Review paper

The Polish Working Group for Primary Immunodeficiency

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Abstract

Primary antibody deficiencies have variable autoimmune manifestations. Immunodeficiency and A national project with the aims of building up a Polish national registry of primary immunodeficiency diseases (PID), harmonizing existing Polish diagnostic guidelines based on the ESID proposal, developing therapeutic guidelines at a national level, improving patient care in Poland, and raising awareness of PID across the country, was initiated by the Polish Working Group for PID, established in March 2005. The Group has been assembled from six main Polish centres for the diagnosis and therapy for PID. The project has been supported by grant PBZ-KBN-119/P05/04 from the Polish Ministry of Science, and European Union grant EURO-POLICY-PID SP23-CT-2005-006411, both granted since 2005 through 2008.

Key words: *the Polish Working Group for PID, primary immunodeficiency.*

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Introduction

PIDs are rare chronic diseases. Many of the autosomal recessive forms affect less than one in a million individuals, whereas the X-linked recessive forms affect about one in a hundred thousand individuals or less. Thus, each disease affects only a few individuals in each country. However, due to the fact that more than 100 different disease entities are known, all PIDs considered collectively have a significant impact on public health [1, 2]. In particular, new groups of genetically determined PIDs are emerging, including selective susceptibility to specific pathogens (mycobacteria, pneumococci, etc.) and disorders of leukocyte trafficking [3]. The very large number of rare forms, together with the variable symptomatology and treatment, make PID a highly versatile disease group [4, 5].

Advances in molecular genetics are challenging our classification of PID, which is still based on clinical and immunological grounds [6]. This offers hope for gene therapy, which is used with success in numerous diseases, mostly in the severe form of primary immunodeficiency.

Aim of the study

The national project with the aims of improving patient care, resulting in early clinical recognition and improved diagnostic and treatment strategies, and raising awareness of PID across the country was initiated by Polish immunologists. The Polish Working Group for PID was established in March, 2005. The Group has been set up from six main Polish centres for the diagnosis and therapy of PID (table 1), covering the whole of Poland (figure 1). The main objectives of the Group's activity are:

1. to build up a Polish national registry of PID,
2. to harmonize existing Polish diagnostic guidelines based on the ESID proposal, and to develop therapeutic guidelines at a national level,

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Table 1. Polish Working Group for PID

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3. to increase awareness of PID among paediatricians and general practitioners,
4. to achieve the development of channels for the active dissemination of information about PID among patient organizations, media and public health groups, government and non-government organizations in Poland.

Polish National Registry of PID

The prevalence of immunodeficiency disorders varies extensively, depending on the type of disease. Furthermore, multiple aetiologies and distinct clinical subtypes exist for some diseases, where each subtype is represented by a limited number of patients in each major referral centre. Genetic and/or therapeutic studies usually involve a large number of patients. Identification and localization of patients is therefore necessary for the successful completion of these studies. Access to a sufficiently large number of patients thus constitutes the basis for clinical trials, and it is only by pooling the resources from different centres that we will solve the molecular basis of these disorders, and thus will be able to institute efficient therapeutic measures.

The Polish National Registry has been developed in co-operation with Bodo Grimbacher from the Division of Rheumatology and Clinical Immunology, Department of Medicine, University Hospital, Freiburg. The registry is located on a server in Freiburg and will automatically be a part of the Pan-European PID patient registry system online. Training concerning the introduction of individual PID patients to the Pan-European PID patient registry system online has been provided for physicians from Polish centres for diagnosis and therapy of PID in both Freiburg and in Warsaw. Based on the Polish registry, demographic data regarding age, gender and ethnicity will be statistically analysed, as well as disease type and method of treatment. To date the Polish registry, has collected data on 412 patients with PID from the whole of Poland. The Children's Memorial Health Institute (CMHI), Warsaw, occupies the leading position for the Polish National Registry of PID. The responsible person from the Warsaw centre attended "1st ESID Online Registry Training Class: Set-up of Documenting – centres", which was held in Freiburg on 22 July, 2004. All efforts to receive the approval of local authorities were successful, and finally the approval of the Polish Ethics Committe was issued on 15.09.2004. The first agreement between the Warsaw centre and Freiburg was signed in December 2004, and after that date registering of patients started. The second agreement, between the Kraków centre and Freiburg, was signed in 2005. A new agreement between the Warsaw centre and Freiburg for a Polish National Documenting Centre within the ESID On-line Registry was signed in January 2006.

