Maternal plasma and amniotic fluid chemokines screening in fetal Down syndrome

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Objective

Chemokines (chemoattractive cytokines) exert different inflammatory responses which can potentially be related with certain fetal chromosomal abnormalities. The aim of the study was to determine the concentration of selected chemokines in plasma and amniotic fluid of women with fetal Down Syndrome.

Methods

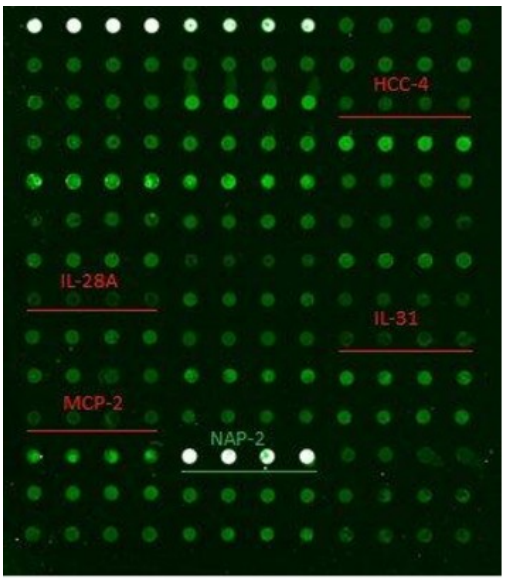
Out of 250 amniocenteses we had 8 patients with confirmed Down syndrome. For the purpose of our control we chose 14 women without confirmed chromosomal aberration. To assess the concentration of chemokines in the blood plasma and amniotic fluid, we used a protein macroarray, which allows the simultaneous determination of 40 chemokines per sample. The sets consist of the following chemokines: 6Ckine, Axl, BTC, CCL28, CTACK, CXCL16, ENA-78, Eotaxin-3, GCP-2, GRO (GRO).

Results

We showed a significant decrease in concentration of 4 chemokines: HCC-4, IL-28A, IL-31, MCP-2 and an increase in the concentration of 1 chemokine: NAP-2 in plasma of women with fetal Down Syndrome. Furthermore we showed a decrease in the concentration of 4 chemokines: 6Ckine, ITAC, MCP-3 MIF and an increase in the concentration of 3 chemokines: IP-10, MPIF-1 and NAP-2 in amniotic fluid of women with fetal Down Syndrome. We created ROC curves for all significant chemokines in maternal plasma, which set the threshold values and allowed for predicting the likelihood of Down Syndrome in fetus with specific sensitivity and specificity (minimal sensitivity was set to 0. 7). The area under the ROC curve for HCC-4 was 0. 73, for IL-28A it was 0. 79, for IL-31 it was 0. 79, for MCP-2 it was 0. 83 and for NAP-2 it was 0. 79. We demonstrated a significantly higher risk of Down Syndrome when the plasma concentration of HCC-4 < 1574, 65 pg/mL (sens. 0. 86, sp. 0. 71, p value= 0. 0412), IL-28A < 397. 33 pg/mL (sens. 1, sp. 0. 71, p value= 0. 0016), IL-31< 443. 6 pg/mL (sens. 0. 71, sp. 0. 85, p value= 0. 0017), MCP-2 < 30, 27 pg/mL (sens. 1, sp. 0. 71, p value= 0. 0001) and NAP-2 > 171, 56 pg/mL (sens. 0. 86, sp. 0. 71, p value= 0. 0015).

Conclusion

On the basis of our findings, it seems that the chemokines may play role in the pathogenesis of Down Syndrome. Defining their potential as biochemical markers of Down Syndrome requires further investigation on larger group of patients.



Macroarray in plasma sample