

Grand Rounds



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10/15/10

History

- CC: Headache and double vision
- HPI: 90 y/o WM with a 3 day history of a left sided headache and a 2 day history of binocular, vertical diplopia. He denied blurry vision, but did say he saw “zig zags” with his left eye during this time period
- POHx: Pseudophakia OU
- PMH: HTN, dyslipidemia, depression

History

- Medications: Losartan, metoprolol, simvastatin
- Allergies: Lisinopril, fluoxetine
- ROS: Positive for fatigue and low grade fevers. Negative for weight loss, jaw claudication, night sweats

Exam

VA(sc): 20/20 OU

Pupils: 3 → 2 mm with no APD

External exam: left sided scalp tenderness

EOM: Right hypertropia, worse in left gaze and with right head tilt

SLE/DFE: PCIOL OU, no optic nerve abnormalities

Assessment

- Assessment: Acute cranial nerve 4 palsy
- DDX:
 - Giant cell arteritis
 - Ischemic (nonarteritic)
 - Tumor with compression
- Plan:
 - ESR → 82 mm/hr
 - CT head → WNL
 - IV steroid bolus followed by 60mg/day PO
 - TEMPORAL ARTERY BIOPSY!

Course

- A left temporal artery biopsy was performed 3 days after presentation:
 - Small focus of granulomatous inflammation associated with elastic tissue degeneration (granulomatous arteritis)
 - Severe subintimal sclerosis with almost total occlusion of the arterial lumen

Course

- The patient's headache and scalp tenderness resolved within 24-48 hours of initiating steroids
- The 4th nerve palsy resolved sometime between day 8 and day 17 of treatment
- His vision remained 20/20 OU, though he had a small APD OD

Giant Cell Arteritis

- Systemic inflammatory vasculitis affective medium and large arteries.
- The most commonly involved arteries include the temporal, posterior ciliary, ophthalmic, and vertebral, though almost any artery can be affected.

Symptoms

- Visual symptoms include transient or persistent blurring of vision in addition to diplopia
 - 50-60% of these cases result in permanent vision loss
- Jaw claudication, scalp tenderness, headache, fevers, anorexia, weight loss, fatigue, depression, neuropathy

Signs

- So what might we see clinically as ophthalmologists
 - AION, CRAO, BRAO, CN palsy