Fig. 1. Polish Working Group for PID – diagnostic centres. (1) Warsaw, (2) Wrocław, (3) Łódź, (4) Kraków, (5) Poznań, (6) Białystok

Efforts on co-operation with other Polish centres involved in the diagnosis and management of primary immunodeficiencies resulted in co-ordination and the final establishment of a local network involving six other centers, with 8 physicians engaged.

Harmonization of existing Polish diagnostic guidelines based on the ESID proposal and development of therapeutic guidelines at a national level

The development of diagnostic guidelines and treatment strategies has already been initiated for a cohort of diseases under the guidance of the European Society for Immunodeficiencies (ESID), http://www.esid.org. The initial attempt to identify the diagnostic and treatment regimens for a single disease demonstrated a rather large variation among different centres. The task force of the Polish Working Group for PID is to develop diagnostic and therapeutic guidelines with the aim of harmonizing its strategy.

Report of the Task Force

Standarization existing diagnostic and therapeutic guidelines, and in the organization and provision of training has already started. The complete set of diagnostic and therapeutic guidelines for chronic granulomatous disease (CGD) was established by the Group on December 9, 2006 in Warsaw. These include ESID diagnostic criteria (table 2), laboratory diagnostic (table 3) and therapeutic (table 4) guidelines. The agreed standard guidelines for common

Table 2. Diagnostic criteria for chronic granulomatous disease (CGD)

Diagnostic criteria for chronic granulomatous disease by ESID (European Society for Immunodeficiencies) and the Polish Working Group for PID
Definitive diagnosis Male or female patient with abnormal NBT or respiratory burst in activated neutrophils (less than 5% of control) having one of the following: 1. Mutation in genes for gp91, p22, p47 or p67 components of NADPH oxidase 2. Absent mRNA for one of the above genes by northern blot analysis 3. Maternal cousins, uncles or nephews with an abnormal NBT or respiratory burst
Probable diagnosis Male or female patient with abnormal NBT or respiratory burst in activated neutrophils (less than 5% of control) who has one of the following: 1. Deep-seated infection (liver, perirectal or lung abscess; adenitis; or osteomyelitis) due to Staphylococcus, *Serratia marcescens*, Candida or Aspergillus 2. Diffuse granuloma in respiratory, gastrointestinal or urogenital tracts 3. Failure to thrive and hepatosplenomegaly or lymphadenopathy
Spectrum of disease Patients with the X-linked form of CGD (60-70% of patients) tend to present earlier and have more severe disease than patients with autosomal recessive forms. Most patients with X-linked CGD present with failure to thrive, severe bacterial adenitis, abscesses or osteomyelitis within the first year of life. Pneumonia and lymphadenitis due to catalase-positive organisms (particularly Staphylococcus) or fungi are the most common infections. Symptoms of intestinal or urinary tract obstruction can be caused by granuloma formation. Rarely, in both the X-linked and autosomal recessive forms, the first severe symptoms are not recognized until adulthood
Differential diagnosis 1. LAD 2. Sarcoidosis 3. Hyper IgE syndrome

Table 3. Chronic granulomatous disease – laboratory guideline

Laboratory guideline for chronic granulomatous disease D71 – by the Polish Working Group for PID
1. NBT slide test utilizes the ability to reduce water soluble nitroblue tetrazolium into insoluble formazan deposits by superoxide produced by neutrophils
2. PMA-stimulated NBT slide test enables preliminary differentiation between patients with X-linked and autosomal recessive chronic granulomatous disease, as well as detection of carriers
3. PMA-induced respiratory burst in cells preloaded with 123DHR utilizes the difference between fluorescent signals emitted by dihydrorhodamine (DHR) and rhodamine produced in presence of H_2O_2 and O_2^- generated during the process. Both signals are measured by flow cytometry. The test enables establishing the diagnosis, preliminary differentiation of the inheritance patterns, and detection of female carriers of CGD
4. Chemiluminescence utilizes the ability of neutrophils to emit light during the respiratory burst. Apart from the diagnosis of CGD the test enables identification of carriers
5. Genetic analysis detects mutations in components of NADPH oxidase complex (CYBB, CYBA, NCF1, NCF2)
6. Prenatal diagnosis

variable immunodeficiency (CVID) started with adoption of the ESID diagnostic criteria and differential diagnosis for agammaglobulinemia (tables 5, 6) and with new therapeutic guideline (table 7) [7, 8].

