

Arthrocentesis was performed and sterile synovial fluid was found. Magnetic resonance images displayed a bone fragment detachment from the humeral condyle of the right elbow with synovium thickening and persistent effusion: the diagnosis of OCD was pointed out.

The patient showed minor dysmorphisms (i.e. dolicocephaly, hypotelorism, arched palate and brachydactyly of the IV finger of both hands) and parents reported a previous episode of OCD when he was 12: at that time, symptoms resolved with non-weightbearing and non-steroidal anti-inflammatory therapy after few days. Furthermore, the patient went under regular endocrinologist follow-up for short stature since he was 8. At the age of 10, his height was 123 cm, SDS 2.4, and growth hormone (GH) stimulation tests showed partial response to insulin tolerance test (GH peak 6.27 ng/mL). Bone age at the X-Ray of right hand and wrist was delayed of 12 months. Human recombinant GH replacement therapy was administered without significant growth-velocity improvement. Although the patient came to observation because of suspected elbow septic arthritis, we re-considered the diagnosis: namely, i. recurrent episodes of OCD; ii. short stature that was poorly responsive to the human recombinant GH treatment, iii. mild skeletal and facial dysmorphisms, led us to hypothesize a form of aggrecanopathy. Molecular analysis of the *ACAN* gene revealed the novel missense variant c.6970T>C, p.Trp2324Arg in the G3 domain of the protein. Notably, another mutation of the G3 domain (c.7249G>A) has been previously related to aggrecanopathy2. Intra-familial molecular analysis allowed us to detect the same gene variant in other three subjects (the mother and 2 siblings) affected only by brachydactyly and short stature.

Conclusion: A patient carrying a novel mutation of the *ACAN* gene presented an atypical form of aggrecanopathy mimicking inflammatory and/or septic arthritis associated with slight short stature and bone dysmorphisms. Further studies are needed to investigate a possible role of this novel *ACAN* gene variant in the inflammatory articular involvement.

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AB0091 SYNDECAN-4 IS INCREASED IN OSTEOARTHRITIC KNEE, BUT NOT HIP OR SHOULDER, ARTICULAR HYPERTROPHIC CHONDROCYTES

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Background: Syndecan-4 plays a critical role in cartilage degradation during osteoarthritis (OA).

Objectives: To investigate the expression and localization of syndecan-4 in different OA joint tissues.

Methods: Syndecan-4 mRNA levels were quantified by RT-PCR in human OA primary cells to compare non-hypertrophic vs hypertrophic articular chondrocytes, non-sclerotic vs sclerotic subchondral osteoblasts and normal/reactive vs inflamed fibroblasts-like synoviocytes. Syndecan-4 was localized by immunohistochemistry in knee, hip or shoulder OA bone/cartilage biopsies. Syndecan-4 was quantified by immunoassay in chondrocytes culture supernatant and cell fraction.

Results: By immunohistochemistry, syndecan-4 was observed in chondrocytes clusters in the superficial zone of OA knee, but not in OA hip or shoulder cartilage. No staining was observed in the deep zone of cartilage and in subchondral bone.

No difference between syndecan-4 expression level in sclerotic and non-sclerotic osteoblasts was observed. Syndecan-4 tended to be increased in inflamed synoviocytes compared to normal/reactive ones but difference was not significant. Differentiated hypertrophic chondrocytes from knee, but not from hip cartilage, expressed more syndecan-4 than non-hypertrophic cells. Using an immunoassay for the extracellular domain of syndecan-4, we found 68% of the syndecan-4 in the culture supernatant of OA chondrocytes culture, suggesting that a large majority of the syndecan-4 is shed and released in the extracellular medium. The shedding rate was not affected by hypertrophic differentiation state of the chondrocytes or their joint origin.

Conclusion: Syndecan-4 could be related to the hypertrophic differentiation of the OA chondrocytes, but the pathway seems to be knee specific. Even if chondrocytes clusters are seen in OA knee, hip and shoulder cartilage and hypertrophic differentiation appears in knee and hip OA articular chondrocytes, syndecan-4 synthesis only increased in knee. These findings suggests the presence of biochemical difference between articular cartilage according to their location and that syndecan-4 could be a biochemical marker specific for knee OA.

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AB0092 SERUM LEVELS OF COLL2-1, A SPECIFIC BIOMARKER OF CARTILAGE DEGRADATION, ARE NOT AFFECTED BY SAMPLING CONDITIONS, CIRCADIAN RHYTHM, SEASONALITY AND PHYSICAL ACTIVITY

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Background: Coll2-1 is a nine amino acid sequence (HRGYPLDG) specific of type II collagen which is released during cartilage degradation. This peptide is located in the triple helicoidal part of type II collagen molecule(1,2,3).

Objectives: This study aims to assess intra-individual biological variability of serum cartilage specific biomarker Coll2-1 and define the best standardized conditions for blood sampling in clinical trials.

Methods: Blood samples were taken from 122 subjects with diagnosed knee osteoarthritis (KOA) at a single timepoint as well as from 15 healthy subjects under various conditions, including fasting condition (before or after breakfast and lunch), sampling time (at 8am, 9am, 12pm, 2pm and 5pm), sampling season (at baseline and after 2, 16, 52 and 68 weeks), physical activity (after a resting weekend versus working day), blood treatment (blood clotting from 1h to 24h at room temperature or 4°C; centrifugation at room temperature or 4°C) and type of blood collection tube (dry tube versus dry tube with gel separator). Type II collagen-specific biomarker Coll2-1 was measured using ELISA (Artialis Groups SA, Liège, Belgium) on all collected samples.

Results: There was no significant difference on Coll2-1 values between samples collected at any of the five sampling times (p=0.85) or at any of the sampling days measured (p=0.58). None of the sampling parameters tested had a significant impact on Coll2-1 value (clotting time, clotting temperature and temperature of blood centrifugation (p=0.93), type of tube: p=0.38) when all data from healthy subjects were pooled (n=631 samples). On the contrary, subjects with knee OA had a significantly higher Coll2-1 concentration than healthy subjects (OA: 481±/144nM vs Healthy 192±/32nM, p<0,001).

Conclusion: Coll2-1 assay is sufficiently robust for use during OA clinical trials. Coll2-1 measurement is not affected by subject specific conditions such as fasting, resting state, circadian rhythm, seasonality, nor by sampling process factors such as type of dry tube, clotting patterns and centrifugation temperature.

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