



# A headache for us all...

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# CASE 1

## – MR X

### 73M

- 2 wks of exertional SOB & chest pains with a dry cough & lethargy -?angina
  - Vague history of sweats/subjective fevers & weight loss
  - COVID swab negative x2 and CTPA - NAD
- PMHx:
  - Aortic stenosis - AVR 2015
  - COPD – Budesonide/formoterol
  - Hypothyroid – thyroxine
  - HTN – perindopril/amlodipine
  - BPH – previous TURP
  - Previous R) THR
  - Severe OSA – on CPAP
  - Ex-smoker – 15 PYH
- Investigations
  - Normal BNP, serial troponins, CTPA NAD; CRP 34, afebrile
  - Iron deficiency anaemia
  - EST : symptomatically & electrically positive

# CASE 1

## – MR X

### 73M

- 3<sup>rd</sup> day of admission
  - 3 wks of unilateral headaches, jaw claudication & shoulder pains
  - O/E: mild B/L temporal tenderness
  - ESR – 80
- Rheum opinion – temporal artery US + hold off on pred given atypical history + ongoing Ix for IHD
- US: 1mm concentric wall thickening of the R) frontal branch of temporal artery - ?equivocal
- Commenced prednisone 50mg daily
- Urgent outpatient TAB

# Histopathology Report

## MICROSCOPIC

Right temporal artery biopsy: The sections show a muscular artery shows been transected into four pieces. In one of the pieces, chronic inflammatory cells are seen within the media along with partial disruption of the elastic lamina. One possible multinucleated giant cell is seen in the examined levels. There is an associated area of intimal hyperplasia adjacent to the area of inflammation. The three remaining pieces have a normal appearance. Although focal, the appearance would be consistent with giant cell arteritis.

This case has been shown to Dr S Pillai who agrees with the above assessment.

## SUMMARY

Right temporal artery biopsy: Consistent with giant cell arteritis.

CASE 1  
– MR X  
73M

Rheum OPD – pt self weaned prednisone to 25mg daily → recurrence of jaw claudication  
CRP <5, ESR 15; increased back to 40mg with weaning plan

# CASE 2 – MRS Y 75F

## Recurrent presentations:

- 30<sup>th</sup> May (ED 1): back/shoulder pain and blurry vision
  - No headaches
  - ESR 67, CRP 10 – was for Ophthal & Rheum review, but discharged against medical advice; given pred 60mg daily cover
- 10<sup>th</sup> July (ED 2): alternating left and right temporal headache
  - ESR 95 + CRP 29 – self weaned pred; d/c from ED with follow-up
- 20<sup>th</sup> August (ED 3): ongoing vague headaches, shoulder and hip girdle pain & jaw discomfort
  - Had recommenced pred 10mg daily; ESR 77, CRP 16
  - Seen by Rheum – pred increased to 25mg daily
  - For PET scan & OPD TAB

CASE 2  
– MRS Y  
75F

PET SCAN: No FDG-PET/CT evidence of GCA or PMR. No FDG avid lesions demonstrated elsewhere within the body.

26<sup>th</sup> August (ED 4): blurry vision – discharged as had close follow-up and inflammatory markers downtrending

3<sup>rd</sup> September (Rheum OPD): asymptomatic – though had again self weaned prednisone to 10mg – ESR 58, CRP 4.4

# Histopathology Report

## MICROSCOPIC

Right temporal artery biopsy: The sections show a medium sized artery with transmural inflammatory cell infiltrate comprising lymphocytes, plasma cells and occasional giant cells. Fragmentation of elastic fibres in the vessel wall is seen.

## SUMMARY

Right temporal artery biopsy: Temporal (giant cell) arteritis.

Continues on high dose pred

CASE 2  
— MRS Y  
75F

# CASE 3

## MRS Z - 76F

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- Headaches & facial pain, malaise & sore throat
  - pain on chewing and swallowing food and a swollen tongue sensation
  - Nil visual changes; shoulder stiffness for same period of time
  - Some weight loss and night sweats; nil fevers
- PMHx:
  - HTN – on Ramipril
  - Hypothyroidism – on thyroxine
  - Previous superficial melanoma
  - Bilateral cataracts
  - Fuch’s corneal dystrophy
- O/E:
  - TMJ tenderness; nil temporal artery tenderness, not pulsatile
  - Oral white plaques over tongue and hard palate with ulcerations



# CASE 3

## MRS Z - 76F

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- Bloods
  - CRP 123, ESR 82
  - ALP 147, GGT 91, ALT 38
- Admitted under GM for further investigation and Gastro consult with impression of ?oesophageal candidiasis
  - Endoscopy – negative
- Unclear cause and was discharged with CRP 101 with GP to monitor

# CASE 3

## MRS Z - 76F

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- 2 months later referred into ED with complete R) eye vision loss..
  - CRP 80, ESR 82
- Onset 3 weeks prior to presentation
- Reviewed by Rheum & Ophthal
  - Right arteritic optic neuropathy with ~95% vision loss
- Commenced IV methylprednisolone
- Urgent TAB

# CASE 3

## MRS Z - 76F

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## Histopathology Report

### **MICROSCOPIC**

**Right temporal artery biopsy:** The sections show a small muscular artery and confirm changes of giant cell arteritis (GCA). There is histiocytic infiltration of the wall accompanied by elastic lamina fragmentation, thrombosis and recanalisation. No aneurysm formation is seen.

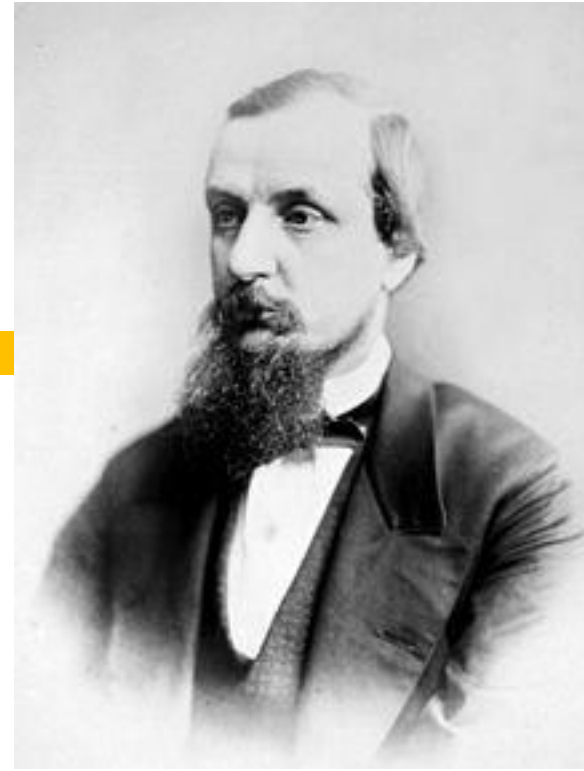
### **SUMMARY**

**Right temporal artery biopsy:** GCA with thrombosis.

Despite high dose prednisone - nil recovery of vision

# GCA – what is it?

- Chronic inflammatory disease involving large/medium sized arteries
- Pathogenesis: initial triggering event in a genetically predisposed person with risk factors
- Inflammatory vascular remodelling → intimal hyperplasia and lumen occlusion → stenosis and aneurysms - the source of the ischaemic complications of the disease
- Overall lifetime risk is 1.0% in women, and 0.5% in men



# GCA Classification Criteria

The American College of Rheumatology 1990 GCA Classification Criteria.

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## GCA Classification Criteria

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- (1) Age at onset  $\geq 50$  years     **80% of patients >70 years**

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- (2) A new headache

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- (3) Temporal artery abnormality such as tenderness to palpation or decreased pulsation     **Surrogate: scalp tenderness**

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- (4) Erythrocyte sedimentation rate  $\geq 50$  mm/h

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- (5) Abnormal artery biopsy showing vasculitis with mononuclear cell or granulomatous inflammation, usually with giant cells

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At least three of the five parameters must be present, which yields a sensitivity of 93% and a specificity of 91%, in relation to controls with other vasculitides.

