Autoantibodies

Autoantibodies are antibodies (immunoglobulins) directed against the body's own antigens. The antigen may be proteins, glycoproteins, nucleic acids, phospholipids and glycophospholipids. Autoantibodies can be divided into organ-specific and organ-non-specific -> **specific** or only **associated** with a certain disease.

Autoantibodies are formed physiologically (natural antibodies) and are important for physiological autoreactivity (labelling and removal of inappropriate autoantigens). Increased production of autoantibodies occurs on the basis of various pathogenetic mechanisms and leads to damaging organs or tissues (type II, III and IV of immunopathological reaction). Autoantibodies, which are part of the immune system, play an important role in the body's defence and are polyreactive, low-affinity and IgM isotype. Autoantibodies of the IgG and IgA isotypes subject to somatic mutations can be highly specific against individual autoantigens and are demonstrated in a variety of autoimmune diseases.

Autoantibodies serve as a marker of autoimmune disease. Autoantibodies may prevent the clinical manifestation of the disease, accompany the clinical manifestation, persist after the clinically manifesting disease, or may exist without the disease. The positivity of autoantibodies does not have a clear diagnostic significance; only in the case of clinical suspicion of an autoimmune disease will it support the diagnosis. Otherwise, it forces the examiner to analyze the patient's symptomatology in more detail, not to overlook a possible more serious immunopathological disease. A number of methods are used to detect autoantibodies, such as indirect immunofluorescence, enzyme-linked immunosorbent assay (EIA), radioimmunoassay (RIA) and immunoblotting (western blot).[1]

Non-organ specific antibodies

Non-organ-specific autoantibodies react with the body's own antigens, which are common to all tissue or organ systems.

ANA – antinuclear antibodies

Antinuclear antibodies target a complex of different nuclear autoAgs. **Clinical use:** when systemic autoimmune diseases are suspected (e.g. systemic lupus erythematosus, systemic scleroderma, mixed connective tissue disease, rheumatoid arthritis, etc.). If ANA is positive, other nuclear Ags are tested for specific epitopes. ANAs are the most common autoantibodies, they have a limited differential diagnostic significance - they occur in older people, especially women, sometimes after infections, after immunostimulatory therapy. The ANA test serves as a **screening test**, if positive, it is necessary to perform a more detailed analysis and examination of other autoantibodies. If we do not indicate ANA together with ENA (see below), we may not get a reliable differential diagnosis. ENA positivity, which accompanies a number of systemic diseases, can be an isolated finding with negative ANA detection.

ENA – antibodies against extractable nuclear antigens

Antibodies against extractable nuclear antigens are associated with systemic autoimmunities, especially mixed connective tissue disease, Sicca-Sjogren's syndrome, and others. Autoantibodies to individual Ags are tested for ENA positivity: SS/A autoantibodies - occur in HLA-DR3-associated SLE, primary or secondary Sjogren's syndrome, isolated keratoconjunctivitis, isolated xerostomia, the cutaneous form of LE, neonatal SLE, SLE in defects of complement components system and about 1/4 of RA patients and overlap syndrome. In pregnant patients with SLE, the presence of autoantibodies to SS/A may pose a risk of fetal congenital cardiac atrioventricular block. These autoantibodies, passively transmitted by the mother to the fetus, can sometimes be associated with only transient changes in ventricular depolarization.

SS/B autoantibodies

It is most often found in SLE and Sjogren's syndrome. In paraproteinemia (monoclonal gammopathy), the presence of anti-SS/B autoantibodies indicates an association with systemic non-malignant haematological disease (secondary monoclonal gammopathy). Autoantibodies to Scl-70 are considered highly specific for systemic scleroderma, but not a circumscriptive form. CREST syndrome (calcinosis, Raynaud's phenomenon, oesophageal dysfunction, sclerodactyly and telangiectasia) is described in some patients with systemic scleroderma. These individuals also have positive anti-Scl-70.

ACA autoantibodies – against centromeres

They can be demonstrated in patients with Raynaud's syndrome, CREST syndrome and systemic scleroderma, in whom antibodies against Scl-70 were negative. The autoantibodies of the ENA group also include a number of autoantibodies, the significance and target structure of which (intracellular enzymes - topoisomerase, synthetases) are being studied in more detail. They are examined for dermato-polymyositis, but their incidence is relatively low (3–10%). Clinically used include autoantibodies labelled Jo-1 (dermatomyositis sometimes complicated by pulmonary fibrosis), PL-7, PL-12, and others. Autoantibodies against Sm antigen are highly specific for SLE, resp.

overlap syndrome with features of scleroderma, polymyositis and rheumatoid arthritis. Overlap syndrome with a positive finding of autoantibodies against Sm antigen often progresses to SLE with renal impairment. Other non-organ-specific autoantibodies:

