IgG4 associated disease

IgG4 associated disease (**IgG4-RD**, eng. *IgG4-related disease*, german. *IgG4-assoziierte Erkrankung*) is a systemic inflammatory and fibrotic diseases affecting a wide range of organ systems. The first case corresponding to IgG4-RD was described in 1961, but a detailed study of the disease dates back to the 21st century. It turns out that many of the previously described diseases are most likely organ manifestations of IgG4-RD.

Epidemiology

The incidence is reported as 0.28–1.08 / 100,000 inhabitants. It mostly affects patients in the sixth decade of life, men are more often affected.

Clinical picture

The clinical manifestation is usually **localized swelling** in the affected organ, with the exception of multifocal occurrence in several organs. **Subacute course** is common, but cases with an acute course in the form of the dramatic failure of the affected organ are also known. About half of the patients have a history of **alergies, asthma, eczema orchronic sinusitis**. Fever or night sweats are rather rare. A number of organs can be affected, in particular:

- pancreas
- bile ducts
- liver
- gastrointestinal tract
- salivary glands
- lacrimal glands
- orbit
- retroperitoneum
- mesenterium
- aorta
- thyroid
- lung
- kidneys
- breast
- skin
- pineal gland and meninges
- prostate
- lymph node
- pericardium

Biochemical examination

Elevation of IgG4

Elevation of IgG4 above 1,4 g/l can be demonstrated in 70–80% of patients. Thus, a normal level of IgG4 does not rule out a diagnosis, it is probably associated with a milder clinical course. However, IgG elevation also occurs in approximately 5% of healthy people, and elevation is relatively common in patients with pancreaticobiliary malignancy, with inflammatory or infectious disease.

Serum electrophoresis

In patients, a polyclonal band may appear in the faster migrating γ fraction, leading to the phenomenon of β–γ bridging. t can be shown that this fraction consists of IgG4.

Other changes

Other changes occur quite often, but are only slightly specific:

- elevation of total IgG;
- IgE elevation;
- elevation of inflammatory markers (FW, CRP);
- serum ANAs are detectable in about half of patients;
- Rheumatoid factor is detectable in about one-fifth of patients.

Decreased levels of complement proteins have also been detected and the presence of a number of antibodies has been demonstrated; the diagnostic significance of these findings is not yet clear.

Imaging methods

The radiological picture can show varying degrees of disability, distinguishing from malignancy is usually difficult or impossible.

Histopathology

The histopathological finding is relatively characteristic. The Triassic is classically described:

1. lymphoplasmocytic infiltration;
2. fibrosis, usually storiformly arranged;
3. obliterative venulitis.

Furthermore, an **eosinophilic infiltrate** may be visible, in some cases even significant. Granulomas do not belong to the picture, their detection makes the diagnosis of IgG4-RD unlikely. Individual features may be present in a wide range of fibroproductive inflammatory disorders, IgG4-RD is characterized by their combination.

In addition to its own morphology, the key evidence is the **infiltration of the IgG4 lesion by positive plasma cells**. Both the distribution and the number of IgG4 + cells in the lesion can fluctuate; a threshold of the average number of cells per field of view at maximum magnification (HPF) is used to support the diagnosis. Older works recommended a threshold value of 10 cells/HPF, more recently a higher threshold, 20 cells/HPF.

Diagnostics

There are several diagnostic criteria to diagnose IgG4-RD. These include **clinical behavior, laboratory, and histopathological findings**. **Organ-specific diagnostic criteria** are available for some organs.

The following self-defined diseases are now considered to be **organ-specific manifestations of IgG4-RD**:

- autoimmune pancreatitis;
- sclerosing cholangitis;
- Mikulicz syndrome;
- Küttner's tumor;
- Riedel's thyroiditis;
- Ormond's disease;
- Mediastinal fibrosis;
- orbital pseudotumor;
- eosinophilic angiocentric fibrosis ;
- multifocal fibrosclerosis;
- idiopathic hypocomplement tubointerstitial nephritis with extensive tubulointerstitial deposits.

In some cases, the classification as an IgG4-associated disease is based on the analysis of only a small number of patients, so it is possible that it is in fact an IgG4-associated disease in only some cases.

Therapy and prognosis

Currently, there are not sufficiently large controlled studies with sufficient follow-up in general for IgG4-RD.

IgG4-RD responds well to **corticosteroid** therapy for a minimum of 3-6 months. The risk of relapse is high. Within 6 months, about a third of patients relapse, during the year more than half of patients and after three years, less than a tenth of patients are without relapse.

In the experimental phase, therapy aimed at reducing the number of B cells with rituximab. Though, only at the level of case reports is there evidence of clinical success with proteasome inhibitor therapies bortezomib.

Links

Related articles

- IgG4 related disease/PGS

References

- CULVER, E.L. – BATEMAN, A.C.. General principles of IgG4-related diseace. *Diag Histopatol.* 2013, vol. 19, no. 4, p. 111-118, ISSN 1756-2317.