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Giant Cell Arteritis

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Abstract Giantcell arteritis (GCA) involves the major branches of the aorta with predilection for the extracranial branches of the carotid artery. It occurs in individuals older than 50 years, and the incidence increases with age. The signs and symptoms of GCA can be classified into four subsets: manifestations of cranial arteritis (mainly headache, jaw claudication and visual manifestations), extracranial arteritis, systemic symptoms and polymyalgia rheumatica. Patients may develop any combination of these manifestations, which are associated with laboratory evidence of an acute-phase reaction. The only test that confirms the diagnosis is a temporal artery biopsy showing vasculitis with mononuclear cell or granulomatous inflammation usually with giant cells. However, areas of vasculitis may be missed by the biopsy and the histological examination is normal in about 15% of the cases. Some imaging modalities may aid in the diagnosis of GCA. Among these, color duplex ultrasonography of the temporal arteries is more commonly used. There are no independent validating criteria to determine whether GCA is present when a temporal artery biopsy is negative. The American College of Rheumatology (ACR) criteria for the classification of GCA may assist in the diagnosis. However, meeting classification criteria is not equivalent to making the diagnosis in individual patients, and the final diagnosis should be based on all clinical, laboratory, imaging and histological findings. Glucocorticoids are the treatment of choice for GCA. The initial dose is 40–60 mg/day for most uncomplicated cases. Addition of low-dose aspirin (100 mg/day) has been shown to significantly decrease the rate of vision loss and stroke during the course of the disease.

Keywords Temporal arteries · headache · sedimentation rate · glucocorticoids

Description of the Disease

Giant cell arteritis (GCA) involves the major branches of the aorta with predilection for the extracranial branches of the carotid artery, including the temporal arteries. The aorta and other large arteries may also be involved.

GCA is more common among people of north European decent than among Mediterranean people and is rare among African Americans, Native Americans and Asians. GCA occurs in individuals older than 50 years, and the incidence increases with age. The age-specific incidence rates per 100,000 population increase from 2 in the age group 50–59 years to 52 in the age group 80 years and older (1). The estimated prevalence is about 1:750 persons older than 50 years (2). Women are two to three times more commonly affected.

The signs and symptoms of GCA can be classified into four subsets: manifestations of cranial arteritis, extracranial arteritis, systemic symptoms and polymyalgia rheumatica (Table 13.1). Among these, tender, prominent temporal arteries with absent pulses, jaw claudication and diplopia have the highest positive likelihood ratios for GCA diagnosis (3, 4). Patients may develop any combination of these manifestations. Patients with systemic symptoms and increased inflammatory response in laboratory testing such as very high erythrocyte sedimentation rate (ESR), anemia of inflammation and thrombocytosis tend to present less often with ischemic intracranial manifestations (5). The onset of GCA symptoms may be abrupt but in most instances symptoms develop gradually over a period of several weeks. Elevated ESR is found in more than 90% of the patients, and in 30–60% it is very high (>100 mm/h). This and other abnormalities in laboratory tests are elaborated in Table 13.2.

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TABLE 13.1. Signs and symptoms of giant cell arteritis (GCA).

Clinical feature		Frequency (%)
Cranial arteritis	Headache, facial pain	70–85
	Scalp tenderness	20–40
	Prominent or tender temporal arteries	30–60
	Jaw claudication	30–40
	Vision symptoms: sudden vision loss (transient or permanent), diplopia or other ophthalmic manifestations	15–45
	Stroke, transient ischemic attacks and other neuropsychiatric manifestations	<15
	Vestibulo-auditory manifestations: hearing loss, tinnitus, vertigo	5–25
	Tongue or scalp infarction	<5
Extracranial arteritis	Aortic arch syndrome, aortic-valve insufficiency, aortic aneurysm and dissection	<15
	Clinically significant involvement of other arteries	10–20
	Peripheral neuropathies	<15
	Respiratory symptoms (cough, sore throat, hoarseness)	<15
Systemic symptoms	Fever, malaise, fatigue, anorexia, weight loss	30–60
Polymyalgia rheumatica	Bilateral aching and stiffness of the shoulder girdle, sometimes the neck and hip girdle	20–65

TABLE 13.2. Abnormalities in laboratory tests in giant cell arteritis (GCA).

Test		Frequency (%)
Acute-phase reactants	Elevated erythrocyte sedimentation rate (ESR)	90–95
	ESR $\geq$100 mm/h	30–60
	Elevated ESR *and/or* elevated C-reactive protein (CRP)	>95
Blood count	Anemia	35–65
	Thrombocytosis	30–60
	Leukocytosis	10–30
Liver function tests	Elevated alkaline phosphatase	30–60
	Elevated transaminases	<20
	Low albumin	10–30
Autoantibodies	Anticardiolipin	30–80

TABLE 13.3. Predictive values of temporal artery (TA) duplex ultrasonography and biopsy for giant cell arteritis (GCA) diagnosis.

	TA biopsy (%)	TA ultrasonography (%)
Positive predictive value	~100	50–90
Negative predictive value	80–90	90–95

Diagnosis and Diagnostic Criteria

The diagnosis of GCA is made primarily on clinical grounds and is bolstered by laboratory evidence of an acute-phase reaction. The only test that confirms the diagnosis of GCA is a temporal artery biopsy showing vasculitis with mononuclear cell or granulomatous inflammation usually with giant cells.

