I. Streszczenie w języku angielskim

Primary Epstein-Baar virus infection may occur in 10-20% of people, of which 30-50% develop infectious mononucleosis (IM). EBV infection most often occurs in children and adolescents. IM manifests itself mainly through: fever, pharyngitis and tonsillitis, enlarged lymph nodes, and enlarged liver and spleen. In the case of an atypical course of the disease and difficulties in distinguishing the acute phase of IM from other infectious diseases, laboratory tests are helpful in the diagnosis, especially the determination of specific antibodies directed against EBV antigens.

In response to EBV infection, cells involved in the host's immune response produce numerous cytokines, including: IL-2, IL-6, IFN-γ or TNF-α. There are also cytokines that are induced and engaged during EBV infection, but have not been thoroughly studied and described as yet. Interleukin 35 (IL-35) belongs to this group. It is an anti-inflammatory cytokine. Regulatory T lymphocytes and, to a lesser extent, B lymphocytes, macrophages and dendritic cells are responsible for the production and secretion of IL-35. IL-35 inhibits the growth of Th1 and Th17 lymphocytes, reduces the number of pro-inflammatory macrophages, increasing the number of anti-inflammatory macrophages.

The main aim of the study was to assess the concentration of IL-35 in the serum of children suffering from infectious mononucleosis. Additionally, the level of antibodies directed against selected EBV antigens (EBNA-1, EBNA-2, LMP-1, VCA p18, VCA p23, EA-D p54, EA-D p138, EA-R p85, ZEBRA, Rta, gp85, and gp350) as well as hematological and biochemical parameters were assessed in a group of children in the acute and chronic phases of EBV infection.

The study group included 68 children of both sexes with symptoms of infectious mononucleosis and a positive serological result for EBV infection. Based on the results of serological tests, two subgroups of patients were distinguished: in the acute phase and in the chronic phase of infection. The control group consisted of 20 children of both sexes without symptoms of infectious mononucleosis, with negative serological results for EBV infection. Screening tests assessing the presence of anti-VCA IgM and anti-VCA/EA IgG antibodies were performed on the VIDAS analyzer. The concentration of IL-35 was determined using the ELISA method, and specific IgM and IgG antibodies against recombinant EBV antigens were determined using the Microblot-Array EBV IgM and IgG kits.

The group tested in the acute phase of EBV infection presented higher IL-35 concentrations ($p<0.0001$) compared to the control group, and in the group tested in the

chronic phase of infection ($p<0.001$) than in the control group. There were no significant correlations between the level of IL-35 and other selected parameters measured in the study group in the acute and chronic phases of infection. IL-35 (AUC 0.913; $p<0.0001$) turned out to be a very good predictor of the occurrence of the acute phase of infectious mononucleosis. The analysis of the occurrence of antibodies directed against EBV antigens showed that in the study group, in the acute phase of EBV infection, the most common antibodies were: VCA p18 (IgM: 85%; IgG: 52%), EA-D p54 (IgM: 42%; IgG: 52%) and ZEBRA (IgM: 33%; IgG: 55%), and in the chronic phase of infection: VCA p18 (IgG: 94%), EBNA-1 (IgG: 66%), VCA p23 (IgG: 31%) and ZEBRA (IgG: 31%). The most frequently presented serological profile in patients in the acute phase of infection, there was the simultaneous presence of antibodies in both classes against the antigens: VCA p18, EA-D p54 and ZEBRA, and in the chronic phase in the IgG class: VCA p18 and EBNA-1.

Additionally, antibodies against the antigens: VCA p18 (IgM: AUC 0.971 and IgG: AUC 0.896), EA-D p54 (IgM: AUC 0.784 and IgG: AUC 0.862), ZEBRA (IgM: AUC 0.796 and IgG: AUC 0.893) and VCA p23 (IgG: AUC 0.874) turned out to be the best predictors of the acute phase of EBV infection ($p<0.05$), and VCA p 18 (IgG: AUC 0.951), EA-D p54 (IgG: AUC 0.751), EBNA-1 (IgG: AUC 0.979) and VCA p23 (IgG: AUC 0.901) of the chronic phase of infection ($p<0.05$). The group examined in the acute phase of EBV infection showed a significantly higher number of white blood cells, lymphocytes, monocytes and higher levels of AST, ALT and CRP compared to the control group and the group of children in the chronic phase of infection ($p<0.05$).

Higher concentration of IL-35 in children with infectious mononucleosis compared to the group of healthy children indicates that it plays a role in the pathogenesis of this disease. The high AUC indicates that IL-35 can be used as an additional parameter in the confirmation of mononucleosis infection in children. The lack of statistically significant differences in IL-35 levels between the studied groups suggests that this cytokine cannot be used as an indicator differentiating the acute phase from the chronic phase of infection EBV. However, the Immunoblot method can complement the diagnostics of children with IM, especially when the patient's results are questionable. The determination of IgM and IgG antibodies directed against the following antigens: EA-D p54 and ZEBRA may be helpful in the differential diagnosis.