

Conservative and surgical approach to intra-articular chondrosarcoma in dogs

Abordagem conservativa e cirúrgica do condrossarcoma intra-articular em cão

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ABSTRACT: Chondrosarcoma (CSA) is a malignant mesenchymal neoplasm. Diagnosis is made through imaging and histological examinations. The prognosis is guarded, and treatment is predominantly surgical in most cases. The objective of this report is to describe an unusual case of intra-articular CSA associated with a cranial cruciate ligament (CrCL) rupture in a dog. A male mixed-breed canine patient, weighing 10.1 kg and nine years old, presented with a history of lameness in the left pelvic limb. After an orthopedic examination, knee radiography and synovial fluid analysis were performed. The results suggested arthritis, joint effusion, and CrCL injury. During surgery, a yellowish mass was identified in the infrapatellar fat pad region, adherent to the cranial portion of the tibial plateau. The mass was excised, and the knee was stabilized using the fabelo-tibial suture technique. Histologically, the tumor exhibited morphological characteristics of well-differentiated chondrosarcoma. The neoplastic cells expressed S100, did not express 1A4, Desmin, AE1AE3, and Osteocalcin, and showed partial expression of Ki67. Adjuvant chemotherapy with doxorubicin and cyclophosphamide was established. The patient had an excellent recovery and was followed up for 455 days postoperatively with no signs of recurrence. In conclusion, a less aggressive surgical approach with limb preservation is an alternative for the treatment of low-grade CSA and should be considered in patients with multiple orthopedic lesions that may compromise ambulation and quality of life.

KEYWORDS: Neoplasm; oncology; limb preservation; cranial cruciate ligament; arthropathy.

RESUMO: O condrossarcoma (CSA) é uma neoplasia mesenquimal maligna. O diagnóstico ocorre por meio de exames de imagem e histológicos. O prognóstico é reservado e o tratamento é na maioria dos casos cirúrgico. O objetivo deste relato é descrever um caso incomum de CSA intra-articular associado a ruptura do ligamento cruzados cranial (LCCr) em cão. Um paciente, canino, sem raça definida, macho, com 10,1 kg, nove anos de idade, foi atendido com histórico de claudicação no membro pélvico esquerdo. Após o exame ortopédico realizou-se radiografia do joelho e análise do líquido sinovial. Os resultados foram sugestivos de artrose, efusão articular e lesão do LCCr. No transoperatório foi identificada uma massa de coloração amarelada em topografia de gordura infrapatelar, aderida a porção cranial do platô tibial. A massa foi excisada e o joelho estabilizado pela técnica da sutura fabelo-tibial. Histologicamente o tumor mostrou características morfológicas de condrossarcoma bem diferenciado. As células neoplásicas expressaram S100, não expressaram 1A4, Desmina, AE1AE3 e Osteocalcina e expressaram parcialmente o Ki67. Foi instituída quimioterapia adjuvante com doxorubicina e ciclofosfamida. O paciente teve uma excelente recuperação e foi acompanhado até o 455º dia de pós-operatório sem sinais de recidiva. Conclui-se que a abordagem cirúrgica menos agressiva, com preservação do membro é uma alternativa para o tratamento do CSA de baixo grau e deve ser considerada em paciente com múltiplas lesões ortopédicas que possam comprometer a deambulação e qualidade de vida.

PALAVRAS-CHAVE: Neoplasia; oncologia; preservação de membros; ligamento cruzado cranial; artropatia.

