Adipocytes into synovial fluid

Contributors

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Specimen

Direct smears from the synovial fluid of the left knee

Signalment

A 2-year-old neutered male, Bullmastiff, dog

History

The animal was presented with a history of chronic lameness of the left hindlimb that had progressively worsened over time. The dog had not been on any treatment and had no other previous clinical illness.

Clinical findings

Physical examination revealed a left hindlimb lameness VI/X. No other remarkable finding was found. Orthopedic examination showed left stifle effusion, medial buttress without cranial tibial thrust. The dog had a body condition of 7 of 9.

Diagnostic test

Radiography of the left stifle joint showed increased soft tissue opacity compatible with joint effusion and signs of new bone formation at the patella apex (Figure 1).

Complete blood cell count and standard serum biochemical profile carried out as a pre-anesthetic evaluation were within the reference values.

Due to radiography results an MRI was performed. MRI showed increase in synovial fluid, extension of the joint space caudomedial and proximal to the patella. Thinning of the cranial cruciate ligament, with mildly increased signal on proton density (DP), fat suppression (FS) and STIR sequences was detected. An irregular appearance of the synovium, similar to the subcutaneous adipose tissue, was also detected on T2 and DP FS sequences (Figure 2).

A synoviocentesis was performed and direct smears were prepared from the synovial fluid for cytological evaluation (Figures 3 to 6).

Questions

1. **What is your description of the synovial fluid smears?**
2. **What is your cytological interpretation?**
3. **Which other tests would you recommend in this animal to confirm the preliminary diagnosis?**

Interpretation/Diagnosis

- Moderate to marked mononuclear inflammation (degenerative arthropathy)
- Fat tissue – highly suggestive of synovial lipomatosis

Additional information

On cytology, the smears presented high cellularity with adequate cellular morphology. The background was pinkish with granular to ropy appearance and sporadic smudge cells.

An average of 20 nucleated cells were detected per 40x field (estimated count 8.000 cells/µL). The cell population was mostly inflammatory with a predominance of mononuclear cells (small lymphocytes and macrophages). Some of the macrophages observed contain clear vacuoles and cellular debris material within the cytoplasm. Sporadically bi-, tri- and multinucleate macrophages were seen. Synovial lining cells or synoviocytes were also frequently observed.

On a 200 nucleated cellular differential count, 94% large mononuclear cells (macrophages and synoviocytes) and 6% small mononuclear cells (lymphocytes of small size) were identified.

Also, abundant round and big cells, distributed in cohesive aggregates or isolated compatible with adipocytes were identified. These cells displayed marked eccentric round nuclei with stippled to coarse chromatin, one prominent nucleoli and a large fat-compatible vacuole occupying the entire cytoplasm. The nuclei: cytoplasm ratio was low. Mild anisocytosis and anisokaryosis were noted.

Neither microorganisms nor neoplastic cells were detected in the examined cytological preparations.

In order to stifle stabilization a Tibial Plateau Leveling Osteotomy was performed. In addition, a minimal arthrotomy was carried in order to sample the fat pad and the joint capsule tissue for histopathology examination and bacteriology culture. This procedure revealed an edematous and irregular appearance of the synovium.

Macroscopically, intra-articular surgically extracted samples consisted in tan, yellow soft tissue fragments of about 5 to 7 mm each. After submission, they were fixed in 4% formaldehyde for 24 hours and then cross trimmed and routinely processed for histology. Subsequently, sections of 3-4 cm

paraffin-embedded tissue were stained with hematoxylin and eosin for microscopic evaluation. Histological investigation revealed 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 7). A diagnosis of synovial lipomatosis was made rely on histopathological examination.

Follow up and clinical outcome

The patient underwent stifle stabilization (Tibial Plateau Leveling Osteotomy), he developed a surgical site infection that was treated with antibiotics based on culture and sensitivity tests. The lameness resolved completely.

Discussion

Synovial lipomatosis or lipoma arborescence is a rare disorder of the synovium, sometimes considered a “tumor-like” condition (1-3). It is characterized by the extensive and diffuse synovial proliferation of fatty tissue (3). In humans, it has been described affecting different and simultaneously several joints (elbow, hip, metatarsophalangeal, glenohumeral, etc.) (4-6), this entity affects mainly 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 casuistry to determine age or breed predispositions. 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 aetiology of this condition remains unknown, although in human medicine, joint trauma, inflammation or instability and systemic disturbed lipid metabolism situations, such as obesity or short bowel syndrome, has been proposed as possible causes of joint fat deposition (1, 4, 12). The two cases of dogs with stifle joint synovial lipomatosis, including the dog presented in this case, had a partial cranial cruciate ligament rupture, which could have contributed to the development of the disease (10). In addition, in the previous published report, the dog was overweight (10).

