Received: 22 September 2023 | Revised: 19 December 2023 | Accepted: 4 January 2024

DOI: 10.1111/vcp.13330

Veterinary Clinical Pathology
An International Journal of Laboratory Medicine
WILEY

CASE REPORT

Adipocytes in synovial fluid cytology: An approach for diagnosing synovial lipomatosis

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Abstract

A 2-year-old neutered male bullmastiff dog was presented with chronic left hind limb lameness. Physical examination revealed left stifle effusion and medial buttress without cranial tibial thrust. Radiographs showed joint effusion and new bone formation at the patella apex. Magnetic resonance imaging showed increased synovial fluid, widening of the joint space, abnormal infrapatellar fat body and thinning of the cranial cruciate ligament. Synoviocentesis and cytologic evaluation of synovial fluid revealed marked mononuclear inflammation with abundant fatty tissue, suggesting synovial lipomatosis in conjunction with the imaging findings. The disease was confirmed histologically after sampling the lesion during arthrotomy. Synovial lipomatosis, characterized by extensive synovial adipose tissue proliferation of the synovial membrane, is a rare "tumor-like" disorder that usually affects the stifle. Although the etiology remains unclear, joint trauma, inflammation, instability, and lipid abnormalities have been proposed as causes. Inflammatory factors may promote synoviocyte and adipocyte hyperplasia that perpetuate the process. Surgical removal may be suggested to eliminate triggers and prevent future recurrences. The report provides the first cytological description of adipocytes in synovial fluid associated with the diagnosis of synovial lipomatosis in dogs. This case report underscores the potential effectiveness of cytologic analysis of synovial fluid smears, in combination with magnetic resonance imaging (MRI), for diagnosing this condition and reducing complications associated with arthrotomy for sampling purposes. Additionally, the case highlights that synovial lipomatosis should be considered as a potential differential diagnosis for synovial masses in dogs. Further cases are needed to validate these observations in veterinary medicine.

1 | CASE PRESENTATION

A 2-year-old neutered male bullmastiff dog was presented with a history of chronic left hind limb lameness (more than one month) that had progressively worsened over time. The dog had not received any prior treatment and did not exhibit any other clinical illnesses.

During the physical examination, left hind limb lameness III/V was observed. No other significant abnormalities were noted. Orthopedic assessment revealed left stifle effusion and medial

buttress without cranial tibial thrust. The dog had a body condition score of 5 out of 9.

Radiographs of the left stifle showed increased soft tissue opacity compatible with joint effusion and evidence of new bone formation in the patella apex, femoral trochlea, and tibial plateau (Figure 1).

Complete blood count and standard serum biochemistry profile performed as a pre-anesthetic evaluation were within reference intervals.

Magnetic resonance imaging (MRI) was conducted for further examination of the radiographic findings. MRI showed synovial distention with effusion, heterogeneous synovium, and widening of the joint space. Thinning of the cranial cruciate ligament with mildly increased signal intensity on proton density (DP), fat suppression (FS), and short tau inversion recovery (STIR) sequences was noted, suggestive of patellar desmopathy. An irregular appearance of the synovium, with regions that showed partial attenuation in T2w fat-suppressed sequences and STIR, suggestive of fat, was also detected (Figure 2).

The orthopedic examination findings, together with the MRI images, suggested the presence of a partial cranial cruciate tear.

Synoviocentesis was then performed, and direct smears of synovial fluid were taken for cytologic evaluation (Figures 3 and 4).

Cytologically, the smears presented high cellularity, and the cells were well-preserved for cytologic evaluation. The background was pinkish with a granular to ropy appearance and sporadic smudge cells. An average of 20 intact nucleated cells were detected per 40× field. The estimated number of cells from direct smear count was 8000 cells/μL. The cell population was mainly inflammatory, with a predominance of mononuclear cells: macrophages and a few small lymphocytes. Some of the macrophages observed contained clear vacuoles and cellular debris within the cytoplasm (Figure 4). Bi-, tri-, and multinucleated macrophages were seen sporadically. Synovial lining cells or synoviocytes were also frequently observed. In a differential count of 200 nucleated cells, 94% were large mononuclear cells, both macrophages and synoviocytes, and 6% were small mononuclear cells, lymphocytes of small size. Additionally, 33% of large mononuclear cells contained vacuoles. Abundant round and large cells, distributed in cohesive aggregates or isolated, compatible with adipocytes, were also identified. These cells had pronounced eccentric round nuclei with stippled to coarse chromatin, a prominent nucleolus, and a large fat-compatible vacuole occupying the entire cytoplasm. The nuclear to cytoplasmic ratio was low. Mild anisocytosis and anisokaryosis were observed. The cytologic interpretation was moderate to marked mononuclear inflammation compatible with degenerative arthropathy and fatty tissue, highly suggestive of synovial lipomatosis based on the description of the lesion.

