9/L$ ) and protein (35 g/L; normal value: < 25 g/L) and with a differential of lymphocytes (87%) and fewer neutrophils (13%; normal value: < 10%), suggestive of septic arthritis or possibly secondary to mild cellulitis from the superficial wound over the hock. No bacteria were recovered from the joint fluid.

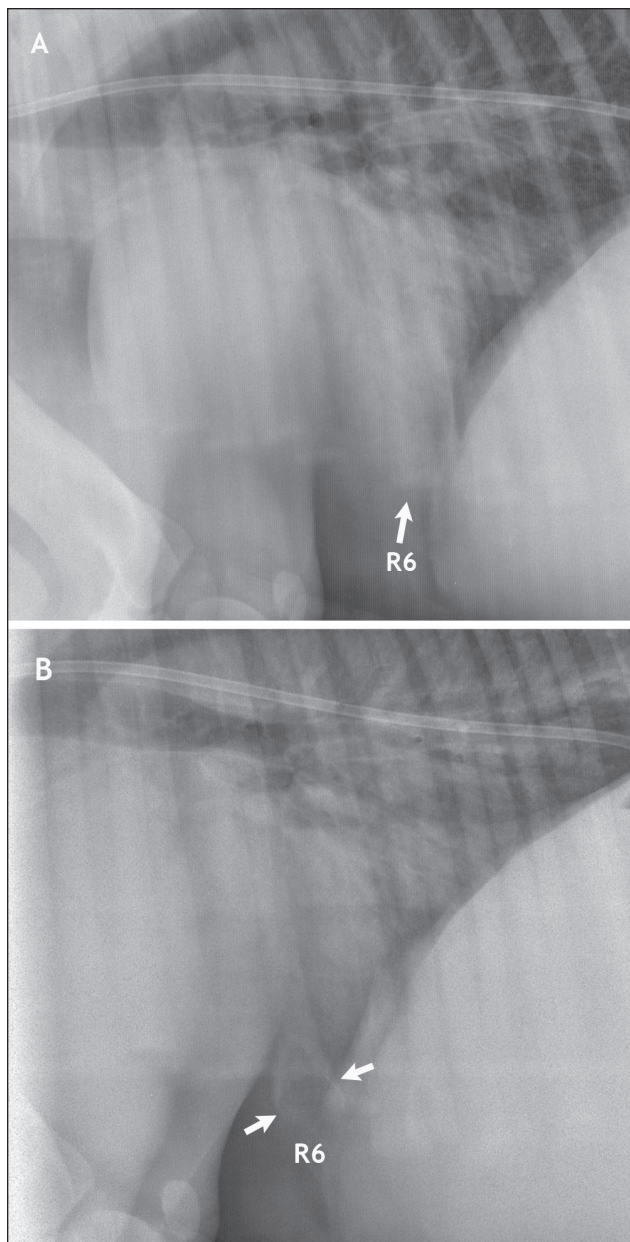
The filly was initially treated with sodium penicillin (penicillin G; Novopharma, Toronto, Ontario), 22 000 IU/kg BW, IV, q6h and amikacin (Amiglyde-V; Fort Dodge Animal Health, Fort Dodge, Iowa, USA), 20 mg/kg BW, IV, q24h. The foal was sedated (xylazine, Rompun; Bayer Health Care), 0.2 mg/kg BW, IV and the left tibiotarsal joint was flushed with 1 L of 0.9% NaCl using thru-and-thru needle lavage. Amikacin (250 mg) was injected into the tibiotarsal joint post-lavage. *Escherichia coli* was isolated from blood culture and determined to be susceptible to penicillin and amikacin. On initial radiographs (day 1), punctate lucencies were suspected on the medial margin of the talus, in association with regional soft tissue swelling, suggesting septic arthritis. Also, the soft tissue around the joint was swollen. On day 2, the left tibiotarsal joint was examined by ultrasound and significant fibrin accumulation in the medial and lateral plantar compartment of the joint was identified. Repeat

