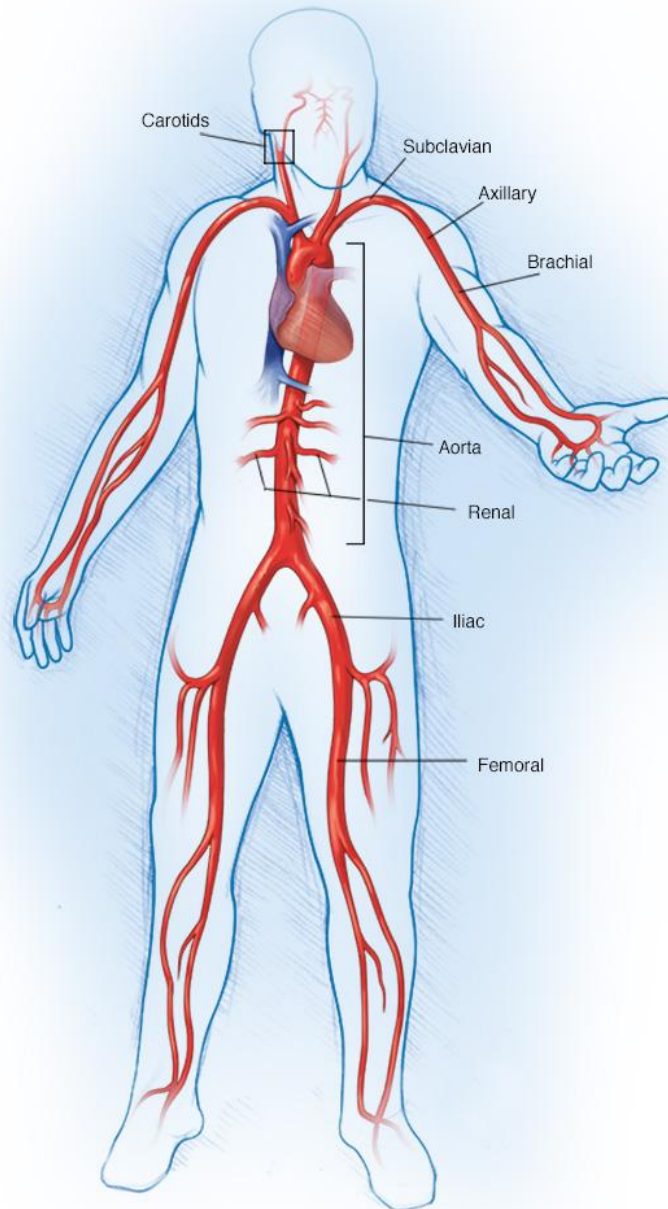


TAKAYASU'S ARTERITIS

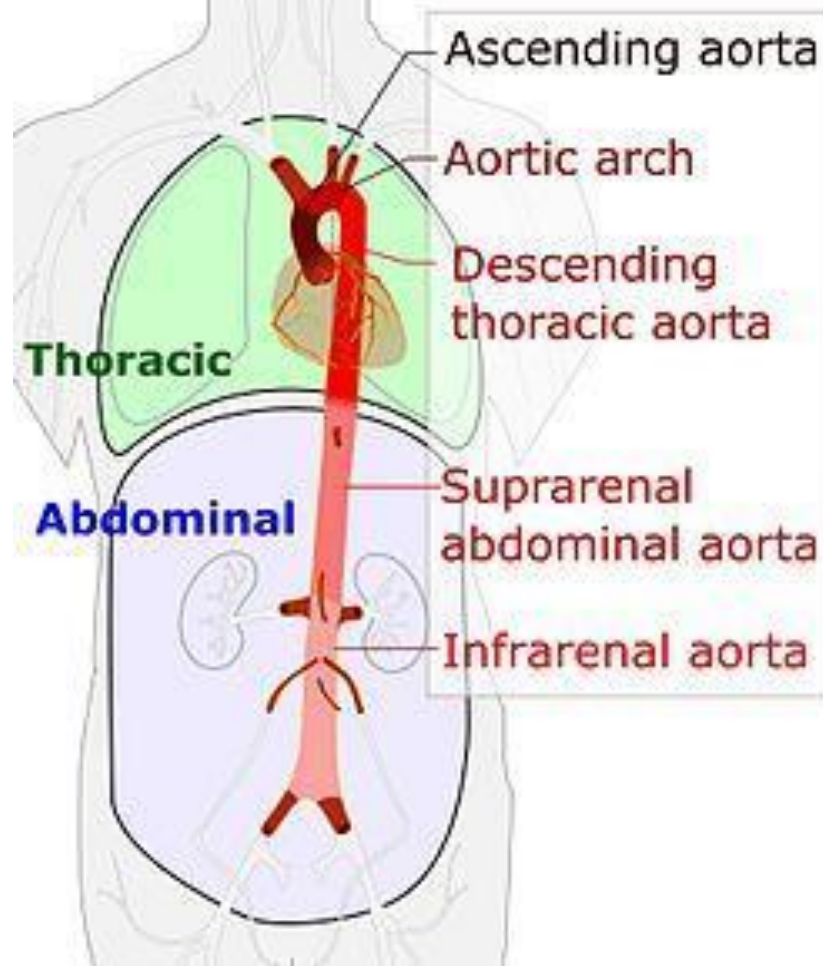
Dr Katya Dolnikov

2017

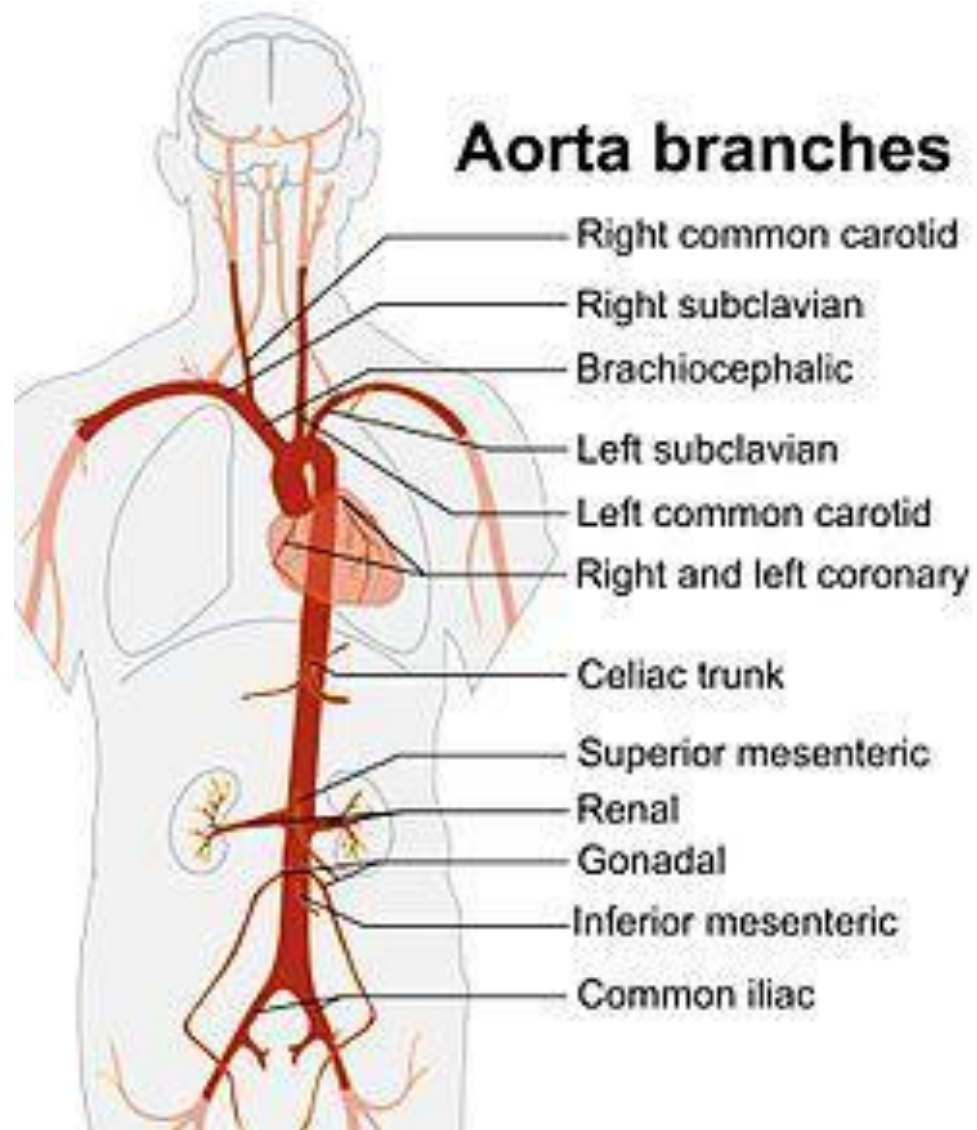
D_katya@rambam.health.gov.il

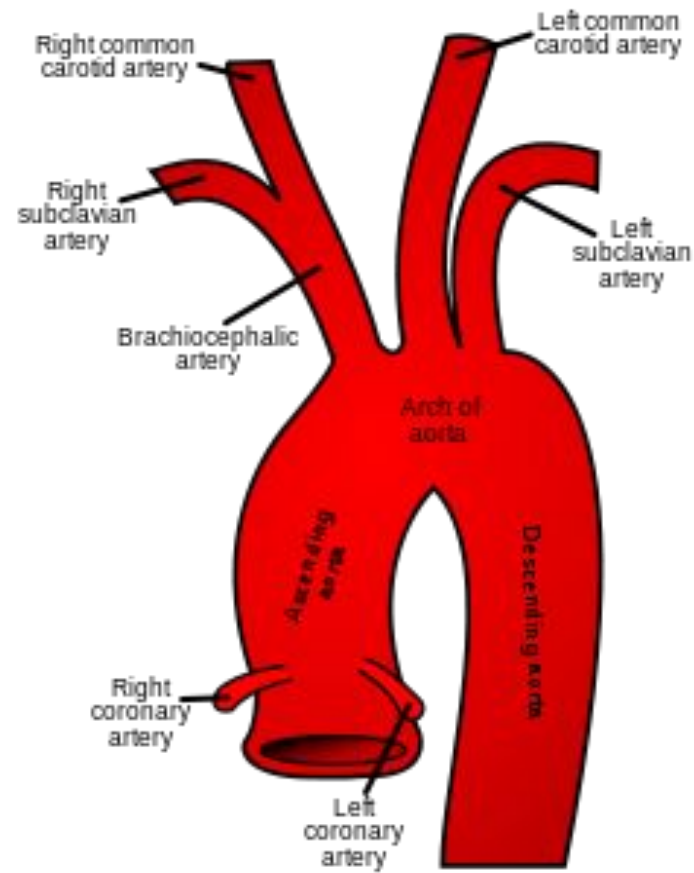


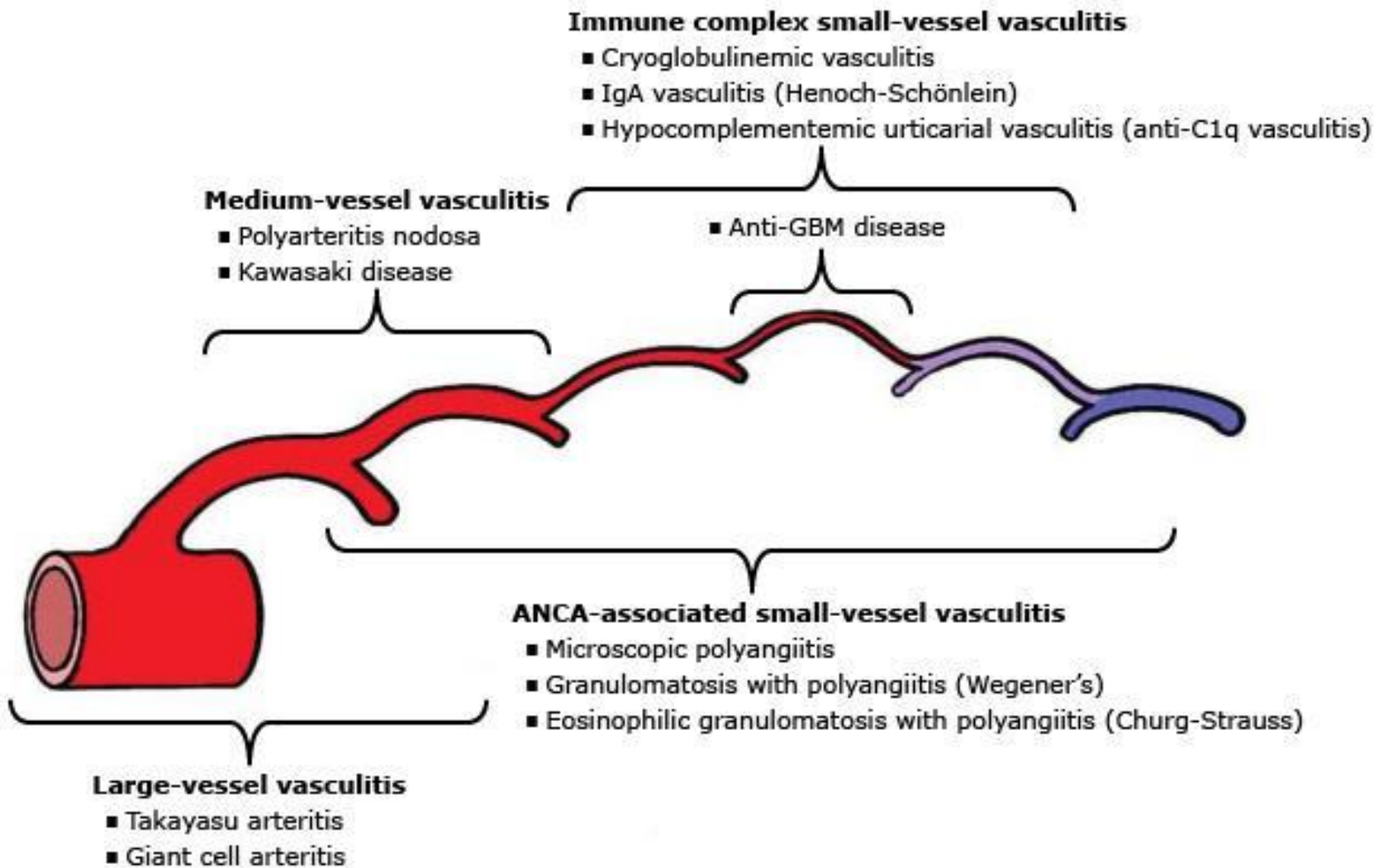
Aorta segments



Aorta branches







Epidemiology

- More case reports from Japan ,India, South-east Asia, Mexico
- No geographic restriction
- No race – immune
- Incidence-2.6/million/year-N.America/Europe
- The incidence in Asia is 1 case/1000-5000 women.