# GCA – clinical features

- 2/3 of patients with GCA present with headache
  - Generally temporal, but can occur in other locations
  - Resistant to standard analgesia
- 50% of patients report scalp dysaesthesia
- ~50% report jaw claudication
- 20% of patients experience partial or total visual loss
- 10% of patients develop amaurosis fugax – 50% progress to blindness
- 50% have systemic symptoms (fever, fatigue, weight loss)
  - 15% present only with systemic symptoms
- 10% present with cough



# Signs & Symptoms



**Table 2.** Comparison of the sensitivity and specificity of potential criteria variables for giant cell (temporal) arteritis\*

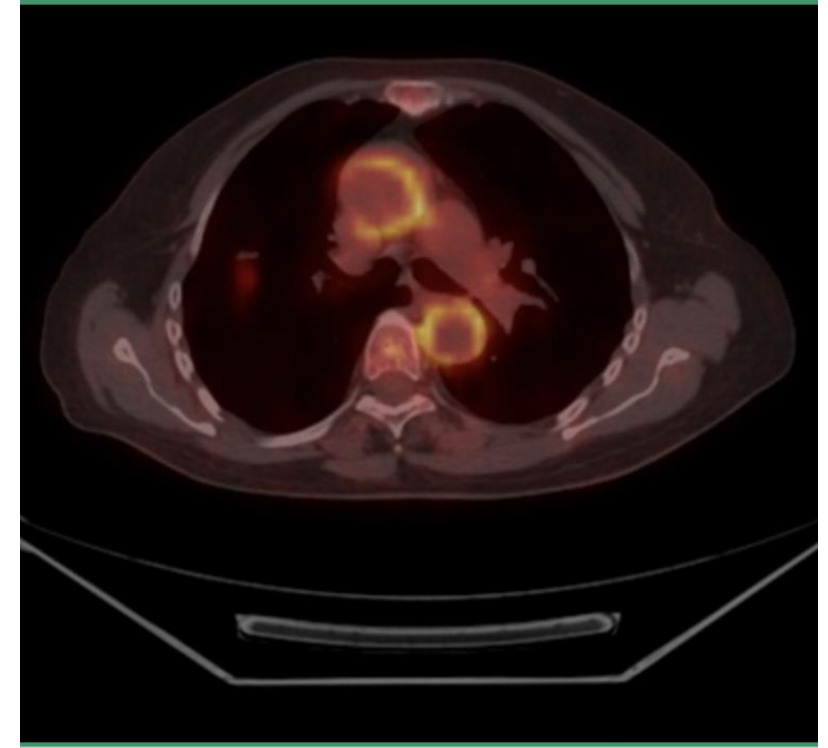
Criterion	No. of patients (n = 214)	No. of controls (n = 593)	Sensitivity (%)	Specificity (%)
<b>History</b>				
1. Age at disease onset $\geq 50$ years <sup>†‡§</sup>	213	588	98.6	63.8
2. Headache, new, localized <sup>†‡§</sup>	214	590	64.5	81.9
3. Jaw claudication	213	579	38.5	97.9
4. Tongue claudication	213	578	2.8	99.8
5. Claudication on deglutition	212	577	4.2	99.0
6. Claudication, variables 3–5 <sup>†§</sup>	212	576	40.6	97.6
7. AM stiffness neck/torso	211	586	50.2	86.5
8. AM stiffness shoulders/arms	210	586	52.9	77.5
9. AM stiffness hips/thighs	211	586	46.9	79.7
10. Polymyalgia rheumatica, variables 7–9 (2 out of 3) <sup>†</sup>	210	585	52.9	79.3
11. Diplopia	213	587	11.3	93.9
<b>Physical</b>				
12. Ischemic optic neuritis	212	580	7.5	98.4
13. Amaurosis fugax	214	588	11.2	95.7
14. Partial unilateral loss of vision	213	587	4.2	99.0
15. Complete unilateral loss of vision	212	585	3.3	99.7
16. Partial bilateral loss of vision	214	584	2.3	99.1
17. Optic atrophy	212	586	4.7	99.0
18. Visual abnormality, variables 11–17 <sup>†</sup>	210	573	27.6	88.8
19. Right TA tenderness	212	495	23.1	99.6
20. Decreased right TA pulse	210	477	35.2	97.9
21. Left TA tenderness	211	494	21.3	99.2
22. Decreased left TA pulse	209	476	28.7	97.9
23. TA abnormality, variables 19–22 <sup>†‡§</sup>	211	473	57.3	96.8
24. Scalp tenderness	212	584	40.6	97.9
25. Scalp nodules	212	585	13.7	99.5
26. Scalp tenderness or nodules <sup>†§</sup>	212	581	43.9	97.4



Aortitis in GCA on MR angiography



FDG PET scan of GCA patient with aortic involvement



# Large vessel involvement phenotype

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1/5 patients develop large vessel involvement



# Why we worry so much

- Delayed treatment = irreversible vision loss
- Vision loss in fellow eye
  - 30% in one day
- Despite correct treatment
  - Up to 30% further deterioration in same eye
  - Up to 10% lose vision in fellow eye
- GCA can be fatal if not treated promptly
  - Posterior circulation strokes, myocardial ischemia etc





# Pearls from Hayreh

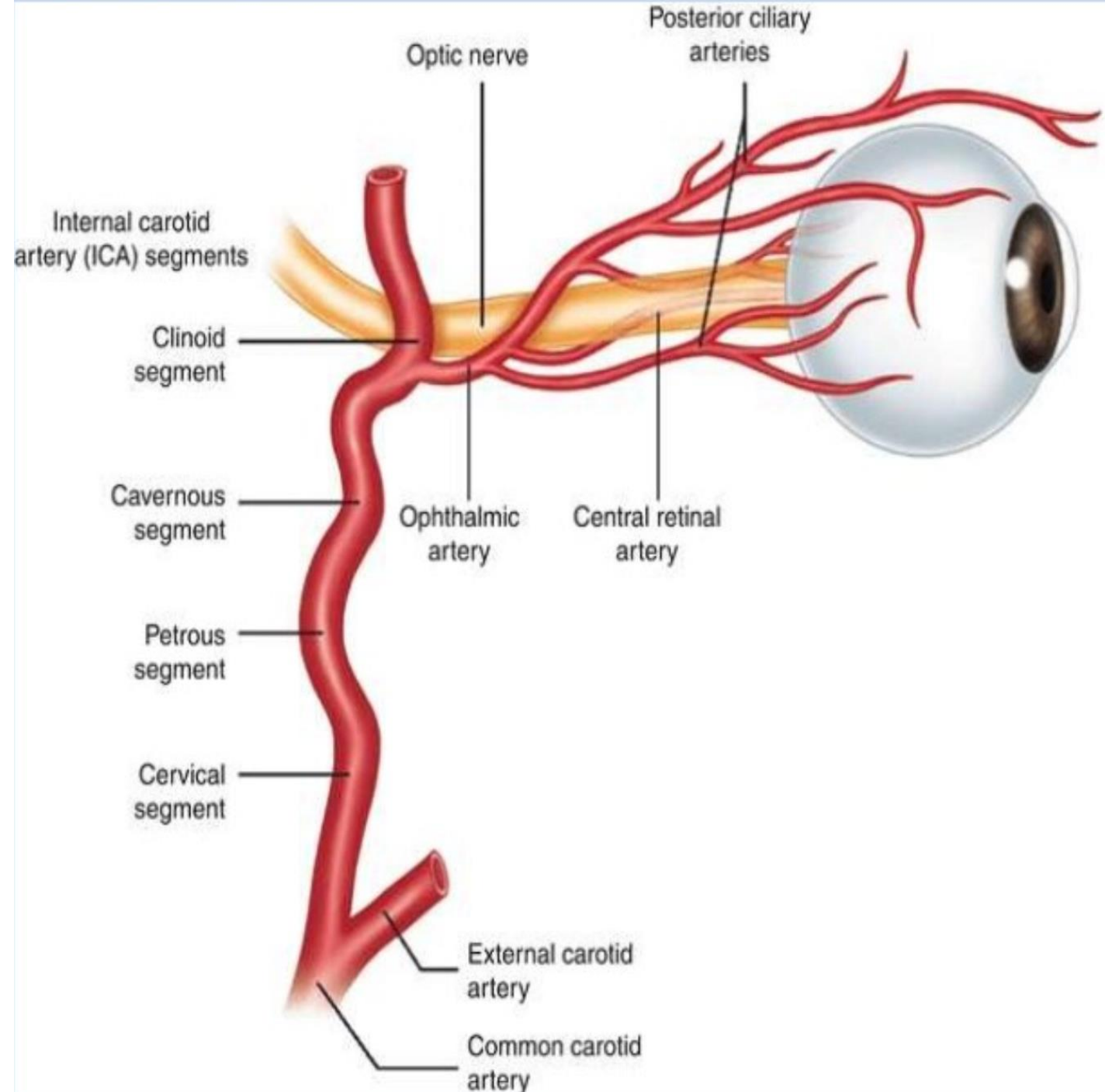
1. Normal ESR does not exclude GCA
2. CRP – sensitivity 100%, specificity 80%  
- not influenced by age/gender
3. Platelets – sensitivity 60%, specificity 97%
4. Vision loss with positive biopsy  
– 21% had NO systemic symptoms of GCA

Hayreh SS, Zimmerman B. Management of giant cell arteritis. Our 27-year clinical study: new light on old controversies. *Ophthalmologica*. 2003 Jul-Aug;217(4):239-59. doi: 10.1159/000070631. PMID: 12792130.

