Giant Cell Arteritis

Case History

This is the case of C.S., a 51-year-old Portuguese known female patient who presented in February 1994 with blurring of vision and temporal headaches.

She claims that for the past few weeks she has been feeling very sluggish. She has had poor vision previously however she noted a further decrease in her visual acuity. She has more difficulty recognizing objects during the past few days. In addition she has been experiencing a new onset temporal headache which has been nagging her ever so effectively. Past ocular history

Cataracts, OD
Band keratopathy, OD
H/o Uveitis, OU
H/o Retinal vasculitis, OU
H/o angle closure glaucoma
S/p yag iridotomy and cyclophotocoagulation

Past medical history

Hypertension
Migraine headaches
Lupus suspect (ANA 1:128 speckled)
APS suspect
Plaquenil (for ANA titer)
Aspirin (for anticardiolipin antibody positivity)

Family medical history

Non-contributory

Personal and social history

Non-contributory

Ocular examination

VA OD NLP
VA OS 20/100

Gross exam

Quiet white eyes

EOMs full OU
AT OD 22

AT OS 17

Funduscropy

OD No view

OS good red-orange reflex, clear vitreous media, slightly indistinct disc borders, slight pallor inferiorly, cup:disc ratio difficult to ascertain, artery:venous ratio 2:3; no signs of vasculitis, retina attached, foveal reflex dull

Introduction
Giant cell arteritis (GCA)

Synonyms: Temporal arteritis, Cranial arteritis

- Systemic granulomatous vasculitis involving medium- and large-sized vessels.
- First clinically described c/o Hutchinson in 1890.\[1\]
- First histologic description c/o Horton et al in 1932.\[2\]
- Differs from other forms of vasculitis by:
  - Patient’s age
  - New onset of localized headache
  - Temporal artery tenderness or pulselessness
  - Elevated ESR
  - Temporal artery biopsy findings.

Epidemiology

- Age
  - Mostly in patients over 50 years of age
  - Incidence (0.49 to 50/100,000) increasing with age and peaking (nearly 1%) in the eighth decade.\[3\]-\[20\]

- Sex
  - M:R 1:2-41 \cdot 2 \cdot 3

- Race
  - Higher incidence rates in Caucasians of European descent
  - Rare in African-Americans and Asians.

Clinical Features

Systemic Manifestations

- Prodromal symptoms (days to weeks)
  - Anorexia
  - Fever
  - Malaise
  - Myalgia
  - Night sweat
  - Weight loss
- Hallmark symptom
  - New onset localized headache.\[5,6,11\]
  - Usually localized to the temporal or occipital area.
  - Occasionally diffuse or bilateral.
  - Scalp tenderness
- Gently stroking the GCA patient’s hair results in a characteristic complaint of pain distinctively seen only in patients suffering from GCA.
- Rizzo anecdotally describes this as the single most important clinical finding for GCA.[xxii]
- Dudenhoefer described scalp necrosis with GCA seen in 2 elderly patients.[xxiii]
  - Other cranial symptoms
    - Temporal tenderness or pulselessness
    - Jaw claudication
    - Facial pain
    - Earache
    - Toothache
    - Tongue pain
    - Palate pain
    - Odynophagia.
  - Other clinical features
    - Pulselessness and/or tenderness and inflammation along the course of the temporal artery
    - Bruits in the cranial or neck area
    - Jaw claudication
    - Atrophy of temporal and tongue muscles
    - Temporal artery blood flow measurements may be reduced.

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- Cerebrovascular disease
  - 1% to 25% of patients,[xxiv][xxv][xxvi][xxvii][xxviii]
  - Most common cause of death in GCA patients.26 27
- Neurologic disease[xxviii][xxix] 25 26[xxx][xxxi][xxxii][xxxiii][xxxiv]
  - Myopathy
  - Neuro-otologic syndromes
  - Neuro-psychiatric syndromes
  - Peripheral neuropathies
  - Seizures.