INTRODUCTION

Chondrosarcoma (CSA) is a malignant neoplasm originating from chondrocytes. It is the second most common among mesenchymal-origin neoplasms, accounting for 5 to 10% (Nelson; Couto, 2023). It can arise in any location containing cartilage,

with the most commonly affected structures being the nasal cavity, followed by ribs, sternum, pelvis, long bones, vertebrae, digits, and the penile bone (Vail; Thamm; Liptak, 2019). Intra-articular presentation is rare. The neoplasm is described in medium to large-sized dogs, with no sexual predilection,

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and typically occurs between the ages of 5 to 15 years (Nelson; Couto, 2023). Several factors that contribute to its occurrence are known, such as traumas, chronic inflammatory processes, constant exposure to ionizing radiation, use of orthopedic implants, genetic mutations, and bone infarctions (Vinayak *et al.*, 2018). Medical history, anamnesis, physical and orthopedic examinations are not sufficient for a definitive diagnosis, and radiographic examination does not yield conclusive findings (Fossum *et al.*, 2021). Therefore, histopathological and immunohistochemical analysis is necessary (Shimada *et al.*, 2023; Vinayak *et al.*, 2018). The prognosis is guarded and varies depending on the tumor size, degree of tumor invasion, and the presence of metastases. In most cases, surgical treatment is recommended, often involving limb amputation (Fossum *et al.*, 2021; Shimada *et al.*, 2023). The aim of this study is to describe a rare and atypical case of intra-articular CSA in a dog, with an emphasis on an alternative treatment approach that allows for the preservation of the affected limb.

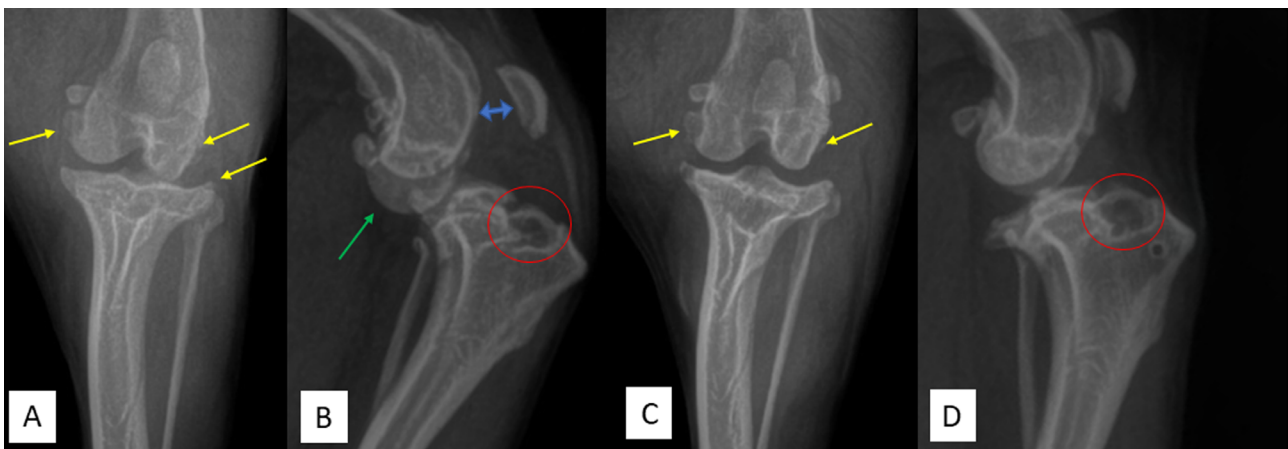
CASE REPORT

A male mixed-breed dog, weighing 10.1 kg and nine years old, was presented at the Pulo do Gato Veterinary Clinic with a complaint of lameness in the left pelvic limb. The patient exhibited normal appetite, normal water intake, normal urination, and normal defecation. He had a history of patellar luxation and cranial cruciate ligament (CrCL) rupture in the contralateral (right) knee, which were treated two years ago.

During the clinical examination, a heart rate of 120 bpm, a respiratory rate of 40 rpm, a rectal temperature of 36.9°C, and a capillary refill time of 2 seconds were observed. In the musculoskeletal system, crepitus was noted in the left knee, along with slight drawer motion when the joint was semi-flexed. Upon analyzing

the animal in motion, lameness in the left pelvic limb with partial weight-bearing was observed. Subsequently, synovial fluid analysis and radiographic examination of the left knee were performed. The physicochemical analysis of the synovial fluid showed a pale-yellow color, mild turbidity, and a glucose level of three crosses. The cytological analysis revealed a total nucleated cell count of 31,000 cells/mm³ and erythrocytes at 56,000 cells/mm³, with a differential count comprising 94% lymphocytes and 6% macrophages. Microscopic examination showed mild cellularity characterized by reactive macrophages, typical lymphocytes, intact and degenerate neutrophils, as well as red blood cells and cellular debris, suggestive of chronic inflammation. In the radiographic examination (Figure 1), it was possible to visualize radiolucent cystic images in the subchondral margin, cranial to the tibial plateau; the presence of enthesophytes on joint margins, cranial displacement of the tibia, and the patella displaced cranially in relation to the trochlea.