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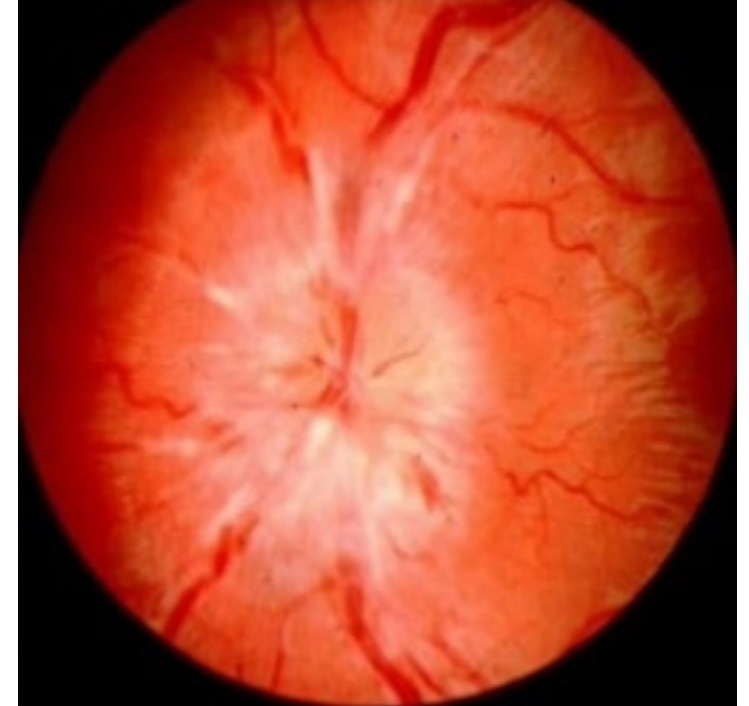
# Anatomy

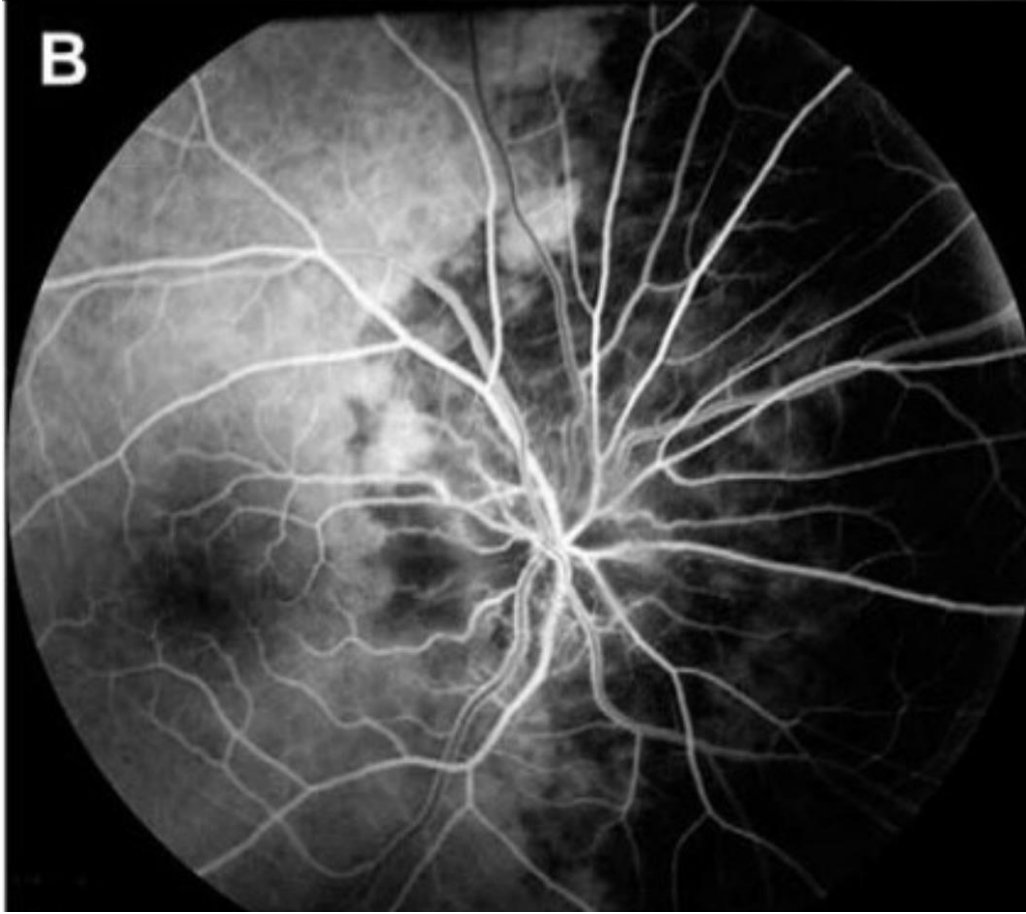
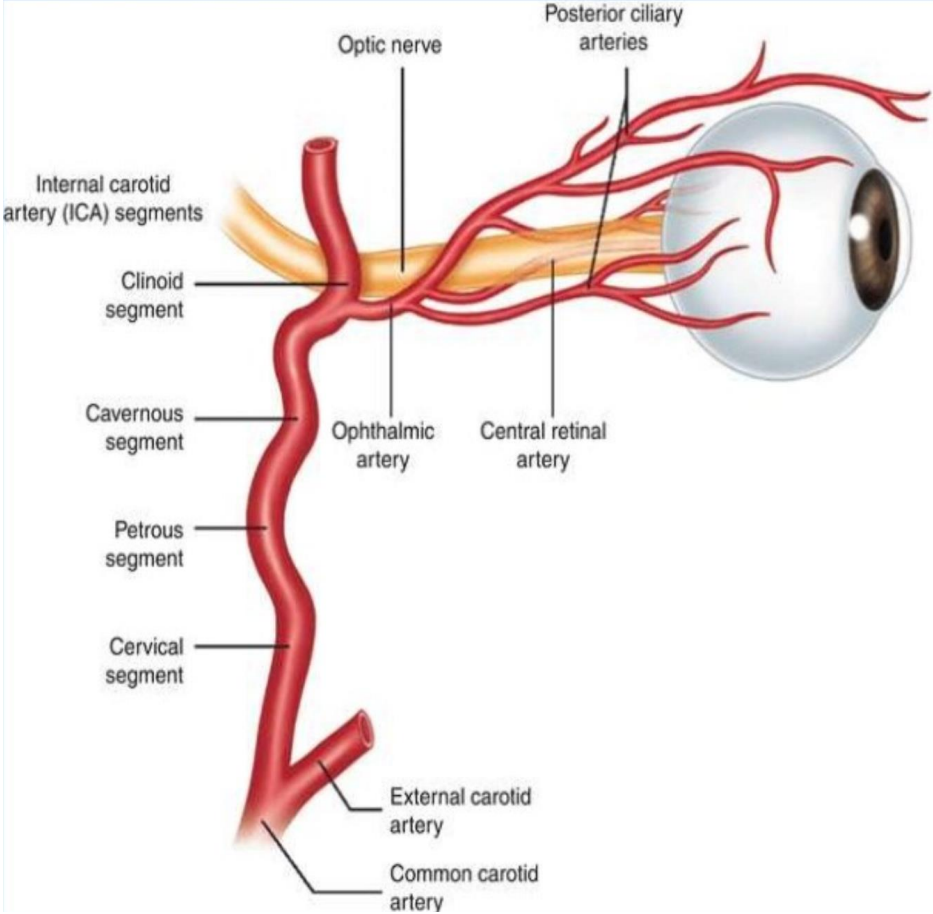
- Posterior ciliary arteries of the eye are affected → optic nerve infarction with subsequent Anterior Ischemic Optic Neuropathy (AION)
- Occlusion of the posterior ciliary arteries may, in addition to arteritic AION, cause patches of choroidal infarcts



# Ocular Signs of GCA

- VA: profound unilateral reduction
  - 60% worse than 6/60
- RAPD: positive
- Visual Fields: extensive
- Colour vision: dyschromatopsia unilateral
- Fundoscopy
  - Optic nerve swollen, pale/hyperemic
  - Normal retinal vasculature
- ? Fluorescein fundus angiogram
  - Choroidal ischemia