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**Figure 1.** Initial (A) and follow-up (B) computed radiographs of the thorax in foal 1. A – On day 1, increased soft tissue opacity is present in the caudoventral lung field, consistent with pneumonia. This increased opacity limits one's ability to visualize the overlying ribs, which appear normal. A nasogastric tube is visible dorsal to the trachea and cardiac silhouette. R6, 6th rib. B – On day 7, the distal portion of the 6th rib (R6) is now enlarged (arrows) and associated with expansile bony lysis. Proximally, this lytic reaction shows an ill-defined and heterogeneous transitional zone. An interstitial pattern is also present in the caudal lung field indicative of pneumonia.

arthrocentesis of the left tibiotarsal joint at day 3 revealed an elevation of leukocytes ( $14.1 \times 10^9/L$ ) and total protein (38 g/L), suggesting a septic arthritis. An arthrotomy of the left tibiotarsal was performed under general anesthesia to improve efficacy of joint flushing and debridement.

Follow-up radiographs of the left hock on day 7 confirmed the presence of ill-defined bone lysis involving approximately 2 cm of the medial ridge of the talus, indicating

progressive osteomyelitis, despite systemic antimicrobial therapy. Additionally, the foal developed joint distension of the left carpus on day 8. On radiographic examination, the medial and proximal subchondral plates of the intermediate carpal bone were ill-defined compared with other bone surfaces, suggesting early bone reaction. Arthrocentesis of the left carpal joint performed under sedation (xylazine, Bayer Health Care), 0.3 mg/kg BW, IV yielded fluid that was moderately suppurative with an elevated leukocyte count ( $63.0 \times 10^9/L$ ) and protein (42 g/L). Septic arthritis was suspected based on the elevated neutrophil count in the sample. The joint fluid was not submitted for bacteriological examination. Follow-up thoracic radiographs obtained on day 8 revealed expansile bone lysis with proliferation at the level of the 6th CCJs (Figure 1B). On ultrasound, the left 6th CCJ appeared enlarged and heterogeneous with a central hyperechoic focus, compared with the neighboring junctions. Ultrasound-guided fine-needle aspiration of the CCJ was attempted without success. An umbilical ultrasound revealed enlargement of the right umbilical artery and hypoechoic foci caudal to the umbilical stump suggesting fluid accumulation between the urachus and both umbilical arteries. Due to financial constraints and the poor prognosis, euthanasia was performed after 9 days of hospitalization.

Necropsy revealed fibrinous to purulent arthritis of the left tibiotarsal, radiocarpal, and intercarpal joints, purulent omphaloarteritis and osteomyelitis of the 6th left rib localized at the costochondral junction which was enlarged and filled with purulent material. Histologically, the lesions corresponded to a subacute purulent osteomyelitis localized at the metaphysis and costal growth plate. A subacute villous arthritis was present in the tarsus and the carpus. Small foci of neutrophils were observed in the liver parenchyma. There was no change in the lungs, heart, spleen, ileum, and kidneys. *Escherichia coli* was isolated from the CCJ and the umbilicus.

## Foal 2

A 5-day-old Appendix colt arrived at the VTH with colic of 2 days duration and difficulty standing. Despite medical treatment (mineral oil; Laboratoire Atlas, Anjou, Quebec) by nasogastric intubation, and flunixin meglumine (Banamine; Schering-Plough, Kirkland, Quebec), 1 mg/kg BW, IV from the referring veterinarian the colt remained uncomfortable and became progressively weaker.

Upon arrival the foal was depressed and anorectic. Physical examination revealed hyperthermia ( $39.8^\circ C$ ), tachycardia (120 bpm), mild tachypnea (40 breaths/min), a purulent draining umbilicus and bilateral tibiotarsal, femorotibial and radiocarpal joint effusion. Hematologic findings included a leukocytosis ( $15.9 \times 10^9/L$ ), with a neutrophilia ( $13.4 \times 10^9/L$ ), and an elevated fibrinogen (11 g/L), suggestive of an inflammatory process. Semi-quantitative analysis of serum IgG by ELISA (Snap® Foal™, Idexx Laboratories) yielded a result of  $> 8$  g/L. Arthrocentesis of both tibiotarsal joints was performed under sedation (xylazine, Bayer Health Care), 0.3 mg/kg, IV on day 2. The cytological examination showed increased leukocytes in the left ( $35.6 \times 10^9/L$ ; neutrophils 92%) and right tibiotarsal joints ( $14.7 \times 10^9/L$ ; neutrophils 90%). Phagocytosed bacteria

were identified in the right tibiotarsal joint fluid. *Klebsiella pneumoniae* was isolated from both hocks. Both tibiotarsal joints were lavaged with 1 L of 0.9% NaCl using a thru-and-thru large gauge needle (day 2). Post-lavage, 125 mg of amikacin was injected into each joint.