Following the radiographic examination, the diagnostic impressions were suggestive of arthritis, subluxation of the femorotibial joint, cranial cruciate ligament (CrCL) injury, and osteomyelitis. Surgical exploration of the joint for biopsy and CrCL treatment was recommended. Preoperative exams, including a complete blood count, biochemical analyses [glutamic-pyruvic transaminase (GPT), glutamic-oxaloacetic transaminase (GOT), gamma-glutamyl transferase (GGT), total proteins and fractions, creatinine, urea, alkaline phosphatase, glucose, triglycerides, total cholesterol and fractions], electrocardiography, and echocardiography, were performed, and all results were within the normal range. Then, a left knee arthrotomy was performed (Figure 2). Degerming and alcoholic chlorhexidine was used for surgical site antisepsis. With the animal under anesthesia, a cranial-lateral approach to the femorotibialpatellar

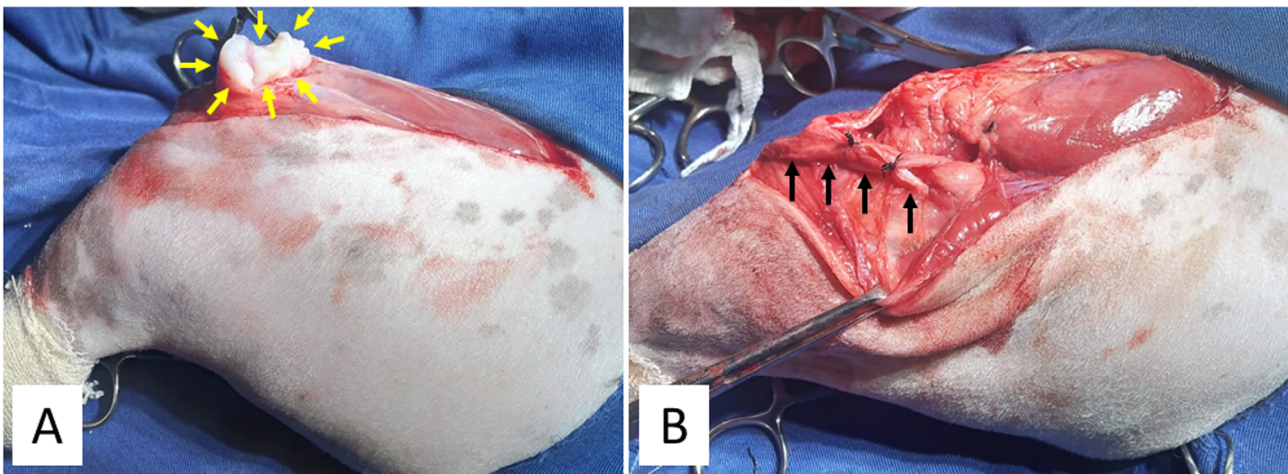


Source: Author's collection.

Figure 1. Radiographic examination of the left femorotibialpatellar joint in a dog with intra-articular chondrosarcoma before surgical resection (A and B) and on the 455th postoperative day (C and D). Note in the preoperative images the cranial displacement of the tibia, the femoral condyles displaced caudally to the tibial plateau (green arrow - image B), the patella separated from the trochlear groove (blue arrow - image B); radiolucent cystic images between the insertion of the patellar ligament and the tibial plateau (red circle - images B); and the presence of osteophytes and enthesophytes on joint margins (yellow arrows - images A). Note in the postoperative images the restoration of the anatomical position of the knee structures (femur, tibia, and patella), stable degenerative joint disease (yellow arrows - images C), and the persistence of the radiolucent cystic area even after surgical curettage (red circle - images D).

