Primary antibody deficiencies in Estonia

Sirje Velbri
Tallinn Childrens' Hospital, Estonia

Introduction

- Antibody deficiencies are the main group of immunodeficiency in the primary immunodeficiency registries in European countries.
- We have analysed the cases of primary immunodeficiency during 1980 -2005 in Estonia

Material

- Cases of primary immunodeficiency were analysed, detected in different hospitals of Tallinn serving mainly North-Estonia.
- As risk groups were studied:
  943 children with recurrent infections;
  29 first degree relatives of patients with antibody deficiency.
- IgA screening was made in 4152 blood donors from North-Estonian Blood Center.
- Some patients with antibody deficiency were followed clinically and immunologically up to 20 years.

Methods

- Immunological study included the following analysis depending on the clinical data of the patient:
- IgG, IgA, IgM, IgE, IgG subclasses, T- and B-lymphocytes and T-subpopulations.
- In detection of immunodeficiency the analyses were repeated.
- Immunodeficiency was diagnosed according to WHO criteria of primary immunodeficiency.

Results

- Different forms of antibody deficiency were detected **in 159 patients**: in 87 children and 72 adults. Male/female ratio was 70 /89.
- **13 cases** of immunodeficiency were found among children with recurrent infections (**1,4%**) and **4 cases** among relatives (**13,8%**).
- IgA deficiency was found in 9 from 4152 **donors 0,22 % or 1 :461**.

Primary antibody deficiencies in Estonia

Immunodeficiency	All	M/ N	Adults	Children
XLA	2	2/ 0	-	2
CVID	17	14 /3	8	9
Hyper-IgM-syndrome	1	1 /0	-	1
IgA deficiency	121	43/78	59	62
IgG subclass deficiency	11	5/6	5	6
Transient hypogamma-globulinemia of infancy	7	5/2	-	7
All	**159**	70/89	**72**	**87**

Primary immunodeficiency in the risk groups

Risk groups	n	All	CVID	IgA defi-ciency	Transient hypogam maglobu-linemia of infancy
Children with recurrent infections	943	13 1,4%	1	10 1,1%	2
First degree re-latives of pa-tients with anti-body deficiency	29	4 13,8%	1	3 10,3%	-

X-linked agammaglobulinaemia

- Two brothers (5 and 4 years old) in Estonian family. Agammaglobulinemia was diagnosed at 7 and 2 months of age. Regular IVIG therapy started.
- Clinically recurrent infections and neurological symptoms (sensonineural impairment of hearing, absence of speech).
- Immunologically IgG <0,1 -1,39 g/l; IgA <0,03 g/l, IgM <0,04 g/l, IgE <2 U/ml, B-lymphocytes <1%.
- Genetic study (Karolinska Institute): a large deletion of Btk gene and exon 1 and part of exon 2 of TIMM8A gene. The latter mutation is characteristic for the neurodegenerative Mohr-Tranebjaerg syndrome.

Common variable immunodeficiency

- **17 patients**: 13 male anf 4 female patients
  The age of patients during final diagnosis 2 -74 years.
  Patients have followed 2 -20 years.
- **Clinically:**
- Respiratory infections: recurrent bronchitis, pneumonia, bronchectasia;
- Other infections: sinusitis, otitis, meningitis, pericarditis;
- Lymphadenopathia;
- Autoimmune diseases: arthritis, hemolytical anemia

Common variable immunodeficiency

- **Immunologically**:
- IgG 0,06 -2,4 g/l
- IgA <0,01 -0,2 g/l
- IgM 0,1 -1,2 g/l
- IgE < 2 U/ml
- B lymphocytes 0,1 -15 %
- CD3 and CD4 – transient decrease in 2 patients

Common variable immunodeficiency

- **Therapy:**
- Intramuscular IG and plasma at the beginning
- Intravenous IG from 1993

Hyper-IgM-syndrome

- 15 years old boy
- **Clinically**: recurrent pneumonia, haemolytical anaemia
- Immunologically
- IgG < 1 g/l
- IgA < 0,05 g/l
- IgM 1,2 -10 g/l

Transient hypogammaglobulinaemia of infancy

- **7 children**: 5 boys and 2 girls
- **Clinically** recurrent infections (otitis, bronchitis), in 4 cases combined with allergy
- **Immunologically**: IgG < 2,5 g/l or total Ig < 4 g/l at least during 6 months.
- **Therapy**: in 3 cases IVIG of short duration
- **Follow-up during 2-6 years**: the normalization of total IgG but the low level of IgG3, IgG4 and/or IgA remained

IgA deficiency
Clinical characteristics

Pathology	N of patients	Adults	Children
Infections	59	10	49
Intestinal disorders	9	7	2
Autoimmune diseases	43	33	10
Malignant diseases	5	4	1
Others	6	5	1

IgA deficiency
Immunological characteristics

- Total IgA deficiency (IgA <0,05 g/l) – 104 patients
  Partial IgA deficiency (IgA 0,06-0,3) – 17 patients
- IgG was mostly increased, IgM normal;
- IgG subclass deficiency (IgG2, IgG3 and/or IgG4) in 29 % of IgA deficient patients;
- IgE was increased in 44 % of patients besides more often in children (60%);
- During long-term following (up to 15 years) of patients level of IgG and IgM did not decrease.

IgG subclass deficiency

- **11 patients**: 5 adults and 6 children
- **Clinically** recurrent infections
- **Immunologically** IgG2, IgG3 and/or IgG4 deficiency
- Immunological criteria used: low values of IgG subclasses during one year
  IgG2 < 0,3 g/l; IgG3 < 0,15 g/l; IgG4 < 0,01 g/l
- **Therapy**: in 3 cases IVIG of short duration

Conclusion

- Primary antibody deficiency was found more frequently in children with recurrent infections and in relatives of patients with antibody deficiency than in other groups of patients and in donors.
- Among the patients with antibody deficiencies there was predominantly IgA deficiency.
- The patients with severe forms of antibody deficiency are treated regularly with IVIG.
- The frequency of IgA deficiency in donors was similar to that in other European countries.