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DIAGNOSIS OF CANINE RHEUMATOID ARTHRITIS

(Diagnóstico da artrite reumatoide canina)

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ABSTRACT

Canine rheumatoid arthritis is a chronic inflammatory disease that affects the joints of dogs. The inflammation can cause damage to cartilage and bones and early diagnosis is the main factor determining treatment success. This report describes an unusual case of rheumatoid arthritis in a dog, highlighting the relevance of radiographic examination in association with histopathology in the definitive diagnosis. An 8 year old, male German Spitz dog, weighing 5kg was admitted with a history of cruciate ligament rupture and grade IV patella dislocation. Previously, surgery had been performed to correct the cranial cruciate ligament rupture, without success. On physical examination, the dog showed a palmigrade stance, severe pelvic limb lameness, and pain on palpation of all joints. Blood count and biochemical analysis were within normal ranges. Orthogonal radiographs of the joints of the pelvic and thoracic limbs were performed. The lesions were bilaterally symmetrical. Samples were taken from the patellofemoral joints for cytology, microbiology, and histopathologic analysis. Rheumatoid factor antibody assay was negative. In conclusion, the combination of more than one clinical sign and diagnostic tests, such as radiographs suggestive of rheumatoid arthritis, histopathologic analysis of the joints, and rheumatoid factor testing is required to reach a definitive diagnosis of rheumatoid arthritis.

Keywords: Dog, rheumatoid arthritis, rheumatic diseases, rheumatoid factor.

RESUMO

A artrite reumatóide canina é por definição uma doença crônica inflamatória que acomete as articulações de cães. Como resultado, a artrite reumatoide pode causar lesões na cartilagem e nos ossos e o diagnóstico precoce é o principal fator para o sucesso do tratamento ideal. Este relato de caso objetivou descrever um caso incomum de artrite reumatóide em um cão, destacando a relevância do exame radiográfico associado à histopatologia no diagnóstico definitivo. Foi atendido um cão da raça Spitz Alemão, 8 anos, com 5kg de peso. Anteriormente, foi realizada procedimento cirúrgico para correção da ruptura bilateral de ligamento cruzado e luxação de patela grau IV, porém sem sucesso. Ao exame físico, o cão apresentava posição palmígrada, intensa claudicação dos membros pélvicos e sensibilidade dolorosa de todas as articulações à palpação. As análises de hemograma e bioquímica sérica básica estavam dentro dos limites normais. Foram realizadas radiografias ortogonais das articulações dos membros pélvicos e torácicos. A distribuição das lesões foi simétrica e em ambos os lados. Considerando esses achados, foram obtidas amostras biológicas das articulações para análise citológica, microbiológica e análise histopatológica. O anticorpo fator reumatóide também foi realizado e o resultado foi negativo. Diante do exposto, é necessária a associação de mais de um sinal clínico e diferentes exames, como por exemplo, radiografias sugestivas de artrite reumatóide, análise histopatológica das articulações e anticorpo fator reumatóide para alcançar o diagnóstico definitivo de artrite reumatóide.

Palavras-Chave: Cão, artrite reumatoide, doenças reumáticas, fator reumatoide.

INTRODUCTION

Rheumatoid arthritis is an uncommon erosive non-infectious arthropathy in dogs. It can affect dogs of any age – from young animals to adults, and small breeds appear to be

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predisposed. The pathogenesis is still unclear and there is little published epidemiological data (SHAUGHNESSY *et al*., 2016). It is an uncommon arthropathy with <2/25,000 dogs developing rheumatoid arthritis (KIMURA, 2017).

The clinical signs include joint pain and swelling, usually bilaterally symmetrical. Less frequently, dogs present with lameness and difficulty walking or an abnormal gait. Nonspecific signs such as fever, weight loss, hyporexia, lethargy, vomiting, and diarrhea may also be present (CHAVES *et al.,* 2015).

Neoplastic, infectious, and primary inflammatory diseases should be ruled out by complementary examinations such as blood count, biochemical analysis, urinalysis, thoracic radiographs, and abdominal ultrasound (LATORRE, 2015).

Orthogonal radiographs of the limbs must be performed to exclude congenital or traumatic bone deformities that may cause degenerative joint diseases. Radiographs may show specific lesions and suggest the diagnosis of erosive arthritis (KIMURA, 2017).

The most common lesions are swelling of periarticular soft tissues, distension of the joint capsule, erosions in the joint margins, often associated with periosteal reaction, lysis of the subchondral bone, subluxation, and reduction of the joint space (KIMURA, 2017).