The foal was administered broad spectrum antimicrobials, sodium penicillin, (Novo-Penicilline G, Novopharma), 22 000 IU/kg BW, IV, q6h and amikacin (Amiglyde-V; Fort Dodge Animal Health), 10 mg/kg BW, IV, q12h; metronidazole (APO-metronidazole; Apotex, Toronto, Ontario, Canada), 15 mg/kg BW, PO, q6h, and cimetidine (APO-cimetidine; Apotex), 25 mg/kg BW, PO, q6h, and mineral oil (400 mL) by nasogastric intubation.

A pure culture of *Klebsiella pneumoniae* susceptible to penicillin and amikacin was isolated from the hemoculture and articular fluid. On day 3, arthrocentesis of both femorotibial and both radiocarpal joints revealed an abnormal macroscopic articular fluid but no cytological examination was performed because of financial limitations. We suspected septic processes in all 4 synovial structures. All affected joints were lavaged with 1 L of 0.9% NaCl with thru-and-thru large gauge needles and 125 mg of amikacin was locally injected. Ultrasonography of the thorax revealed rib fractures near CCJs from the 3rd to the 6th left ribs with several hyperechoic foci. Several of these ribs appeared irregular and deformed on a ventro-dorsal radiograph; however, CCJ involvement was not clear. Ultrasonography of the draining umbilical structures showed a patent urachus. All septic joints were regularly flushed under sedation. Phenylbutazone (Phenylbutazone; Univet Pharmaceuticals, Milton, Ontario), 1.1 mg/kg BW was added to therapy for pain control. On day 10 radiographic re-evaluation of the right carpus and both tibiotarsal joints revealed osteolytic lesions involving the distal radial and tibial physis, as well as joint effusion. As the foal's condition deteriorated despite antimicrobial therapy and because of a poor prognosis, euthanasia was elected by the owner 10 days after admission.

At necropsy, multiple rib osteomyelitis, suppurative polyarthritis, suppurative omphalitis, intramuscular abscesses on both quarters and lung atelectasia were diagnosed. On macroscopic examination, the CCJ of the 3rd through the 8th left ribs were enlarged and abscessed on cut section. Hemorrhage was present within the right 7th and 8th CCJ. Microscopically, the CCJ region of the abscessed ribs was remodeled: the cartilage and bone were replaced by fibrinonecrotic material including degenerate neutrophils and fragments of necrotic bone and cartilage. Proliferation of fibrous tissue and increased osteoclastic activity were noted in the surrounding tissues. Woven bone was produced under the adjacent periosteum. Infiltration of lymphocytes and some degree of fibrosis were present in the intercostal muscles. One synovial membrane was diffusely thickened by edema and neutrophils. Portions of necrotic mineralized material associated sometimes with neutrophils; macrophages and rare giant cells were present at the surface and within the synovial membrane. In the other synovial membranes, there was synovial cell hyperplasia, villous hyperplasia and neutrophilic and lymphocytic infiltrations. Small foci of neutrophils were present in the hepatic sinusoids. No significant change was noted in the

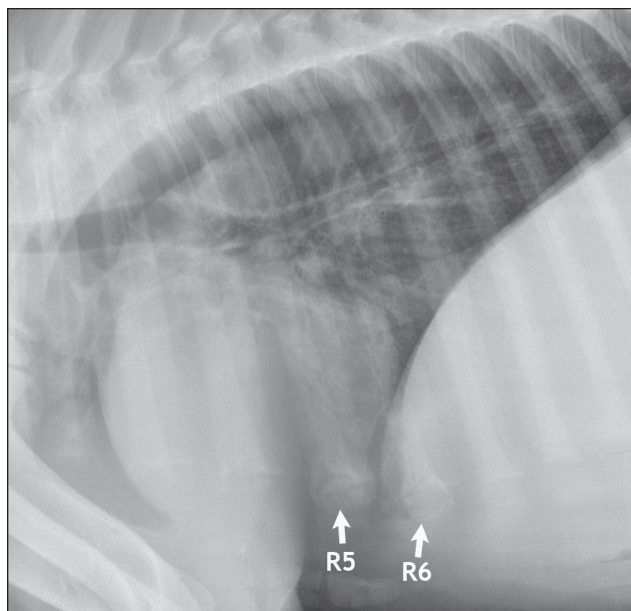
spleen, lungs, and heart. For technical reasons, bacterial culture could not be performed on the tissue samples.

