THE ROLE OF MONOCYTIC TLR2 AND TLR4 IN PATHOGENESIS OF CELIAC DISEASE

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SUMMARY

In this work was detected expression of Toll-like receptor 2 (TLR2), Toll-like receptor 4 (TLR4) and prolactin (PRL) mRNA produced by monocytes (PBM) and this expression was compared between patients with celiac disease and healthy subjects. Expression of TLR2 and TLR4 was upregulated in patients with celiac disease, but expression of PRL was higher in controls.

INTRODUCTION

Celiac disease (CD) is an organ-specific autoimmune disease with prevalence about 1% in Europe [1]. It is caused by abnormal immune response to gluten in the diet in genetically predisposed individuals. For part of genetic predisposition are responsible genes located on the short arm of chromosome 6, HLA-DQ and HLA-DQB. Clinical manifestations of CD are highly variable (i.e. diarrhea, abdominal extension and pain, weakness, bad absorption and anemia), and can occur both in childhood and in adulthood. The only possible treatment of CD is lifelong gluten-free diet. The emergence of CD is involved in both adaptive and innate immunity. The key molecules of innate immunity are Toll-like receptors (TLRs); their signalization is necessary for maintaining intestinal homeostasis. TLRs are important for recognition of bacterial components and play central role in initiation and maintenance of immune response. Patients with active CD of mammary glands and lactation, but PRL is also produced by immune cells as an organ (PBM) and this expression was compared between patients with celiac disease and healthy subjects. Expression of TLR2 and TLR4 mRNA in duodenal mucosa [2]. Similarly, increased values of TLR2 and TLR4 in the lower gastrointestinal tract were observed in patients with active gastrointestinal disease [3]. Prolactin (PRL) is a pituitary hormone which promotes growth and differentiation of mammary glands and lactation, but PRL is also produced by immune cells as dendritic cells, lymphocytes and monocytes. PRL is involved in the activation of a number of immunological responses and stimulates the immune system [4]. Hypoprolactinemia in serum was observed in large number of autoimmune disease, including celiac disease [5]. In contrary, in cases where the immune response fails, the serum PRL is reduced, as documented by hypoprolactinemia observed in children with mutigen failure [6].

RESULTS I

We observed striking increase in both, TLR2 and TLR4 mRNA expression in PBM derived from CD patients compared to healthy subjects (52.7 times higher (P < 0.0001) and 6.7 times higher (P < 0.0001), respectively). These results support the hypothesis that activation of immune response leads to increase in gene expression of TLR2 and TLR4. TLRs can recognize the “toxic” peptide and then express protein of proinflammatory cytokines and chemokines.

RESULTS II

The physiological PRL mRNA levels in circulating monocytes are very low (median 141,4; 97,79 - 236,3) , however, this expression in PBM derived from diseased people was even 4.1 times lower (median 34,83; 1861 - 139,2). Given the known functions of PRL in autoimmune diseases and allergy [9], we expected higher expression of PRL mRNA in patients with CD. This surprising contrary data may result from relatively small sample size (N=12) in four (33.3%) of analyzed patients PRL mRNA could not be detected.

CONCLUSIONS

Our results indicated that TLR2 and TLR4 expressed by PBM play a role in the immune response in pathogenesis of celiac disease. Nevertheless, we could not confirm the role of monocytic PRL in activation of the immune system in autoimmune reaction initialized by gluten.

REFERENCES


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