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Histopathological modifications in blood-induced haemophilic artropathy

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Haemarthrosis triggers haemophilic arthropathy (HA), involving mainly the larger joints. Mechanisms and pathways of blood-induced joint damage are still not completely clear. The molecular triad OPG/RANK/RANKL tightly controls the bone turnover and any change in the balance between OPG and RANKL leads to bone pathological conditions. The aim of this study was to evaluate the expression of RANK/RANKL/OPG system in synovial tissue of haemophilic patients (pts) with severe HA, compared to osteoarthritic (OA) pts.

Synovial biopsies from 20 HA pts and from 16 OA pts, obtained during arthroplasty of the knee, were routinally processed for light microscopy. The severity of HA was evaluated according to i) Ultrasonography (US) score, ii) World Federation of Haemophilia orthopaedic joint scale (WFH) and iii) radiographic Petterson method. Synovial sections were stained with H&E to evaluate pathological changes. The expression of RANK, RANK-L, OPG was examined by immunohistochemistry. Moreover, serum levels of sRANKL and OPG from 67 HA pts and 30 controls were measured by ELISA assay.

The mean US, WFH and Pettersson score in HA pts were 11(range 0-21 with cut off>5), 39,5 (range:12-57), and 10,4 points (range: 6-12), respectively.

Microscopically, the synovium from HA pts showed a large amount of intra- and extracellular haemosiderinic deposits. The lining layer showed mild proliferation and in the sublining area the vessels showed thickened wall, due to a local and chronic inflammatory stimuli. A lower expression of OPG was found in HA synovium compared to OA. RANK and RANK-L positivity was strongly expressed in the lining and sublining both in HA and OA synovial tissue. Serum levels of sRANKL and OPG resulted lower than in controls.

Our preliminary data show that, in HA pts, the synovium highly expressed RANK and RANKL, whereas OPG positivity decreased, suggesting an osteoclastic activation. Tissue expression of OPG correlates with serum level of this protein in HA pts and with severity of HA, as assessed by US score.

Keywords: Haemophilic Arthropathy; synovium; RANK/RANKL/OPG