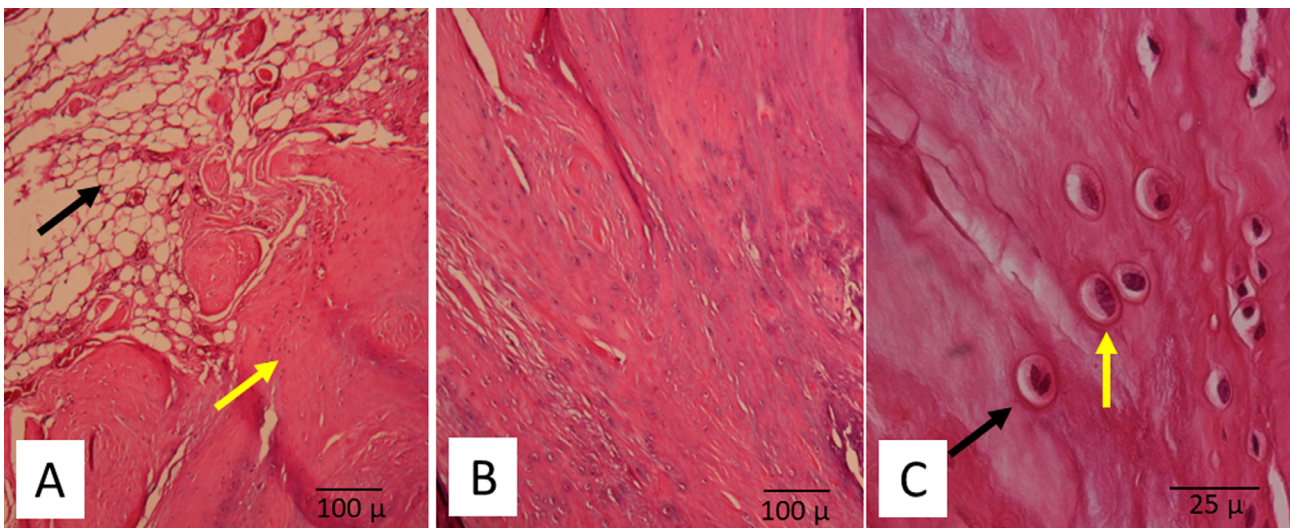
joint was performed. After the arthrotomy, a mass measuring 4.5 x 4.0 x 2.0 mm with a yellowish color and smooth surface was observed in the infrapatellar fat pad region, infiltrating the bone cranial to the tibial plateau and caudal to the insertion of the patellar ligament. The mass was also adhered to the cranial portion of the meniscus, particularly to the cranial edge of the medial meniscus. The structure and cranial edge of the medial meniscus were excised, and the bone was curetted to remove as much tissue as possible. Additionally, a complete rupture of the CrCL was confirmed, and the fabelo-tibial suture technique (FOSSUM *et al.*, 2021) was employed for joint stabilization using 1 mm thick polyamide suture and fascia lata. Tissue closure was performed layer by layer in a simple interrupted pattern with 2-0 polyamide suture.

Microbial (bacterial and fungal) cultures and antimicrobial sensitivity testing were performed on collected samples, but no growth was observed. The excised mass was fixed in 10% formalin and sent for histopathological analysis, which revealed the presence of mature cartilaginous tissue within a fibrous stroma (Figure 3). Typical chondrocytes forming solid and cord-like arrangements were observed, interspersed with basophilic chondroid material and groups of spindle-shaped cells with moderate pleomorphism, alternating areas of nuclear enlargement and prominent nucleoli. Four mitotic figures were observed in 10 fields at 400x magnification. Immunohistochemical evaluation (IHC) showed that the neoplastic cells were positive for S100, negative for 1A4, desmin, AE1/AE3, and osteocalcin. Ki67 expression was positive in approximately 10% of the neoplastic cells.



Source: Author's collection.