It can be hypothesized all these situations induce an inflammatory articular stage where the released pro-inflammatory substances promote the hyperplasia of the synovium synoviocytes and adipocytes (1). Some authors consider that the fatty synovial proliferation may come from fat cells normally presented in the subsynovial tissue or from multipotent mesenchymal stem cells niches located in the articular fat pads (13, 14). Synoviocyte and adipocyte hyperplasia gives rise over time to the characteristic villous lesions of the disease (1, 15). This entity has been included in some studies into the lipomatosis concept, understood as an overgrowth of non-encapsulated adipose tissue in various locations (16). In dogs, lipomatosis has been described in parotid salivary glands (17), pancreas (18) and epidural space (11).

As all the cases reported both in human and veterinary medicine, the dog presented in the current report showed pain and swelling of the joint and synovial fluid effusion. These clinical signs might be consequence of the synoviocytes proliferation that results in joint effusion, as well as the articular pain

could be due to the effect of pressure or to the nervous network and abundant substance P fibers located in the articular fat pads (1, 13).

For its diagnosis, imaging techniques, such as radiography or ultrasound, are able to show soft tissue swelling, joint effusion and the presence of masses arising from the joint capsule among other associated alterations (10, 19). However, the possible differential diagnosis of intra-articular masses includes synovial lipoma, synovial chondromatosis, pigmented villonodular synovitis, synovial hemangioma, and rheumatoid arthritis (1). Magnetic resonance imaging (MRI) is the preferred diagnostic imaging modality for synovial lipomatosis because it can exhibit the fatty nature of the lesion with signal intensities like subcutaneous fat, and it can demonstrate a villous mass appearance of the synovium (10, 20).

The cytological evaluation of the synovial fluid can be very helpful during the diagnosis procedure. As in our case, the identification of lipid globules in the synovial fluid direct smear of a patient diagnosed with articular lipomatosis has been previously reported (21). Synovial fluid sample collection for cytological evaluation is a minimally invasive and inexpensive diagnostic technique. Both a synovial lipoma and joint lipomatosis or even extra-articular fatty tissue contamination could lead to the observation of adipocytes in a joint cytological smear (1). Nevertheless, fatty tissue recognition in the cytology in addiction to a compatible MRI image can closely reach the diagnosis to synovial lipomatosis, limiting arthrotomy to the treatment and not only to the histopathological confirmation of the disease.

Regarded treatment, most studies propose the surgical excision of the lesion through arthrotomy or arthroscopy, being essential to eliminate the triggering cause at the same time to avoid relapses (22). This approach may be based on the idea that the hyperplastic adipocytes and synoviocyocytes continue producing synovial fluid and pro-inflammatory substances and might 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 (23).

On the contrary, Rao and co-workers have speculated that if there is no evidence of fibrosis in histology, a reversal state is still possible, if the predisposing factor is removed or treated (1). This hypothesis could justify the clinical signs recurrence in the previously reported case of a dog with synovial lipomatosis despite the resolution of the triggering causes, because fibrosis was observed histologically (10). In our case, given the absence of fibrosis in the histological evaluation, a complete remission was achieved by the stifle stabilization. However, further studies are needed to corroborate these findings in veterinary medicine.

In conclusion, this clinical report highlights the importance of including synovial lipomatosis in the differential diagnosis of synovial masses in the canine joints. A cytological evidence of lipid globules in the synovial fluid smears in addiction to a compatible MRI image can help in reaching the diagnosis, limiting the use and the possible complications of arthrotomy or arthroscopy for diagnosis procedure. Furthermore, more synovial lipomatosis cases in dogs are required to confirm these observations.

Figures

Figure 1. Lateral stifle radiograph demonstrating increase soft tissue opacity at the level of the fat pad (arrowheads) and new bone formation at the apex of the patella (arrow).