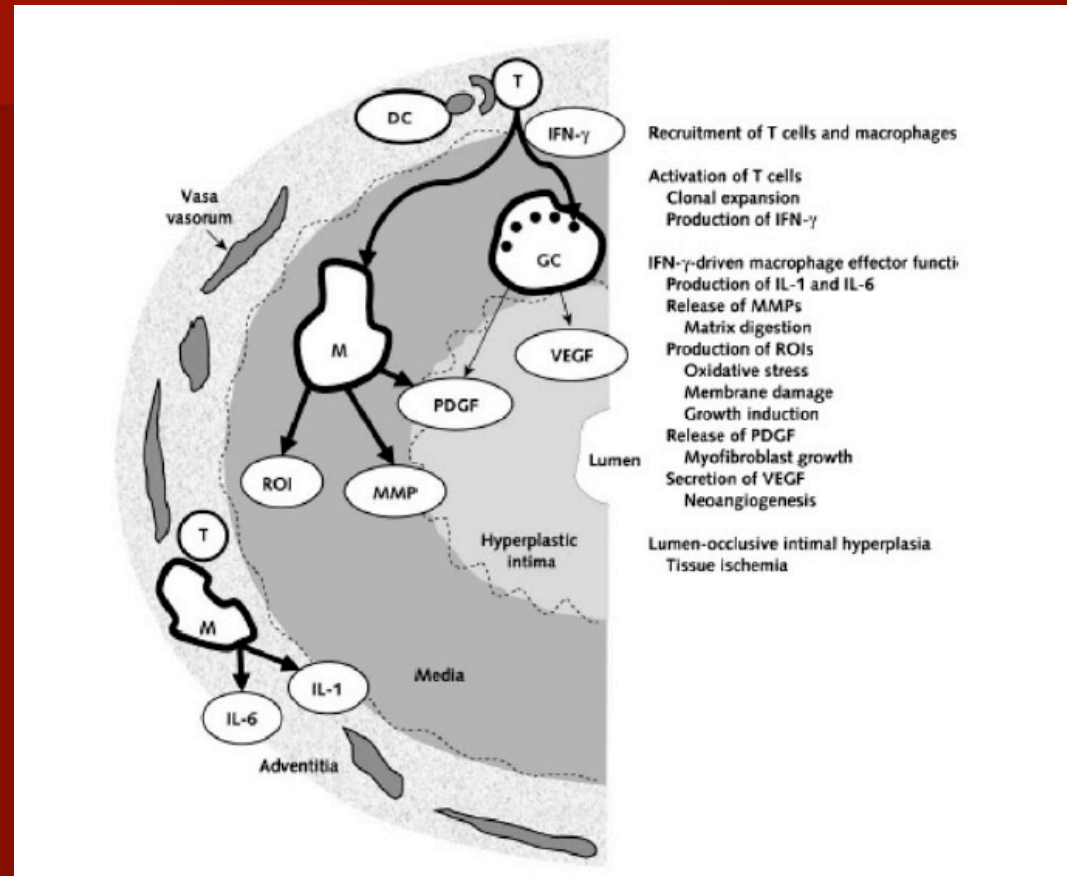
Systemic Findings

- The aortic arch is commonly involved and can result in aortic aneurysms, aortic dissection, and aortic regurgitation
- Branches from the aortic artery results in decreased upper extremity pulses, arm or leg claudication, TIAs, coronary ischemia, and abdominal angina

Pathophysiology

- Autoimmune disease of unknown etiology
- Dendritic cells native to the vessel adventitia function as antigen presenting cells for T lymphocytes
- This leads to macrophage mediated damage to the vessels
 - Reactive oxygen and nitrogen intermediates damage endothelium
 - Metalloproteinases disrupt the internal elastic lamina allowing migratory fibroblasts to access the intimal layer
 - VEGF secretion promotes vascularization of the normally avascular intima
 - **OCCLUSION**

Pathophysiology



- Schematic demonstrating the immunology of GCA

Pathophysiology

- In addition to focal inflammation, patients with GCA develop systemic inflammation resulting in constitutional symptoms
- These patients have elevated levels of circulating IL-1, IL-6 (from macrophages and monocytes)
- This helps to explain the relationship between GCA and polymyalgia rheumatica

Diagnosis

- Clinical suspicion based on history and physical
- Elevated inflammatory markers (ESR, CRP, platelets)
- Imaging with PET/CT can demonstrate acute inflammation within the aorta and other larger arteries
- The gold standard is temporal artery biopsy
 - At least 1cm is recommended as there are frequently areas of no inflammation between involved areas
 - Initiate corticosteroid therapy

Diagnosis

- The gold standard is temporal artery biopsy
 - At least 1cm is recommended as there are frequently areas of no inflammation between involved areas
 - Initiate corticosteroid therapy prior to biopsy
 - The biopsy can be performed 1-2 weeks after initiating therapy

Diagnosis



- H&E stain showing intimal hyperplasia, inflammation, and luminal narrowing

Treatment

- The mainstay of treatment continues to be corticosteroids
 - Initial bolus of IV steroid may be useful
 - Daily maintenance 1mg/kg/day
 - Very slow taper
- Corticosteroids suppress IL-1 and IL-6 production, but do not significantly alter IFN- γ production
- Th1 vs. Th17 (immuno4)

Treatment

- Corticosteroids suppress IL-1 and IL-6 production, but do not significantly alter IFN- γ production
- Corticosteroids selectively suppress Th17 cells without suppressing Th1 cells → smoldering arteritis continues even after long term treatment.
- Targeting IFN- γ (fontolizumab) or IL-12 (SC ABT-874) may be beneficial

Treatment

- Sirolimus – anti IL2
- Infliximab, etanercept – TNFa
- Methotrexate – antimetabolite messes with folate metabolism and therefore DNA synthesis
- Cyclosporin – t cell inhibitor
- Azathioprine – DNA synthase inhibitor, purine analog
- Cyclophosphamide – alkylating agent, cross links DNA therefore kills cells

Treatment

- Other immunomodulatory drugs have been tried with limited success
 - **Methotrexate** appears to provide a modest benefit in terms of decreasing the steroid dose or discontinuing steroids altogether
 - **Azathioprine** has a statistically, but not clinically significant steroid sparing effect
 - **Infliximab, cyclosporine, and others** appear to be ineffective
- Low dose aspirin decreases the risk of cardiovascular and cerebrovascular events as well as the rate of vision loss in patients actively losing vision

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