

Chlamydia-induced septic polyarthritis in a dog

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ABSTRACT

A systemic disease associated with pyrexia, lymphadenopathy, and arthropathy of several joints of the appendicular skeleton in a dog is described. *Chlamydia*-like organisms were detected on light-microscopic examination of a smear made from joint fluid aspirated from one of the affected joints. A group-specific lipopolysaccharide antigen shared by all *Chlamydia* spp. was demonstrated by direct fluorescent antibody staining of joint fluid, which also proved positive for chlamydia by means of the relevant polymerase chain reaction test. An indirect fluorescent antibody test on serum was also positive, although the complement fixation test was negative. Attempts to grow the organism from joint aspirates in the yolk sac of embryonating hens' eggs and on appropriate tissue cultures, however, failed. *Chlamydia* spp. are considered to have played an aetiological role in this case, making it the first substantiated case of naturally-occurring arthropathy in a dog due to chlamydiosis. The origin of the infection could not be traced.

Key words: *Chlamydia*, septic arthritis.

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INTRODUCTION

Infectious arthritis is defined as an inflammatory joint condition from which an infective agent can be isolated⁴. In dogs this condition usually involves a single joint (monarticular), and is most commonly caused by bacteria such as *Staphylococcus*, *Streptococcus*, *Erysipelothrix*, *Corynebacterium*, *Salmonella*, and *Brucella* spp.^{12,22}. Less commonly implicated agents include bacterial L-forms, fungi, the spirochaete *Borrelia burgdorferi*, *Mycobacterium tuberculosis*, the rickettsial organisms *Rickettsia rickettsi* and *Ehrlichia canis*, *Mycoplasma spumans* and *Leishmania donovani*^{2–4,21}.

In young or debilitated, large-breed dogs, infective agents may gain entry to the joint from a remote focus via the haematogenous route^{4,5}. More commonly, however, pathogens reach the joint by direct introduction from either penetrating wounds or extension of adjacent infections, for example osteomyelitis^{4,5}.

Chlamydia organisms are ubiquitous, obligate intracellular parasites implicated in a number of disease conditions in humans, other mammals, and birds.

There are, however, few reports of naturally-occurring clinical chlamydial infections in dogs, although antibodies to the organism have been demonstrated, possibly indicating a greater prevalence of subclinical infections⁸. A naturally-occurring outbreak of psittacosis was described in a household where 3 humans, a cockatiel and 2 of 3 dogs were diagnosed as having *Chlamydia psittaci* infections¹⁰. Both dogs showed clinical signs of pneumonia and tricuspid endocarditis, while the 3rd dog, although not clinically ill, had complement-fixing antibodies to *C. psittaci*. Both clinically-affected animals recovered after antimicrobial treatment. *C. psittaci* was isolated from the pleural effusion of a dog with pyrexia and shifting lameness, which made a complete recovery after treatment with ampicillin and oral prednisolone¹. The cause of the lameness was not explained. *C. psittaci* was cultured from the stool of a Yorkshire terrier with a cough and radiographic opacity of the right diaphragmatic lung lobe after eating carcasses of dead budgerigars from which the same organism had been isolated⁷. *C. psittaci* has been implicated as a cause of superficial keratitis⁵ and encephalitis⁶ in dogs. Dogs experimentally infected with chlamydial organisms isolated from ovine polyarthritis demonstrated fever, anorexia, depression, pneumonia, muscle and joint pain, as well as diarrhoea¹⁴.

Pathological changes found in similarly infected dogs included focal hepatitis, splenic hyperplasia, leptomeningitis and fibrinopurulent polyarthritis²⁶. This report outlines the 1st reported case of polyarthritis in a dog associated with a natural *Chlamydia* sp. infection.

CASE HISTORY

A 9-year-old, cross-bred, castrated male Maltese dog with a body mass of 8 kg was referred to the Onderstepoort Veterinary Academic Hospital for evaluation of progressive hind-limb lameness of 5 months' duration. There had been a rapid deterioration during the month preceding admission. The owner reported that the animal's habitus and appetite were normal. Clinical evaluation revealed non-weightbearing lameness of the right hind limb, pyrexia (39.5 °C) and enlargement of all the peripheral lymph nodes. The right stifle was swollen, painful and unstable, exhibiting an anterior drawer sign. The left stifle joint and both tarsal and carpal joints were moderately enlarged on palpation. Survey radiographs revealed joint effusion and moderate osteoarthritic changes of both stifle joints, cranial displacement of the tibia relative to the femur in the right stifle, erosion of the lateral and cranial aspects of the right lateral femoral condyle, minor osteoarthritic changes of the right carpal and both tarsal and elbow joints, and varus deviation of left carpus owing to relative shortening of the ulna. Thoracic survey radiographs indicated no radiographic abnormalities. Abdominal ultrasound examination demonstrated enlarged iliac lymph nodes.