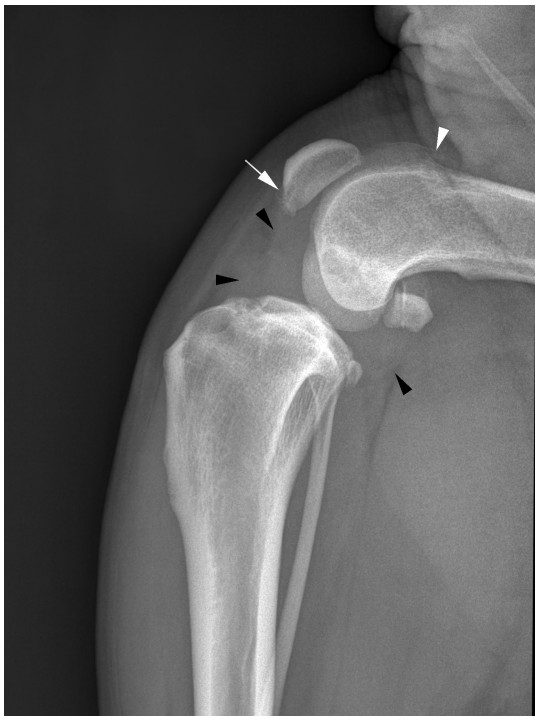

FIGURE 1 Radiographic image from a 2-year-old bullmastiff dog with left stifle lameness. Mediolateral radiograph of the left stifle showing increased soft tissue opacity in the synovial space (black arrowheads) causing displacement of the fat opaque fascial planes and compression of the infrapatellar fat body. There is periarticular new bone/osteophyte formation in the apex of the patella (long white arrow) and femoral trochlea (white arrowhead).

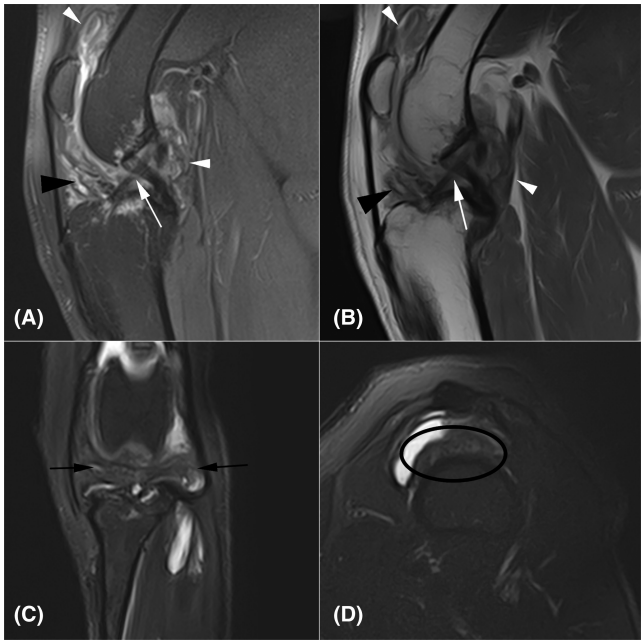

FIGURE 2 (A–D): magnetic resonance images (MRI) from a 2-year-old bullmastiff dog with left stifle lameness. Sagittal PDFS (A), T2w (B), dorsal STIR (C), and transverse T2wFS (D) MRI images of the left stifle. There is moderate synovial distension (white arrowheads, A and B) with heterogeneous signal intensity in the fat-suppressed sagittal sequence (A). The margins of the synovial space are irregular. The infrapatellar fat body is compressed and shows abnormal signal intensity on T2wFS and T2w (black arrowheads). There are signs of cranial (long white arrows, A and B) and caudal cruciate desmopathy. On STIR (C, long black arrows) and T2wFS (D, oval) the synovium is partially suppressed, suggesting the presence of fat within the distended joint space.