Some imaging modalities may aid in the diagnosis of GCA. Among these, color duplex ultrasonography of the temporal arteries is more commonly used. A periluminal hypo-echoic halo, probably representing vessel-wall edema, is considered highly specific for GCA (6). A recent meta-analysis concluded that when the pre-test probability of GCA is low, a negative result of ultrasonography practically excludes GCA (7). It appears that ultrasonography better serves to rule out GCA due to its high negative predictive value, whereas a positive test needs to be confirmed by a temporal artery biopsy, as the positive predictive value varies considerably among different studies (Table 13.3).

High-resolution contrast-enhanced magnetic resonance imaging (MRI) of the temporal arteries also enables evaluation of possible inflammation of the vessel wall. Preliminary results show high sensitivity of this imaging modality (8). Angiography of the aortic arch and its branches may serve to diagnose large-vessel involvement (9). Non-invasive modalities, such as positron-emission tomography, may also be employed to detect large-vessel involvement (10), but data on their predictive values are limited.

GCA affects the vessels focally; therefore, areas of vasculitis may be missed and the histological examination is normal in about 15% of GCA patients (biopsy-negative GCA) (11). A threshold temporal artery biopsy size of 1 cm is associated with increased diagnostic yield (12). Obtaining biopsies from both temporal arteries increases the chance of a positive result by 1–14% (13, 14). It is preferable to perform the biopsy as soon as possible, but the specimen may show signs of arteritis even after 2–4 weeks of treatment (15).

There are no independent validating criteria to determine whether GCA is present when a temporal artery biopsy is negative. The American College of Rheumatology (ACR) criteria for classification of GCA (16) may assist in diagnosis.

These criteria include:

1. age at onset $\geq$50 years
2. a new headache
3. temporal artery abnormality such as tenderness to palpation or decreased pulsation
4. ESR $\geq$50 mm/h

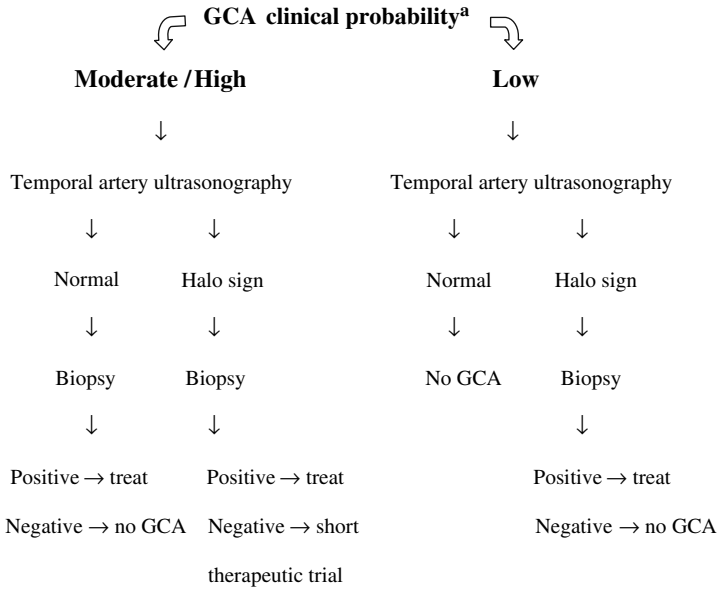

FIGURE 13.1. Suggested approach to giant cell arteritis (GCA) diagnosis.
[a] The pre-test probability is considered moderate if one of the following clinical manifestations is present *in addition* to elevated ESR and/or CRP: new headache, jaw claudication, sudden vision loss (permanent or transient), diplopia, prominent and tender temporal arteries. The probability is higher if more than one of these clinical manifestations is present, or when polymyalgia rheumatica, cerebral ischemic symptoms or systemic symptoms are present in addition to one of these manifestations.

5. abnormal artery biopsy showing vasculitis with mononuclear cell or granulomatous inflammation, usually with giant cells.

At least three of the criteria must be present, which yields a sensitivity of 93% and a specificity of 91%.

However, it is important to note that these are not diagnostic criteria. These classification criteria serve mainly to differentiate GCA from other types of vasculitis. They cannot effectively serve to differentiate GCA from other disease conditions. Such classification criteria work best in studying groups of patients with vasculitis and less well when used for diagnosing individual cases (17). Meeting classification criteria is not equivalent to making the diagnosis in individual patients, and the final diagnosis should be based on all clinical, laboratory, imaging and histological findings.

Based on the predictive values of tem biopsy and temporal artery duplex studies (Table 13.3), long-term experience with diagnosing and treating GCA, and data synthesis from studies, a practical approach to GCA diagnosis in suspected patients is suggested (Table 13.4).

Therapy and Course

Glucocorticoids are the treatment of choice for GCA. The initial dose is 40–60 mg/day for most cases. Starting treatment with intravenous methylprednisolone 500–1000 mg/day for 3 days may be considered in patients with vision loss (transient or permanent), diplopia, transient ischemic attacks or stroke (18).

Rapid improvement of clinical manifestations following treatment initiation is characteristic. Prompt treatment is crucial in GCA to prevent irreversible complications of acute vision loss and stroke. Thus, treatment may be started prior to confirming the diagnosis.

The average duration of treatment is 2–3 years. Relapses are experienced by 25–65% of GCA patients. Most relapses are mild, but some patients may develop vision loss or stroke while tapering glucocorticoid dosage or after discontinuation of therapy. Addition of low-dose aspirin (100 mg/day) has been shown to significantly decrease the rate of vision loss and stroke during the course of the disease, probably mediated by its anti-platelet effect (19). It is not clear whether the presence of anticardiolipin antibodies increases the rate of intracranial ischemic complications (5).

Individual cases vary greatly; therefore, the exact doses and the duration of treatment should be adjusted to the needs of the individual patient, considering both disease manifestations and glucocorticoid adverse effects. No steroid-sparing agent was proven to be widely effective thus far.

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