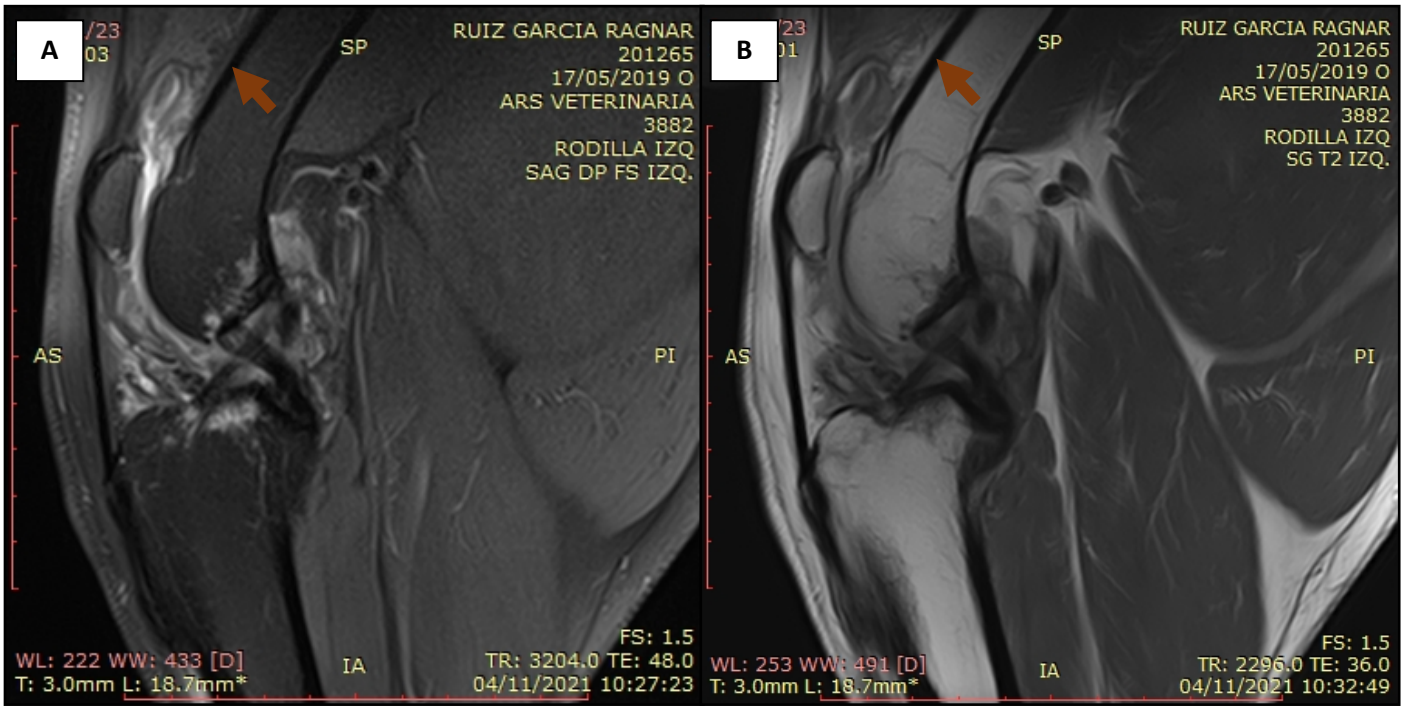

Figure 2. Irregular appearance of the synovium (arrows) with sagittal DP FS (A) and sagittal T2 (B)

