Dysregulation of the immune system in children with Graves disease – the role of NK and NKT-like cells

Maria Klatka¹, Agnieszka Polak², Ewelina Grywalska², Witold Kollataj¹, Jacek Rolinski²

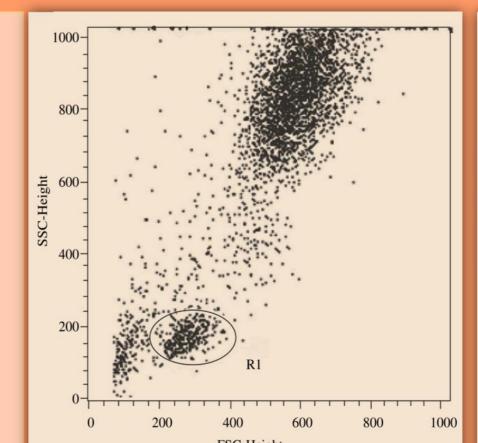
1- Department of Endocrinology, Medical University of Lublin, 2 Chodzki Street, Lublin, Poland 2- Department of Clinical Immunology, Medical University of Lublin, 4a Chodzki Street, Lublin, Poland

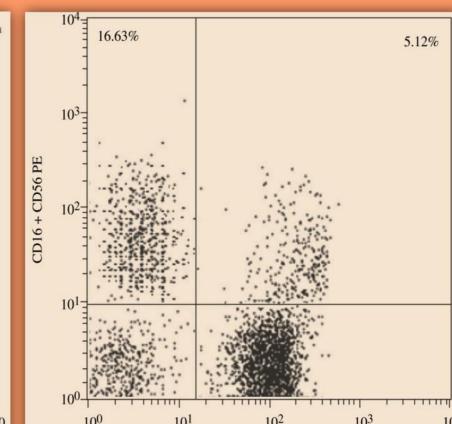
Introduction

Almost all cases of hyperthyroidism in children result from Graves' disease (GD). Recent studies have confirmed a significant role of T cells in the development of autoimmune diseases. However, the interactions between NKT-like cells and NK cells in GD are still poorly understood [1-3].

Objectives

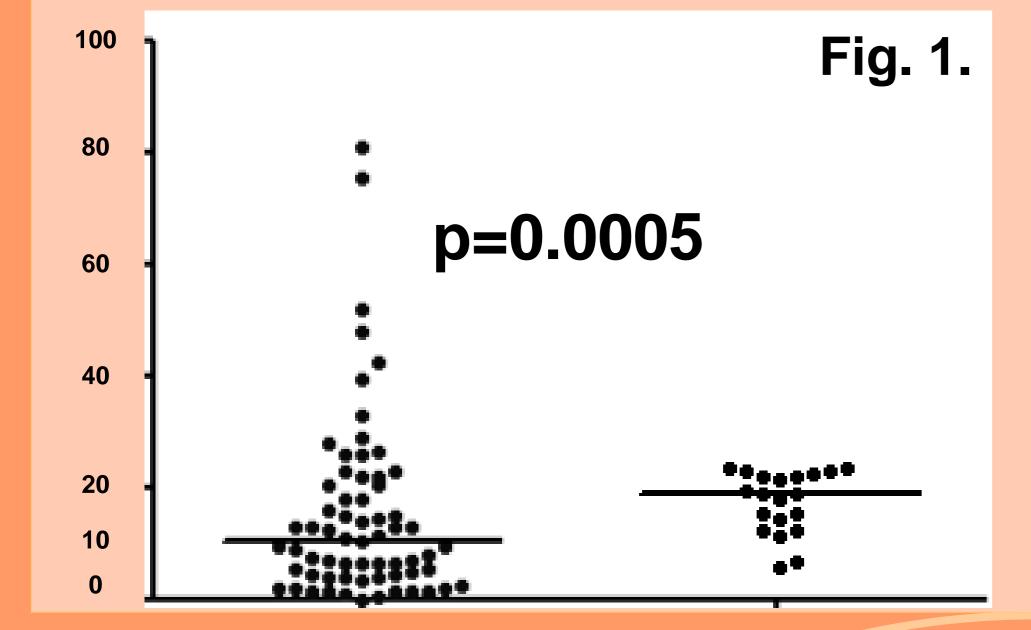
The aim of the study was to assess the frequencies of peripheral blood T, NK and NKT-like cells in children with GD.

