Temporal Arteritis aka Giant Cell Arteritis and Temporal Artery Biopsy Technique

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Temporal Arteritis aka Giant Cell Arteritis and Temporal Artery Biopsy Technique

Case Example Temporal Arteritis with Tongue Necrosis

GENERAL CONSIDERATIONS

1. Definition
   a. Temporal Arteritis (TA) aka Giant Cell Arteritis (GCA) or Horton’s disease, named after the first physician to describe pathologically confirmed GCA
   b. Chronic vasculitis of medium-large sized arteries especially temporal and other cranial arteries

2. American College of Rheumatology 1990: 3 of 5 required to meet the classification criteria for GCA (Reported sensitivity of 93.5% and specificity of 91.2% for GCA compared with other vasculitides):
   a. Age 50 years or older,
   b. New-onset localized headache,
   c. Temporal artery tenderness or decreased temporal artery pulse,
   d. Erythrocyte sedimentation rate of at least 50 mm/h, and
   e. Abnormal artery biopsy specimen characterized by mononuclear infiltration or granulomatous inflammation.

3. Prevalence/Demographics
   a. GCA is the most common vasculitis in individuals > or = 50 y.o. occurring in 1-30/100,000
   b. Very rarely affects individuals < 50 y.o.
   c. GCA occurs most commonly in populations of Scandinavian descent
   d. Women > Men
   e. Prevalence of GCA is increasing

4. Pathogenesis
   a. Data suggests GCA is T cell-mediated and/or due to inappropriate dendritic cell activity in the adventitia leading to T-cell activation
   b. To date, no clear association has been found between any particular infectious agent or genetic component and GCA
   c. Intimal hyperplasia may lead to partial/complete lumen occlusion and cause ischemic complications

5. Complications and Associated Conditions
   a. Vision loss: arteritis of branches of the ciliary or ophthalmic arteries leading to optic nerve ischemia
   b. Polymyalgia rheumatica
   c. Stroke in ~2-4% of GCA patients, usually vertebrobasilar territory
   d. Peripheral neuropathy
   e. Claudication of extremities: upper and/or lower, uni/bilateral
   f. Aortitis or aortic aneurysm, usually clinically silent or result in fever of unknown origin; rarely may manifest in aortic dissection
   g. Normochromic, normocytic anemia
   h. Speech and respiratory features in giant cell arteritis have been described, but infrequently (~)
      i. Suggested that vasculitis in cases of GCA with speech or respiratory features may show a preference for branches of the external carotid artery (larynx supplied) over the internal carotid (supply the eye) (Ali 2005)
      ii. Involvement of the aorta and branches is recognized with GCA and has been associated with Ortner's syndrome causing dysphonia associated with laryngeal paralysis through to be caused by involvement of the RLN near the aorta (Endrees 2012)

EVALUATION

1. History
1. Chief Complaint
   a. Headache: most common initial complaint, classically sudden onset, severe, predominantly temporal region, but may occur in occipital, frontal, parietal regions
   b. Jaw claudication in ~50% patients
   c. Vision manifestations ~30%; vision loss ~15%. Visual deficit may be intermittent initially, but once established, it becomes irreversible.
   d. Constitutional symptoms: fatigue, general malaise, fever, anorexia, weight loss, and night sweats
   e. Fever of Unknown Origin
   f. Rarely tongue pain, ulceration and necrosis, see Case Example Temporal Arteritis with Tongue Necrosis

2. Review of Systems
   a. Polymyalgia rheumatica: sudden/gradual onset morning stiffness, neck, shoulder or hip pain, and pain during the night

3. Differential Diagnosis
   a. Vasculitides
      i. Wegeners Granulomatosis, polyarteritis nodosa, and microscopic polyangiitis rarely affect the temporal artery. Involvement of respiratory tract, kidney, or skin and ANCA positivity differentiate these from GCA
      ii. Takayasu’s arteritis affects the aorta and its branches, but occurs in patients younger than 40 years, whereas GCA is rarely seen in people younger than 50
   b. Infection
   c. Malignancy

4. Imaging
   a. Duplex sonography (DS) has been recommended for inclusion as a diagnostic criterion for GCA with reservation of temporal artery biopsy for patients with negative DS results. DS may reveal hypoechoic circumferential arterial wall thickening (halo sign) which disappears after 2-3 weeks of therapy. Two meta-analyses showed unilateral halo sign specificity of 89-91%, sensitivity of 69-75% for GCA; bilateral halo sign specificity of 100%, sensitivity of 43%
   b. High-resolution MRI has been reported to have very similar diagnostic power as DS but more data are needed before it can be recommended as a diagnostic tool in GCA
   c. PET has shown promise in some case reports