- Cardiovascular, pulmonary, gastrointestinal, renal, and dermatologic manifestations may also occur.28 29 34[xxxvi][xxxvii][xxxviii][xxxix][x][xi][xii][xiii][xiv]

**Ophthalmic manifestations**
- **Visual symptoms**
  - ~50% of patients
  - Transient visual blurring
  - Diplopia
  - Eye pain
  - Sudden loss of vision, etc. [xlvi]
- Transient repeated episodes of blurred vision are usually reversible.
- Sudden loss of vision is an ominous sign and is almost always permanent.
- Vision loss incidence, either partial or complete, is variably reported to be 10% to 60%. 6·7·8·17·24·25·27

- **Anterior ischemic optic neuropathy (AION)**
  - The most common cause of vision loss.
  - Ischemia of the optic nerve head
    - Supplied mainly by the posterior ciliary arteries.
  - Majority of AION is non-arteritic (87% to 91%). [xlvii] [xlviii] [xlix]
  - GCA is an arteritic AION
  - History of sudden painless loss of vision.
  - Fundus examination
    - May reveal optic disc edema, with or without splinter hemorrhages along the disc margin.
    - Typically presents with a chalky white edematous optic disc. [li]
  - Automated visual field
    - Typically reveals an inferior altitudinal defect, inferior nasal sectoral defect or central scotoma.48

- **Other important vascular ophthalmic presentations**
  - Posterior ischemic (retrobulbar) optic neuropathy
  - Central retinal artery occlusion
  - Branch retinal artery occlusion
  - Choroidal ischemia.

- **Neuroophthalmic manifestations**
  - Diplopia
  - Ptosis
  - Nystagmus
  - Internuclear ophthalmoplegia (INO)
  - Pupillary abnormalities.
Relationship with Polymyalgia Rheumatica

- Apparent relationship between GCA and polymyalgia rheumatica (PMR). [iv]
- Occasionally, the disease may begin with PMR symptoms
  - Fever
  - Malaise
  - Pain and stiffness
    - Neck
    - Shoulder or hip muscles
    - Without any obvious abnormalities by physical examination, such as muscle wasting or weakness.
- It is important to know that both symptom complexes may manifest in the same individual, or each can occur separately.
- PMR responds remarkably with low doses of corticosteroids.
- The ocular, cardiovascular, and neurologic manifestations of GCA are not associated with PMR. [24]

Laboratory Features

- Erythrocyte sedimentation rate (ESR)
  - Elevation (moderate to > 100 mm/hr) is common
  - Rarely (~3%) normal. [7·8·34]
Highly elevated ESR results are characteristic of a GCA process rather than other vasculitic or rheumatologic entities.

Other acute phase reactants

C-reactive protein (CRP), are elevated and reflect the underlying inflammatory process.

These acute phase reactants may be followed serially and may assist in monitoring for treatment dosing and response.\[li\] \[lii\]

CBC

Most are mildly anemic (normochromic, normocytic).

Lymphocytes hypothesized to proliferate in response to elastin, other arterial wall antigens, or muscle.

Immunoglobulin levels

Standard

Immune complexes are absent.

Hepatic enzymes, alkaline phosphatase and serum aspartate aminotransferase (SGOT)

Elevated in 20% to 30% and 15% of cases respectively.\[liii\] \[liv\]

Imaging studies

Aortic arch and cerebral angiography may show occlusion or alternating stenotic areas.

Computed tomography (CT) and magnetic resonance imaging (MRI) of the brain are not first line diagnostic procedures for GCA, however, they may be useful in patients with a multi-infarct state secondary to cervicocephalic arteritis.56

Superficial temporal artery biopsy (TAB)

Focal granulomatous arteritis, often with giant cells and "skip areas" of normal arterial wall.\[lv\] \[lvi\]

The technique for TAB is reported elsewhere.\[lvii\]

The most symptomatic side should be biopsied initially.

In a patient with suggestive symptoms and a negative initial biopsy on the symptomatic side, performing a TAB on the other side may confirm the diagnosis.57-58

The TAB should be performed ASAP, in the appropriate patient.
Therapy should not be withheld pending the performance or results of the TAB in patients with acute visual loss and extremely high clinical suspicion for GCA.

