Back pain, mechanical musculoskeletal problems, local soft tissue disorders

THU0482

HUMAN LUMBAR SPINE FACET JOINT OSTEOARTHRITIS DISPLAYS PREDOMINANT NGF EXPRESSION AND SIGNALING IN CAPSULAR SYNOVIUM AND SUBCHONDRAL BONE MARROW TISSUES INDEPENDENT OF OSTEOARTHRITIS GRADE

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Background: Increased nerve growth factor (NGF) levels are associated with chronic pain conditions, including low back pain and osteoarthritis (OA). NGF signalling through its receptor TrkA regulates pro-inflammatory neurotransmitters such as substance P (SP). Inhibition of NGF has shown therapeutic efficacy in knee OA [1] and chronic back pain [2], but trials have revealed rare cases of rapidly progressive OA of peripheral joints.

Objectives: To describe the tissue distribution of NGF, TrkA, SP and macrophages in facet joint osteoarthritis (FJOA) of the lumbar spine and their association with FJOA grade.

Methods: FJOA specimens were obtained by facetectomy from patients undergoing intervertebral fusion ($n=10$, average age 69 years, 5 males). FJOA severity and presence of synovial hypertrophy was graded using preoperative magnetic resonance imaging (MRI). Relative abundance of NGF, CD68 (macrophages), TrkA and SP in capsular synovium (SY), cartilage (CL), subchondral bone (SB) and subchondral bone marrow (BM) was evaluated semi-quantitatively on a scale ranging from 0-3 using immunohistochemistry. Association between imaging parameters and tissue expression was determined using Pearson correlation analysis.

Results: Synovial hypertrophy as determined by MRI was present in six cases (60%) and median Weishaupt grade of FJOA was 2 (1.5-3) corresponding with moderate to severe OA. NGF was abundantly expressed in SY (3 [0.5-3]) and to a lesser extent in BM tissues (2 [1-3]), whereas TrkA expression was detected in BM exclusively. NGF abundance in SY and BM showed a strong correlation ($r=0.94$), but did not associate with synovial hypertrophy or FJOA severity. CD68+ macrophages were highly abundant in BM (3 [1.5-3]) and sparse in SY tissues (0.5 [0-1]). The relative abundance of macrophages and NGF was strongly correlated in SY tissue only ($r = 0.78$). SP as a downstream mediator of NGF signalling was also abundantly expressed in SY, CL and BM tissues. Tissue distributions of CD68, NGF and SP are summarized in the figure.

Conclusion: NGF expression and signalling is evident in lumbar spine FJOA specimens, but not strongly associated with synovial hypertrophy or disease severity. These results are in agreement with recent studies of human knee OA, which have shown osteochondral NGF expression as a hallmark of symptomatic OA independently of chondropathy or synovitis [3].

Abstract THU0482 – Figure 1.

REFERENCES:

- [1] Lane NE, Schnitzer TJ, Birbara CA, Mokhtarani M, Shelton DL, Smith MD, Brown MT. (2010) Tanezumab for the treatment of pain from osteoarthritis of the knee. *N Engl J Med*. 363:1521.
- [2] Katz N, Borenstein DG, Birbara CA, Bramson C, Nemeth MA, Smith MD, Brown MT. (2011) Efficacy and safety of tanezumab in the treatment of chronic low back pain. *Pain*. 152(10):2248
- [3] Aso K, Shahtaheri SM, Hill R, Wilson D, McWilliams DF, Walsh DA. (2019) Associations of symptomatic knee OA with histopathologic features in subchondral bone. *Arthritis Rheumatol*. ePub

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DEMOGRAPHICS AND CLINICAL CHARACTERISTICS OF A NATIONAL COHORT OF 280 PATIENTS WITH JOINT HYPERMOBILITY SYNDROME, THEIR SOCIOECONOMIC BURDEN AND THE PERFORMANCE OF THE 2017 INTERNATIONAL CLASSIFICATION CRITERIA OF THE EHLERS DANLOS SYNDROMES

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Background: Joint hypermobility syndromes (JHS) encompass a spectrum ranging from asymptomatic joint hypermobility through to Ehlers Danlos syndromes (EDS) including hypermobile EDS (equivalent to the former diagnosis of EDS type 3). Many EDS patients have significant musculoskeletal pain and other systemic comorbidities including autonomic, bowel and bladder dysfunction. We present data from a cohort of patients with JHS referred to our tertiary centre from December 2015 to May 2017.

Objectives: To increase the awareness of the hypermobility syndrome among general rheumatologists and other health professionals. To assess the impact of this condition on the patient general health and their work disability.

To reflect on the 2017 Ehlers Danlos International Criteria

Methods: We undertook a retrospective analysis of medical records. Statistical analysis utilised non parametric Chi squared analysis for between group comparisons

Results: There were 280 patients: 253 patients (90%) were female and 27 were male (10%) with a female to male ratio of 9:1. The age distribution was from 18 to 66 (mean age 42 years). The age at which they were first diagnosed ranged from 4 to 55 (mean age 29 years); 279 (96%) had Ehlers Danlos Syndrome type 3, one patient had Marfan's, one Kyphoscoliotic EDS, and two patients had Tenascin X deficiency. Family history of hypermobility was reported among 185 patients (66%). In relation to the autonomic dysfunction, 185 patients (66%) had orthostatic intolerance, 126 (45%) had gastrointestinal problems; 109 (39%) had bladder dysfunction with 2.5% of them requiring catheterisation. Chronic joint and muscle pain was reported in 91%; 49.6% of these used opioid analgesia long term. One hundred and twenty patients (43%) had work disability.

Patients taking opioids were more likely to have work disability: 54% vs. 34% ($p<0.001$). Bladder problems were more common in the group taking opioids (46% vs 32%; $p<0.02$). A significant association between orthostatic intolerance and bowel problems was observed. Almost half (47%) of those with orthostatic intolerance had bowel problems, compared to only 19% without ($p<0.001$). Patients with bowel problems were more likely to have bladder problems compared to those without bowel problems ($P < 0.001$).

Conclusion: The 2017 EDS International Classification defined thirteen subtypes of EDS. The molecular basis for the hypermobile Ehlers Danlos Syndrome (previously Ehlers Danlos Syndrome type 3) remains to be identified and diagnosis is clinical, preferentially characterised by joint hypermobility, skin hyper extensibility and tissue fragility. However, this study shows that systemic manifestations are frequently observed and they tend to appear in clusters.

As important is the diagnosis of joint hypermobility, the same is the recognition of every aspect of hypermobility syndrome. A tailored multidisciplinary approach can potentially improve the quality of life and lessen the socioeconomic and NHS burden of these patients. In addition we would strongly discourage use of opioids in patients with hypermobility.

REFERENCE:

- [1] Fransiska Malfait at al : The 2017 international classification of Ehlers – Danlos syndromes. *American Journal of medical Genetics Part C: Seminars in medical Genetics*, Vol 175, Issue 1, March 2017, pages 8-26

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