Giant Cell Arteritis

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Contents

Core Messages

- Iritis may be the first sign of ocular ischemia in giant cell arteritis (GCA).
- The main signs and diagnostic features of GCA are headaches with an increased ESR and CRP in a person older than 50 years of age, with histologically inflammation of the superficial temporal artery biopsy.
- Additional signs and symptoms such as polymyalgia rheumatica (PMR) and jaw claudication are also very important signs for diagnosis.
- Histology of the superficial temporal artery reveals lymphocytic and plasma cell infiltration of the vessel wall; giant cells are not present in every vessel wall specimen.

65.1 Definition

Jonathan Hutchinson (1890) described the first patient with the characteristic signs of giant cell arteritis (GCA) and called the disease "arteritis of the aged." Horton, Magath, and Brown (1932 and 1934) published the clinical and histological signs of the temporal artery inflammation as a clinical entity for the first time. The disease occurs much more often in Caucasians and in cool climates, compared to people from other parts such as Africa or Asia, and is much more frequent in women.

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The American College of Rheumatology 1990 criteria for the classification of giant cell arteritis [8] are:

1. Age at disease onset ≥50 years
2. New headache
3. Temporal artery abnormality
4. Elevated erythrocyte sedimentation rate
5. Abnormal artery biopsy

The incidence of GCA varies geographically. The disease predominantly affects subjects of Northern European descent with estimates of about 20 cases annually per 100,000 persons older than 50 years of age [11].

65.2 Clinical Manifestations

65.2.1 General Involvement

Patients complain about headache and myalgia mainly in the shoulder girdle. Typically, they report jaw claudication when chewing and pain in the neck may also occur as first symptoms. General signs and symptoms develop earlier than ocular ones. Inflammations of all arteries can occur. Life-threatening manifestations are aortitis and inflammation of the coronary arteries.

65.2.2 Ocular Involvement

Ocular symptoms may present as amaurosis fugax (AF) and visual blurring, which occur much more often than other symptoms such as eye pain, peri- or retrobulbar pain, or visual loss for several hours which can be preceded by diplopia.

Ocular signs are inflammation of posterior ciliary arteries and anterior ischemic neuropathy (AION) (Fig. 65.1) which occurs more often than central retinal artery occlusion (CRAO). Ischemic choroidopathy is not an unusual finding (Fig. 65.2). Ischemic iritis or even panuveitis may rarely occur in GCA. Other signs of ischemia are ocular hypotony and cotton-wool spots in the retina [13, 14]. Rajesh and Cole [12] described cells in the anterior chamber and vitreous as well as nongranulomatous keratic precipitates. The development of iritis with anterior synechiae and gelatinous deposits on the trabecular meshwork with secondary glaucoma in both eyes were also found. Bilateral swelling of the papilla was observed.

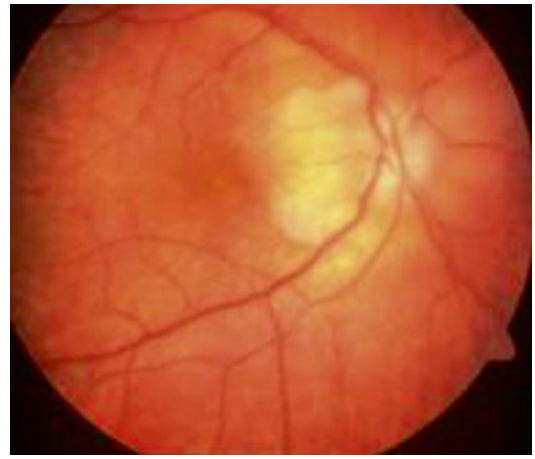

Fig. 65.1 AION with pale optic disc and cotton-wool spots at the superior border in an atrophic area of an 89-year-old woman with GCA

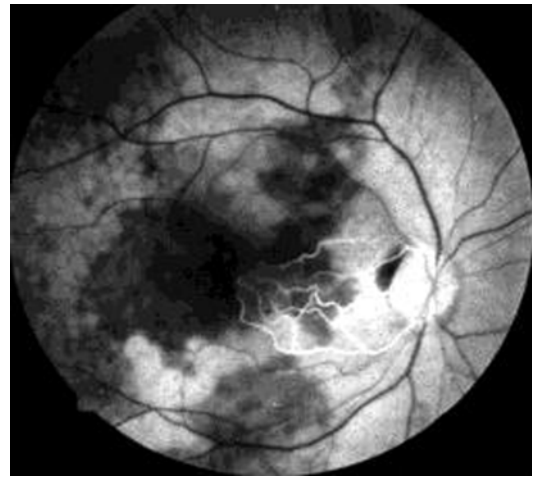

Fig. 65.2 Combined retinal and choroidal infarction in a patient with GCA

Rarely described are branch retinal artery occlusion (BRAO), posterior ischemic neuropathy (PION), and eye muscle paresis.