In addition to the radiographic examination, one or more diagnostic tests such as cytologic and histopathologic evaluation of synovial fluid, serologic testing for rheumatoid factor, measurement of precipitated intraarticular mucin, and more than one associated clinical sign are required for definitive diagnosis (GOELDNER *et al.,* 2011).

This case report describes the radiographic findings and discusses the diagnostic methods in rheumatoid arthritis by reporting an unusual case in a dog. This case highlights the value of radiographic and histopathologic examination for the final diagnosis of rheumatoid arthritis.

PATIENT SERVICE

An 8 year old male German Spitz dog, weighing 5kg was admitted with a history of cruciate ligament rupture and grade IV patella dislocation at the Veterinary Teaching Hospital of the São Paulo State University – School of Agricultural and Veterinary Sciences (UNESP/FCAV). Fabella tibial suture surgery for cruciate ligament repair had been performed 60 days before the appointment, but without success. On physical examination, the patient showed a palmigrade stance, severe pelvic limb lameness, and pain on palpation of all joints. Complete blood count and biochemical analysis were within normal ranges (red blood cells: $6.1x10^6/\mu L$ (reference: 5.7-7.4 $x10^6/\mu L$), hemoglobin: 12g/dL (reference: 14-18g/dL), hematocrit: 39% (reference: 38-47%), reticulocytes: 60.000/µL (reference: 60-200 $x10^3/\mu L$), platelets: 275.000/µL (reference: 200-500$x10^3/\mu L$). Biochemical analyses were within the normal ranges (creatinine: 1.4g/dL (reference 0.5-1.5g/dL), BUN: 50mg/dL (reference 21.4-59.92mg/ L), alanine aminotransferase – ALT 57 (reference: 10-120 U/L), alkaline phosphatase 84 (reference: 20-56 U/L).

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Clinical findings

Orthogonal radiographs of the joints of the pelvic and thoracic limbs were taken There was marked erosion of the articular surfaces and subchondral bones, joint incongruity, and swelling of the soft tissues adjacent to the carpal joints, tarsi, phalanges, elbows, and stifles. Lesions were bilaterally symmetrical (Fig. 01A). There was bilaterally symmetrical marked erosion of the joint surfaces and subchondral bones and joint incongruity. Distension of the joint capsule and synovial effusion in both femurotibial-patellar joints, medial subluxation of the left tibia, and medial dislocation of the carpal bones in both thoracic limbs were also observed (Fig. 01B). The soft tissue adjacent to the carpi, tarsi, phalanges and stifles was swollen (especially in the right stifle) (Fig. 01C). Abdominal radiographic abnormalities were restricted to hepatomegaly confirmed by ultrasound examination. There were no abnormalities on thoracic radiographs.

Samples were taken from both patellofemoral joints for cytologic, microbiology, and histopathologic analysis. Rheumatoid factor antibody assay was also performed.

Cytologic examination revealed a moderate inflammatory infiltrate with no bacterial component. The microbiologic analysis of joint fluid was negative. Although the rheumatoid factor assay was negative, radiographic examination findings and the chronic arthritis with deposition of fibrotic cells associated with the lymphoplasmacytic component on histopathology strongly suggested the diagnosis of rheumatoid arthritis.

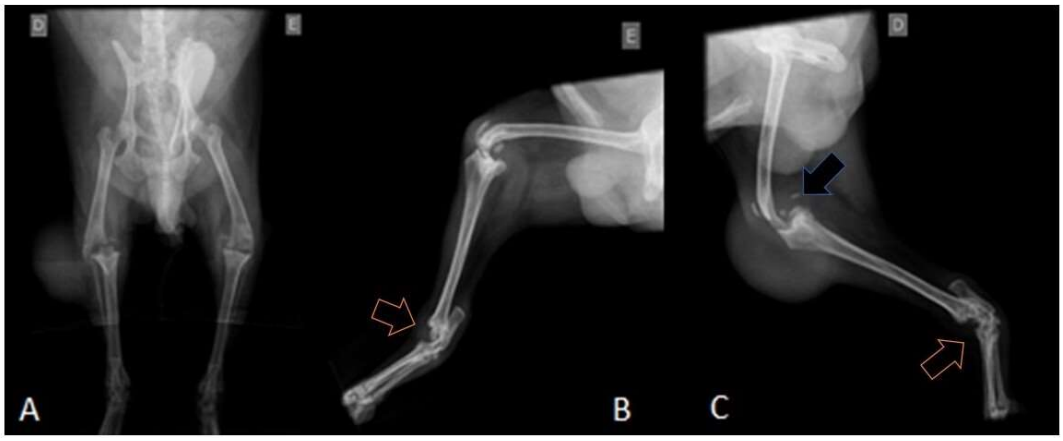

Figure 01: Radiographs of a male, German Spitz dog, 8 years old with a history of pelvic limb lameness and pain on palpation of all the joints.