Plans for the future

A project is already under way to establish and evaluate harmonised guidelines for flow cytometry diagnosis in PID. This project is being realized in co-operation with Professor Jacques J.M. van Dongen at the Erazmus University, Rotterdam. A meeting concerning standarisation of cytometrics in PID will be held on May 17-18, 2007, in Poznań. The meeting is planned for a group of participants from 11 Polish centres, involved in PID diagnosis. Each centre will send 3-4 specialists; paediatricians/clinical immunologists, scientists involved directly in laboratory analyses.

Table 4. Chronic granulomatous disease – Therapeutic guideline

Chronic granulomatous disease D 71 – Therapeutic guideline by the Polish Working Group for PID
Management of infections – the algorithm 1. Empirical, intensive antibiotic therapy covering the most common pathogens (mainly *S. aureus*) which is continued or modified according to bacteriological tests. Surgical management of skin and organ abscesses (most commonly liver abscess) followed by antibiotic treatment 2. In case of fever persistence longer than 72-96 hours despite broad-spectrum antibiotic therapy empirical treatment of potential *Aspergillus* infection 3. Spontaneous or resulting from infection granulomas (points 1 and 2) are treated with prednisone in an initial dose of 1 mg/kg for 2 weeks, subsequently reduced to the minimal effective dose 4. Interferon gamma and leukocyte transfusions are not recommended in treatment of acute infections treatment. They may be considered in individual, exceptional cases 5. BMT indications are considered individually, especially in patients with a severe clinical course of disease 6. Gene therapy has not been successful till now
Prophylaxis of infections 1. General and careful dental hygiene, injury avoidance, cleaning of skin abrasions with hydrogen peroxide solution 2. Appropriate living conditions, and avoidance of places with high evidence of *Aspergillus* spores (hay, compost, dovecots, old flats, lofts) 3. Permanent, regular antibiotic prophylaxis: Cotrimoxazole: 0-6 mo 1x 120 mg/day; 6 mo-5 yo 1x 240 mg/day 6 yo-12 yo 1x 480 mg/day; >12 yo 1x 960 mg/day Itraconazole, or less effective ketokonazole in doses 3-5 mg/kg/day In patients with *Aspergillus* infections in past history only Itrakonazole 4. Efficiency of interferon gamma as a prophylactic agent is not confirmed by meta-analysis 5. Immunization according to Recommended Childhood and Adolescent Immunization Schedule except live bacterial vaccines: BCG and typhoid ones. Additionally *H. influenzae* type b and *S. pneumoniae* vaccines are recommended

Table 5. Common variable immunodeficiency – CVID D 83

Diagnostic criteria for common variable immunodeficiency – D 83 by ESID (European Society for Immunodeficiencies) and by the Polish Working Group for PID
Probable Male or female patient who has a marked decrease of IgG (at least 2 SD below the mean for age) and a marked decrease in at least one of the isotypes IgM or IgA, and fulfills all of the following criteria: 1) Onset of immunodeficiency at above 2 years of age 2) Absent isohemagglutinins and/or poor response to vaccines 3) Defined causes of hypogammaglobulinemia have been excluded (*see table 6 'Differential diagnosis of hypogammaglobulinemia'*)
Possible Male or female patient who has a marked decrease (at least 2 SD below the mean for age) in at least one of the major isotypes (IgM, IgG and IgA) and fulfills all of the following criteria: 1) Onset of immunodeficiency at above 2 years of age 2) Absent isohemagglutinins and/or poor response to vaccines 3) Defined causes of hypogammaglobulinemia have been excluded (*see table 6 'Differential diagnosis of hypogammaglobulinemia'*)
Spectrum of disease Most patients with CVID are recognized to have immunodeficiency in the second, third or fourth decade of life, after they have had several pneumonias; however children and older adults may be affected. Viral, fungal and parasitic infections as well as bacterial infections may be problematic. The serum concentration of IgM is normal in about half of the patients. Abnormalities in T cell numbers or function are common. The majority of patients have normal numbers of B cells; however, some have low or absent B cells. Approximately 50% of patients have autoimmune manifestations. There is an increased risk of malignancy

