

Giant cell arteritis

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Abstract

Giant cell arteritis (GCA) or temporal arteritis is a systemic vasculitis which involves large and medium-sized vessels, especially the extracranial branches of the carotid artery, usually in persons older than 50 years. Feared complications of GCA are permanent visual loss, ischaemic strokes and thoracic and abdominal aortic aneurysms. The treatment consists of high-dose steroids. Mortality in patients with GCA seems to be similar to that of controls, probably due to a correct diagnosis and management. GCA is the most common systemic vasculitis in Western countries. The incidence rates described in European countries are around 20:100 000 persons older than 50 years.

Key-words

vasculitis, giant cell arteritis, temporal arteritis, Horton's arteritis, large and medium-sized vessels disorder.

Disease names

Giant cell arteritis
 Temporal arteritis
 Horton's arteritis

Definition

Giant cell arteritis (GCA) is a relatively common systemic vasculitis in Europe. GCA involves large and medium-sized vessels in patients usually older than 50 years. It is a granulomatous arteritis of the aorta and its major branches, especially the extracranial branches of the carotid artery.

Table 1: The Chapel Hill Consensus Conference on the Nomenclature of Systemic Vasculitis

Large Vessel Vasculitis
Giant cell arteritis
Takayasu arteritis
Medium Vessel Vasculitis
Polyarteritis nodosa
<u>Kawasaki's disease</u>
Small Vessel Vasculitis
<u>Wegener's granulomatosis</u>
<u>Churg-Strauss syndrome</u>
<u>Microscopic polyangiitis</u>
<u>Henoch-Schonlein purpura</u>
<u>Cryoglobulinemic vasculitis</u>
Cutaneous leukocytoclastic vasculitis

Epidemiology

GCA almost exclusively affects persons older than 50 years. GCA is the most common systemic vasculitis in Western countries. The highest incidence rates are described in Scandinavian countries and in North American populations of the same descent (table 2). GCA is more common among women than men. In the last years, a progressive increase in the incidence has been reported.

Table 2: Incidence of GCA

Country	Years	Incidence*
Norway (Aust Agder)	1987-94	29
Iceland	1984-90	27
Sweden (Goteborg)	1973-75	18
United States (Minnesota)	1950-85	17
Spain (Lugo)	1988-97	11
Israel (Jerusalem)	1980-91	10
France (Loire-Atlantique)	1970-79	9
Italy (Reggio Emilia)	1980-88	7

* Incidence per 100.000 persons older than 50 years.

Etiology

GCA is a chronic inflammatory disorder involving large and medium-sized arteries. Some familial accumulation and the association with the HLA-DR4 haplotype suggest a genetic predisposition. Epidemiological observations may indicate an infectious origin. Immunological research demonstrates an antigen-driven disease with local T-cell and macrophage activation in the vessel wall with an important role of the proinflammatory cytokines. The initial process may be a foreign-body giant-cell attack on calcified internal elastic membrane in arteries. The prerequisite of a calcified artery is a possible explanation for that GCA almost exclusively affects persons older than 50 years. Although progress towards the understanding of GCA pathogenesis during the last decade are encouraging, the etiology remains unknown.

Clinical manifestations

Most of these manifestations occur prior to steroid therapy, but they may also develop during the early phase of therapy, or during tapering of the dose of steroids.

Common clinical manifestations

- Constitutional syndrome (asthenia, anorexia, and weight loss)
- Low-grade fever
- A new onset headache or a new type headache
- Thickened, nodular, tender and erythematous temporal arteries with decreased or absent pulses
- Jaw claudication
- Visual ischaemic complications are observed in about 25% of patients, and irreversible blindness, mainly due to anterior ischaemic optic neuropathy and frequently

preceded by amaurosis fugax, is found in 1-15%. Predictors associated with an increased risk of permanent visual loss are a history of amaurosis fugax and cerebrovascular accidents, the absence of anaemia and a higher platelet count. The presence of constitutional symptoms and polymyalgia rheumatica are associated with a reduced risk.

- Audiovestibular manifestations (nystagmus and hearing loss).
- Polymyalgia rheumatica, a clinical syndrome characterized by pain and stiffness in neck, shoulder girdle and pelvic girdle.