### Foal 3

A 2-week-old Thoroughbred filly was referred to the VTH for fever and diarrhea. The foal displayed signs of dysmaturity at birth and a fever of unknown origin since 3 days of age. She had been treated with intramuscular ceftiofur sodium (Excenel; Pfizer Animal Health, Pfizer Canada, Kirkland, Quebec), 2.2 mg/kg BW, q12h, but developed abscesses at the neck injection sites, so antimicrobial therapy was switched to oral trimethoprim-potentiated sulphonamides (Novo-Trimel DS; Novopharm/Tevapharm, Toronto, Ontario). The diarrhea started the same day as the foal's admission to the VTH.

On arrival the filly had an elevated body temperature (39.4°C), tachycardia (160 bpm), and a mild tachypnea (28 breaths/min). Signs of dehydration (dry mucosa, capillary refill time at 3 to 4 s) were observed. The right tibiotarsal joint and right metacarpophalangeal joints were effused. An abscess was present on the left side of the neck and was surgically opened upon arrival. Irregular swellings were also observed on both sides of the neck. Semi-quantitative analysis of passive transfer showed a blood IgG level of > 8 g/L. The CBC revealed an inflammatory leukocytosis ( $39.2 \times 10^9/L$ ), characterized by a mature neutrophilia ( $35.7 \times 10^9/L$ ) and hyperfibrinogenemia (6 g/L). Biochemical analysis revealed abnormalities including elevated serum urea (20.3 mmol/L; RR: 4.1 to 7.6 mmol/L) and creatinine (215  $\mu\text{mol/L}$ ; RR: 87 to 150  $\mu\text{mol/L}$ ) and severe metabolic acidosis (pH at 7.1 and  $\text{HCO}_3^-$  at 13.5 mmol/L). The foal was administered IV fluids (Plasmalyte A 148; Baxter Corporation, Toronto, Ontario), 200 mL/kg BW, q24h, sodium bicarbonate (Hospira, St-Laurent, Quebec), 2 mEq/kg BW, broad-spectrum antimicrobials (penicillin, amikacin, metronidazole) and cimetidine at the dosages stated for Case 2. Hemoculture, multiple fecal cultures for *Salmonella*, and an ELISA test for rotavirus were all negative.

Arthrocentesis of the right tibiotarsal joint revealed a severe suppurative arthritis based on elevated leukocytes ( $119.2 \times 10^9/L$  RR) and protein (48 g/L). Radiographic examination of the right tarsus revealed a circular lucency 3 mm in diameter on the lateral margin of the talus and on the plantar margin of the calcaneus. No radiographic abnormalities were noted in the right front metacarpophalangeal joint. The right tibiotarsal joint was flushed with 1 L of 0.9% NaCl using a thru-and-thru large gauge needle system and 250 mg of amikacin was injected in the joint post-lavage. The joint flush was performed with the foal under sedation (xylazine), 0.2 mg/kg BW, IV. Umbilical ultrasonography was interpreted as normal. Thoracic radiographs revealed an alveolar pattern involving the caudo-ventral lung field, compatible with bronchopneumonia. Expansive osteolysis with heterogeneous new bone formation was observed at the 5th and 6th CCJs (Figure 2). Thoracic ultrasound revealed abnormalities of the right 4th, 5th, 6th, and 7th CCJs by the second day of hospitalization (Figures 3A and 3B). Arthrocentesis of the left tibiotarsal and both femorotibial joints was performed on day 3 because they were effused. Cytology of the fluid that was removed was within normal limits