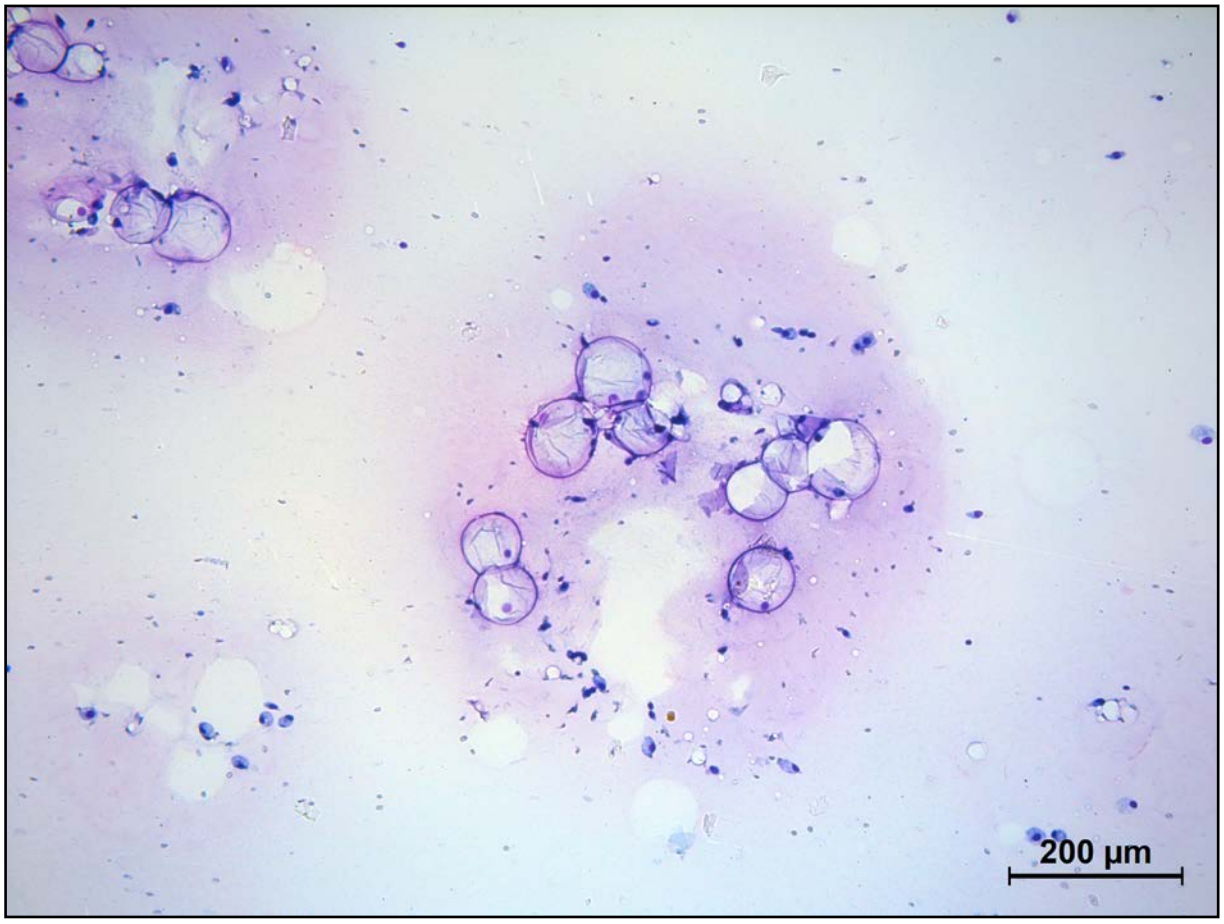

Figure 3. Cytological photomicrograph of the left stifle synovial fluid direct smear. Aqueous Romanowsky stain, x10 objective. At low magnification cohesive aggregates or isolated adipocytes are frequently seen.