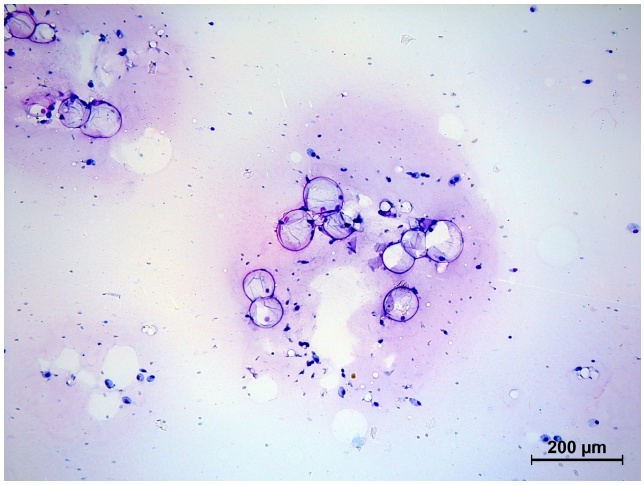

FIGURE 3 Cytological photomicrograph of a direct smear of synovial fluid from the left stifle joint from a 2-year-old bullmastiff dog with synovial effusion. (Aqueous Romanowsky stain). Cohesive aggregates or isolated adipocytes are often seen at low magnification together with a mixed population of large mononuclear cells (vacuolated macrophages and synoviocytes) (×10 objective).

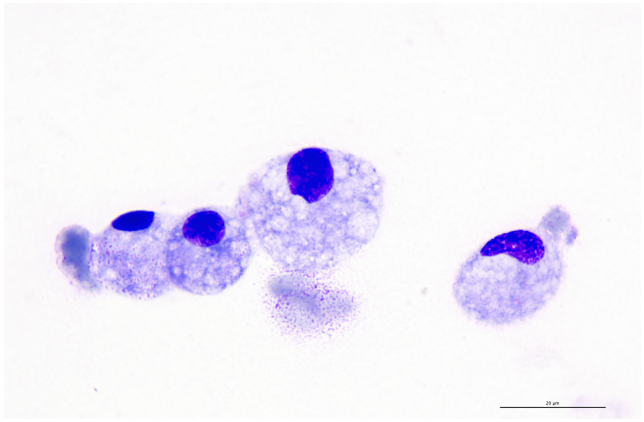

FIGURE 4 Cytological photomicrograph of a direct smear of synovial fluid from the left stifle joint from a 2-year-old bullmastiff dog with synovial effusion (Aqueous Romanowsky stain). High magnification of large mononuclear cells containing clear vacuoles (×100 objective).

To stabilize the stifle, a tibial plateau leveling osteotomy (TPLO) was performed. In addition, a minimal arthrotomy was carried out to sample the lesions in the fat pad and the joint capsule for histopathology and bacteriology culture. The arthrotomy revealed an edematous and irregular appearance of the synovium.

Macroscopically, intra-articular surgically extracted samples consisted of tan, soft yellow tissue fragments of about 5–7 mm each. After submission, they were fixed in 4% buffered formaldehyde for 24 h and then routinely processed for histology. Subsequently, sections of 3–4 µm paraffin-embedded tissue were stained with hematoxylin and eosin for microscopic evaluation. Histological investigation revealed that all seven fragments consisted of irregular rounded papilliform projections of mainly mature adipose tissue covered by a thin layer of dense fibroconnective tissue lined by a single cell layer of cells consistent with synoviocytes. Only occasional superficial perivascular lymphocytes were noted (Figure 5). The macroscopic and microscopic findings were consistent with synovial lipomatosis.

After the TPLO, the dog developed a surgical site infection that was treated with cefalexin 20 mg/kg BID PO based on culture and sensitivity tests (the isolated microorganism was *Staphylococcus pseudintermedius*, sensitive to first-generation cephalosporins at a minimum inhibitory concentration of 2 mg/L using VITEK 2 system [Biomérieux]). The patient was lameness-free at the last check-up, which was 9 months after surgery.