# Radiology tests to consider:

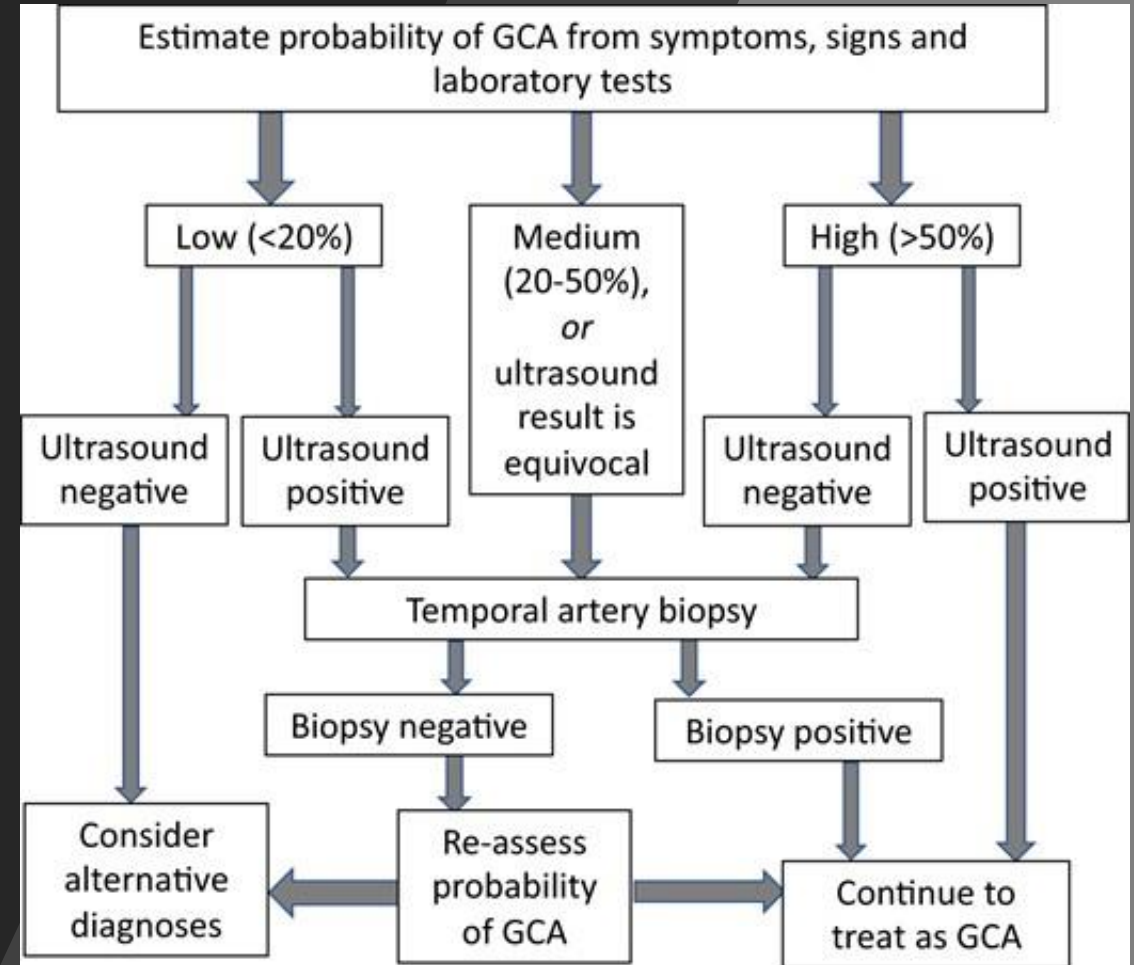
- US
- CT
- MR
- Nuclear Medicine – PET/CT



# What test answers which question?

- US – screening of low or moderate clinical suspicion from history, CRP and ESR
- Halo sign – disappears post 2-4 weeks of steroids

**Negative study does not exclude GCA or temporal artery involvement of GCA**



# What test answers which question?

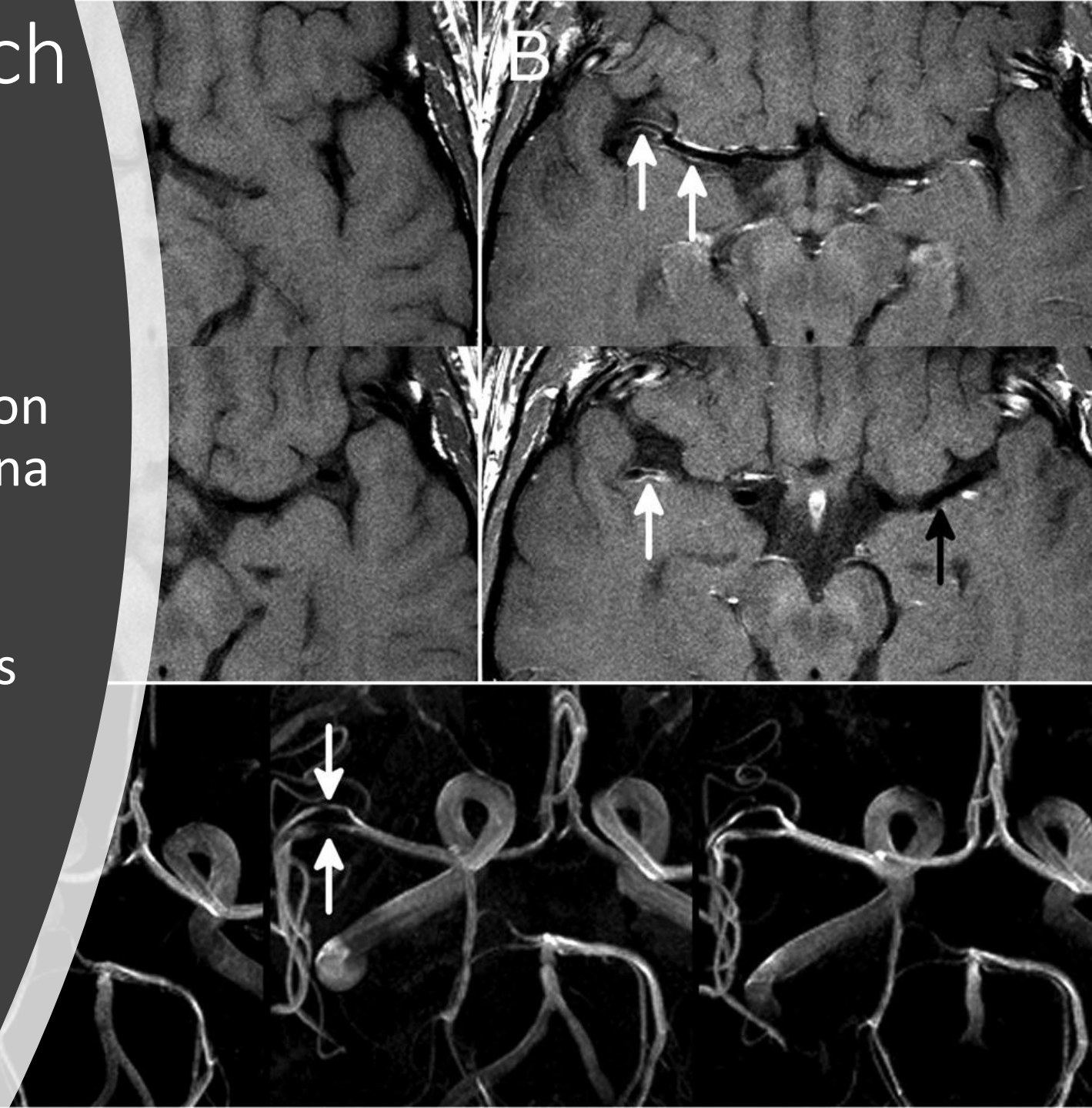
- CT arterial phase
- Confirmed vasculitis looking for aortic or other large vessel involvement
- Acute ophthalmic sx - ?embolic phenomena ?occluded ICA
- Not for temporal artery assessment