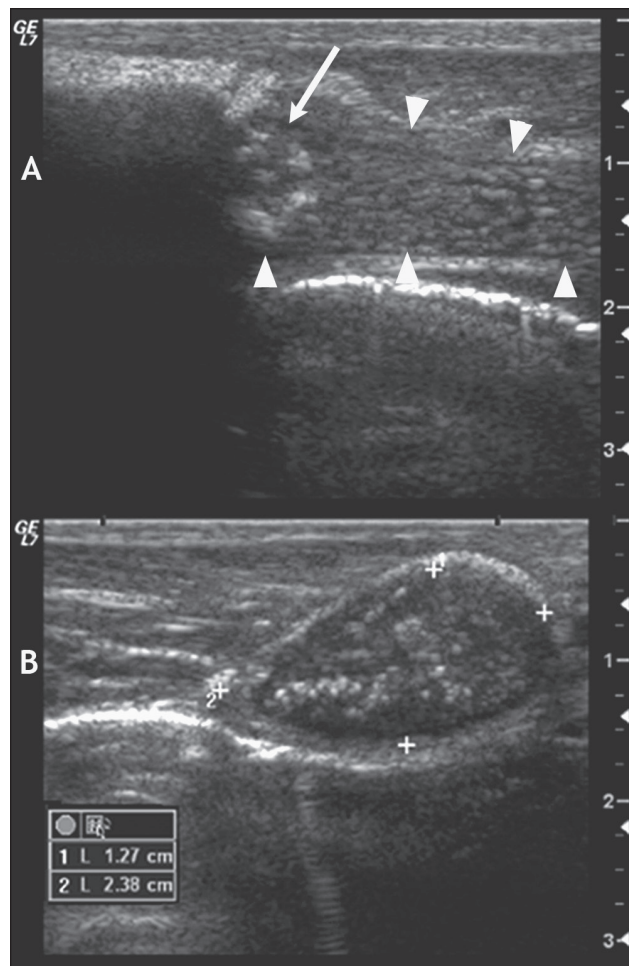
**Figure 2.** Lateral computed radiograph obtained on day 1 in foal 3. The distal portion of the 5th (R5) and 6th (R6) ribs is enlarged at the costochondral junction and shows a mixed lytic and osteoproliferative bony reaction, consistent with osteomyelitis.

and no bacteria were isolated on aerobic culture. Considering the absence of improvement of the foal's condition, the owner elected euthanasia of the filly 3 days after arrival.

Postmortem examination revealed disseminated pulmonary abscesses of up to 0.5 cm in diameter that yielded a pure growth of *Staphylococcus aureus*. Two small thin-walled abscesses were also noted between the sternum and pericardium. There was a mild to moderate fibrinous polyarthritides involving both tibiotarsal joints and stifles. Histologically, the synovial lining of affected joints showed villous hyperplasia with a mild multifocal lymphoplasmocytic infiltration. In some sections, the synovial membrane was either focally covered with a fibrinoleukocytic exudate or eroded with an underlying inflamed granulation tissue. Macroscopically, the right 3rd to 7th CCJs were swollen and the right 4th and 5th CCJs were more mobile than other junctions. On section, there were necrosuppurative lesions affecting osteochondral tissue (Figure 4). Histological examination of the right 4th, 5th, and 6th CCJs showed lesions of chronic active osteomyelitis characterized by a center of necrotic bone infiltrated by neutrophils and a peripheral fibrous replacement of bony tissue. Similar lesions affected the costal cartilage. *Staphylococcus aureus* and rare *Lactobacillus* were obtained from one of the affected CCJs. Direct immunofluorescence on intestinal sections was positive for rotavirus.

## Discussion

Osteomyelitis, an inflammatory process of the medullary cavity, cortex, and periosteum of bone (1), is generally associated with a bacterial infection, and constitutes one of the potential consequences of septicemia in foals. It most commonly affects the epiphyses of long bones and osteochondral junctions, such as metaphyseal plates or articular facets of vertebral bodies (2). There have been few reports of rib osteomyelitis in foals (1,3).



**Figure 3.** Longitudinal (A) and transverse (B) ultrasonographic images of the right 4th costochondral junction (CCJ) affected with osteomyelitis in foal 3. The cartilaginous portion of the rib (arrowheads) can be followed proximally to the CCJ that presents several hyperechoic foci (arrow). The CCJ is also enlarged (callipers on transverse image A).