Figure 2. Photograph of the left femorotibialpatellar joint of a dog during surgery to excise an intra-articular chondrosarcoma and joint stabilization to treat cranial cruciate ligament rupture. Note the intra-articular mass with a yellowish-white color in the infrapatellar fat pad region (yellow arrows - image A) and the reinforcement of the fabelo-tibial suture with the fascia lata (black arrows - image B).



Source: Author's collection.

Figure 3. Photomicrograph of intra-articular chondrosarcoma in a dog's knee (Hematoxylin and Eosin stain). In image "A," observe the infrapatellar adipose tissue (black arrow) and newly formed cartilaginous tissue (yellow arrow). In image "B," typical chondrocytes interspersed with basophilic chondroid material can be seen. In image "C," note pleomorphism, nuclear enlargement, and prominent nucleoli (yellow arrow), as well as a binucleated cell (black arrow).

The immediate post-operative treatment consisted of enrofloxacin (Biofloxacin® - 5 mg/kg, orally, once daily, for 10 days), firocoxib (Previcox® - 5 mg/kg, orally, once daily, for 10 days), and tramadol (Cronidor® - 2 mg/kg, orally, three times a day, for 5 days). The patient had a good post-operative recovery, and skin sutures were removed at 15 days. Adjuvant chemotherapy was initiated, consisting of four sessions of doxorubicin (Fauldoxo® - 1 mg/kg, intravenous, with a 21-day interval between each session). Prior to the sessions, complete blood counts, thoracic and affected joint radiographs, and abdominal ultrasound were performed. Echocardiographic evaluation was conducted every two sessions. Additionally, metronomic chemotherapy was established using carprofen (Carproflan® - 4.4 mg/kg, orally, once a day, for 30 days) and cyclophosphamide (Genuxal® - 12.5 mg/m², orally, once a day, for 30 days). After 30 days of treatment, the drugs were alternated, with carprofen administered on one day and cyclophosphamide on another day, until completing six months of treatment. After the conclusion of chemotherapy, the patient was followed quarterly until the 455th day through clinical, radiographic, and ultrasonographic evaluations. The patient remained well with joint stability, no pain, and no signs of recurrence.

DISCUSSION

The primary sites of origin for CSA are the nasal bones, ribs, and pelvis. In general, they are more commonly observed in flat bones of the axial skeleton (Vail; Thamm; Liptak, 2019). The affected region in this case was the femorotibialpatellar joint, making it an intra-articular neoplasm with a rare presentation, highlighting the uniqueness and significance of this case report.

The radiographic examination and synovial fluid analysis, requested in this patient's case report, are essential when joint injury is suspected. They were useful in identifying degenerative joint disease and the CrCL injury by showing marked cranial displacement of the tibia. However, they were of limited assistance in diagnosing the CSA. Since it is a non-exfoliative tumor, the chance of finding neoplastic cells in synovial fluid analysis is minimal (Vail; Thamm; Liptak, 2019), and due to its low-density extracellular matrix within the intra-articular location, which also results in a negative image, the tumor mass is not visible on radiographs. Computed tomography provides more accurate images than radiography and could have been used, but magnetic resonance imaging (MRI) is the preferred diagnostic tool for this case, as it produces precise images of soft tissues (Shimada *et al.*, 2023). Arthroscopy would also be an option that, in addition to aiding diagnosis, allows for minimally invasive treatment of lesions.

When observing osteolytic lesions like the one in this patient's case report, it is important to establish a differential diagnosis between neoplasms, osteomyelitis, bone infarcts, and bone cysts, as they are radiologically indistinguishable (Alexiev *et al.*, 2023).

The choice of the fabelo-tibial suture technique for knee stabilization was made due to its faster execution and because the technique had been employed with excellent results in the contralateral knee of the same patient approximately 2 years prior. Although polyamide is not absorbable, it can undergo hydrolysis and lose up to 20% of its strength each year (Rahal *et al.*, 1997), which may lead to rupture over time. This is why fascia lata was used to reinforce the fabelo-tibial suture. Other materials, such as polyester and polypropylene threads, could also have been used (Fossum *et al.*, 2021).