Epidemiology

Age

- Mc-2nd & 3rd decade
- May range from infancy to middle age
- Indian studies-age 3- 50 y

Gender diff

- Japan-F:M=8-9:1
- India-F:M ratio varies from 1:1 - 3:1

Genetics

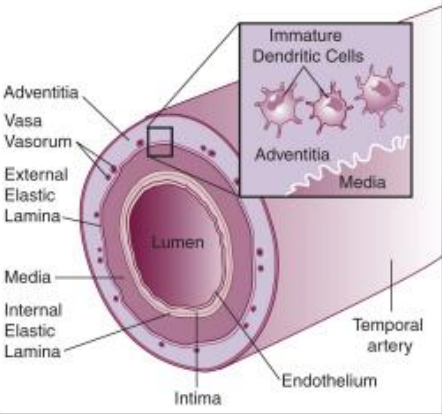
- Japan - HLA-B52 and B39
- Mexican and Colombian patients - HLA-DRB1*1301 and HLA-DRB1*1602
- India- HLA- B 5, -B 21

Histopathology

- Idiopathic inflammatory arteritis of elastic arteries resulting in occlusive/ ectatic changes
- Large vessels – Aorta and its main branches (brachiocephalic, carotid, SCL, vertebral, RA)
- Coronary and PA involvement
- Aorta - usually not beyond IMA
- Multiple segments with skipped areas or diffuse involvement

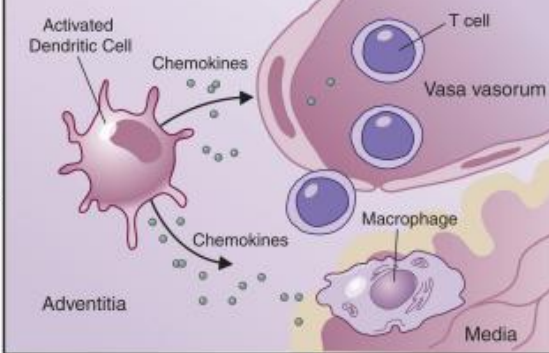
Pathogenesis

In **healthy medium-sized arteries**, immature, nonactivated dendritic cells reside in the adventitia near the adventitia-media border. When immature dendritic cells present antigen to T cells, the T cells are inhibited, which may be important in maintaining immune tolerance.

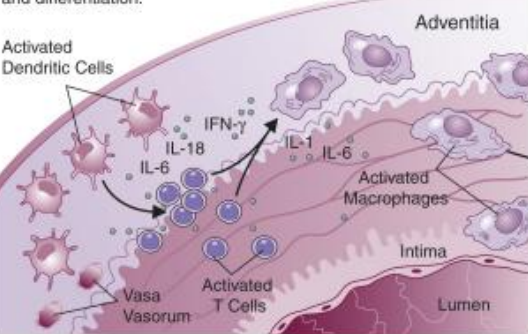


In **temporal arteritis**, a triggering antigens (e.g., an infectious agent, drug, toxin, or autoantigen) activates dendritic cells resident in the arterial wall.

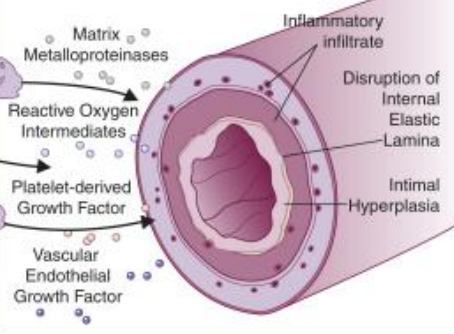
The activated dendritic cells release chemokines that attract T cells from the vasa vasorum and macrophages into the arterial wall. Binding of those chemokines to the dendritic cells traps them in the evolving inflammatory infiltrate.



The activated dendritic cells express receptors and release inflammatory cytokines (interleukin [IL] 6, IL-18) that promote activation of T cells and vascular inflammation. IL-18 up-regulates the release of interferon (IFN) γ from T cells. IFN- γ released from activated T cells promotes inflammation, granuloma formation, and macrophage activation and differentiation.

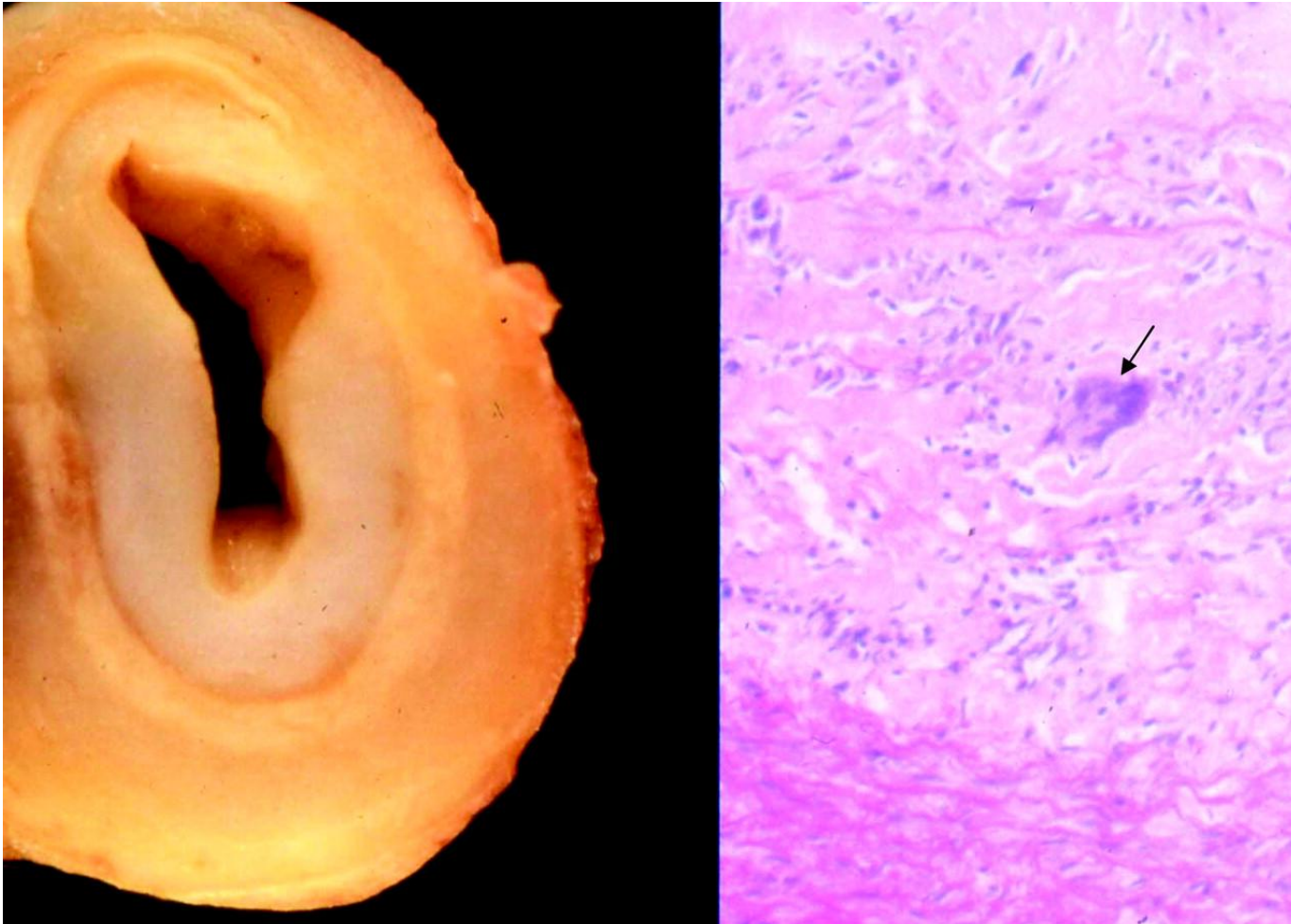


Activated macrophages produce a variety of mediators that lead to progressive vascular inflammation, endothelial damage, disruption of the internal elastic lamina, and intimal hyperplasia. Macrophages also release cytokines (IL-1, IL-6) that may contribute to systemic features of temporal arteritis.



