Preventing blindness: Ultrasound in Giant cell arteritis

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DISCLOSURES

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- No relevant financial relationship reported
OUTLINE

• What is giant cell arteritis?
• Vision loss, stroke and other morbidities of giant cell arteritis
• Ultrasound in diagnosis of giant cell arteritis
• Collaborating to prevent vision loss and stroke: The fast track clinic
Giant cell arteritis

Normal artery

Giant cell arteritis

Granulomatous inflammation of the large and medium sized arteries
Demographics: Elderly patients of Northern European descent
Arteries affected by GCA
Symptoms of GCA/temporal arteritis (%)

- Headache 68
- Decreased temporal artery pulsation 46
- Jaw claudication 45
- Constitutional symptoms 40-50
- Joint pain and stiffness of shoulders, neck and hips (PMR) 39
- Neurologic (vertebrobasilar stroke) 15 (7)
- Visual loss 14

Calamia, KT Clin Rheum Dis 1980; 6:389
Giant cell arteritis of the temporal artery:
temporal arteritis
GCA: lingual artery involvement
Visual loss in GCA

Double vision (cranial nerves III, IV, VI)

Transient visual loss can precede permanent loss: Amaurosis fugax

Permanent visual loss due to thrombosis of the short posterior ciliary arteries to optic disc (anterior ischemic optic neuropathy-AION)
Rapid recognition of symptoms and treatment is essential in preventing visual loss

• Prevention of vision loss is imperative as there is almost never return of sight – only 4% have some improvement
• Vision loss in 1 or 2 eyes occurs in 15-35% of most series and usually at presentation before initiation of corticosteroid treatment
• Vision loss rare after 8 weeks of prednisone >40mg q d
Projected worldwide disease burden from GCA by 2050


- Giant cell arteritis most common vasculitis in persons > age 50
- Incident cases will increase due to aging population
- Literature review of publications indicating incidence rate from primary care data bases or hospital records
- By 2050:
  - 3 million people diagnosed with GCA in N. America, Europe and Oceania
  - 500,000 visually impaired
  - $70 billion estimated cumulative cost of visual impairment in US
Table 3. 1990 criteria for the classification of giant cell (temporal) arteritis (traditional format)*

<table>
<thead>
<tr>
<th>Criterion</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Age at disease onset ≥ 50 years</td>
<td>Development of symptoms or findings beginning at age 50 or older</td>
</tr>
<tr>
<td>2. New headache</td>
<td>New onset of or new type of localized pain in the head</td>
</tr>
<tr>
<td>3. Temporal artery abnormality</td>
<td>Temporal artery tenderness to palpation or decreased pulsation, unrelated to arteriosclerosis of cervical arteries</td>
</tr>
<tr>
<td>4. Elevated erythrocyte sedimentation rate</td>
<td>Erythrocyte sedimentation rate ≥50 mm/hour by the Westergren method</td>
</tr>
<tr>
<td>5. Abnormal artery biopsy</td>
<td>Biopsy specimen with artery showing vasculitis characterized by a predominance of mononuclear cell infiltration or granulomatous inflammation, usually with multinucleated giant cells</td>
</tr>
</tbody>
</table>

* For purposes of classification, a patient shall be said to have giant cell (temporal) arteritis if at least 3 of these 5 criteria are present. The presence of any 3 or more criteria yields a sensitivity of 93.5% and a specificity of 91.2%.
Difficulties with TA Biopsy

• False negatives: 10-20%, negative biopsy does not rule out GCA
• Sensitivity 30-40%
• 26% of patients with negative biopsy still were treated with prolonged corticosteroids
• Invasive

## Diagnostic tests for GCA

<table>
<thead>
<tr>
<th>Diagnostic test</th>
<th>TA biopsy</th>
<th>FDG-PET/CT</th>
<th>MRA (multi contrast HR of vessel wall)</th>
<th>color duplex ultrasound</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity/specificity (percent)</td>
<td>40/100</td>
<td>83/90</td>
<td>89/75</td>
<td>67-100/95 Temporal, Common Carotid and axillary arteries</td>
</tr>
<tr>
<td>Safety</td>
<td>Invasive, facial n. injury, infection</td>
<td>radiation exposure</td>
<td>contrast</td>
<td>N/A</td>
</tr>
<tr>
<td>Assessing disease activity</td>
<td>contralateral biopsy for recurrence?</td>
<td>in remission may remain positive</td>
<td>unknown</td>
<td>under study</td>
</tr>
<tr>
<td>Cost</td>
<td>$541</td>
<td>$5,185</td>
<td>$7,348</td>
<td>$388</td>
</tr>
<tr>
<td>Limitations</td>
<td>does not assess extra-temporal vessels</td>
<td>cannot assess temporal artery</td>
<td>limitations for MRI in general</td>
<td>aorta</td>
</tr>
</tbody>
</table>

Rapid recognition of disease and instigation of treatment: The Fast Track Clinic

• Similar to MI and CVA educational programs: public and MDs—GPs, FPs, IM, Ophthalmologists, Neurologists and Vascular Surgeons—must recognize typical and atypical presentations (without HA, fever, PMR, jaw claudication)