2 | DISCUSSION

Synovial lipomatosis or lipoma arborescens is a rare disorder of the synovium, sometimes considered a "tumor-like" condition.[1–3] It is characterized by extensive and diffuse synovial proliferation of adipose tissue.[3] In humans, it has been described to affect different and multiple joints simultaneously (elbow, hip, metatarsophalangeal, glenohumeral, etc),[4–6] although it primarily manifests in the knee.[7–9] In the canine species, there are only two previous descriptions, one involving the stifle[10] and the other the tibio-tarsal joint.[11]

In veterinary medicine, there is not enough causality to determine age or breed predisposition. It is noteworthy to mention that both our clinical case and the other case of stifle joint lipomatosis were presented in bullmastiff dogs.[10]

The etiology of this condition remains unknown. In human medicine, joint fat deposition has been suggested to result from joint trauma, inflammation, instability, and systemic disturbance of lipid metabolism (such us obesity or short bowel syndrome).[1,4,12] The two cases of dogs diagnosed with synovial lipomatosis of the stifle joint (including the dog reported in this study) presented with partial rupture of the cranial cruciate ligament. Joint instability may contribute to the development of the disease in these cases.[10] In addition, the dog in the previously published report was overweight.[10] It can be hypothesized that all these conditions induce an inflammatory articular state where the released pro-inflammatory substances promote the hyperplasia of the synovium, synoviocytes and adipocytes.[1] Some authors suggest that the fatty synovial proliferation may originate from adipocytes normally present in the subsynovial tissue or from multipotent mesenchymal stem cell niches located in the articular fat pads.[13,14] Synoviocyte and adipocyte hyperplasia leads over time to the characteristic villous lesions of the disease.[1,15] This entity has been included in some studies of the concept of lipomatosis, understood as a benign process characterized by the overgrowth of unencapsulated adipose tissue in various locations.[11,16,17] In dogs, lipomatosis has been described in the parotid salivary glands,[18] pancreas,[19] and simultaneously in the tarsal joint and epidural space.[11] Therefore, in cases of clinical

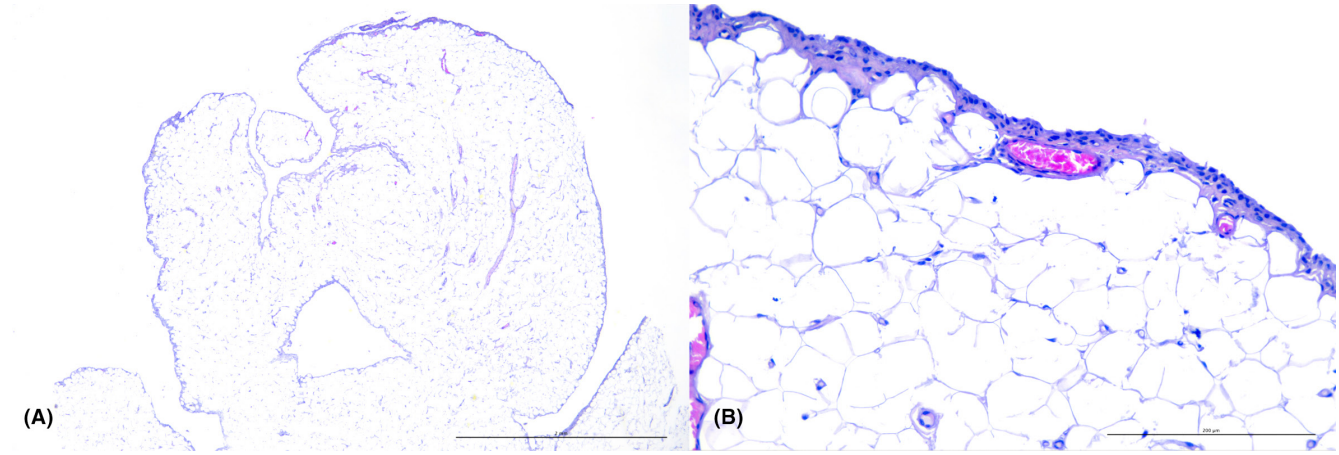

FIGURE 5 (A, B): Histological photomicrographs of an intraarticular tissue from a 2-year-old bullmastiff dog with an articular capsule lesion (hematoxylin and eosin stain). (A) Synovial tissue with papillary architecture is composed mainly of adipose tissue (bar = 1 mm). (B) Detail of the surface of the Synovial tissue. Adipocytes are lined by a thin layer of fibrovascular tissue and synoviocytes (Bar = 50 μm).