- Antigen-driven disease, with the site of immunologic recognition events being the adventitia.
- DC in adventitia activated by AG release IL-18 and chemokines that “recruit” T cells from vasa vasorum to the vessel wall
- CD4+ T cells secrete interferon- γ → stimulate macrophages and multinucleated giant cells
- The results of this inflammatory cascade are :
 - granulomatous inflammation
 - destruction of the internal elastic lamina
 - arterial wall hyperplasia, smooth muscle cell proliferation, intimal thickening, vascular occlusion

Pathological findings in Takayasu arteritis.



A

B

Heather L. Gornik, and Mark A. Creager *Circulation*.
2008;117:3039-3051

Macroscopic

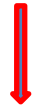
Gelatinous plaques-early

White plaques-collagen

Diffuse intimal thickening



Superficial– deep scarring



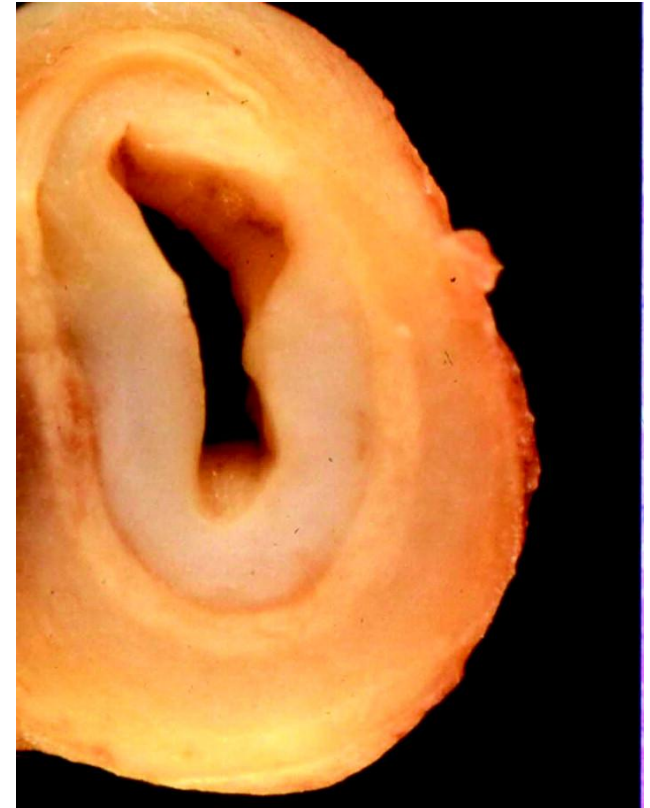
circumferential  stenosis

Mural thrombus

2^o atheromatous changes

long standing,

HTN

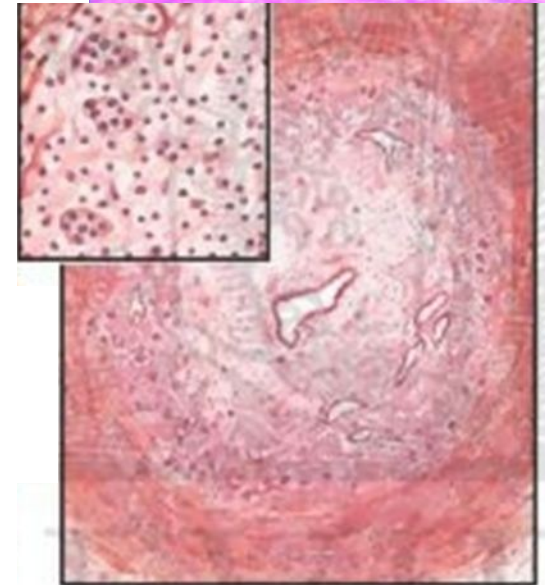
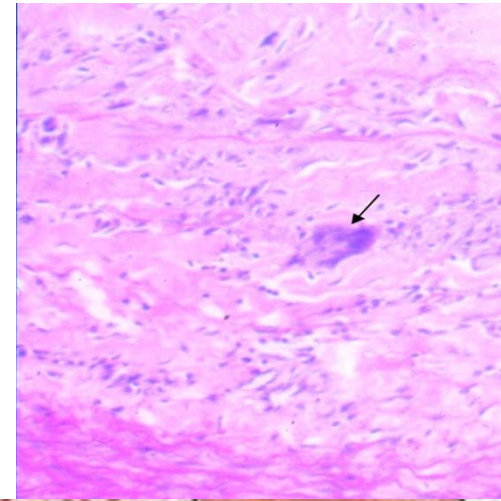


Macroscopic

- Wall thickening, fibrosis, stenosis, thrombus formation → end organ ischemia
- More inflammation → destroys arterial media → Aneurysm (fibrosis inadequate)
- Most patients with aneurysms also have stenosis

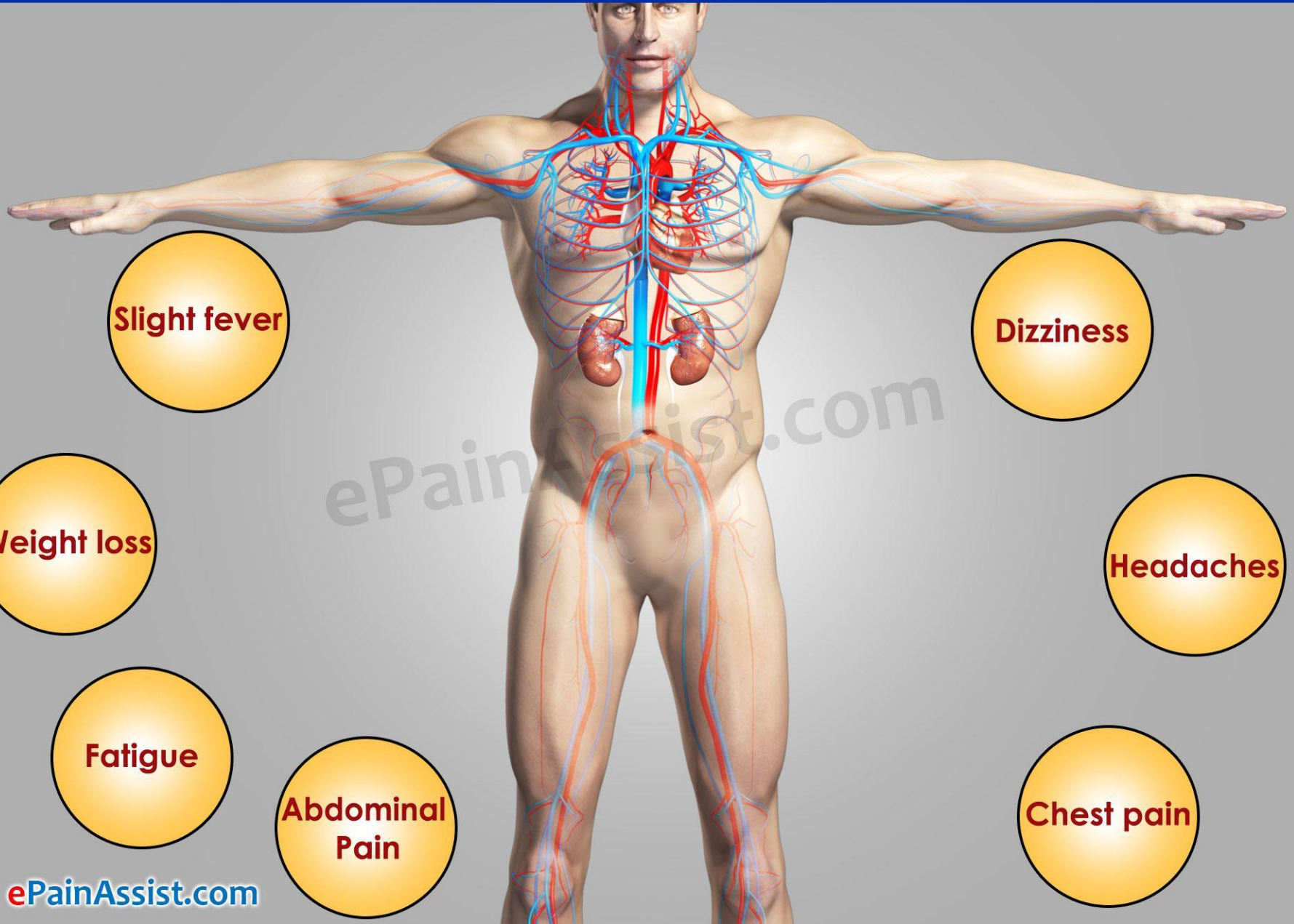
Microscopic

- Panarteritis with inflammatory mononuclear cell infiltrates within the vessel wall with frequent giant cell formation
- There is proliferation of the intima and fragmentation of the internal elastic lamina