5. Laboratory Analysis
   a. Serum Studies
      i. ESR, CRP are elevated in >90% of patients
      ii. LFTs, especially AlkPhos, elevated in ~1/3 of patients
      iii. May have thrombocytosis and normocytic normochromic anemia

   a. A 1-2 cm biopsy should be taken on the more symptomatic side. Routine bilateral biopsy is not recommended since additional diagnostic yield is deemed to be too low
   b. At the University of Iowa, temporal artery biopsies are evaluated by the Ocular Pathology section, which logs in specimens and grosses them once a day in the afternoon. For this reason, all specimens must come to them in formalin, not in saline like for surgical pathology.
   c. Pertinent Anatomy
      i. Biopsies taken from within the ‘danger zone’ may result in frontalis palsy due to the proximity of the frontal branch of the superficial temporal artery to the frontal branch of the facial nerve. As described by Yoon et al.(1), the ‘danger zone’ is “bounded by (A) the tragus of the ear, (B) the junction of the zygomatic arch and lateral orbital rim, (C) the area 2 cm superior to the superior orbital rim, and (D) the point superior to the tragus and in horizontal alignment with (C).”
Danger Zone delineated by dotted box showing proximity of frontal branch of facial nerve to the frontal branch of superficial temporal artery.

ii. Occasionally, the frontal branch of the facial nerve may cross the superficial temporal artery at an unusually high location as shown below:

iii. To reduce the risk of frontalis paralysis, biopsy the parietal branch (rather than the frontal branch) of the superficial temporal artery as pictured below:
Inflammatory infiltrate in at least the tunica adventitia and media with elastic lamina fragmentation with or without giant cells provides the most definite evidence of GCA.

A positive result is not 100% specific for GCA. It has a sensitivity of 70% to >90%. Negative biopsy does not exclude GCA; some patients must be diagnosed on clinical grounds alone.

Biopsy confirmation of GCA is important for preventing unnecessary prolonged steroid therapy.

1-2 weeks steroid treatment before biopsy has little effect on positivity rate. But, with longer steroid treatment, histology may become less typical.

Histopathology (see slides in Case Example Temporal Arteritis with Tongue Necrosis):

- Inflammatory infiltrate of all 3 arterial tunicae (intima, media, adventitia);
- Granuloma forming giant cells in the media and intima–media border;
- Destruction of elastic lamina and smooth muscle of tunica media; smooth muscle replaced by fibrous tissue;
- Significant variability between patients and even within same sample;
- Giant cells detected in ~60-70% of samples since may be absent in early or late stages of disease.

MANAGEMENT

1. Upon strong clinical suspicion of GCA, start glucocorticoid treatment immediately as it remains the only means to prevent irreversible visual loss and other catastrophic ischemic events.

2. Current EULAR (European League Against Rheumatism) guidelines:
   a. Initial dose of prednisolone/prednisone at 1 mg/kg body weight, not exceeding 60 mg/day, x 4 weeks, followed by gradual tapering.
   b. If severe ischemic complications, like visual loss or stroke, are present: 0.5-1g of IV pulse methylprednisolone x 3 days is recommended, followed by oral dosage/tapering.
   c. In the absence of relapsing disease, prednisolone/prednisone should reach 10-15 mg/d by month 3, and 5 mg/d by month 6 after diagnosis. Prednisolone/prednisone should then be maintained at 5 mg/d for at least 12 months.

3. Fever, headache, and PMR symptoms of GCA respond very rapidly to corticosteroid therapy resolving within hours to days.

4. Usually after 2-4 weeks, when all reversible signs/symptoms have resolved and ESR has returned to normal, corticosteroids should be gradually tapered. Avoid tapering to alternate day therapy since it increases risk of relapse.

5. 40-50% of patients relapse during steroid tapering or after steroid withdrawal. Main clinical manifestations of relapse are headaches, PMR, and constitutional symptoms. Chronic relapsing may require indefinite low-dose corticosteroid therapy.

6. Steroid sparing/Disease Modifying Anti-Rheumatic Drug (DMARD): Methotrexate at 10-15 mg/week subQ confers a modest benefit in reducing cumulative steroid dose and is indicated in relapsing disease.

7. Adverse effects of long term steroid therapy include posterior subcapsular cataract, infections, HTN, GI bleeding, DM, osteoporosis with bone fractures and avascular...
8. Duplex sonography and PET/CT screening are valid options given high prevalence of aortic and limb arteritis. Beyond the early phase of the disease, GCA may impact patient care given the probably increased incidence of aortic aneurysms.

SUGGESTED READING