Haematological evaluation revealed an elevated total white cell count due to moderate neutrophilia with left shift and monocytosis. Serum chemistry indicated an elevated concentration of globulins primarily due to an increase in IgM (400 mg/dl), and a mild increase in the serum activity of alanine phosphatase (382 U/l). Mild hyperplastic changes and plasma cell infiltration were seen in smears made from fine-needle aspirates of several of the enlarged peripheral lymph nodes. The results of routine analysis of urine collected by cystocentesis were within normal range.

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Joint fluid aspirated aseptically from the right stifle and left carpus was voluminous, brownish and turbid. Specific gravity of the fluid was greater than 1.035, the protein content was 80 g/l and a nucleated cell count of 80 000/mm³ comprising predominantly neutrophils and active macrophages was recorded. Sparse, extracellular, *Chlamydia*-like organisms were seen on smears made of these aspirates, stained with a rapid Romanowski stain (CAM's Quick Stain, C A Milsch) and examined under a light microscope. Samples of these aspirates were also submitted for aerobic and anaerobic bacterial as well as *Brucella* culturing, but these results were negative. As chlamydial infection was not suspected at the time of sampling, specific techniques used to grow this organism were not employed on the initial samples. Subsequent joint aspirates taken the following day from both stifles and carpi, after a single oral treatment with doxycycline (Mildox, Centaur) at 10 mg/kg and enrofloxacin (Baytril, Bayer) at 5 mg/kg, yielded very small volumes. These joint fluids were each placed in 2 ml of a chlamydial transport medium, and stored at -70 °C until culture systems became available²³. Representative volumes were then inoculated into the yolk sac of 7-day-old, specific pathogen-free, embryonating hens' eggs and into cycloheximide-treated McCoy cell monolayer cover slip cultures^{11,24}. No growth occurred in either of the culture systems.

The indirect fluorescent antibody (IFAT) staining technique (Chlamydia-Cel Vet IF test, Cellabs, Australia) for the detection of group-specific lipopolysaccharide antigen shared by all members of *Chlamydia* spp. was performed by 2 separate laboratories on 3 separate joint aspirates taken at daily intervals. All were positive, as evidenced by bright intracellular fluorescence of the chlamydial elementary and reticular bodies. A joint fluid specimen from the right stifle submitted for examination for *Chlamydia* spp. by polymerase chain reaction (PCR) proved positive. Paired serum samples collected at patient admission and a month later were submitted for complement fixation test (CFT) and IFAT. In the latter test a *C. psittaci* sheep isolate grown in McCoy cell cultures was used as antigen. The CFT proved negative for the presence of chlamydial antibodies but the IFAT was positive to a serum dilution of 1:40. An enzyme-linked immunosorbent assay (ELISA) was not performed because the kits were not available.

Additional serological tests performed to exclude certain other causes of arthritis

were included for the detection of antinuclear antibody for immune-mediated arthropathies, rheumatoid factor, and antibodies for *Borrelia burgdorferi* and *Ehrlichia canis*. All proved negative. A canine distemper virus serology test indicated a 1:80 IgG titre which was compatible with a fully vaccinated animal.

Treatment with 5 mg/kg enrofloxacin (Baytril, Bayer) once a day p.o. commenced in-hospital, and the patient was discharged with treatment for an additional month and instructions to the owner to return the dog at the end of the course of treatment and to reduce the animal's weight. The owner initially declined surgical stabilisation of the right stifle.

On re-admission, the animal's habitus was good, rectal temperature was normal, the peripheral lymph nodes were of normal size, and the joint swelling had partially subsided. There was still marked lameness of the right hind limb and the laxity of the stifle joint had increased. Radiographs of the affected joints did not demonstrate increased severity of the described changes except that the erosive lesion on the right femur was more extensive. No microorganisms were evident with light microscopy in smears of multiple joint aspirates, but evidence of mild inflammation was still present.