Biopsy specimen of superficial temporal artery: almost total obliteration of lumen with some recanalization. High-power insert shows infiltration with lymphocytes, plasma cells, and giant cells; fragmentation of elastica

The Symptoms Of Takayasu Disease /Aortic Arch Syndrome



Slight fever

Dizziness

Weight loss

Headaches

Fatigue

**Abdominal
Pain**

Chest pain

Clinical features

Early pre-pulseless/gen manifestations

- Fever, weight loss, headache, fatigue, malaise, night sweats, arthralgia
- Splenomegaly, cervical, axillary lymphadenopathy

Late ischemic phase

- Sequel of occlusion of Ao arch/br
- Diminished/absent pulses (84–96%)
- Bruits (80–94%)
- Hypertension (33–83%)
- RAS(28–75%)

CLINICAL MANIFESTATIONS

ARTERY	Potential Clinical Manifestations
Subclavian	Arm claudication, Raynaud's phenomenon
Common carotid	Visual changes, syncope, transient ischemic attacks, stroke
Abdominal aorta ^a	Abdominal pain, nausea, vomiting
Renal	Hypertension, renal failure
Aortic arch or root	Aortic insufficiency, congestive heart failure
Vertebral	Visual changes, dizziness
Coeliac axis ^a	Abdominal pain, nausea, vomiting
Iliac	Leg claudication
Pulmonary arteries	Dyspnea, chest pain, hemoptysis
Coronary arteries	Chest pain, myocardial infarction

CVS	<p>↓/– pulses (84–96%) -claudication & BP Diff ,Bruits (80–94%) -carotids, subcl & abd vess.</p> <p>HTN- (33–83%) –Mcc RAS (28–75%),↓Ao capacitance,atyp CoA, baroreceptor reactivity</p> <p>CHF-(28%)- HTN, AR, DCM-5%</p> <p>AR-(7-24%) Ao root dil > valve inv, annuloaortic ectasia Coronary & vascular involvement</p>
CNS	Cerebral ischemia 2 ^o to obliterative arteritis, seizures etc
RENAL	RAS & Ischemic Nephropathy
SKIN	Erythema nodosum, Raynauds disease, leg& hand ulcers
PULMONARY	<p>15-27%, stenosis/ occlusion of lobar/segmental pul art</p> <p>UL>LL, R> L—INDIA (Panja et al 1997)</p>

Coronary involvement in TA

- Occurs in 10~30%
- Often fatal
- Classified into 3 types

Type1:stenosis or occlusion of coronary ostia

Type2:diffuse or focal coronary arteritis

Type3:coronary aneurysm

Occular involvement

Hypertensive retinopathy

- Common
- Arteriosclerotic –art narrowing, av nipping, silver wiring
- Neuroretinopathy-exudates and papilloedema
- Direct ophthalmoscopy

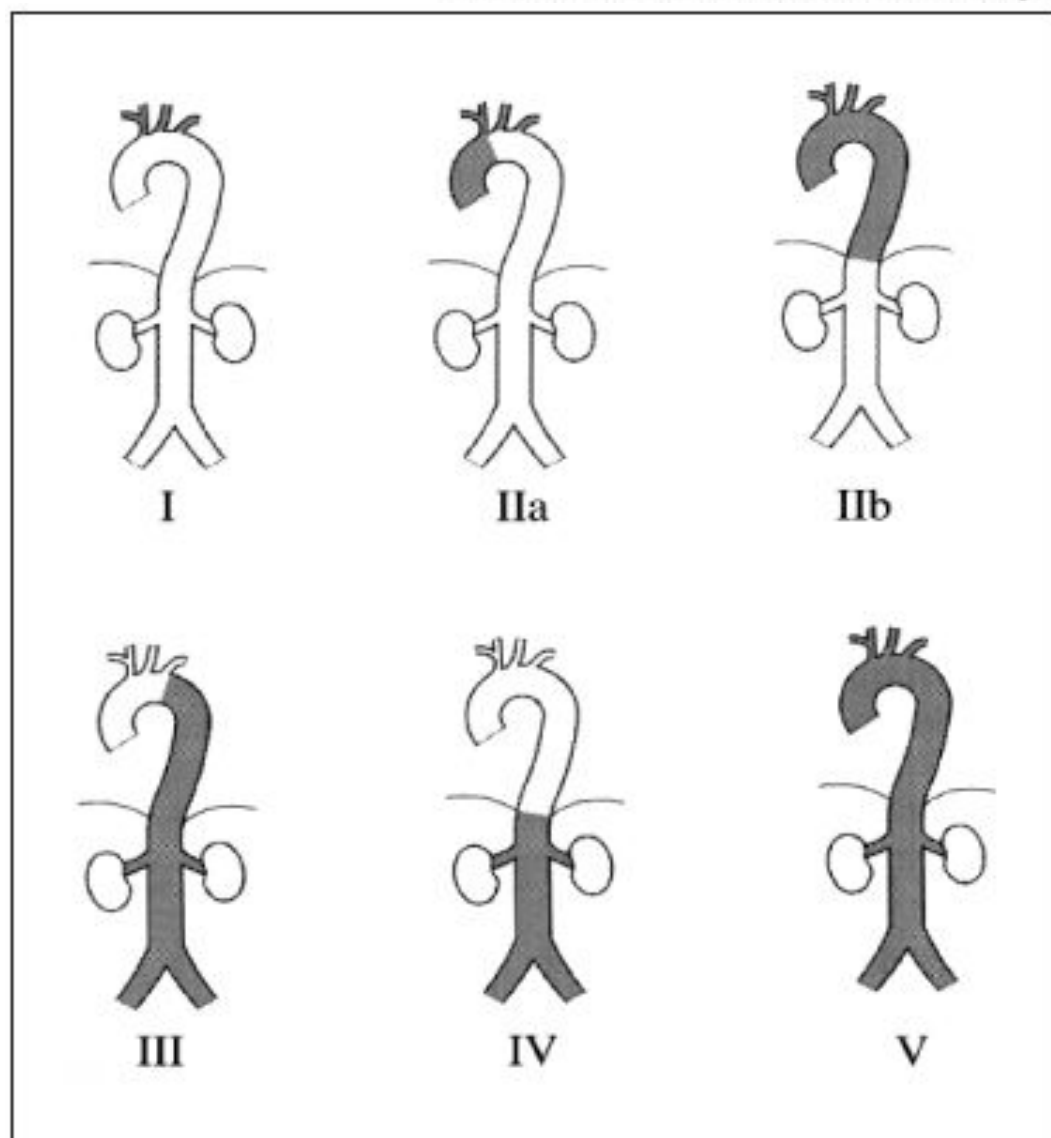
Nonhypertensive retinopathy

- UYAMA & ASAYAMA CLASS
- stage 1- Dil of small vessels
- stage 2- Microaneurysm
- stage 3- Art-ven anastomoses
- stage 4- Ocular complications