Table 6. Differential diagnosis for hypogammaglobulinemia

Drug induced
Antimalarial agents
Captopril
Carbamazepine
Glucocorticoids
Fenclofenac
Gold salts
Penicillamine
Phenytoin
Sulfasalazine
Genetic disorders
Ataxia Telangiectasia
Autosomal forms of SCID
Hyper IgM Immunodeficiency
Transcobalamin II deficiency and hypogammaglobulinemia
X-linked agammaglobulinemia
X-linked lymphoproliferative disorder (EBV associated)
X-linked SCID
Some metabolic disorders
Chromosomal Anomalies
Chromosome 18q-Syndrome
Monosomy 22
Trisomy 8
Trisomy 21
Infectious diseases
HIV
Congenital Rubella
Congenital infection with CMV
Congenital infection with Toxoplasma gondii
Epstein-Barr Virus
Malignancy
Chronic Lymphocytic Leukemia
Immunodeficiency with Thymoma
Non Hodgkin's lymphoma
B cell malignancy
Systemic disorders
Immunodeficiency caused by hypercatabolism of immunoglobulins
Immunodeficiency caused by excessive loss of immunoglobulins (nephrosis, severe burns, lymphangiectasia, severe diarrhea)

Increase awareness of PID among paediatricians and general practitioners – plan for dissemination of information on PID – starting point and future events

Website platform

One of the most important parts of the plan for the dissemination of information on PID is a Website platform. The website http://immunologia.czd.pl, located on a CMHI server, has been set up in September 2006. A newly--created website includes the following elements: the up-to--date Polish registry of PID patients, diagnostic guidelines for PID, information on Polish and major international meetings and symposiums on PID, and helpful links to other websites related to PID including ESID. It also includes general information about PID, a list of information about Polish PID diagnostic centres, information about Polish Association of Parents of Children with PID and other related organizations from Poland and all over the world is also shown.

This year the project is planned to disseminate information on PID to another Website platform in Poland, to make all this information more available. The first objective is the platform granted by the Polish Ministry of Science PBZ-KBN-119/P05/04 project, conducted by Professor Jan Żeromski on behalf of the Polish Society of Experimental and Clinical Immunology: http://www.diagnostyka.immuno.pl. During the third year of the project it will still be under development, and two websites will be created on new topics related to vaccination in immunodeficiency patients and Polish Association of Parents of Children with PID. There are partly provided by patients and/or their parents.

Activity to build up the necessary capacity in order to increase awareness about PID in the EU will be continued during the next two years of the project. Following our long-term experience is a plan to initiate a prospective and retrospective study of PID recorded at CMHI. It will be based on PID patients referred by physicians/paediatricians from 17 Polish provinces. The expected result of this analysis is to identify a target physician group, which could be involved in the early diagnosis of PID. The other parameters to be analysed include types of recurrent infection, time to make diagnosis, etc.

Adult patient care

The number of centres for diagnosis and treatment of adult patients with PID is insufficient in Poland. The initiation of close co-operation between paediatricians and internists plays a crucial role in the further management of PID patients. One of the objectives of the Polish Working Group for PID is to improve patients care for those over18 years of age. The first step was to increase or initiate collaboration with adult centres from five main academic centres in Poland. We are at present establishing a database of detailed addresses and responsible adult clinicians from particular centres in all regions of Poland. It is planned to put the collecting data on a website to made them more available. Next, detailed information about diagnostic and treatment possibilities in each centre will be completed. It is planned to initiate in each region (for the first time in the Mazovian district), regular meetings of paediatricians together with internal medical clinicians and persons responsible for laboratory investigation, to discuss the list and also specific cases of PID patients who have became adults. The first protocols on CGD has recently been finished and will be distributed to all collaborating centres for adult patients. We will also provide dissemination of information to different targeted groups of physicians other

