SEMAPHORIN 3A: A POSSIBLE MARKER FOR DISEASE ACTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Sema 3A is concerned in the pathogenesis of many autoimmune diseases because it is involved in regulation of immune responses and maintenance of self-tolerance. Regulatory T cells play an important role in maintaining immunological self-tolerance by suppressing autoreactive T cells. Sema3A promotes regulatory T cells by enhancing IL-10 production.

Objectives: The current study aimed at testing the possible role of Semaphorin 3A (Sema 3A) in activity and in remission in rheumatoid arthritis patients and to assess whether this level correlates with interleukin 10 (IL-10) level.

Methods: Sixty Egyptian patients with rheumatoid arthritis (RA) were divided into three groups according to modified Disease Activity Score (DAS28), RA in high activity (group II, n=20), RA in moderate activity (group III, n=20) and RA in remission (group IV, n=20) and compared to 20 normal individuals (group I). Serum levels of Sema 3A and IL-10 were measured and correlated with ESR, CRP, Rheumatoid factor, DAS28 and Health Assessment Questionnaire (HAQ).

Results: Serum Sema 3A levels were significantly lower in high activity (55.7 ± 15.5 pg/ml) than in moderate activity groups (72.9 ± 14.6 pg/ml, p = 0.002) and both levels are lower than those in remission group (77.2 ± 13.1pg/ml, p < 0.001 compared to high activity one also). A significant negative correlation was detected between Sema 3A and each of ESR, CRP, DAS28 and HAQ. Serum IL-10 was higher in patient groups, with highest mean among group IV. The negative feedback mechanism is well described for hepatocytes, but seems to be inactive in synovial fibroblasts from patients with rheumatoid arthritis (RASF). Neangiogenesis, which is mediated partially by local fibroblasts, is increased due to inflammation and tissue hyperplasia in RA synovium.

Conclusion: reduced serum level of Sema 3A was found to be correlated with disease activity and indicating its usefulness marker for RA disease activity.

Disclosure of Interests: None declared


ACTIVIN A AND FOLLISTATIN AFFECT THE INTERACTION OF ENDOTHELIAL CELLS AND RHEUMATOID ARTHRITIS SYNOVIAL FIBROBLASTS

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Background: Activin A and its antagonist follistatin are part of an autoregulatory cycle, which is well known in the hypothalamic-pituitary-gonadal axis. Activins also have an important function in autoimmune diseases, such as rheumatoid arthritis (RA). Due to inflammation, activin A is released systemically, causing an induction of its antagonist follistatin. The negative feedback mechanism is well described for hepatocytes, but seems to be inactive in synovial fibroblasts from patients with rheumatoid arthritis (RASF). Neangiogenesis, which is mediated partially by local fibroblasts, is increased due to inflammation and tissue hyperplasia in RA synovium. Despite the fact that RASF contribute to cartilage destruction in RA and RASF are able to interact with endothelial cells, less is known about the effect of activin and follistatin in this context.

Objectives: The aim of this study was to examine the effect of activin A and follistatin on the interaction of RASF and endothelial cells.

Methods: Endothelial cells (HUVEC) were commercially obtained and RASF were isolated from synovial tissue of patients with RA undergoing joint replacement surgery. RASF and HUVEC were stimulated in mono-, or coculture with activin A (15ng/ml), follistatin (500ng/ml) and/or IL-1β (1ng/ml). The concentrations of activin A, follistatin, VEGF and IL-6 were measured by ELISA.

Results: IL-1β induced the release of activin A 8-fold in RASF alone (p < 0.01, n=5) as well as in direct coculture with HUVECs 4-fold (p < 0.05, n=5). The stimulation with follistatin together with IL-1β reduced the activin A concentration produced by HUVECs 9-fold (p < 0.01, n=5) as well as in cocultures (10-fold, p<0.01) in comparison to stimulation with IL-1β alone. This reduction could not be observed in RASF monocyte.

In HUVECs, the IL-6 release was reduced by 37.6% after stimulation with activin A and IL-1β (n=5,p<0.05) in comparison to the stimulation with IL-1β alone. In RASF monocyte the release of IL-6 was induced by 61.0% after stimulating with activin A combined with IL-1β in comparison to the stimulation with IL-1β alone. In direct coculture neither the induction, nor the reduction of the IL-6 concentration could be detected when stimulated with activin A and IL-1β.

The release of VEGF was induced in RASF with IL-1β (89%), activin A (55%), activin combined with IL-1β (148%), follistatin and IL-1β (84%) compared to unstimulated control. In coculture with HUVECs, the induction was less distinct than in direct coculture with no induction in coculture compared to stimulation with activin A and IL-1β.

Conclusion: The autoregulatory cycle of activin A and follistatin is active in endothelial cells and inactive in RASF. Due to the interaction of endothelial cells and RASF, the proinflammatory response of the RASF is weakened. This was shown in direct coculture with no induction in coculture compared to stimulation with activin A and IL-1β in RASF monoculture. Interestingly, in direct coculture, the effects of HUVECs appear to dominate resulting in a significant reduction of the activin A concentration in the presence of follistatin and IL-1β in comparison to monoculture of RASF.

Disclosure of Interests: None declared