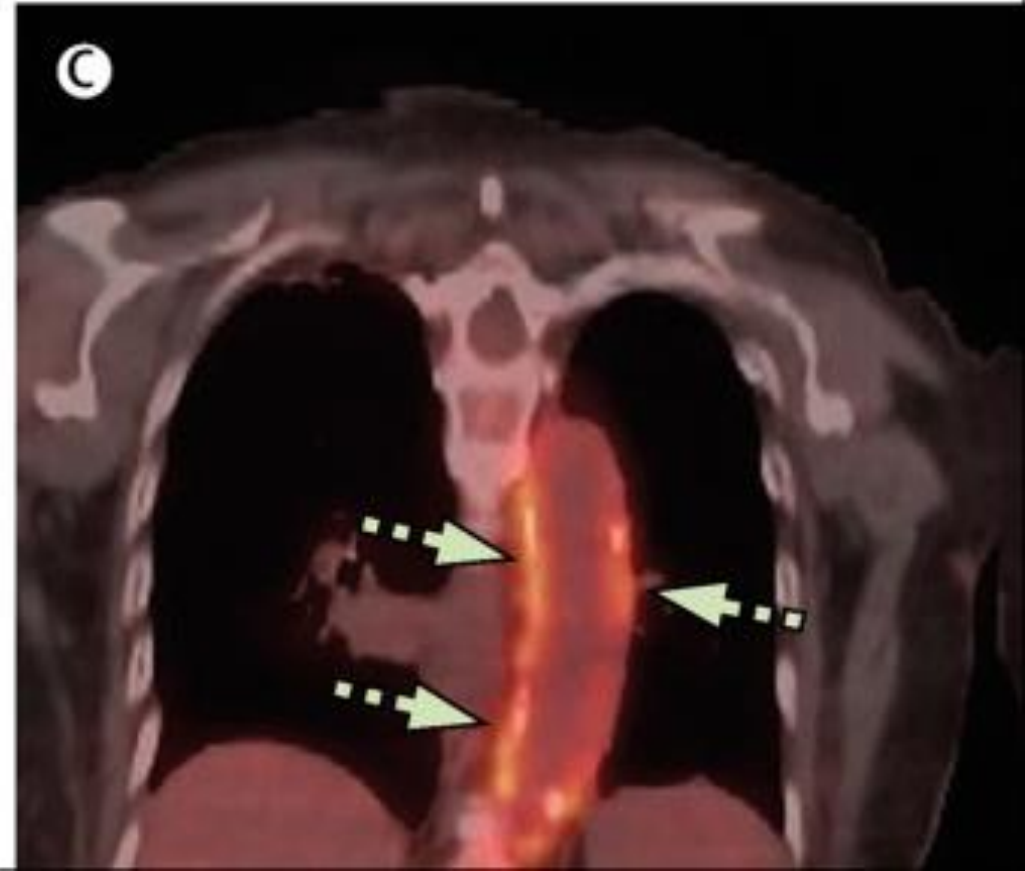
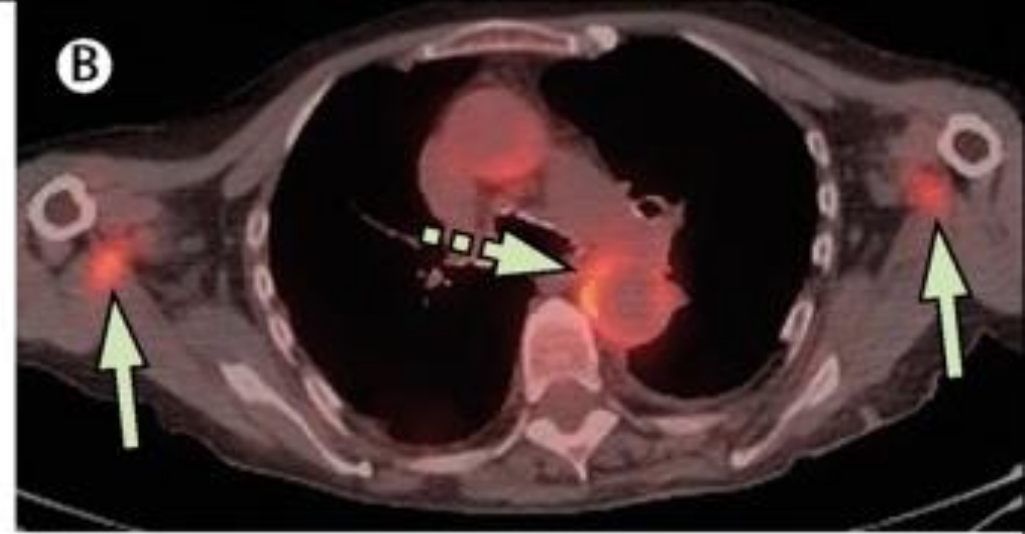
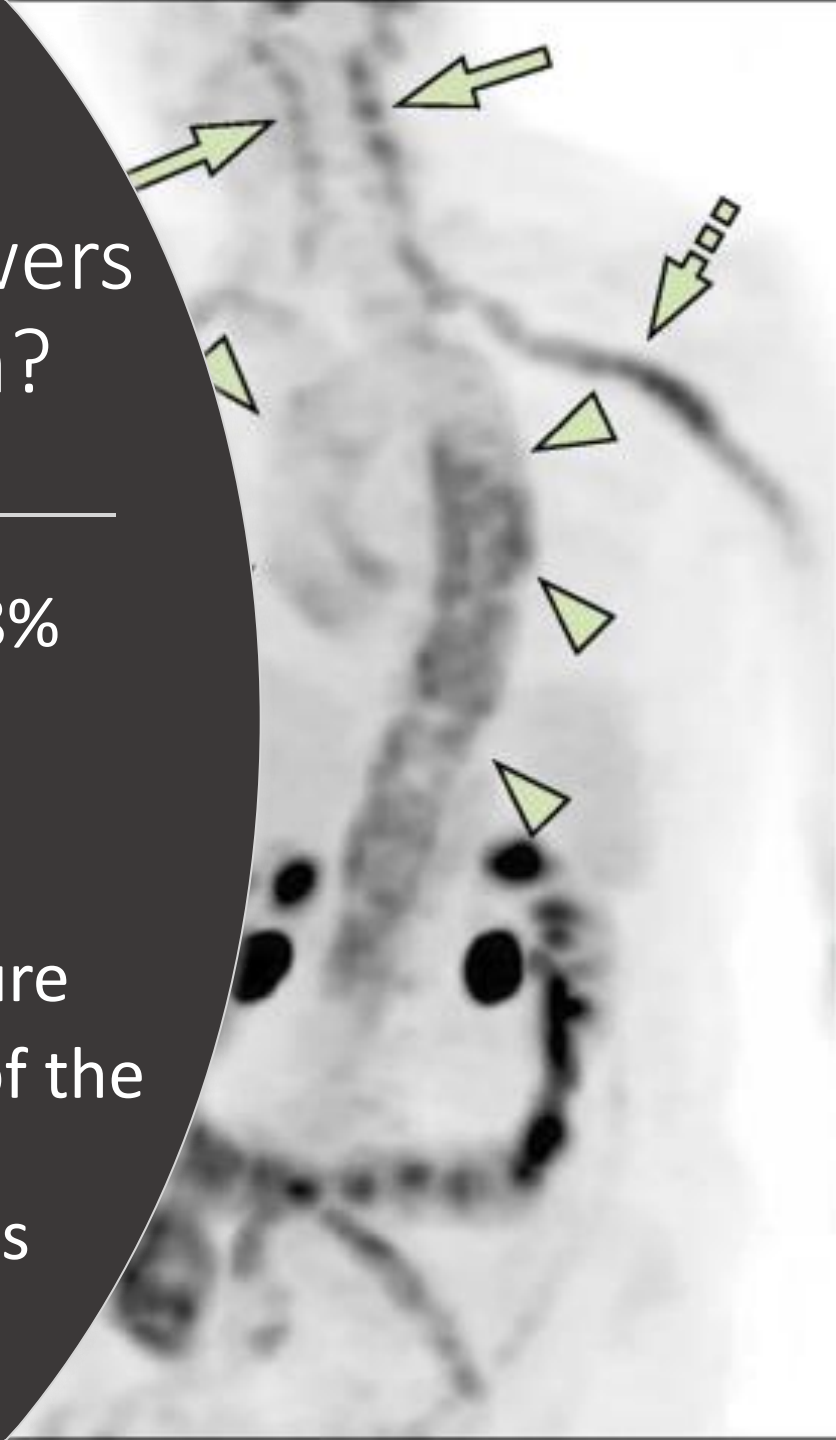
# What test answers which question?