Table 7. Common variable immunodeficiency – CVID D 83: Therapeutic guideline

Therapeutic guideline for common variable immunodeficiency – D83 by the Polish Working Group for PID		
Prophylaxis		
1. Replacement therapy with immunoglobulins:		
• Intravenous immunoglobulins (IVIG) – initial dose of 0.5-0.8 g/kg b.w., next doses approximately 0.4-0.6 g/kg b.w., every 2-4 weeks. The dose depends on clinical course of the disease and should control the infections. IgG trough level should achieve at least 5.0-6.0 g/l. In case of bronchiectases it should be even higher and reach IgG >7.0-9.0 g/l		
• Subcutaneous immunoglobulins (SCIG) – the same month dose as during IVIG therapy split into 4 equal week dosages, approximately 0.1-0.15 g/kg/week		
2. Prophylaxis of infections (in some patients):		
Cotrimoxazole:	0-6 mo 1 x 120 mg/day;	6 mo-5 yo 1 x 240 mg/day
	6-12 yo 1 x 480 mg/day;	>12 yo 1 x 960 mg/day
Amoxycylina:	20 mg/kgb.w./day in single dose	
Ospen:	<5 yo 2 x 250 000 U	>5 yo 2 x 500 000 U
Possible prophylaxis with azithromycine or ciproflaxacine		
3. General hygiene, drinking boiled water!		
4. Immunisations with alive attenuated vaccines are not recommended; inactivated vaccines may be recommended in special conditions – depending on IgG level		
Management of infections		
1. Additional infusion of immunoglobulins preparation in case of significant IgG trough level drop or severe infection. The frequency and dose of infused immunoglobulins should be revised		
2. Empirical, intensive antybiotic therapy covering the most common pathogens (mainly *Haemophilus influezae*, *Streptococcus pneumoaniae*, *Staphylococcus aureus*, *Pneumocystis carinii*, *Mycoplasma pneumoniae*), to be continued or modified according to bacteriological tests		
3. Empirical treatment of potential fungal infections caused by *Aspergillus*, *Candida albicans* (Itraconazole, Ketokonazole, Flukonazole)		
4. Therapy of parasitic infections (metronidazole)		
5. Probiotics therapy (Lacidofil, Lakcid, Trilac, Enterol) together with antibiotics		
6. Immunosuppresive drugs (prednisone in initial dose of 1 mg/kg, or in special cases cyclosporine, or imuran, or infliximab) should be considered in treatment of spontaneous or resulting from infection granulomas		

than in only specialists in paediatrics and immunology, e.g to specialists in internal medicine, otolaryngology, neurology, and rheumatology etc., during the meetings.

Educational programme for young immunologists

The School of Clinical Immunology

The School of Clinical Immunology has been a great success so far. It has been organised every year since 2002, in various attractive places of Poland. These are fully supported by the following European Union grants: PERFECT QLG1-CT-2002-90358 project, provided by The Children's Memorial Health Institute (CMHI) as a Paediatric Research Centre – Focusing on Effective Child Treatment, 2002-2005; EURO-PID-NAS, 2002-2004 and EURO-POLICY-PID SP23-CT-2005-006411, 2005-2008. It is a tradition of CMHI, to invite young immunologists and doctors interested in clinical immunology from all of Europe. The last school was held in Ruciane-Nida, 8-10 June, 2006. The next one is planned for 2007 in Zakopane. A group of young immunologists from both Central-Eastern and Western European countries take part in the meetings, including a group of young Polish immunologists, together with physicians specializing in clinical immunology. The School of Clinical Immunology provides study opportunities for a new generation of young clinical immunologists and scientists. The meeting gives a chance to attend lectures given by experts in immunology from all over Europe. It also creates a forum to exchange their own experiences, as well as to discuss difficult cases and diagnostic and therapeutic problems. About 40-70 participants from both Central/Eastern and Western European countries have attended these meetings.

Young immunologists from CMHI took part in the annual ESID spring meeting, held in Prague on May 8th and 9th, 2006. It was an annual meeting dedicated to primary immunodeficiencies, especially to aspects of diagnostic and therapeutic procedures.

A meeting of the European Society for Immunodeficiency was organized in Budapest, October 2-6, 2006. Fourteen immunologists, members of the Polish Working Group for PID attended this meeting, presented eight abstracts on PID, and CMHI immunologists together with colleagues from the Czech Republic chaired a session of the Central-Eastern PID Group during this meeting.