Review articles mention the costochondral area as a potential site of infection in equine neonates, but the condition itself is not well-described (2).

Several papers report rib osteomyelitis in human infants, despite the rarity of this condition (4–6). The source of rib infection is typically contiguous, although hematogenous spread has also been described, mainly in the youngest patients. In addition, rib osteomyelitis has been occasionally reported in goats, turkeys, and snakes (7–9). In all cases, infection was secondary to systemic spread of a primary disease (7–9).

In most species, including the horse, neonates are more susceptible to bone infections than are mature individuals (1). Osteomyelitis in humans of the pediatric age group almost always occurs by colonization of growing bones by bacteria, usually *S. aureus*, that arrive by the hematogenous route (10). In 2 of 3 foals reported here, the bacterial species isolated at necropsy from affected CCJs (*E. coli*, *S. aureus*) included bacteria commonly isolated in cases of septicemia in foals (2,11). In Case 1, *E. coli* was isolated from the blood, the umbilicus, and the costochondral junction, suggesting hematogenous spread of



**Figure 4.** Enlarged costochondral junction (CCJ) showing a large and irregular area of suppurative osteomyelitis and chondritis (left rib) compared to a normal CCJ (right rib).

the infection. In Case 3 the route of infection was less obvious, but *S. aureus* was isolated from the lung and several CCJs on postmortem examination. This finding could either be explained by a contiguous spreading, or more likely, by hematogenous dissemination of the infection.

Bone lesions following bacteremia have a strong predilection for sites of active endochondral ossification as is found in the metaphysis and epiphysis. This appears to be related to the unique vascular architecture found at the physis and at the equivalent site (“metaphyseal equivalent zone”) corresponding to epiphysis (the articular-epiphyseal cartilage complex) of the immature skeleton (12,13). At these junctions between cartilage and bone, sharp loops of marrow capillaries open into wide sinusoids and produce sluggish circulation (12). These capillaries are fenestrated and permit escape of bacteria into the bone marrow while sluggish sinusoidal circulation tends to favor the development and persistence of infection (12,13). In contrast to human neonates, in which the metaphysis is the predilection site, hematogenous osteomyelitis in the young foal occurs most often at the junction of bone and cartilage of the epiphysis of long bones (12). The term “metaphyseal equivalent zone” indicates that osteomyelitis occurs at the junction of cartilage and bone in various kinds of bone (long, cuboidal, flat) (12). In ribs, as in long bones, hematogenous disease is likely to occur in areas having the largest blood supply, where the bone is more metabolically active (14). In humans, the area near the CCJ is favored for infection, and is the most commonly (76%) affected region of the rib (5). The anatomy of the blood circulation in the equine neonatal CCJ may be similar to the epiphyses of the long bones, which may similarly predispose them to infection.

Although the final diagnosis of bacterial osteomyelitis of the costochondral junction (CCJ) came following necropsy in the 3 cases, some of the complementary techniques used *in vivo* yielded helpful information for the diagnosis of costal infection. These included physical examination, radiography, ultrasonography, needle aspiration, and bacterial culture.

Conventional radiography is recommended as the first step in the imaging assessment of suspected osteomyelitis in humans. However, bone lysis and periosteal reaction may only be obvious 10 to 21 d after onset of the infectious process (15). In the foals reported here, radiographic lesions were observed at 13 and 15 days of age, respectively. Following what is reported in humans (15), this suggests that the infectious process may have started *in utero* or in the early neonatal period in our foals.

Several advantages including rapidity and its minimally invasive nature make ultrasonography an attractive modality, especially in children, in whom ionizing radiation is avoided as much as possible (10,15). Ultrasonography also allows the early detection of bone infections, as in some soft tissue abnormalities, which are usually demonstrable only 1 or 2 days after the onset of clinical signs (10). Pericostal edema is a strong indicator of rib osteomyelitis in infants, especially when clinical suspicion is present (4,16). Other consistent findings included an enlargement of the CCJ and the presence of multiple hyperechoic foci generating a heterogeneous echotexture. Similar findings may also be encountered with rib trauma, osteochondrosis, or neoplasia (10,17,18), which may complicate the diagnosis. This is particularly true for rib trauma, which was recognized in these foals, and as previously described (16). In these cases, osteochondrosis and neoplasia were considered unlikely due to the age of the foal and the absence of specific ultrasonography findings.

