Defects of humoral immunity

Humoral immunity defects are congenital or acquired abnormalities of B-lymphocytes, all or only some classes of immunoglobulins or complement.

Primary immunodeficiencies are rare and manifest with recurrent infections in early childhood. Some are incompatible with life in a normal environment. Humoral immunodeficiencies are more common in the population than cellular immunodeficiencies. Disorders of B-cell and antibody production are the cause of frequent infections with extracellularly proliferating bacteria. T-cell disorders lead to reduced resistance to parasites and intracellular bacteria and viruses.

Components of humoral immunity

Components of humoral immunity include B-lymphocytes, antibodies and complement. Antibodies are used in the defence against extracellular encapsulated bacteria (pneumococci, streptococci, neisseriae...); as opsonins facilitating phagocytosis; they form immunocomplexes with antigens, to which some components of the complement bind; by binding to antigen, they activate complement and thus mediate cytolysis of unwanted cells or microbes; they neutralise viruses and toxins. Complement is involved in inflammatory reactions and anaphylaxis, removal of immunocomplexes, opsonization of microbes, and cytolysis of cells. In primary humoral immunodeficiencies, impaired antibody production is due to molecular defects in B-lymphocytes or defects in the interaction of B- and T-lymphocytes.

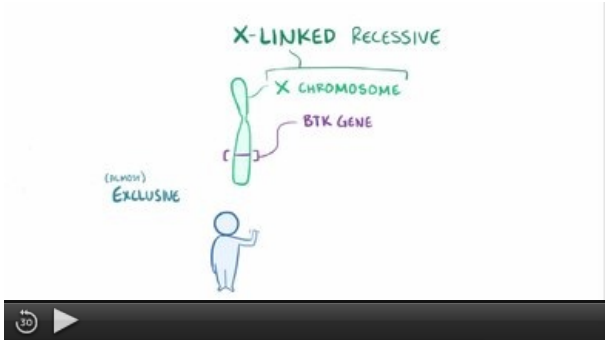
Clinical picture of humoral immunodeficiencies

Antibody deficiency is typically manifested by a susceptibility to recurrent, often severe upper and lower respiratory tract infections, especially with encapsulated bacteria (Streptococcus pneumoniae, Haemophilus influenzae). In children, recurrent otitis media, sinusitis and pneumonia are typical manifestations. There is also an increased susceptibility to viral infections of the respiratory and gastrointestinal tracts and their more severe course.

Other typical manifestations include short stature, failure to thrive, recurrent febrile illness, impaired school attendance and performance, chronic diarrhea, autoimmune disease, mesenteric lymph node hyperplasia, and unexplained hepatosplenomegaly.

Nosological units

- Autosomal inherited agamaglobulinemia.
- Bruton's X-linked agamaglobulinemia (prevalence 1:50,000 to 100,000 population)
  - Tyrosine kinase gene mutation → impaired differentiation of pre-B-lymphocytes into B-lymphocytes → missing B-lymphocytes and immunoglobulins;
  - X-linked → only in boys;
  - Manifestation after disappearance of transplacentally transferred maternal antibodies, i.e. after 6 months of life;
  - repeated severe respiratory infections → bronchiectasis, fibrotic changes; arthritis;
  - Treatment: lifelong immunoglobulin replacement, adequate therapy for infections; vaccination contraindicated.



Bruton's agamaglobulinemia

- Common variable immunodeficiency (prevalence 1:50,000 population)
  - Common variable immunodeficiency (prevalence 1:50,000 population)
  - Manifestation usually in the 2nd and 3rd decades;
  - after an unexplained stimulus, antibody production is attenuated → reduced IgG and IgA levels, IgM normal/reduced, normal B-lymphocyte count;
  - disturbances in the regulation of the immune response, development of autoimmune diseases (especially hematopoietic series), gastrointestinal tract often affected, granuloma formation, lymphoproliferative diseases,...
  - treatment: immunoglobulin replacement, adequate antibiotic therapy for infections, possibly prophylactic antibiotics.
- Selective IgA deficiency (incidence 1/600 to 1/1000)
  - most common antibody immunodeficiency;
  - inability to form IgA isotype antibodies, including secretory IgA (serum level < 0.05 g/l);
  - most often asymptomatic;
  - frequent upper respiratory tract infections, otitis, occasional diarrhoea;
  - associated with autoimmune diseases (e.g. rheumatoid arthritis);
  - repeated administration of blood derivatives is a risk of anaphylactic reaction;
  - treatment: symptomatic.

- Transient hypogammaglobulinemia of childhood.
  - Delayed onset of production of own immunoglobulins → more frequent infections after maternal antibody decline;
  - Usually corrects spontaneously by 2(-4) years of age.
- Specific antibody deficiencies.
- Deficiency of IgG subclasses.
  - Alone or in combination with IgA deficiency (IgG2, IgG4).
- IgM hyperimmunoglobulinemia syndrome (rare)
  - Disturbance of the processes of IgM to other Ig classes - different molecular causes and different pathogenesis;
  - clinically manifests as combined immunodeficiency - opportunistic infections (pneumocystis, toxoplasmosis, cryptosporidia);
  - frequent liver involvement - sclerosing cholangitis;
  - prognosis very serious;
  - Treatment: immunoglobulin replacement, treatment of associated infections, bone marrow transplantation.
- IgE hyperimmunoglobulinemia syndrome - Job syndrome, Buckley syndrome (rare)
  - Very high serum IgE levels (tens of thousands of IU/ml) and eosinophilia, reduction to disappearance of Th17;
  - infections esp. Staph. aureus and Candida albicans, skin infections, abscessed pneumonia;
  - skeletal and connective tissue involvement → "lion's face", dentition disorder

Differential diagnosis

- Combined immunodeficiencies.
- Protein losses (burns, nephrotic syndrome, enteropathy with protein losses)
- Drug-induced hypogammaglobulinemia.
- Other causes of acquired humoral immunity disorders.

Links

Related articles

- Genetic control of antibody production
- Genetics of Ig, B and T receptors
- Defects in cellular immunity
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References

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3. ↑ Skočit nahoru k:a b c d e f g h i LEBL, J, J JANDA a P POHUNEK, et al. *Klinická pediatrie.* 1. vydání. Galén, 2012. 698 s. s. 228-231. ISBN 978-80-7262-772-1.