

Giant cell arteritis

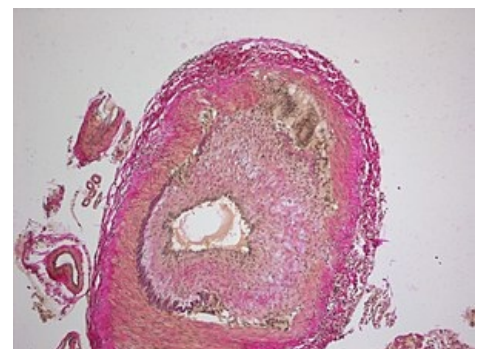
Intro

Giant cell arteritis (*Giant cell arteritis*, GCA) is a chronic systemic vasculitis of medium and large arteries containing *lamina elastica interna*. First described by Dr. Hutchinson in 1890. However, in 1930 Dr. Horton described its histopathology findings (that's why it's also called **Horton's disease**). Another name for this disease is also temporal arteritis (often targets *a. temporalis* *spf.*, *a. ophtalmica*, *a. ciliaris post.*, *aa. vertebrales*). Typical in patients over 50 years old, in younger extremely rare, often seen with *Polymyalgia rheumatica* (PMR – morning neck stiffness, pain of shoulder muscles and pelvis, increased acute phase reactants), approximately 30–50 % has PMR symptoms prior, during or post GCA diagnosis. Association between these two diseases is yet unknown.

GCA develops slowly, in the start of the illness there are complete symptoms (increased temperature, tiredness, nausea, cefalea), later symptoms depend on the location of the targeted vessel: pain when touching *a. temporalis*, claudication of chewing muscles, diplopia, total loss of vision, aortic arch syndrome with upper extremities ischemia, also Raynaud's phenomenon and finger gangrene. Etiology is multifactorial (polygenic heritage, environment). In pathogenesis main role play macrophages, dendritic cells and Th lymphocytes. Biopsy *a. temporalis* and subsequent histological verification is basically always done during diagnostics. Therapy consists of giving corticosteroids (40–60 mg/day).

Histopathology findings

Inflammatory infiltrate in all the parts of the vessel with macrophages and giant cells with multiple nucleuses (in 30–50 % may be missing)^[1], that form into granulomas at the border of media and intima. In case that there are no polynucleus cells apparent, the infiltrate consists then mainly of lymphocytes and small amount of neutrophils and eosinophils. We may also see fragmentation of *lamina elastica interna* and destruction of smooth muscle cells – they are replaced with **fibrosis of media**. Typical sign is hyperplasia of intima – causes occlusion of the vessel (and subsequent ischemia).



Microscopic view of a Giant cell arteritis.

Patogenesis

Main role in patogenesis of GCA play:

1. **cells:** CD4+ T lymphocytes (mainly Th1 and Th17), dendritic cells, macrophages and giant cell multinucleus cells,
2. **enzymes and growth factors:** metalloproteinases, PDGF, VEGF, IFN- γ , IL-6, TNF- α and others.

Causing factors are unknown, even though higher frequency of GCA was described in patients after respiratory infection (*M. pneumoniae*, *Ch. pneumoniae*), alternatively after the infection of parvovirus B19. However, in the beginning of immune system reaction there is most likely unknown antigen(s) in adventicia. It is recognized by T lymphocytes (that get into the adventicia via *vasa vasorum*), undergo clonal expansion and start producing IFN- γ . Activated T lymphocytes exprime MHC II and CD25R – receptors for IL-2, it leads to formation of granulomas, they form at the level of intima and media. It is still unknown mechanism (or route) how this is possible. In presentation of antigen, main role play dendritic cells. They are physiologically in adventicia and when they meet antigen (*toll-like receptor* (TLR) 4 and TLR 5), they get activated. This route is ligand-dependent – different types of bacterial antigens lead to different types of inflammatory process.^[2]

IFN- γ leads to activation and migration of macrophages (main effector cells of GCA), that connects and form **giant multinucleus cells**. In different parts of the vessel, macrophages connect differently:

- in adventicia they produce IL-1 and IL-6, TNF- α and TGF- β , IL-32;
- in intima and media syntetize (due to the IL-1 β and TNF- α) **metalloproteinases** (MMP-2, MMP-9) and **nitric oxide** (active nitric forms). They also exprime VEGF, PDGF (A and B), his expression correlates with intensity of intima hyperplasia.