Rib fractures were present in 2 of the 3 foals, but the limited number of cases does not allow any association between thoracic trauma and costal infection. Nevertheless, the potential hemorrhage and tissue damage that are associated with thoracic trauma could be a predisposing factor for development of osteomyelitis in the affected CCJs.

Ultrasound-guided needle aspiration can be useful in obtaining material for bacterial culture in cases of rib osteomyelitis in humans (10). This procedure was performed in one of our foals (Case 1) without success.

The 3 foals in this study were septic patients with multiple foci of infection. All were treated with broad-spectrum antimicrobials based on culture and sensitivity results; none were treated specifically for the rib osteomyelitis. In human medicine, successful treatment of osteomyelitis includes surgical drainage, removal of necrotic bone, and massive antimicrobial therapy (5). Percutaneous abscess drainage with the help of ultrasonography may be an alternative to surgical drainage when medical therapy alone is inadequate (10). In a review of 106 cases of rib osteomyelitis in humans, 89% had a favorable outcome after antimicrobial therapy with or without surgery (19).

In conclusion, the costochondral junction is a potential site of infection in septic foals. Thoracic trauma at birth may create a suitable environment for bacterial seeding from hematogenous sources. Ultrasonography and radiography are useful for the *in vivo* diagnosis. The report herein reveals that focal osteomyelitis of the ribs at the costochondral junction is an additional potential complication in septicemic foals with suspected thoracic trauma.

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## Book Review

### Compte rendu de livre

### Veterinary Pharmacovigilance: Adverse Reactions to Veterinary Medicinal Products

Woodward KN, ed. 2009. Wiley-Blackwell, Sussex, UK. ISBN 9781-4051-6968-4. 762 pp. \$377.99 CDN.

**A**lthough this book will be an invaluable tool for anyone looking to set up a pharmacovigilance reporting program or who needs in-depth information on the regulatory aspects of veterinary adverse reaction reporting, it will not be useful for the general practitioner looking for information on the frequency and types of reported adverse reactions to veterinary vaccines and drugs. The book's high cost will also make it prohibitive for anyone with less than a devoted interest in veterinary pharmacovigilance.

The focus of this book is on the European regulation of veterinary medicinal products and the regulatory aspects of veterinary adverse reaction reporting. While there are 8 separate chapters devoted to veterinary pharmacovigilance regulation in the European Union, the regulation of veterinary pharmacovigilance in Canada, the United States, and Australia are all covered together in one short chapter. However, there are many similarities between the regulatory requirements for adverse reaction reporting in Europe and North America and so general topics can be applied to multiple regions even though the specific regulations governing those regions will be different.

Understanding government regulations can sometimes be quite challenging and so one of the major strengths of this book

is its tables and figures. Pertinent European regulations and guidelines are clearly listed and several flowcharts illustrate the interrelationships between different groups and how information flows from one area to another and is analyzed.

The chapters devoted to industry will be very useful to those companies looking to set up a pharmacovigilance program. Topics covered include: inspections, preclinical safety testing of drugs and vaccines, reaction causality determination, maximum residue limits for livestock, residue surveillance, and withdrawal periods (drugs only as there are no withdrawal periods in Europe for vaccines).

One topic that I was happy to see was not forgotten was human reactions to veterinary medicinal products caused by inadvertent exposure to the drugs or vaccines. Two chapters are devoted to these types of reaction.

Given the general good quality of the information available in this book, I was very surprised to read about the "anthrax virus" in one place in the book. Such a basic mistake should never have made it into a published veterinary textbook.

In summary, I highly recommend this book to anyone working for industry or for a governmental regulatory agency, and who is involved in veterinary adverse reaction reporting.

*Reviewed by Carolyn Cooper, BSc, DVM, Veterinary Biologics Evaluator, Canadian Centre for Veterinary Biologics, Canadian Food Inspection Agency. Dr Cooper is also responsible for the pharmacovigilance reporting program for veterinary biologics used in Canada.*