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POSTER ABSTRACTS

322.DISORDERS OF COAGULATION OR FIBRINOLYSIS: CLINICAL AND EPIDEMIOLOGICAL

Increased Circulating Levels of YKL-40 Protein in Children and Adolescents with Hemophilia: Correlation with the Degree of Hemophilic Arthropathy

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Introduction: Hemophilia A and B are rare X-linked inherited bleeding disorders caused by complete or partial deficiency of coagulation factors VIII and IX, respectively. Recurrent joint bleeding (hemarthrosis) is the most frequent clinical manifestation of severe hemophilia. Unless appropriately managed, even subclinical hemarthrosis can lead to hemophilic arthropathy, that severely affects the quality of life of patients. Chitinase-3-like protein 1 (CHI3L1), also known as YKL-40, is a 40-kDa heparin-human cartilage glycoprotein without enzymatic activity, that is encoded by the *CHI3L1* gene in humans and its name derives from the one letter code for the three terminal amino acids - tyrosine (Y), lysine (K) and leucine (L). YKL-40 is secreted in vitro and in vivo in the arthritic joint by various cell types, such as activated macrophages, chondrocytes, synoviocytes and neutrophils. Actually, it is a major protein that has been identified in the chondrocytes from arthritic knee joints.In fact, synovial as well as serum YKL-40 levels are found increased in joint diseases like rheumatoid arthritis and osteoarthritis, indicating its potential role as a biomarker of inflammation and tissue remodeling or degradation, whereas it is absent in normal joints. In our knowledge, there are not any reports linking YKL-40 expression with hemophilic arthropathy, thus we aimed to investigate if this protein could be implicated in hemophilic arthropathy severity, by measuring its circulating levels and correlate them with hemophilic arthropathy features and laboratory parameters in children and adolescents with hemophilia A and B.
Patients and Methods: Eighty children and adolescents (median age:14 years, range 10-18 years) with severe (n= 60), moderate (n= 8) and mild (n= 12) hemophilia A or B (n= 7), on prophylaxis or on demand treatment (n= 12) were included in the study, while 35 apparently healthy male individuals matched for age served as controls. No signs of hemophilic arthropathy (NHAP), i.e. Hemophilia Joint Health Score 2.1 $\leq$ 2 and Hemophilia Early Detection Arthropathy with Ultrasound Score $\leq$ 1, were detected in 34/80 patients with median age of 13.5 years. In 37/80 patients with median age of 14.25 years arthropathy (HAP) was confirmed, while 18/80 patients with median age of 15.75 years presented with acute bleeding (AB)-hemarthrosis or muscle bleed- at the time of the laboratory evaluation. In patients and controls YKL-40 concentrations were determined by means of an immunoenzymatic technique.
Results: We found that: a) Circulating YKL-40 levels in patients with hemophilia were significantly higher compared to controls, 21.9±2.3 ng/mL (95% Confidence Intervals of the mean (CI): 19.6;24.2 ng/mL) vs 17.0±2.5 ng/mL (CI: 14.5;19.4 ng/mL), respectively, p=0.003. b) Patients with arthropathy (HAP) tend to express higher circulating YKL-40 levels (25.5±2.0 ng/mL) than patients without arthropathy (NHAP)(20.1±1.8 ng/mL) and patients with acute bleeding (AB) (19.7±2.4 ng/mL), respectively, p-trend=0.06.
Conclusions: To the best of our knowledge, this is the first study to evaluate the potential clinical significance of circulating YKL-40 levels in patients with hemophilia and demonstrated that it could reflect hemophilic arthropathy activity in clinical or even in subclinical level. As YKL-40 in synovial fluid is derived from cells in the inflamed/damaged synovium, such as chondrocytes, we postulate that it may be involved in the pathophysiology of the hemophilic arthropathy processes and reflect local disease activity. Further studies are essential on the role of YKL-40 in the evolution of hemophilic arthropathy, in order to fully elucidate its clinical significance and prognostic utility.

Disclosures No relevant conflicts of interest to declare.

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