Uncommon clinical manifestations

- High-grade fever and unknown origin fever
- Carotidynia
- Enlarged or tender occipital, facial or postauricular arteries
- Claudication of the tongue or the swallowing
- Necrosis of the tongue or the scalp
- Ocular muscle paresis
- Lower limb claudication and aortic arch syndrome resulting in arm claudication
- Thoracic and abdominal aortic aneurysms
- Coronary ischaemia
- Pulmonary artery thrombosis
- Intestinal infarction
- Ischaemic strokes (affecting carotid or vertebrobasilar territories), dementia, spinal cord infarction, mononeuropathies (e.g. brachial plexopathy) and polyneuropathies
- Cough, sore throat, and hoarseness
- Peripheral arthritis
- Secondary amyloidosis

Laboratory findings

Erythrocyte sedimentation rate (ESR) is usually higher than 50 mm/hour, but a lower erythrocyte sedimentation rate is possible. However, a completely normal erythrocyte sedimentation rate (< 30 mm/hour) is exceptional in GCA. C-reactive protein and fibrinogen is usually elevated.

Anaemia, thrombocytosis, and abnormal liver-function tests are frequent. Rheumatoid factor and antinuclear antibodies are usually negative. Previous studies suggest that the circulating CD8 T cells are reduced in patients with active GCA. However, these findings have not been confirmed and the utility of this determination should be re-evaluated. Levels of interleukin-6 may be an indicator of active disease.

Diagnosis

GCA should be confirmed by temporal artery biopsy. Biopsy demonstrates a vasculitis characterized by a predominance of mononuclear infiltrates or granulomas, usually with multinucleated giant cells. A normal temporal artery biopsy does not exclude a GCA

since the lesions may be skipped. Routinely examining a temporal artery biopsy at multiple levels seems not to increase the diagnostic yield, although selective further examination may be indicated in some cases. Patients without visual manifestations, abnormal temporal arteries on examination or constitutional syndrome have a low risk of having a positive temporal artery biopsy.

The American College of Rheumatology proposed a list of criteria for diagnosis of GCA (table 3). The presence of three or more criteria had a sensitivity of 97.5% and a specificity of 78.9% in a French study of patients in whom the diagnosis of GCA was confirmed or ruled out by temporal artery biopsy.

The presence of a halo sign or an inflammatory stenosis in the color duplex ultrasonography of the temporal arteries can effectively predict which patient will need surgical biopsy and eliminate patients who would not benefit from biopsy. It has been suggested that the lack of a halo sign can practically rule out a GCA. However, ultrasonography may be equivalent to a careful physical examination.

Although confirmatory studies are necessary, positron emission tomography may contribute to the noninvasive diagnosis of GCA and to the evaluation of the extent of disease, response to therapy, and disease recurrence. A high temporal 67-gallium uptake is observed in patients with GCA, and the uptake normalizes during remission.

Table 3: The American College of Rheumatology criteria for diagnosis of GCA

Age at onset > 50 years
New headache
Temporal arteries abnormalities on examination
ESR >50 mm/hour
Positive temporal artery biopsy*

ESR: erythrocyte sedimentation rate

*Vasculitis characterized by a predominance of mononuclear infiltrates or granulomas, usually with multinucleated giant cells

Treatment

The treatment of GCA consists of high-dose steroids, usually 40-60 mg per day of prednisone or equivalent. The response appears rapidly, within a few days. Gradual tapering after 1-2 months of therapy should be tried. The objective would be to reach a maintenance dose of 7.5-10 mg per day. Relapse during dose tapering and steroid-related adverse events often complicate management. Steroid resistance is a risk factor for GCA complications.

Visual loss due to GCA treated with intravenous or oral steroids improves only in a few patients. Data suggest that there is a better chance of visual improvement with early diagnosis and immediate start of steroid therapy. Intravenous steroids may offer a greater prospect of

improvement, although there are contradictory results. Steroid therapy may be indicated to prevent complications before confirmatory temporal artery biopsy. Moreover, temporal artery biopsy is useful several weeks after administration of steroids. Calcium and vitamin D supplements must be provided to all patients treated with steroids. Byphosphonates therapy should be considered in patients with osteoporosis.

Methotrexate may be useful to control disease activity or to decrease the cumulative dose and toxicity of steroids. In a Spanish study, treatment with prednisone and methotrexate reduced the proportion of patients who experienced at least one relapse or multiple relapses, and the mean cumulative dose of prednisone was lower in the patients with combined therapy. However, other studies have not confirmed these results.

Prognosis

Death due to cardiovascular diseases may increase in patients with GCA related to either the steroid therapy itself or insufficient control of inflammation. However, mortality in patients with GCA seems to be similar to that of controls, probably due to a correct diagnosis and management. No increased frequency of malignant neoplasms in GCA has been reported in a recent prospective study.

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