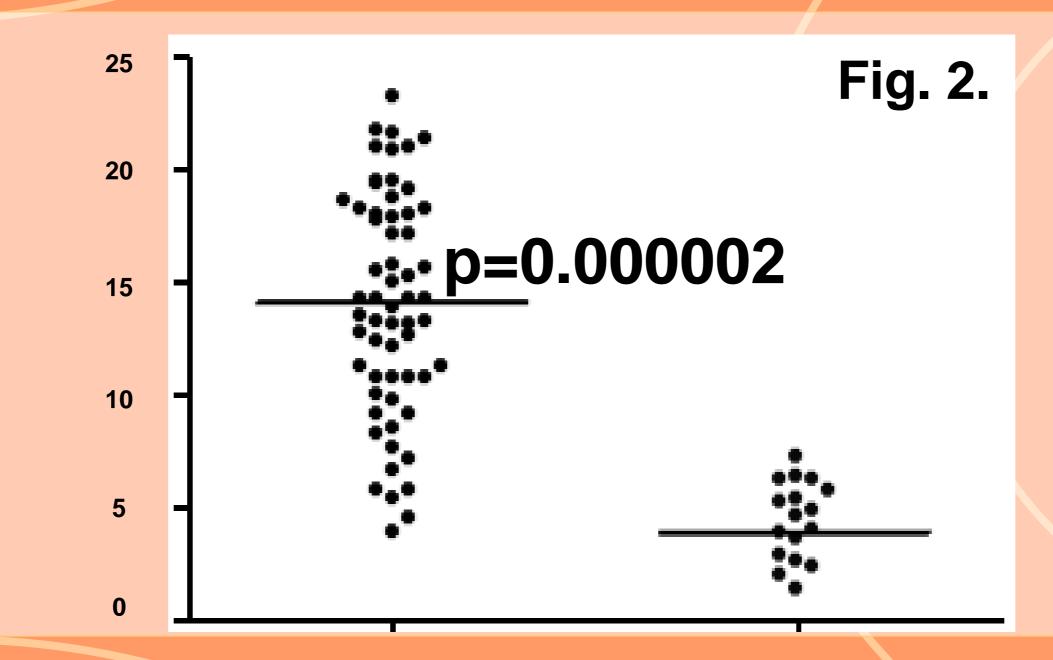


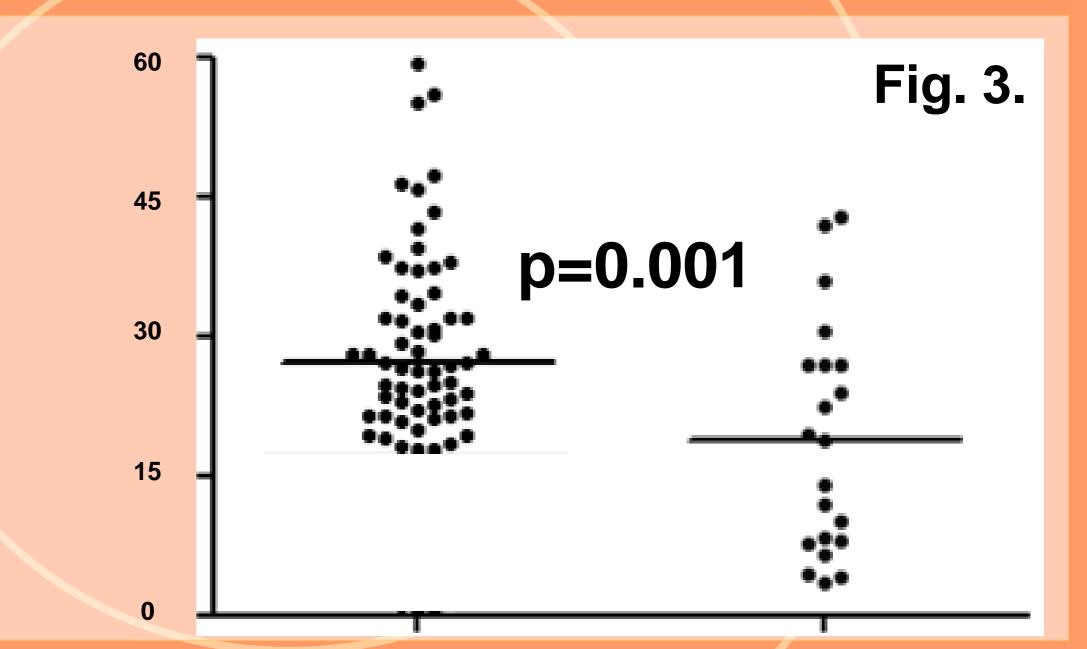


Methods

We studied 50 GD and 20 age- and sex-matched healthy children. Percentages of NK and NKT-like cells were evaluated with flow cytometry using monoclonal antibodies: anti-CD3/FITC, CD16CD56/PE, CD45/PerCP (BD Biosciences), which allowed for simultaneous assessment of CD3+ T lymphocytes and NK (CD16+CD56+) cells. During analysis, the CD3+CD16+CD56+ population was also determined. Immunofluorescence studies on T cell subsets were performed using a combination of the following mAbs: CD3/FITC, CD19/PE, CD8/FITC, CD4/PE, purchased from R&D Systems. Statistical analysis of the results was conducted using Statistica 9.0. A value p less than 0.05 was considered statistically significant.