- MR – MR predominantly focused on vessel wall and embolic phenomena
- Looking for intracranial vessel involvement or embolic infarctions



## What test answers which question?

- PET/CT –NPV of 98%
- Define systemic involvement
- Will show ACTIVE inflamed vasculature
- Poor assessment of the temporal or intracranial arteries







Temporal  
Arteritis in  
Pathology



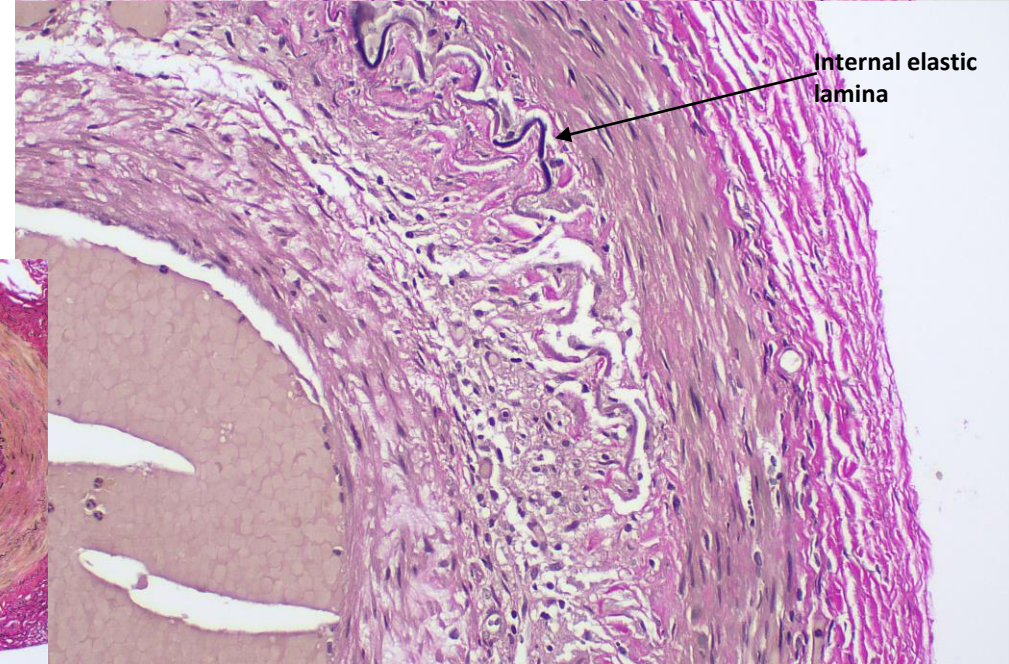
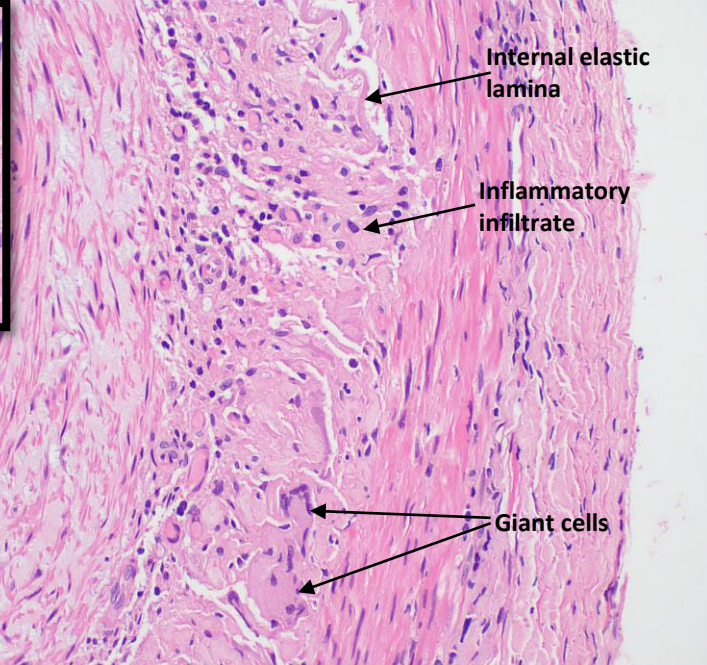
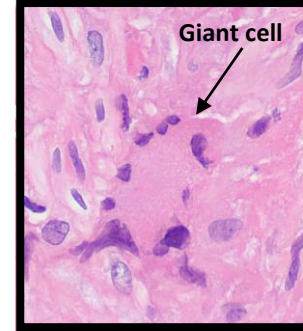
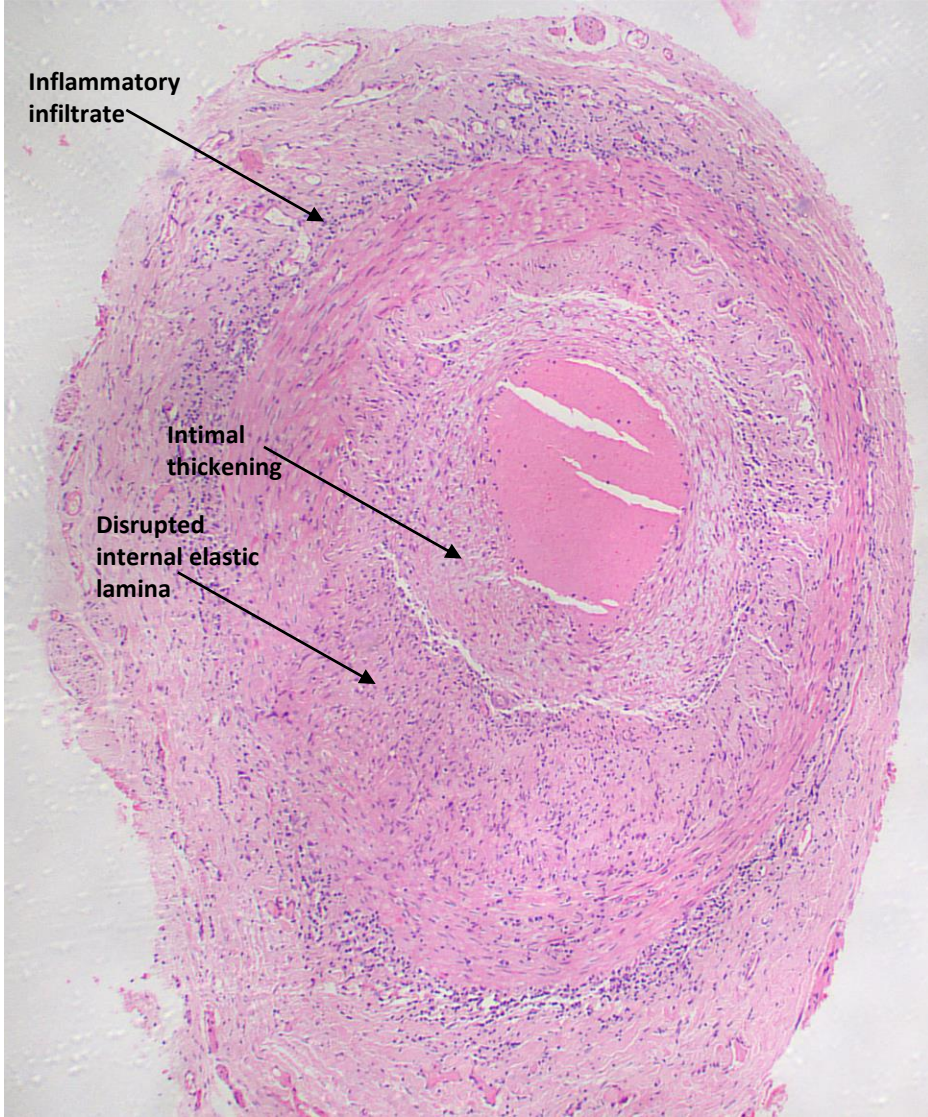
# When we send an artery sample...

- Scientist transversely sections into 2mm segments
  - If “?temporal arteritis” is somewhere on the request form, a special elastin stain is automatically ordered
- Processed for 8-12 hours to replace water in the specimen with paraffin
- Embedded in wax
- Thin sections cut (0.3 microns) and put onto slides
- Stained for H&E and VVG