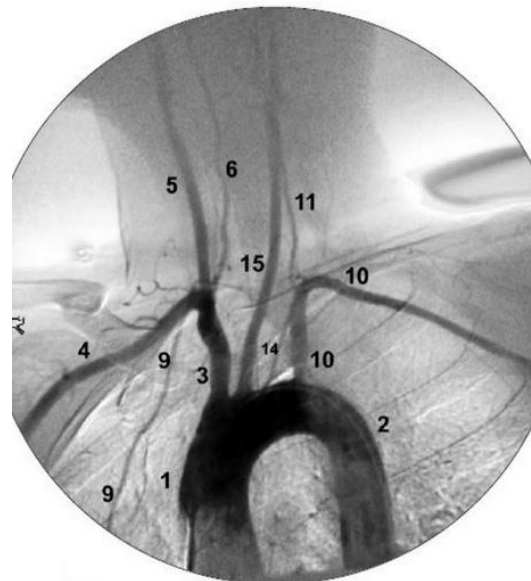
Coronary anastomosis of retinal vessels

New classification of angiogram International Conference on Takayasu Arteritis, 1994

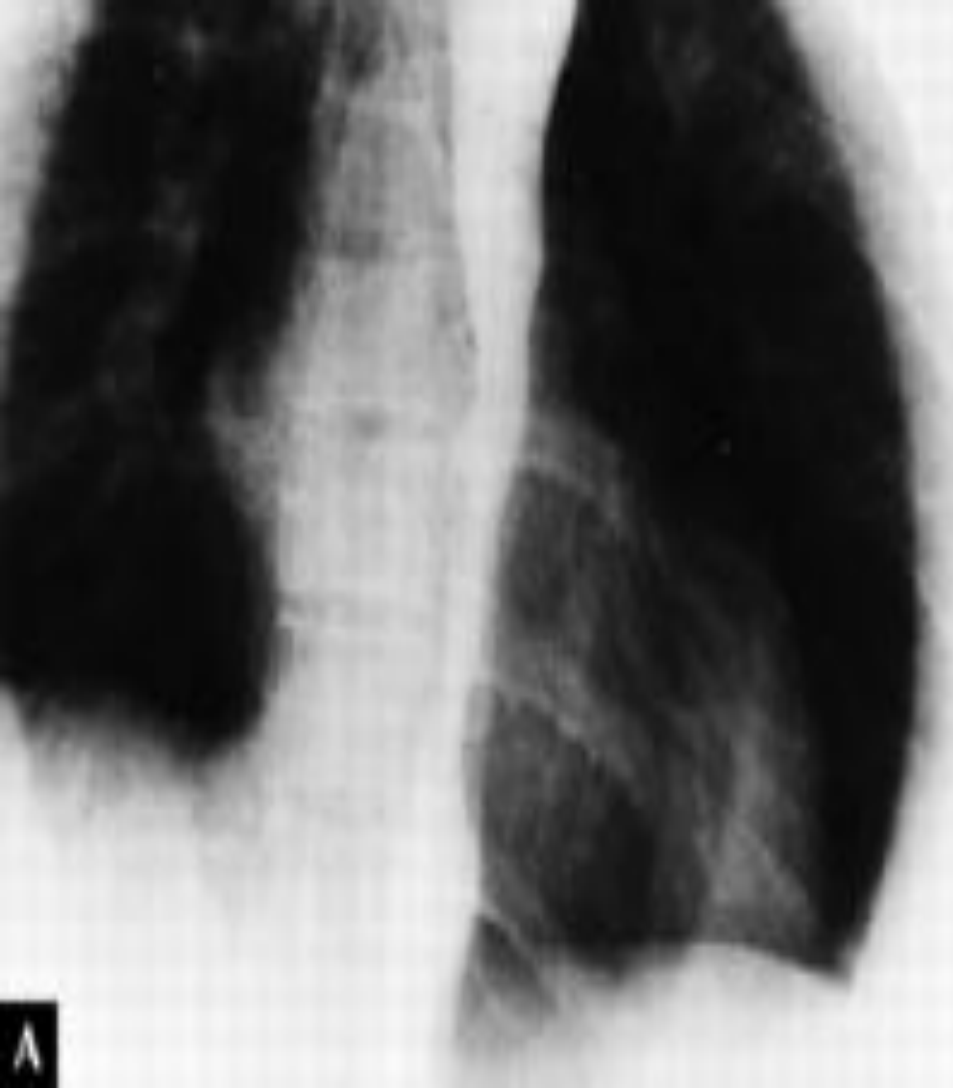


According to this classification system, involvement of the coronary or pulmonary arteries should be designed as C(+) or P(+), respectively.

Severe arteritis with complete occlusion of left carotid and subclavian artery. The right subclavian artery is also occluded