Educational exchanges across Poland

Regular meetings are established all over the country, dedicated to different target physician/scientist groups, such as:

1. **General practitioners and paediatricians working in the country, far away from large or referral medical centres:** Five meetings were organized by the College of Family Physicians in 2006. Basic medical knowledge on various medical disciplines has been provided during these meetings. Among these a clinical immunologist gave a lecture on "Warning signs of Primary Immunodeficiency", focusing on the first symptoms suggesting PID. The aim of this lecture was to disseminate the basic knowledge on clinical immunology, particularly in PID.
2. **Paediatricians and minor groups of clinicians interested in PID:** This group of meetings were organized on behalf of the Polish Paediatric Society: The first one, held on March 16, 2006 in Bydgoszcz was organised by the Department of Paediatrics, Haematology and Oncology, Nicolaus Copernicus University, Collegium Medicum (a very dynamic centre for PID), led by Professor Mariusz Wysocki. The second meeting was held on April 1, 2006 in Warsaw. It was one of the biggest of the year, organized together with the Paediatrics in Review Journal. More than 800 participants attended this meeting. The leading topic was "Emergencies in Paediatrics". The lecture on PID focused on serious ovewhelming infection in PID.
3. **Clinical immunologists/scientists engaged in Polish centre involved in PID, including the Polish Working Group for PID members.** A meeting on "Auto-immunity in Common Variable Immunodeficiency" was organized by Professor Adam Jankowski and held on September 24-26, 2006 in Polanica-Zdrój. Over 40 clinical immunologists, both paediatricians and internists/scientists, attended this meeting. The next meeting was organised for December 8-9, 2006 in Warsaw by CMHI. The Department of Immunology was celebrating this date the twenty-fifth anniversary of the founding of the Department. The leading subjects were as follows: diagnostic and therapeutic criteria for different types of PID, the newest methods of replacement immunoglobulin therapy, haematopoietic stem cell transplant in children with combined immunodeficiencies--qualification and the results of this treatment, autoimmune diseases in PID and vaccinations in children with PID. Further information from both meetings is available on http://www.diagnostyka. immuno.pl.

Contribution to Patient's organization

On December 27, 2006 the Meeting of the Association of Friends of Children with Immunological System Deficiencies was held at the CMHI, Warsaw. The meeting was organised by parents of children with agammaglobulinaemia and patients with CVID. The main topic to be discussed was the problem of inadequate supplies of immunoglobulin preparations on the market for replacement therapy in these patients. A plan to improve this critical situation, developed in some hospitals, has been adopted. The newly-created Association of Parents of Children with Nijmegen Breakage Syndrom took part in this meeting. Both physicians, parents and patients attended the meeting focusing on subcutaneous immunoglobulin replacement therapy, as a good alternative due to the insufficiency of intravenous preparation.

Media communication

The newly-created, new generation of country-wide TV stations on the nTVN platform has started to develop teaching programmes for physicians. The 24hr running programmes are planned to be a part of educational training, and will subsequently provide educational points. The programme on PID will be prepared by CMHI. In 2006, TV and radio station broadcasted several programs on the risk of invasive infectious diseases in immunodeficient children and their prophylaxis.

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References

1. Bernatowska E (2005): The primary immunodeficiency network on European and national levels – where are we now? Centr Eur J Immunol 30: 75-77.
2. Wolska-Kusnierz B, Pac M, Pietrucha B, et al. (2005): Twenty five years of investigations into primary immunodeficiency diseases in the Department of Immunology, The Children's Memorial Health Institute, Warsaw. Centr Eur J Immunol 30: 104-114.
3. Liberek A, Korzon M, Bernatowska E, et al. (2006): Vaccination-related Mycobacterium bovis BCG Infection. Emerg Infect Dis 12: 860-862.
4. Bernatowska E, Mikoluc B, Krzeski A, et al. (2006): Chronic rhinosinusitis in primary antibody immunodeficient patients. Int J Pediat Otorhinolaryngol 70: 1587-1592.
5. Trelinski J, Chojnowski K, Kurenko-Deptuch M, et al. (2005): Successful treatment of refractory autoimmune thrombocytopenia with rituximab and cyclosporin A in a patient with chronic granulomatous disease. Ann Hematol 84: 835-836.
6. Roos D, de Boer M, Koker MY, et al. (2006): Chronic granulomatous disease caused by mutations other than the common GT deletion in NCF1, the gene encoding the p47phox component of the phagocyte NADPH oxidase. Hum Mutat 27: 1218-1229.
7. Gardulf A, Nicolay U, Asensio O, et al. (2006): Rapid subcutaneous IgG replacement therapy is effective and safe in children and Adults with Primary Immunodeficiencies – A Prospective, Multi-National Study. J Clin Immunol 26: 177-185.
8. Pac M, Bernatowska E (2005): Polish experience with immunoglobulin replacement treatment by subcutaneous infusion. Centr Eur J Immunol 30: 78-82.