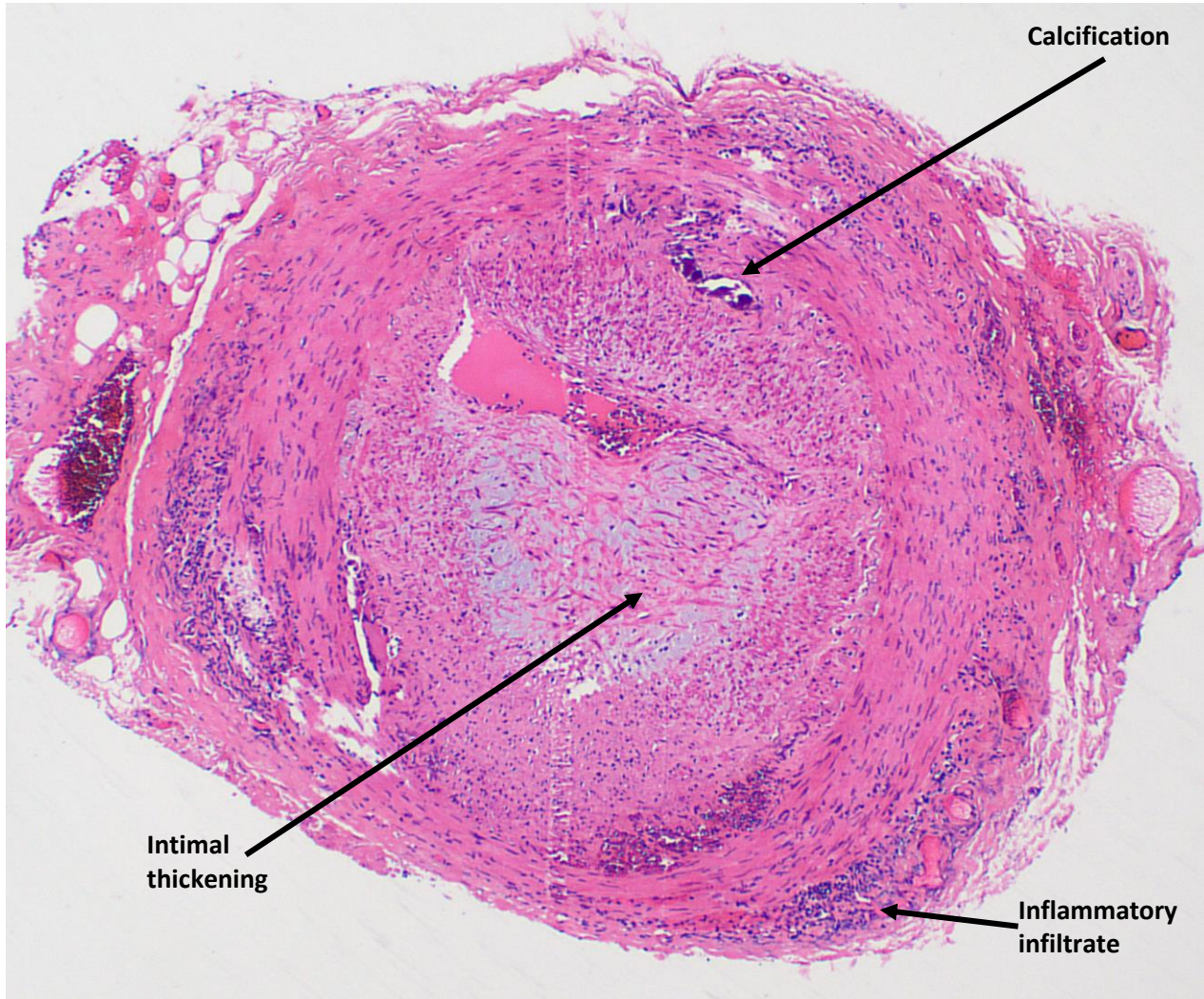


# Classical Features



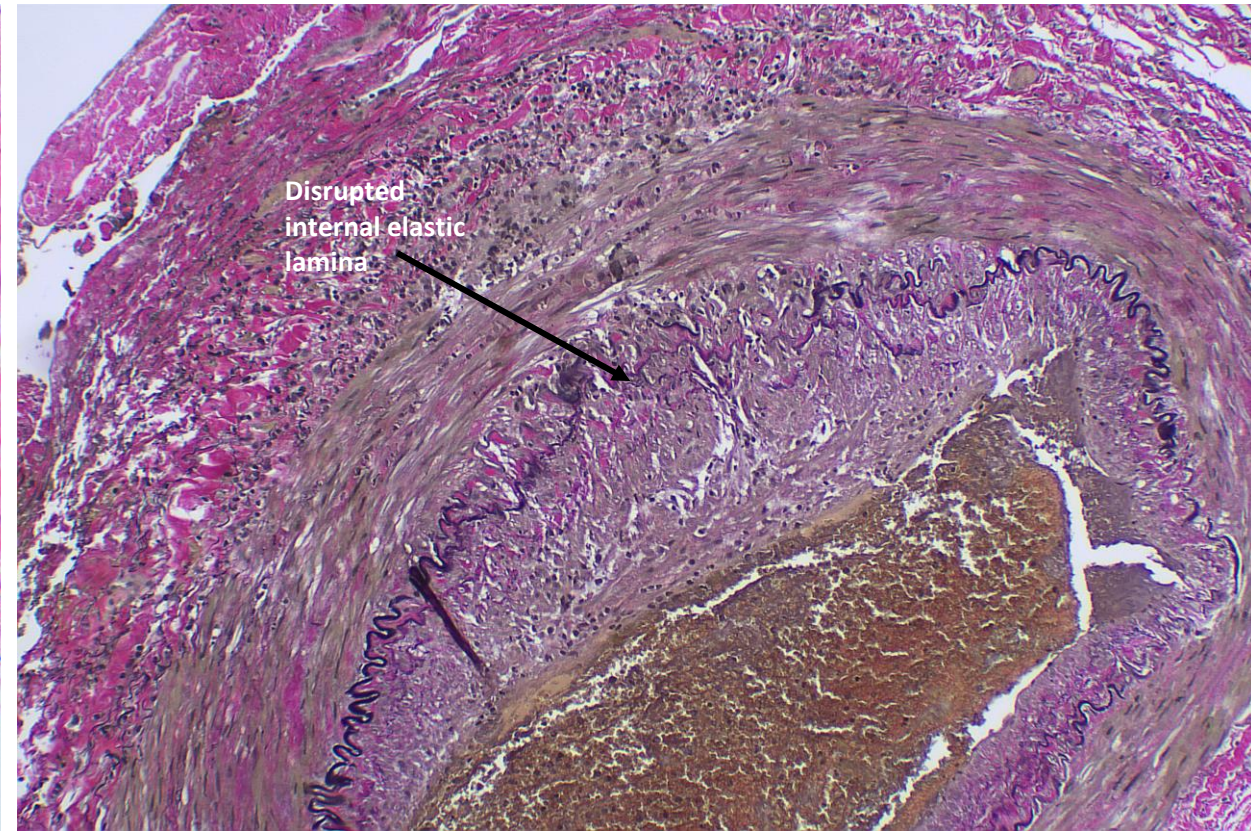
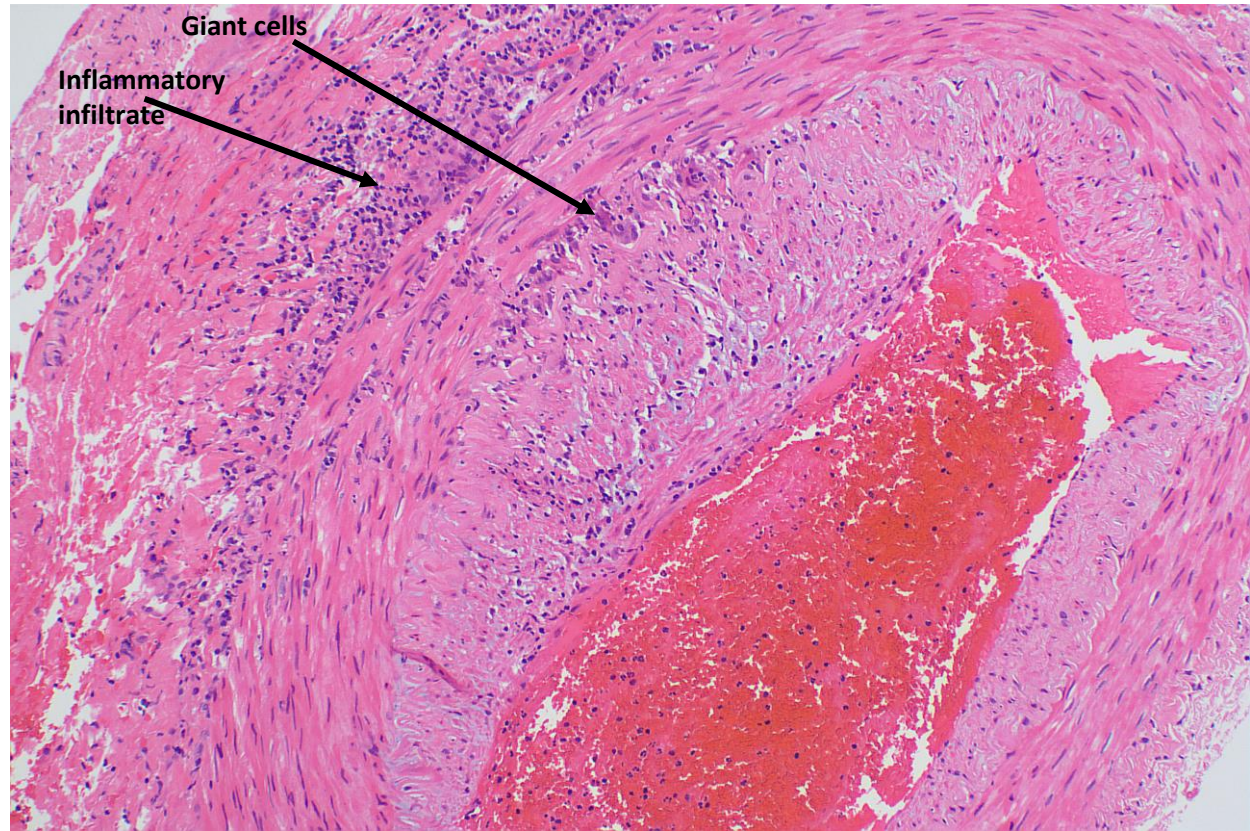