Metalloproteinase's role is in oxidation of macromolecules (lipids, DNA) and in proteolytic activity, they are the main reason of degradation of *lamina elastica interna*. Besides that they „lyse“ cell membranes and released proteolytic enzymes degrade ECM further more. Reactive nitric species cause apoptosis of smooth muscle cells of media. VEGF leads to angiogenesis, destroys the structure of the vessel and lets other lymphocytes to accelerate the process of destruction. IL-6, besides pro-inflammatory effect, stimulates *in vitro* angiogenesis and most likely *in vivo* effects in GCA (there are reports of successful treatment of GCS with IL-6 receptory antibody)^[3]

After the degradation of *lamina elastica interna* myofibroblasts migrate to intima, stay in subendothelial level where they start to proliferate and syntetize ECM components. Besides that, multinucleus cells produce PDGF that stimulates intimal proliferation. That leads, all together, to uncontrolled intimal proliferation and hyperplasia that leads to occlusion of the vessel (this is the reason of some major symptoms: stroke, blindness). In recent years,

Th17 lymphocytes pathogenesis in GCA is studied. Their activation is connected with macrophage production (IL-6, IL-1 β). These cells produce IL-17, that has its receptors on fibroblasts, endothelium and smooth muscle cells of media. Strong stimulation of inflammation is suspected by IL-17.^[4]

Diagnosis

Physical findings are unclear, shows state of continuous inflammation, patients often claim unspecific symptoms. Some pathological laboratory findings are important:

- sedimentation of erythrocytes at least 50mm/h (20 % of patients has normal findings);
- highly increased CRP, may be beneficial to find out levels of IL-6;
- thrombocytosis;
- may be increased liver enzymes levels.

When suspicion of extracranial GCA, arteriography is indicated, CT, MRI angiography. Typical findings on angiography is bilateral stenosis of the affected artery and hyperplasia of the artery due to the inflammation. CT is important when aneurysm is suspected, also aortic dissection (that may be caused by the inflammation). In recent years, we also use 15 FDG PET diagnostics (affected artery catches glucose) and also color Doppler USG of the artery (typical finding is so called „halo sign“).



Main aspects of therapy

Corticosteroids are the first line of treatment in GCA. Recommended dose is 40 – 60 mg of prednisone pro die, when vision symptoms occur, the dosage should be increased to 100 mg daily. Patient is supervised and when the CRP and sedimentation levels drop to 50%, dosages may be decreased. Treatment should be continued for at least 2 years.

Final word

Giant cell arteritis is vasculitis of medium and big arteries, affects mainly older patients and most often affects cranial arteries. Causes occlusion of the lumen with subsequent tissue ischemia. The disease often starts slowly with general symptoms, with progression of the disease, there are more characteristic symptoms typical for each artery location. In pathogenesis, main role play Th lymphocytes and its products IFN- γ and IL-17, also dendritic cells and macrophages with its products that directly destroy the vessel tissue. When GCA is suspected, biopsy is indicated of *a. temporalis*. Therapy consists of corticosteroids with good outcomes.

Links

Other articles

- Kazuistika k tomuto článku
- Obrovskobuněčná arteriitida (stručně)
- Glukokortikoidy
- Hlavní histokompatibilní komplex

References

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- 2.
- 3.
- 4.

Used literature

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Kategorie:Angiologie Kategorie:Imunologie Kategorie:Revmatologie Kategorie:Vnitřní lékařství Kategorie:Patologie