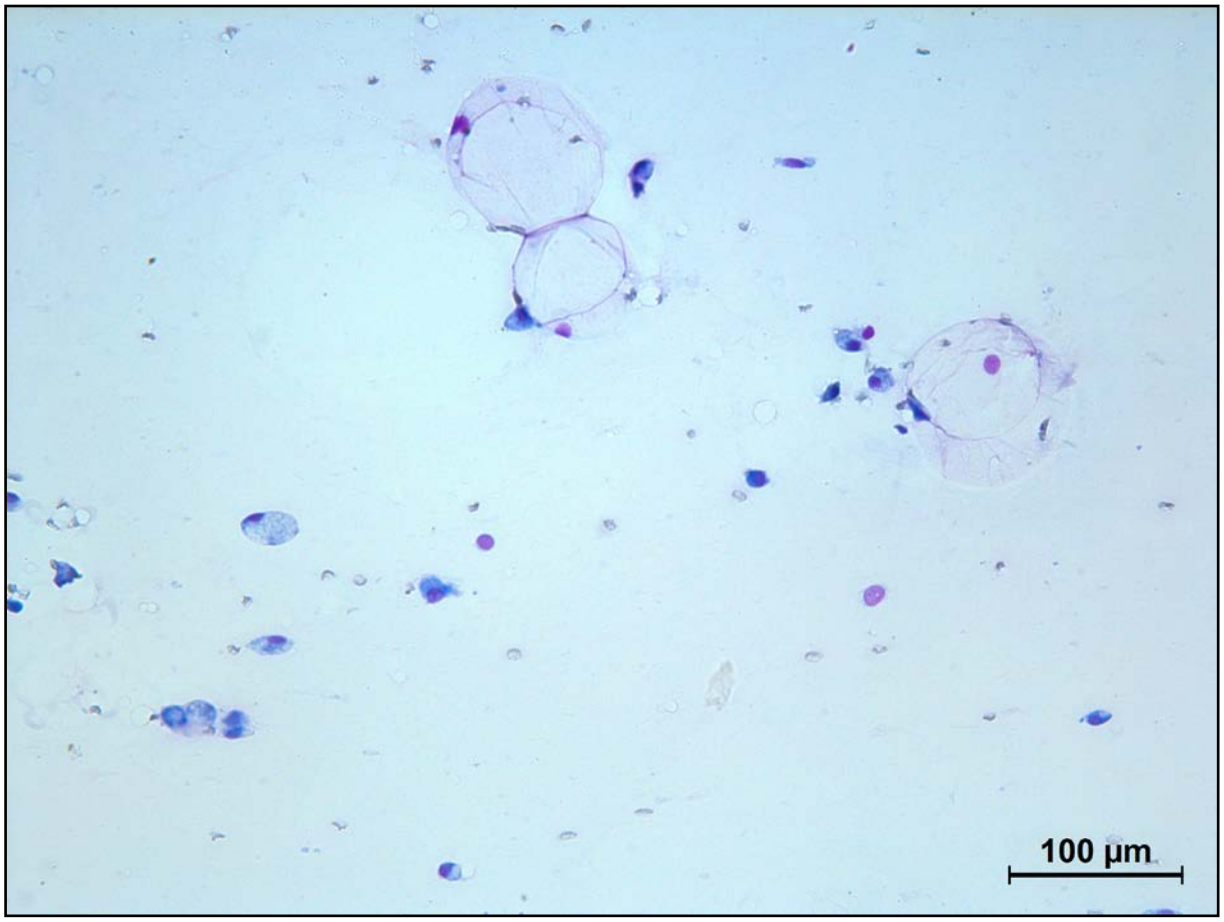

Figure 4. Cytological photomicrograph of the left stifle synovial fluid direct smear. Aqueous Romanowsky stain, x20 objective. Mixed population of adipocytes and large mononuclear cells (macrophages and synoviocytes).

Figure 5. Cytological photomicrograph of the left stifle synovial fluid direct smear. Aqueous Romanowsky stain, x40 objective. Cohesive aggregate of adipocytes with mild atypia.

Figure 6. Cytological photomicrograph of the left stifle synovial fluid direct smear. Aqueous Romanowsky stain, x40 objective. An increase in the number of large mononuclear cells (macrophages or synoviocytes) is observed.

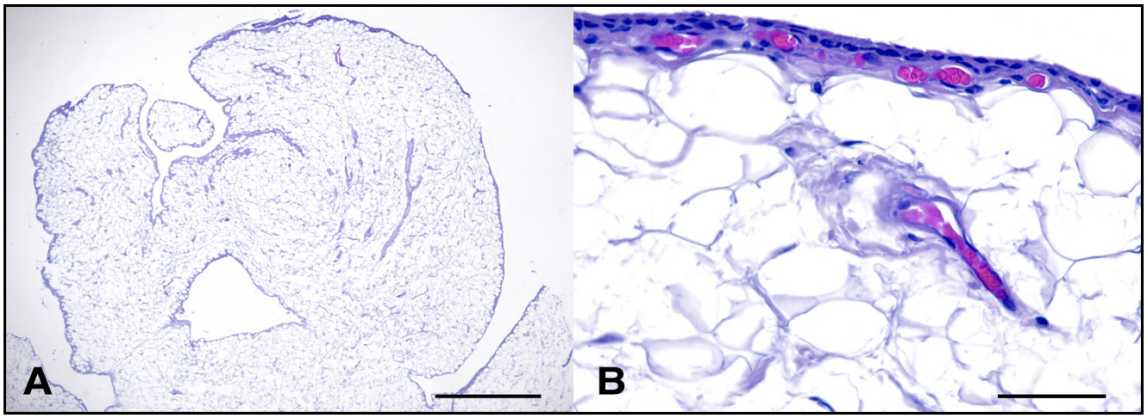

Figure 7. Intraarticular tissue from a dog. A. Synovial tissue with papillary architecture composed mainly of adipose tissue (Bar = 1mm). B. Detail of the surface of the synovial tissue. Adipocytes are lined by a thin layer of fibrovascular tissue and synoviocytes (Bar = 50 µm). Hematoxylin and eosin stain.

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