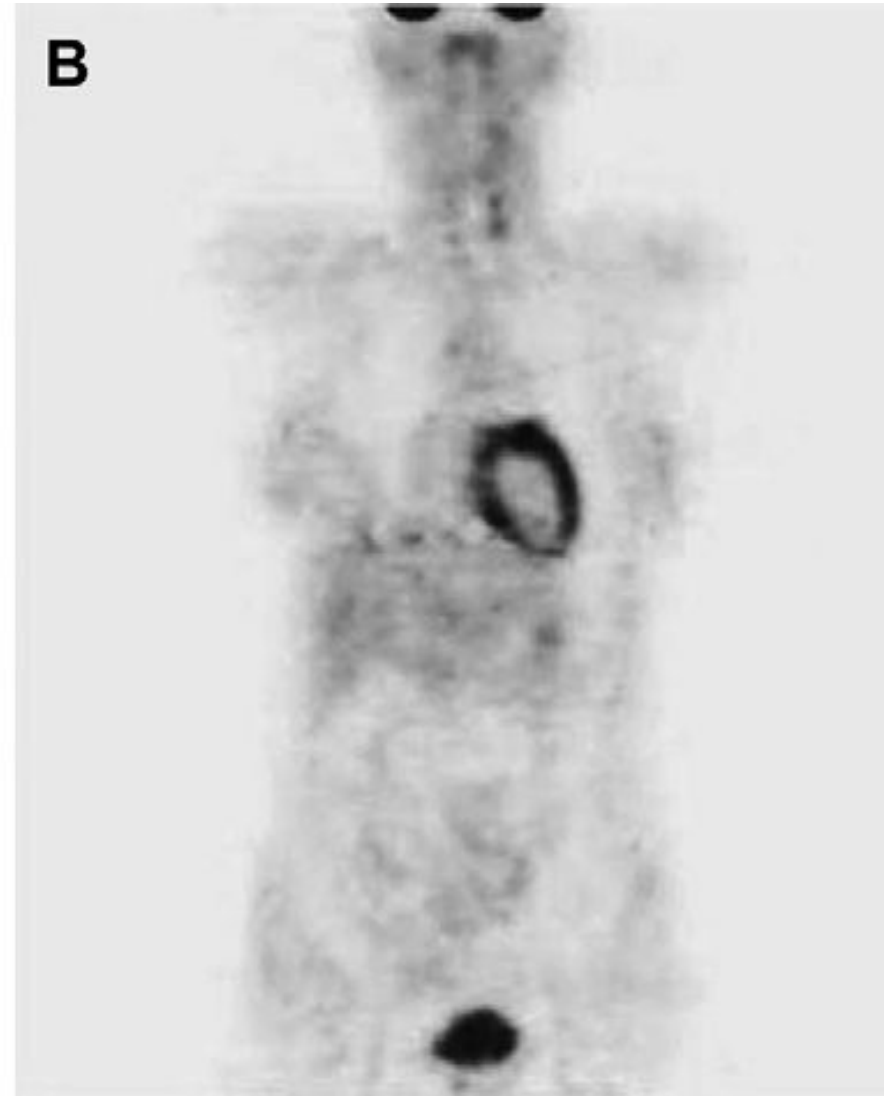
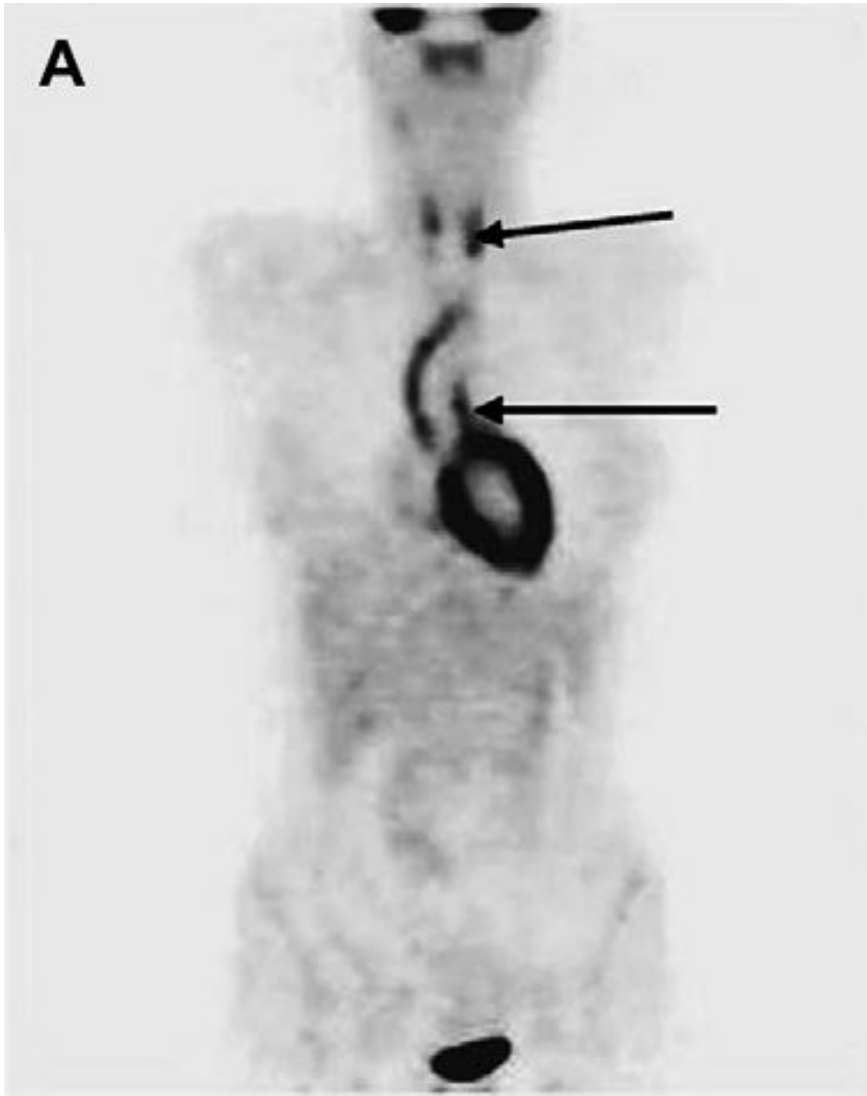
- 1 ascending thoracic aorta
- 2 descending thoracic aorta
- 3 innominate artery
- 4 right subclavian artery
- 5 right common carotid artery
- 6 right vertebral artery
- 9 right internal mammary artery
- 10 left subclavian artery
- 11 left vertebral artery
- 12 left thyrocervical trunk
- 14 left internal mammary artery
- 15 left common carotid artery



A
long-segment diffuse stenotic involvement of
the DTA

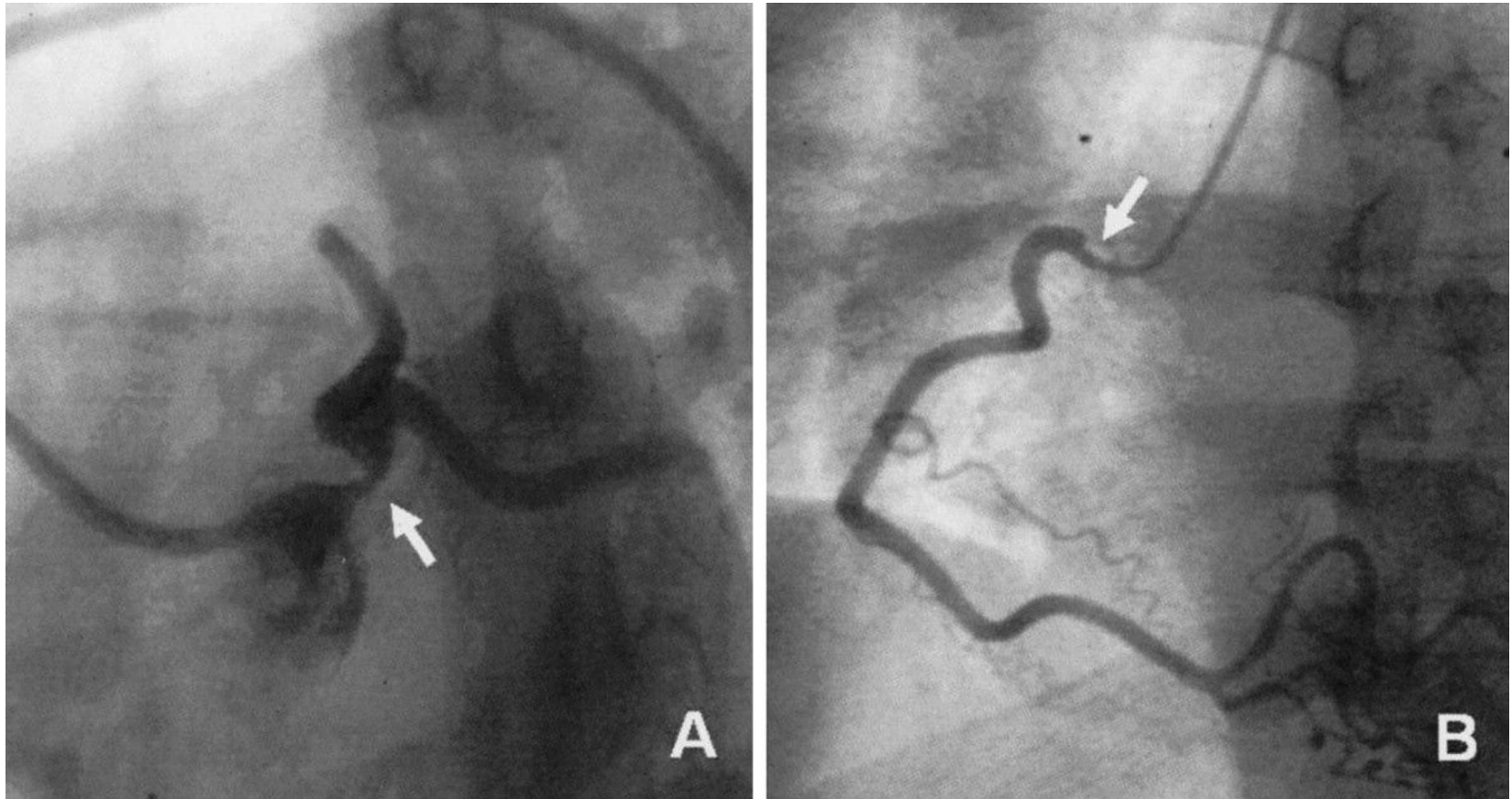


B
after deployment of stents.