ANCA – antibodies against neutrophil cytoplasm

🔎 *For more information see ANCA.*

Antibodies against the neutrophil cytoplasm occur in systemic necrotizing vasculitis and idiopathic rapidly progressing glomerulonephritis. ANCA autoantibody positivity is typical of vasculitic syndromes such as Wegener's granulomatosis (cANCA with specificity against proteinase 3) and microscopic polyangiitis or Churg-Strauss syndrome (pANCA with specificity against myeloperoxidase). ANCA autoantibodies are often positive in chronic intestinal inflammation (ulcerative colitis), cystic fibrosis, sclerosing cholangitis and other immunopathological conditions.

dsDNA – against double-stranded DNA

They are considered highly specific for SLE but may occur in other systemic diseases and in transient immunopathological conditions, such as more severe viral infections.

APLA, ACLA

Anti-phospholipid (APLA) or cardiolipid (ACLA) antibodies. Autoantibodies against cardiolipins (ACLA) are routinely screened and, in case of positivity, supplemented with antibodies against other phospholipids (APLA) phosphatidylserine, phosphatidylinositol, phosphatidylethanolamine, phosphatidic acid and beta2-glycoprotein 1 cofactors, prothrombin. Antibodies directed against the complex of negatively charged phospholipids with beta2-glycoprotein 1 cofactor or prothrombin are used pathogenetically. Clinically, it manifests itself in a triad: thrombosis, thrombocytopenia, and abortion in women. We are talking about antiphospholipid syndrome. It can be secondary (e.g. in patients with SLE) or primary. ACLA and APLA autoantibodies should be investigated in young people with stroke or myocardial infarction, in patients with isolated neurological symptoms such as migraine, chorea and recurrent stroke leading to dementia. In healthy pregnant women, APLA occurs in low concentrations in about 2-7%. The incidence of these autoantibodies increases with age. Infections or even malignancies can accompany them. APLA IgG isotype predominates in venous thrombosis and IgM isotype in habitual abortion.

RF – rheumatoid factor

It is an autoantibody directed against the Fc fragment of IgG immunoglobulins. **Clinical use**: in case of suspected rheumatoid arthritis and systemic immunopathological diseases (lupus erythematosus, Sjögren's syndrome, etc.). RF in the titer of 1: 300 is a typical feature of RA, in high titers they can occur in paraproteinemia (monoclonal gammopathy) and cryoglobulinemia. Higher titers of RF are also found in liver cirrhosis, sarcoidosis, Tbc, after transplantation and chronic inflammation. RF is also determined in isotypes by the Elisa method - RF IgG, IgA, IgM - high titers may correspond to the regulatory efforts of the immune system after exercise (e.g. viral infection, subchronic inflammation, etc.) to restore immunological homeostasis.

AMA – antibodies against mitochondria

Antibodies against mitochondria – detected in 60-90% of patients with primary biliary cholangitis (PBC), may prevent many years of clinical manifestation of this disease. Specific autoantibodies in PBC are type M2. AMAs can occur in the serum of patients with drug SLE, systemic scleroderma, chronic active hepatitis (autoimmune), idiopathic pulmonary fibrosis, lymphomas, syphilitis, Crohn's disease or celiac disease.

SMA – antibodies against smooth muscles

Smooth muscle antibodies - we examine when active chronic (autoimmune) hepatitis is suspected. These autoantibodies may also occur in patients with acute viral hepatitis B and C, infectious mononucleosis, CMV infection, post-infarction or post-pericardial syndrome.

StMAb – antibodies against striated muscles

We examine antibodies against striated muscles when myasthenia gravis or polymyositis is suspected. If the finding is negative, it does not rule out the possibility of this disease, only in the case of myasthenia gravis associated with thymoma, their positivity is a diagnostically valuable indicator. (Clinical use: myasthenia gravis, polymyositis)[1]

Anti-CCP antibodies - against cyclic citrullinated peptide - have a higher specificity for the diagnosis of rheumatoid arthritis than the mentioned RF, at an early stage distinguishes the disease from other systemic diseases such as SLE, scleroderma, Sjogren's syndrome. Their predictive significance for a more severe course with joint damage is considered.

Organ-specific antibodies

Organ-specific autoantibodies occur in a variety of organ immunopathological conditions (autoimmune diseases). Investigation of these autoantibodies has a relatively considerable diagnostic importance.