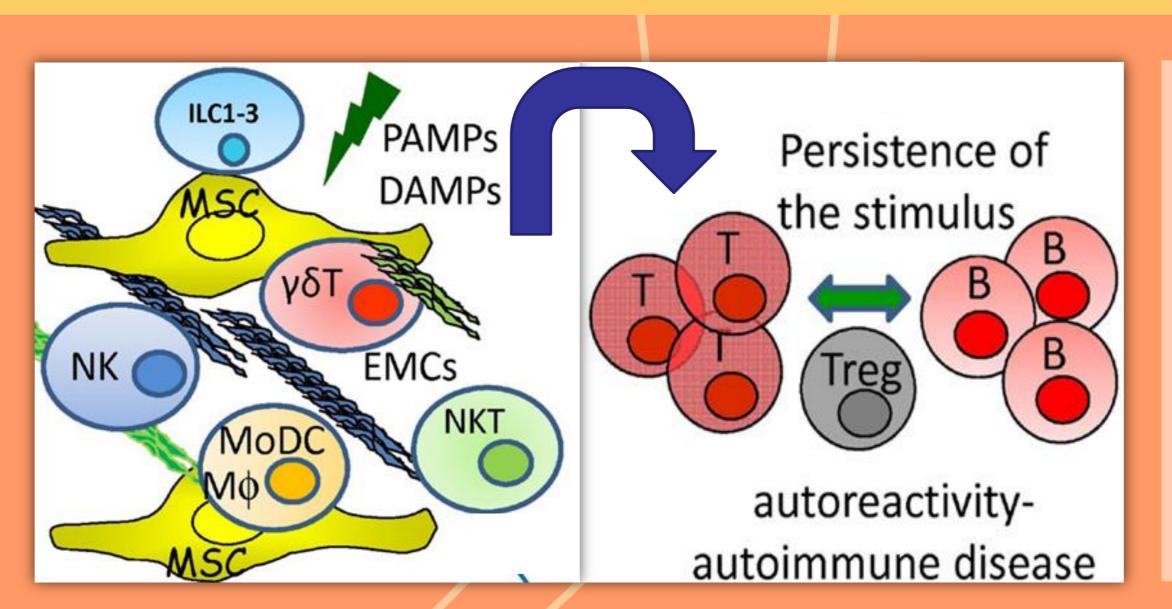


Results

The mean frequency of CD3+CD56+CD16+ NKT-like cells in the peripheral blood of children with GD was 10.93%±11.02% and this value was significantly lower in comparison to the control group (21.15%±9.08%, p=0.0005, Fig. 1). The mean percentage of CD56+CD16+ NK cells in the group of patients was 14.67%±6.89%, and was significantly higher compared to the healthy controls (4.71%±2.99%, p=0.000002, Fig. 2). The mean percentage of CD3+ T lymphocytes in the peripheral blood of children with GD was 67.91%±16.56% and was significantly higher in comparison to the control group (51.7%±24.12%, p=0.02). The mean percentage of CD8+ T lymphocytes in the study group was 28.89%±11.68% and was significantly higher in comparison to the healthy controls (18.72%±6.86%, p=0.001, Fig. 3).

Conclusions

Our findings of the abnormalities in immune cells distribution in peripheral blood of GD children suggest that GD development and progression is related to the dysregulation of the immune system. Low innate response that...



...determines the persistence of the danger signal leads to generation of autoreactive T and B cells. Autoreactive lymphocytes are controlled by Treg cells but chronic stimulation breaks the tolerance leading to autoimmune disease [4].

References:

1. Hwang SM, Kim MS and Lee DY (2016) Predictive factors for early response to methimazole in children and adolescents with Graves disease: a single-institute study between 1993 and 2013. Ann Pediatr Endocrinol Metab. 2016;21(2):70-4. doi: 10.6065/apem.2016.21.2.70.

2. Ting WH, Chien MN, Lo FS, Wang CH, Huang CY, Lin CL, Lin WS, Chang TY, Yang HW, Chen WF, Lien YP, Cheng BW, Lin CH, Chen CC, Wu YL, Hung CM, Li HJ, Chan CI and Lee YJ (2016) Association of Cytotoxic T-Lymphocyte-Associated Protein 4 (CTLA4) Gene Polymorphisms with Autoimmune Thyroid Disease in Children and Adults: Case-Control Study. PLoS One. 2016;11(4):e0154394. doi: 10.1371/journal.pone.0154394.

3. Klatka M, Grywalska E, Partyka M, Charytanowicz M, Kiszczak-Bochynska E, Rolinski J (2014) Th17 and Treg cells in adolescents with Graves' disease. Impact of treatment with methimazole on these cell subsets. Autoimmunity. 2014;47(3):201-11. doi: 10.3109/08916934.2013.879862.

4. Poggi A and Zocchi MR (2014) NK cell autoreactivity and autoimmune diseases. Front. Immunol. 2016; 5:27. doi: 10.3389/fimmu.2014.00027.



Thyroid Maria Klatka