In a retrospective study, Hayreh et al. [6] investigated 170 patients with biopsy-confirmed GCA. Eighty-five patients (50 %) presented with ocular involvement. Visual loss of varying severity occurred in 83 patients (97.6 %), AF in 30.6 %, diplopia in 5.9 %, and ocular pain in 8.2 %. AION was found in 81.2 %, CRAO in 14.1 %, PION in 7.1 %, and ocular ischemic syndrome in 1.2 %.

A delayed perfusion of the choroidal circulation was reported by several authors which implies involvement of the ophthalmic artery [3, 4, 16].

The occult form of the disease presents as a quiet ischemic blindness in one or both eyes, without classical symptoms and signs (headache, weight loss, malaise, and fever). According to Hayreh [5], a fifth of patients with visual loss have occult GCA.

65.3 Etiology and Pathogenesis

Cellular infiltrates are composed of CD4+ T lymphocytes, macrophages, and multinucleated giant cells. The pre-activated T lymphocytes in the adventitia enter the vessel wall through the vasa vasorum. Adventitial CD4+ T cells intermingle with activated macrophages which produce interleukin-1 beta and interleukin-6 [17]. It seems that a distinctive population of vascular dendritic cells (DCs) are present in the vessel wall infiltrates. DCs mainly are present in the adventitia but were also found in the media. It is suggested that DCs participate in the fusion process of phagocytes [18]. The major pathogenic mechanism in GCA is the intimal hyperplasia leading to vessel stenosis. With this process neoangiogenesis develops with new blood vessel formation in avascular zones of the arterial wall. Why uveitis is initiated remains unclear. The cells could very well come from a breakdown of the blood-ocular barrier due to ischemia.

65.4 Diagnosis

The diagnosis of GCA is clinical, but the gold standard for diagnosis is the temporal artery biopsy. Histology of the superficial temporal artery reveals lymphocytic and plasma cell infiltration of the vessel wall; giant cells are not present in every biopsy specimen.

In every patient with an acute visual deterioration, ESR and CRP should immediately be requested. Additional diagnostic tests are imaging methods, such as ultrasonography (US) of the superficial temporal artery and examination with magnetic resonance imaging (MRI) [1, 2, 10]. Gadolinium causes vascular contrast enhancement in temporal arteries due to an inflammatory process. Color duplex ultrasonography (US) combines the imaging capabilities of B-mode US with the flow-velocity determinations of Doppler sonography, and it permits the accurate assessment of both the arterial anatomy and the flow characteristics of the vessel at specific sites [15].

65.5 Differential Diagnosis

GCA is a well-known masquerader. Especially in the case of an occult GCA, diagnosis of a noninflammatory AION due to arteriosclerosis is often made.

65.6 Treatment

The only proven treatment for GCA is the administration of high-dose systemic corticosteroids. Four different strategies are recommended:

1. Hayreh and Zimmerman [7] initially give one intravenous megadose (equivalent to 1 g of prednisone) followed by high-dose (80–120 mg) oral prednisone in patients who present with history of AF or complete or marked loss of vision in one eye or in early signs of involvement of the second eye.
2. Kawasaki and Purvin [9] mentioned the treatment with intravenous steroids (methylprednisolone 250 mg every 6 h) for the first 3–5 days and then continue with high-dose oral prednisone. This prednisone treatment is maintained at least 4–6 weeks. If inflammatory signs and symptoms have subsided and the disease activity (ESR and CRP) has normalized, steroid tapering is necessary. In most patients, the initial reduction in dosage is 5–10 mg/month to a daily dosage toward 20–30 mg. The rate of reduction should further proceed cautiously, usually by 2.5–5 mg/month. When the daily dose is 10–15 mg, tapering should continue by only 1 mg/month. Steroid tapering is highly individualized.
3. Weyand and Goronzy [19] recommended an initial therapy with prednisone at a dose of 1 mg per kilogram of body weight per day. But given the risk of irreversible ischemic complications, intravenous pulse therapy (e.g., 1000 mg of methyl-

prednisolone per day for three consecutive days) is the recommendation by these authors.

4. In a meta-analysis Yates et al. [20] mentioned that prednisolone combined with adjunctive immunosuppression, such as treatment with dapsone, infliximab, adalimumab or hydroxychloroquine is not superior to prednisolone alone.

Threatening visual loss in the first few days is essential for the protection of vision of the second eye. However, during long-term treatment, the dose should be reduced as low as possible – depending on the clinical signs. Hayreh and Zimmerman [7] found that there is little justification for giving aspirin or other platelet-aggregating agents or steroid-sparing agents to prevent visual loss in GCA.

65.7 Prognosis

GCA can be a devastating disease resulting in complete blindness if not promptly treated. In case of an early diagnosis without visual loss, the initiation of anti-inflammatory treatment will result in a good visual prognosis. In case of visual loss in one eye, high-dose corticosteroids can prevent blindness in the fellow eye. However, increase of visual acuity in a patient with visual loss has been rarely observed despite high-dose corticosteroid treatment.

Take Home Pearls

- Giant cell arteritis is one of the prime ophthalmological emergencies because of its threatening visual loss.
- Additional diagnostic procedures are color duplex ultrasonography and magnetic resonance imaging (MRI).
- Early treatment with high-dose systemic corticosteroids is important for the prognosis of GCA.

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