The definitive diagnosis of CSA can be challenging, even with histopathological evaluation. When the neoplasm is poorly differentiated, there can be difficulties in distinguishing CSA from chondroblastic osteosarcoma. In cases similar to the one reported here, where CSA is well-differentiated, the challenge lies in distinguishing it from chondroma, a benign condition (Kim; Lee, 2023). Immunohistochemical evaluation is a valuable tool in such cases and was necessary for the diagnostic conclusion in the case reported here. When dealing with mesenchymal neoplasms, it's important to differentiate between tumors considered cutaneous and subcutaneous soft tissue sarcomas. The markers 1A4 and desmin are indicative of muscular neoplasms, such as leiomyosarcomas and rhabdomyosarcomas. Osteocalcin is a marker for bone neoplasms such as osteosarcoma, which is the main mesenchymal neoplasm affecting dogs. Cytokeratins AE1/AE3 are markers for epithelial cell neoplasms, such as carcinoma (Kumar H *et al.*, 2022). The S-100 protein was initially described as specific to the nervous system, but it is expressed in various tissues, including cartilage and bones. Several members of the S-100 family can be identified in chondrocytes, such as S100A1, S100A2, S100A4, S100A8, S100A9, S100A11, and S100B (Povysil; Kana, 2021; Povysil; Hojny; Kana, 2022). This justifies the choice of these markers, which allowed for a definitive diagnosis. The low expression of Ki67, combined with the morphological evaluation of the tissue in this report, supports the classification of CSA as low-grade. Ki67 quantifies the degree of cellular proliferation and is expressed in all phases of the cell cycle (G1, S, G2, and M), except for the G0 phase (Lashen *et al.*, 2023).

Generally, the most recommended treatment for patients in the early stages of CSA is neoplastic resection with wide surgical margins aimed at a cure, which in the case of the patient in this report would have meant amputation of the affected limb. However, the animal had orthopedic lesions in the contralateral limb and could have had difficulties with mobility if amputated. Concerned about the patient's quality of life, the guardians opted for the resection of the mass even without surgical margins. Limb-sparing treatment should be considered in patients at an advanced stage of CSA, in large and giant patients, and in those who present concurrent orthopedic and neurological lesions that may compromise mobility if the patient is amputated (Fossum *et al.*, 2021). In a study

conducted by Kirpensteijn; Bos; Endenburg (1999), among 44 dogs, 42 showed satisfactory adaptation to mobility with three limbs, and in a faster period than expected by the guardians. Farese *et al.* (2009) observed an average survival of 6 years, 2.7 years, and 9 months in dogs with CSA grade I, II, and III treated exclusively with amputation.

Although there is not substantial evidence of the efficacy of adjuvant chemotherapy in CSA treatment, it was chosen to be employed as a complement to the surgical treatment since it was not possible to achieve clear surgical margins in the resection. Doxorubicin, one of the drugs used in the chemotherapy protocol for the reported case, is indicated for the treatment of some mesenchymal neoplasms (osteosarcomas and soft tissue sarcomas), epithelial (carcinomas), and lymphomas in dogs and cats. However, it can cause adverse effects such as myelosuppression, gastrointestinal toxicity, and cardiotoxicity (Vail; Thamm; Liptak, 2019; Vinayak *et al.*, 2018).

Hence the need for frequent monitoring and reassessments, as performed in the patient of this report. Cyclophosphamide and carprofen, drugs used in the metronomic chemotherapy for this patient, act by altering the tumor microenvironment through antiangiogenic, immunomodulatory, and cytotoxic effects, with minimal side effects.

CONCLUSIONS

In conclusion, chondrosarcoma should be considered among the differential diagnoses for intra-articular tumors in dogs. Histopathological and immunohistochemical examinations are crucial for diagnosis and treatment selection in cases of intra-articular tumors. Resection of the neoplastic mass combined with chemotherapy is an alternative treatment for patients with low-grade chondrosarcomas, especially if they have other comorbidities that make amputation of the affected limb unfeasible.

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