The stifle joint was surgically explored¹⁹ after standard anaesthetic and aseptic preparation. The synovium was found to be thickened and hyperaemic, the articular cartilage was yellow, irregular and dull, and numerous articular osteophytes were present. The cranial cruciate ligament was intact but stretched, permitting an exaggerated anterior drawer laxity. After collection of synovium for histology, electron microscopy (EM), and bacterial culture, the joint was irrigated with a large volume of Ringer-lactate solution (Sabax). The joint was stabilised by an extra-capsular orthopaedic wire technique¹⁷. Histologically, the synovium exhibited oedema and infiltration of macrophages, lymphocytes and neutrophils, but no microorganisms were seen. No elementary or reticulate bodies of *C. psittaci* or any other microorganisms were detected on EM examination. Aerobic and anaerobic bacterial culture as well as culture for the presence of chlamydial organisms using the growth media described above were negative.

Postoperative enrofloxacin treatment was continued for an additional 4 weeks. Two weeks after surgery, a course of an osteoarthritis modifying agent, pentosan polysulphate (Tavan SP 54, Noristan) was administered at 3 mg/kg subcutaneously every 5 days for 5 consecutive treat-

ments²⁰. Telephonic inquiry regarding the dog's progress revealed that the animal only exhibited intermittent spells of lameness.

DISCUSSION

Four species of organisms of the genus *Chlamydia* are recognised¹⁶. These are *C. psittaci*, *C. pecorum*, *C. pneumoniae* and *C. trachomatis*. Infections caused by the last 2 organisms, except for a few isolates from mice, are limited to humans where they cause, among other conditions, trachoma (granular conjunctivitis) and non-gonococcal urethritis, vaginitis, cervicitis, and pneumonia. *C. pecorum* is a pathogen in cattle and sheep, while *C. psittaci* affects both humans and animals¹⁶. The term psittacosis refers to an infection of humans or psittacine birds with *C. psittaci*, whereas ornithosis refers to infections in non-psittacine birds. Isolates of *C. psittaci* from cattle and sheep are associated with abortions, genital and enteric infections, polyarthritides, polyserositis, lymphadenopathy, keratoconjunctivitis, interstitial pneumonia, and meningoencephalitis¹⁸. Single or multiple syndromes may occur.

Although seroepidemiological surveys have detected antibodies to *Chlamydia* in up to 50 % of healthy dogs in some countries⁹, relatively few cases of naturally-occurring disease in dogs have been reported. Lameness was described in 1 report, but no unequivocal evidence that this was caused by the chlamydial organism was presented and its causative role in the lameness could only be inferred¹. Dogs experimentally infected with chlamydial organisms from ovine polyarthritides demonstrated fever, anorexia, depression, pneumonia, muscle and joint pain, and diarrhoea^{14,26}.

In the case under review which showed pyrexia, lymphadenopathy, and polyarthropathy on presentation, confirmation that a chlamydial infection was involved in the condition was afforded by the detection of chlamydia-like organisms on light microscopic examination of joint fluid, demonstration in repeated joint aspirates of a group-specific antigen shared by *Chlamydia* spp., positive PCR on joint fluid, and IFAT using the animal's serum. With the exception of the chronic right stifle lameness, all the other clinical signs resolved following long-term antimicrobial therapy. Despite the fact that no chlamydial organisms were isolated in the culture systems used and the fact that the CFT was negative, there is considerable evidence supporting *Chlamydia* sp. as the cause of the systemic disease with multiple joint involvement suffered by this animal. Failure to culture

the organisms can be explained by the administration of doxycycline and enrofloxacin before sampling as well as the possibility that the inflammatory response within the joints could have inactivated the organisms. Although 2 culture systems were used, it is nevertheless possible that certain *C. psittaci* strains would not grow in either. Alternatively, this may have been a reactive response to chlamydial antigens produced by an extra-articular infection, without the presence of viable intra-articular organisms.

Enrofloxacin inhibits the A subunit of DNA gyrase, thereby inhibiting DNA replication of bacteria and plasmids. It has excellent Gram-negative coverage, particularly for intracellular organisms, and readily enters joints. Its use in the treatment of chlamydiosis has been limited, but it has been found to be effective against psittacosis in birds¹³.

Various causes of cranial cruciate ligament degeneration and subsequent rupture have been suggested, including ageing, conformation abnormalities, and immune-mediated arthropathies¹⁵. In these cases it is believed that osteoarthritis arises within the joint before degeneration, and that enzymes released during the process weaken the ligament until it ruptures¹⁵. The chronic lameness described in this case is believed to represent an aseptic osteoarthritis with progressive weakening and laxity of the right cranial cruciate ligament. It is improbable that the chlamydiosis played a primary role in the degeneration of the cranial cruciate ligament, because the syndrome it produced was rather acute. However, the additional joint inflammation produced by the organism could well have exacerbated the degenerative process.

This is believed to be the 1st substantiated case of naturally-occurring polyarthritides caused by a *Chlamydia* sp. in a dog.

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