• Ongoing attempts in Europe to make diagnosis and begin Rx earlier

• Fast Track clinics in England, Norway, Poland and Germany

We should be doing the same in the United States
Fast Track Clinic & Education: Goals

• Educate public to recognize warning signs and symptoms
• Reduce time from onset of symptoms to seeing any provider
• Reduce time from this provider to diagnosis and initiation of treatment: corticosteroids and IL-6 inhibitor

FTC: Patients seen within 24 hours of referral, with initial telephone advice for starting corticosteroids
**Suggestion for BSR Guidelines**

**suspected GCA‡**
- perform ultrasound *

- low clinical probability
  - US -
  - GCA ruled out

  - US +/±
  - perform biopsy

- intermediate clinical probability
  - US -/±
  - perform biopsy

  - US +
  - GCA confirmed

- high clinical probability
  - US -/±
  - perform biopsy

  - US +
  - GCA confirmed

*Consider PET-CT or other in unclear situation / severe constitutional symptoms

Duffner C. Southend GCA / PMR / LVV Workshop March 2016
Traditional practice vs Fast track clinic

**Treat and biopsy temporal artery**
- Postpone diagnosis
- Involve multiple health care providers
- Surgery with scar
- Increase cost
- When histology returns normal?

**Do ultrasound and decide**
- Rapid diagnosis
- Minimal number of health care providers
- Decrease cost
- Avoid weeks of steroid use in unaffected patients
- Pick up involvement of multiple arteries

Wolfgang Schmidt, MD, Immanuel Krankenhaus, Berlin. Personal communication.
Fast Track Clinics
Appointment within 24 hrs: Clinic & Ultrasound

Irreversible sight loss:
37% → 9%

Irreversible sight loss: 19% → 2%

Inpatient days: 3.6 → 0.6 days


Axillary Artery Ultrasound

Intima – media complex

normal: anechoic

vasculitis: hypoechoic

< 1.0 mm

≥ 1.0 mm

definite vasculitis: ≥ 1.5 mm
GCA Axillary Artery
Giant cell arteritis: temporal artery with halo
Compression sign

Normal temporal artery

GCA temporal artery
## Cut-off Values for Each Artery


<table>
<thead>
<tr>
<th>Artery</th>
<th>N</th>
<th>IMT in mm</th>
<th>Cut-off in mm</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Correctly classified</th>
</tr>
</thead>
</table>
| Common superficial temporal artery | 40 | C: r. 0.22 (SD 0.03)  
L: 0.23 (SD 0.04)  
P: r. 0.23 (SD 0.04)  
L: 0.25 (SD 0.04) | r. 0.42  
L: 0.45 | 100 % | 100 % | 100 % | 100 % |
| Frontal branch                | 34 | C: r. 0.19 (SD 0.03)  
L: 0.19 (SD 0.04)  
P: r. 0.53 (SD 0.19)  
L: 0.55 (SD 0.18) | r. 0.35  
L: 0.34 | 100 % | 100 % | 100 % | 100 % |
| Parietal branch               | 38 | C: r. 0.19 (SD 0.03)  
L: 0.20 (SD 0.03)  
P: r. 0.51 (SD 0.18)  
L: 0.48 (SD 0.16) | r. 0.32  
L: 0.29 | 100 % | 100 % | 100 % | 100 % |
| Facial artery                 | 15 | C: r. 0.24 (SD 0.03)  
L: 0.23 (SD 0.05)  
P: r. 0.55 (SD 0.19)  
L: 0.51 (SD 0.19) | r. 0.37  
L: 0.40 | 92.3 % | 81.8 % | 97.5 % | 94.1 % |
| Axillary artery               | 40 | C: r. 0.59 (SD 0.10)  
L: 0.59 (SD 0.10)  
P: r. 1.80 (SD 0.41)  
L: 1.62 (SD 0.39) | r. 1.1  
L: 1.0 | 100 % | 100 % | 100 % | 100 % |
Technical challenges

• Temporal arteries IMT 0.3-0.4mm
• Easy to over or under fill vessel this small with color either creating or obscuring the halo.
• Distal branch assessment should be performed with caution as slow vessel flow may cause insufficient lumen visualization and reveal false positive halo sign. Compression sign is helpful in assessing for halo

However:

• Compression sign can be helpful in confirming halo
• Higher frequency probes (22-70mHz) commercially available
• Carotid, axillary, subclavian exams do not require color for measurement of IMT
Increasing diagnostic accuracy

• Examine entire artery: Halo sign or increase in IMT may be present only in some branches or appear segmentally

• Examine early:

  Halo disappears quickly after treatment started: 16 days (7-86 days)

  Sensitivity of color duplex US temporal artery 87% → 50% after 4 days of steroids

Schmidt, W NEJM 1997
Hauenstein, C Rheumatology 2012
Summary

• Giant cell arteritis is common and incidence will increase as population ages

• Prompt diagnosis and treatment will prevent blindness and CNS morbidity due to GCA

• Educating the public and medical providers to recognize signs and symptoms of GCA, then referral to fast track clinics will facilitate timely treatment of GCA

• Vascular ultrasound has been an essential part of rapid diagnosis GCA in Europe. Adoption of the use of ultrasound in this way will benefit our patients as well.