Obs.: A: Craniocaudal view highlighting the right and left femoral-tibial-patellar joint (right/pelvic limb). **B and C:** Mediolateral view (left and right pelvic limb) showing femoral-tibial-patellar, tibial-tarsal, intertarsal and tarsometatarsal joints.

Radiographic findings included erosion of the joint surfaces in both stifle joints, lysis of the subchondral bones, especially of the femoral condyles. The joint surfaces were irregular and incongruous with enlargement of the articular joint space of the right stifle and medial tibial subluxation, soft tissue swelling adjacent to both stifles (more evident in the right limb), bilateral distension of the joint capsule, and reduction of joint space in the left stifle, bilateral bone lysis of the patella, and a joint mouse of the right joint (blue arrow), bilateral medial and lateral fabella degeneration. In the mediolateral projections of the tarsal bone region bilaterally

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there was osteolysis of the subchondral bones with an erosion of the tarsal bones (orange arrows).

On ultrasonographic examination hepatomegaly was detected and the urinary bladder was distended with anechoic fluid, similar to cholestasis. These changes were compatible with steroid effects due to prolonged corticosteroid therapy.

Samples of biological material were collected from both patellofemoral joints by fine needle aspiration, needle biopsy, and intra-articular swabbing of the right stifle, and were submitted for cytologic, histopathologic, and microbiologic analysis, respectively. The analysis of synovial fluid revealed increased cellularity with intact and degenerate neutrophils and rare macrophages (an acute inflammatory process). Joint microbiologic analyzes and rheumatoid factor tests were negative.

Areas of fibrosis and tissue organization associated with degenerative foci and lymphoplasmacytic involvement were described on the histopathologic examination. The combination of the radiographic findings, the clinical signs, and joint pain allowed a diagnosis of rheumatoid arthritis to be made.

The dog was prescribed prednisone (1mg/kg/PO, every 12 hours). This dosage was subsequently reduced by 25% after 3 weeks as lameness and joint effusion resolved. Repeat cytology revealed a decrease in the number of abnormalities detected in the synovial fluid samples with an estimated total cell count <3,000 cells/μL.

RESULTS AND DISCUSSION

Rheumatoid arthritis in dogs is uncommon. It affects small breed dogs, between 8 months and 8 years old (KIMURA, 2017). Erosive rheumatoid arthritis is commonly seen in small breeds with a median age of 2.4 years and a weight of 3.4 kg. These data agreed with the findings in this case report (SHAUGHNESSY *et al.,* 2016).

Although the clinical signs, results of histopathologic and cytologic analysis in this case were consistent with reports in the literature, rheumatoid factor assay was negative. Although there are several diagnostic tests for rheumatoid arthritis, none have high specificity when used alone, making the diagnosis difficult (GOELDNER *et al.,* 2011; BRAZ *et al.,* 2018).

The exclusion of neoplastic, infectious, or inflammatory comorbidities for joint injuries, associated with the positive findings in at least two of three diagnostic tests (radiographic images suggestive of rheumatoid arthritis, histopathologic changes in joint samples, or rheumatoid factor testing) are used to make a definitive diagnosis of the disease (JOHNSON e MACKIN, 2012; VIOLA *et al*., 2016).

Although the serological test for the identification of rheumatoid factor is widely used, at least 20% of human patients and 27% of dogs diagnosed with rheumatoid arthritis test negative, as seen in this case report. However, in this case a positive diagnosis was based on the histopathologic findings of lymphoplasmacytic arthritis (BRAZ *et al*., 2012; BRAZ e NASCIMENTO, 2017).

Although the literature recommends analysis of the fluid and tissues from at least three affected joints (JOHNSON e MACKIN, 2012), in this case report, samples were only collected from a single joint, but the findings were helpful in making the final diagnosis.

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CONCLUSIONS

This case report highlights the relevance of complementary exams, emphasizing the use of radiographic and histopathologic evaluation, in the definitive diagnosis of canine rheumatoid arthritis. This disease is a challenging diagnosis in veterinary practice. We hope this case report assists other clinicians to diagnose similar conditions. Further research is needed to better clarify the mechanisms underlying the pathogenesis of canine rheumatoid arthritis, allowing the development of new and more specific therapies.

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