# Case 1

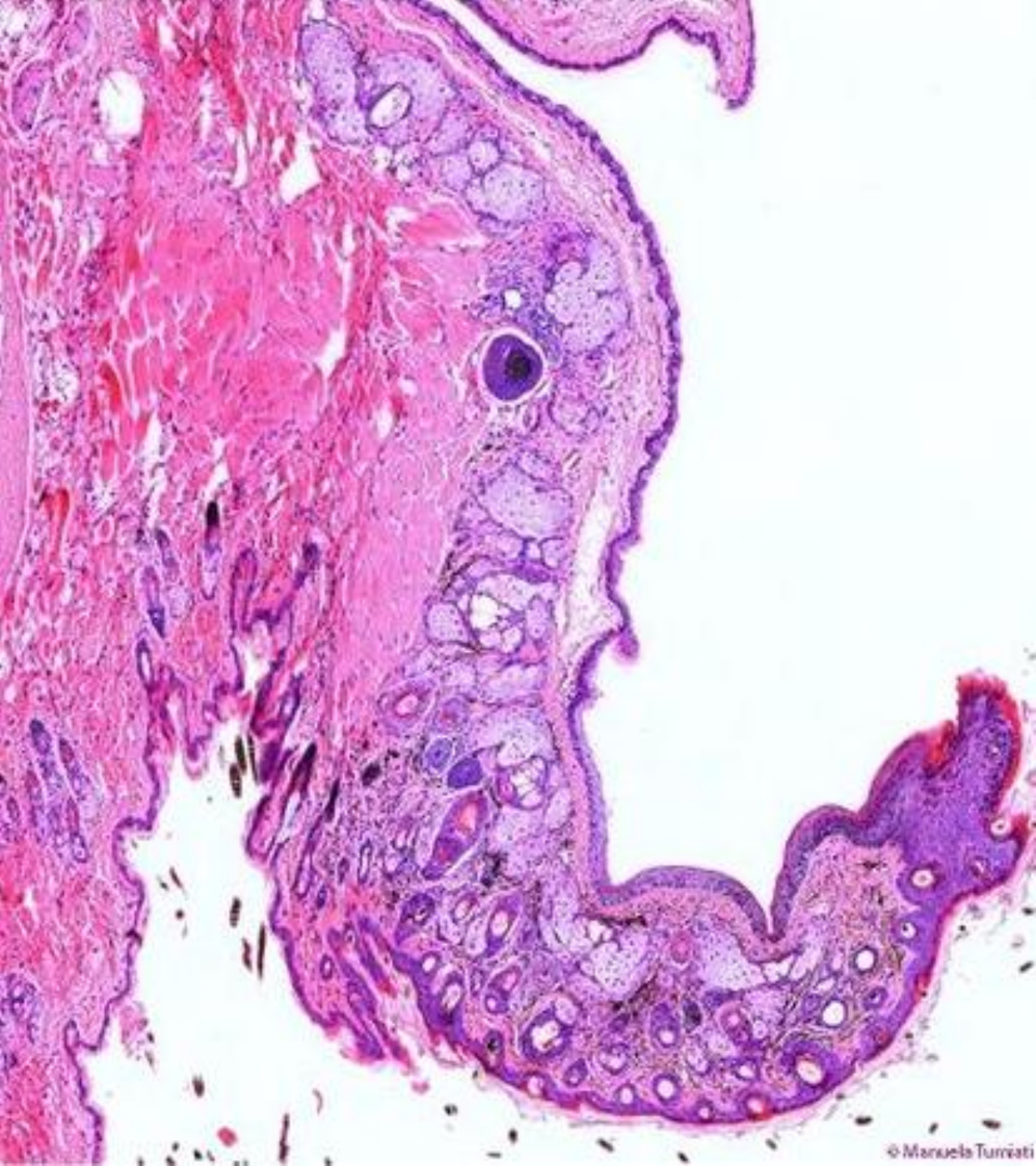




# Case 2







# The Pathology Report

- “Consistent with...” may mean different things depending on the person
- “Some features of...correlate with clinical history”

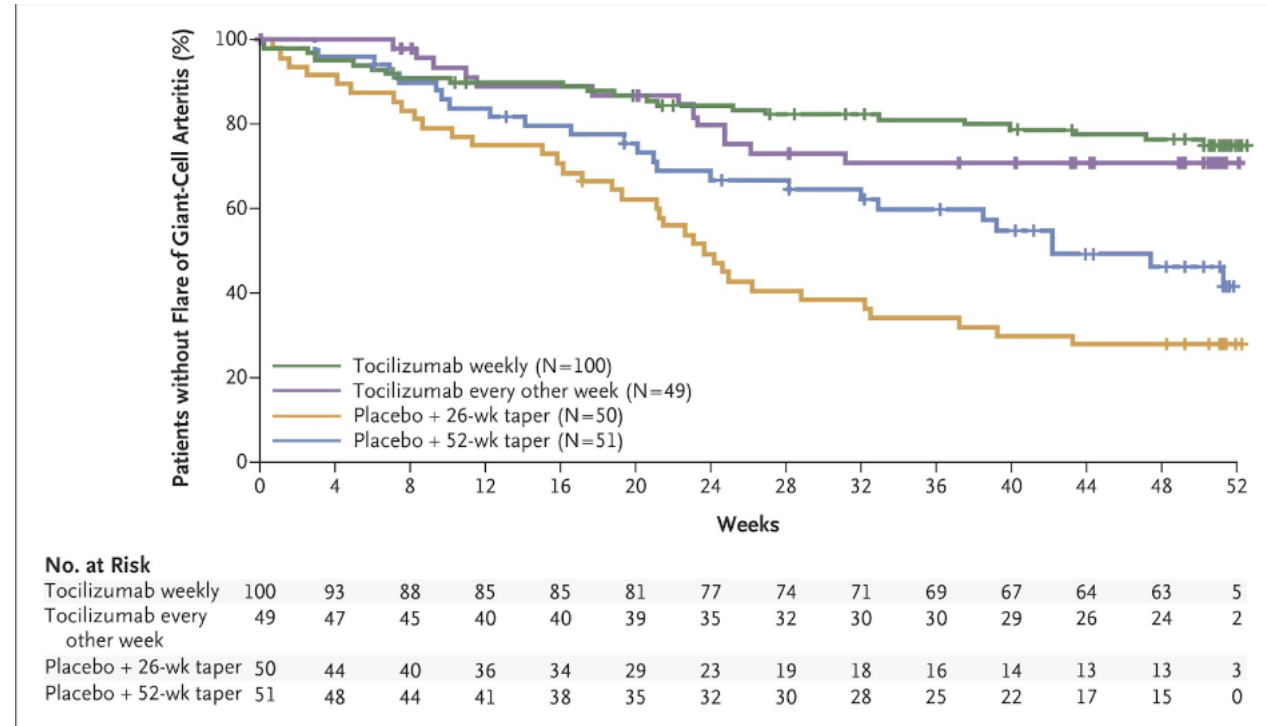


# Treatment

- If no signs of ischemic organ damage (visual loss), initial treatment is prednisone between 40-60 mg/day
- If GCA eye involvement - IV methylprednisolone 1000 mg for 3 days followed by prednisolone 50-60mg oral pred to protect the contralateral eye
- Steroids are weaned slowly over 12-18 mths
- Glucocorticoid-sparing agents (MTX or tocilizumab):
  - Diabetes
  - Osteoporosis
  - Significant obesity
- Bone health +/- PJP prophylaxis +/- gastric protection

# Treatment

- Tocilizumab is an **IL-6** receptor inhibitor
- The GiACTA trial: tocilizumab + steroids had  $\uparrow$  rates of sustained remission vs. steroids alone.
  - reduced steroid-induced adverse effects
- PBS criteria: **ESR >50** or **CRP >24.5** + either **positive MRI** or **PET** or **positive TAB**



**THANK YOU!**



# References

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