suspicion, it may be appropriate to evaluate other potential lesions in animals at the time of diagnosis, given the possibility of systemic or multiple-site involvement.[11,17]

Similar to all cases reported in both human and veterinary medicine, the dog presented in the current report exhibited joint pain, swelling, and effusion. These clinical signs may result from synoviocyte proliferation leading to joint effusion, just as the joint pain could be due to the effect of pressure on the nerve network and abundant substance P fibers located in the articular fat pads.[1,13]

For its diagnosis, imaging techniques such as radiography or ultrasound can show soft tissue swelling, joint effusion, and the presence of masses arising from the joint capsule, among other associated changes.[10,20] However, the possible differential diagnosis of intra-articular masses includes true lipoma, synovial chondromatosis, pigmented villonodular synovitis, synovial hemangioma, and synovial sarcoma, among others.[1,21] MRI is the preferred diagnostic imaging modality for synovial lipomatosis because it can show the fatty nature of the lesion with signal intensities similar to fat and can demonstrate a villous mass appearance of the synovium.[10,22]

Cytologic evaluation of synovial fluid can be very helpful in the diagnostic process. As in our case, the identification of adipocytes in the synovial fluid direct smear of a patient diagnosed with articular lipomatosis has been reported previously.[23] Synovial fluid sampling for cytologic evaluation is a minimally invasive and inexpensive diagnostic technique. Both synovial lipoma and articular lipomatosis or even extra-articular adipose tissue contamination could lead to the observation of adipocytes in an articular cytological smear.[1] Nevertheless, the detection of adipose tissue in cytology, in addition to a compatible MRI image, can narrow the diagnosis to synovial lipomatosis. In this way, the use of arthrotomy for confirmation of the disease could be avoided, and the arthrotomy be performed solely for the purpose of excision of the lesion as treatment.

Regarding treatment, most studies suggest surgical excision of the lesion by arthrotomy or arthroscopy, which is essential to eliminate the triggering cause to prevent recurrence.[24] This approach may be based on the idea that the hyperplastic synoviocytes and adipocytes continue to produce synovial fluid and pro-inflammatory substances, respectively, and may perpetuate the process.[13] In addition, there is evidence that the pro-inflammatory substances produced by articular fat pads (cytokines, interleukins, adipokines, etc) are actively involved in the development of certain joint pathologies such as osteoarthritis.[25]

On the contrary, Rao and coworkers have speculated that in the absence of histologic evidence of fibrosis, a reversible state is still possible if the predisposing factor is removed or treated.[1] This hypothesis could justify the recurrence of clinical signs in the previously reported case of a dog with synovial lipomatosis despite resolution of the precipitating causes because fibrosis was observed histologically.[10] In our case, given the absence of fibrosis in the histological evaluation, complete remission was achieved by stabilizing the stifle. However, further studies are needed to confirm these findings in veterinary medicine.

In conclusion, this report presents the first cytological characterization of adipocytes found in synovial fluid, contributing to the diagnosis of synovial lipomatosis in dogs. This case underscores the potential efficacy of cytological examination of synovial fluid smears when combined with MRI in diagnosing this condition, thereby reducing complications associated with arthrotomy procedures for sampling. Additionally, it emphasizes the importance of considering synovial lipomatosis as a possible differential diagnosis for synovial masses in dogs. Furthermore, more cases are needed to confirm these observations.

CONFLICT OF INTEREST STATEMENT

We have no conflicts of interest to disclose.

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How to cite this article: Agulla B, Vizcaíno N, Velarde R, Estruch J, Domínguez E, Pastor J. Adipocytes in synovial fluid cytology: An approach for diagnosing synovial lipomatosis. *Vet Clin Pathol*. 2024;53:80-84. doi:10.1111/vcp.13330