Pathophysiology

- In GCA, large elastic and medium-sized extracranial muscular arteries are most severely involved.[lxiii]
- The posterior ciliary and ophthalmic arteries are commonly affected.
- The common, external and internal carotid, vertebral, subclavian ayillary, proximal brachial artery may be involved.
- Less commonly, the descending aorta, mesenteric, renal, iliac, femoral, and pulmonary arteries may be affected. 14 ' 23 ' 24 ' 36

- GCA is a disease mediated primarily by an active cellular arm of immunity.
  - CD4+ T-helper cell response to macrophage-presented antigens lead to inflammation typically beginning in the adventitia and progressing to involve the whole vessel wall.
- The vascular occlusion occurs by focal narrowing, due to swelling of the wall without thrombosis or aneurysm formation.
- The internal elastic lamina is invaded and damaged by the primary inflammatory response.[lxiv]
- Giant cells while usually found histologically, is not required for the diagnosis.
- After a period of active inflammation, scarring permanently narrows the vascular lumen.[lxv]
- The impetus for the destructive inflammation is still unknown today. Elastin is highly suspected as being involved in the inciting events leading to this disease.[lxvi]
Diagnosis

- The diagnosis of GCA is primarily based on a clinical suspicion.
- A classification for GCA was created by the American College of Rheumatology.[lxvii]
- Fulfillment of a number of criteria (Table 1.) increases the probability for the diagnosis of GCA.
- The laboratory exams detailed above help strengthen the diagnosis.
- Acquiring a positive TAB is the definitive test.
- The systemic nature of GCA and its catastrophic complications warrants a vigilant approach to its diagnosis and treatment.
- Several authors have stressed in numerous published reports on GCA that one needs to institute therapy immediately on a presumed diagnosis of GCA.69 - 70
- In an appropriate setting, having a strong suspicion precludes the need to wait for the results of other laboratory investigations, or a temporal artery biopsy.

Symptomatic response to systemic steroids (prednisone at 1-2mg/kg/day or methylprednisolone at 250mg every 6 hours), excluding vision, may be dramatic within 24 hours.

Treatment

- Corticosteroids
  - The universally accepted treatment for GCA is high-dose corticosteroid therapy.
  - The major justification for the use of corticosteroids is the impending danger of blindness in untreated patients.
  - A hallmark paper by Birkhead et al showed that corticosteroids were effective in preventing blindness in patients with GCA.[lxviii]
Initially, high doses of corticosteroids may be given at 1 to 2 mg/kg/day until the disease activity is adequately suppressed.

- **ESR determination**
  - Sequential ESR determination may assist in determining the success of the high dose corticosteroid therapy.
  - Once the signs of clinical inflammation is suppressed and the ESR is maintained at a low level, corticosteroid levels may be tapered off slowly.

- **Length of treatment**
  - There is no agreement as to the length of treatment with corticosteroids for GCA.
  - It may be reasonable to maintain the patient on at least two years of treatment in order to lessen the chances of relapses.
  - Even so, relapses have been reported.

- **Immunosuppressives**
  - Foster uses a cyclosporin-azathioprine or cyclosporin-methotrexate combination as a steroid-sparing cocktail or therapy for steroid-resistant cases.

- **Biopsy and treatment**
  - The disastrous nature of the disease may occasionally require the administration of treatment prior to a definitive superficial TAB.
  - It is generally believed that the results of a TAB will not be altered if the procedure is performed within 3 to 5 days of initiating corticosteroid therapy.

Table 1.

**Classification of giant cell arteritis. American College of Rheumatology Criteria for Classification of Giant cell arteritis.**

Traditional (sensitivity, 93.5%; specificity, 91.2%; 3 of 5 criteria must be met)

1. Age of onset of 50 years or older
2. Onset of new headache
3. Temporal artery tenderness or reduced pulsation
4. Elevated (>50 mmHg) Westergren erythrocyte sedimentation rate
5. Abnormal artery biopsy

Alternative (sensitivity, 95.3%; specificity, 90.7%; 3 of 6 criteria must be met)

1. Age at onset of 50 years or older
2. Onset of new headache
3. Temporal artery tenderness or reduced pulsation
4. Claudication of jaw
5. Scalp tenderness or nodules
6. Abnormal artery biopsy

References


Birkhead NC, Waener HP, Shick RM. Treatment of temporal arteritis with adrenal corticosteroids: Results in 55 cases in which the lesion was proved at biopsy. JAMA 1975;163:821.