Endocrine diseases

- Against TPO (*thyroid peroxidase*) - this autoantibody occurs in high titers in Hashimoto's thyroiditis and primary myxedema, in medium titers in thyrotoxicosis. In the normal population, the titer is low in about 8 % of healthy individuals.
- Against **TSH receptor** - (64 kDa Ag on thyroid cells) is found in up to 80 % of patients with thyrotoxicosis. The titer correlates with disease activity. It is transmitted transplacentally (neonatal thyrotoxicosis). Some antiTSHs have a blocking effect on thyroid metabolism (some myxedema), others stimulate growth (goitre, to treat refractory thyroiditis).
- Autoantibodies against T3 and T4 - cause a decrease in thyroid hormones,

Diabetes mellitus type I

- GAD - autoantibodies against glutamic acid decarboxylase. They are not important for the diagnosis of diabetes but have predictive value in children in the preclinical phase of the disease (positivity up to 80%).
- ICA - autoantibodies against islets of Langerhans can be detected many years before the onset of diabetes in 70–80% of patients.

Diabetes mellitus type II

- IA-2 (specific islet antigen 2) - predetermines future dependence on insulin treatment, indicates autoimmune polyendocrinopathy.

Autoimmune adrenalitis (Addison's disease)

- Autoantibodies against adrenal cell cytoplasm, 21-hydroxylase, 17-alpha-hydroxylase. Present in autoimmune adrenalitis, often associated with premature ovarian failure.

Autoimmune hypoparathyroidism

- Autoantibodies against the cytoplasm of parathyroid cells. Very often associated with Addison's disease, pernicious anaemia and vitiligo.

Reproductive autoimmunity - autoantibodies in women

- against zona pellucida - in infertility,
- against ovaries - in primary and secondary amenorrhea, infertility,
- against annexin V - a predictive sign of possible future infertility,
- anti-sperm antibodies - are one of the causes of infertility, they also occur in men.

Digestive and liver diseases

- Celiac disease - autoantibodies against gliadin, reticulin, endomysia, **tissue transglutaminase** (tTG). They are examined when celiac disease is suspected, but their examination is currently recommended as a screening for the severity of celiac disease, which may not be accompanied by gastrointestinal symptoms. They are also tested in isotypes. They are highly specific for the antiendomysial and anti-tTG IgA isotypes. The definitive diagnosis is made by gastroenterologists with a small bowel biopsy. See celiac disease for more.
- Chronic autoimmune hepatitis (CAH) - LKM (liver-kidney microsomes) autoantibodies are considered characteristic of autoimmune hepatitis, they can also temporarily occur in viral acute hepatitis. In practice, a complex of autoantibodies that are characteristic of CAH is used, namely autoantibodies ANA, SMA, sometimes AMA, APLA and ANCA.
- Atrophic gastritis and pernicious anaemia - GPCA (gastric parietal cell antibodies) - autoantibodies against intrinsic factor. In practice, GPCA autoantibodies are investigated in endocrinopathies, where GPCA positivity is often present in polyendocrinopathies.
- Nonspecific intestinal inflammations

ASCA - antibodies against *Saccharomyces cerevisiae*, in Crohn's disease the incidence is estimated at up to 80 %, while in ulcerative colitis the finding of positive autoantibodies pANCA is typical (90–95%).

Kidney diseases

- GBM - antibodies against the basement membrane of the glomeruli - are typical of Goodpasture's syndrome, or other forms of rapidly progressing glomerulonephritis. The examination can be indicated as statim, especially in sudden renal failure, hemoptysis or hematuria.

Skin diseases

- antibodies against the intercellular substance epidermis - in patients with pemphigus vulgaris
- antibodies against the basement membrane of the epidermis - in patients with bullous pemphigoid, sometimes

with herpes gestationis and paraneoplastic pemphigoid.

Neurological diseases

- antibodies against BMP - basic myelin protein are examined in serum or cerebrospinal fluid in all suspected demyelinating diseases (positivity: multiple sclerosis 70 %, optic neuritis 80-90 %, Alzheimer's disease 80-90 %),
- anti gangliosides - Guillan-Barre syndrome, motor neuropathy in paraproteinemia, amyotrophic lateral sclerosis,
- anti MAG (myelin-associated glycoprotein) - occur in demyelinating sensory and motor neuropathies along with autoantibodies against gangliosides.

Paraneoplastic autoantibodies

Paraneoplastic autoantibodies can occur in degenerative disorders of the central or peripheral nervous system without direct tumour invasion. Autoantibodies affect the nervous system and can prevent the clinical manifestation of the tumour for several years. They most often occur in small cell lung cancer, ovarian cancer, uterine cancer, and breast cancer. They can be used as diagnostic markers in patients with neurological symptoms to detect or exclusion of paraneoplastic damage.

- ANNA-1 - antineuronal nuclear antibodies.
- PCA-1 (against Purkinje cells).
- ANNA-2 in neuroblastomas.

Links

Related Articles

- Antibodies
- Immune system
- Antigen
- Autoimmune Diseases

References

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