remission after treatment

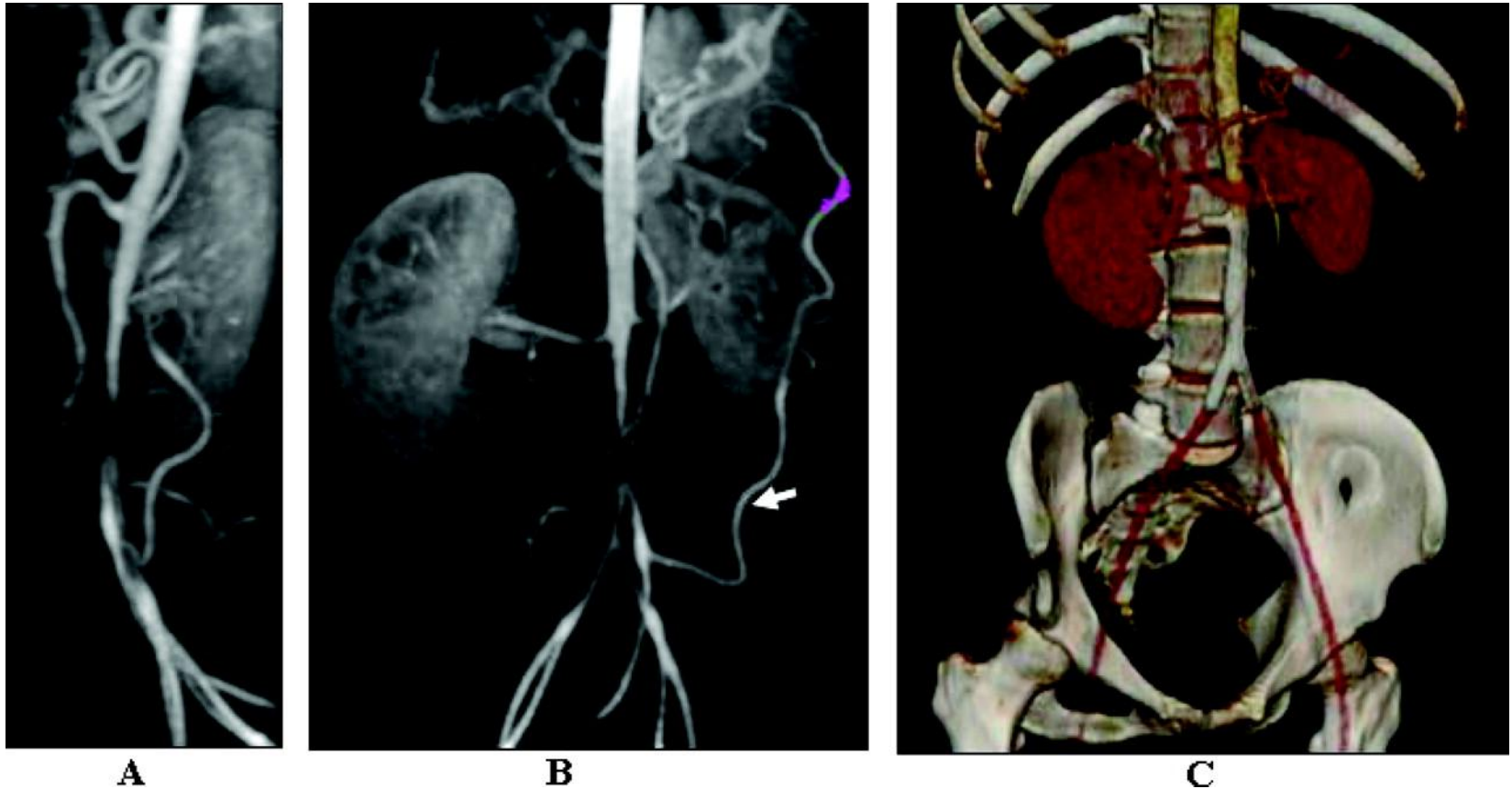
Figure 4. Takayasu arteritis involving the coronary ostia.



Heather L. Gornik, and Mark A. Creager *Circulation*.
2008;117:3039-3051

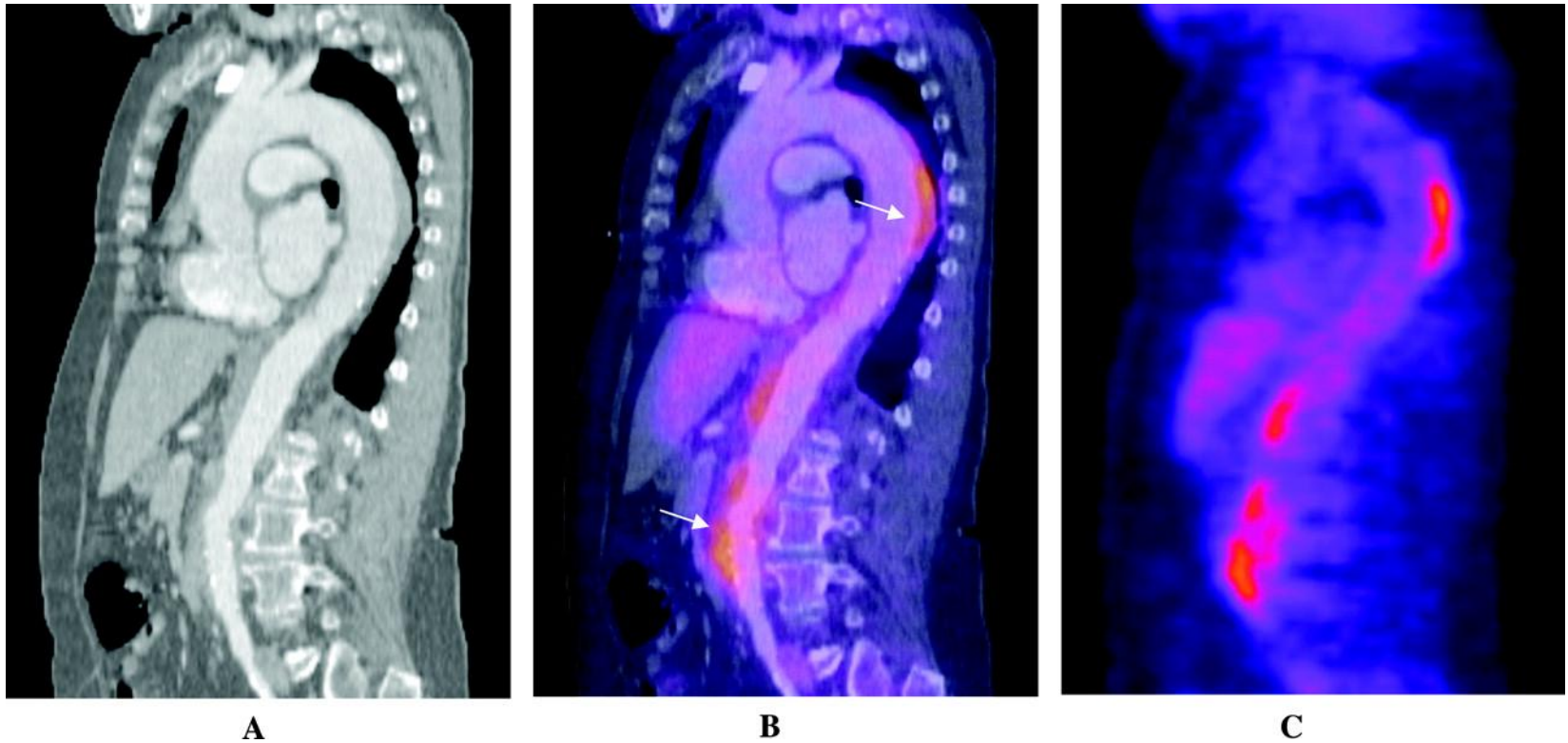


Figure 3. Aortic occlusive disease in a patient with Takayasu arteritis and bilateral leg claudication.



Heather L. Gornik, and Mark A. Creager *Circulation*.
2008;117:3039-3051

Figure 7. Combination of 18F-FDG PET and CTA for assessment of Takayasu arteritis.



Heather L. Gornik, and Mark A. Creager *Circulation*.
2008;117:3039-3051

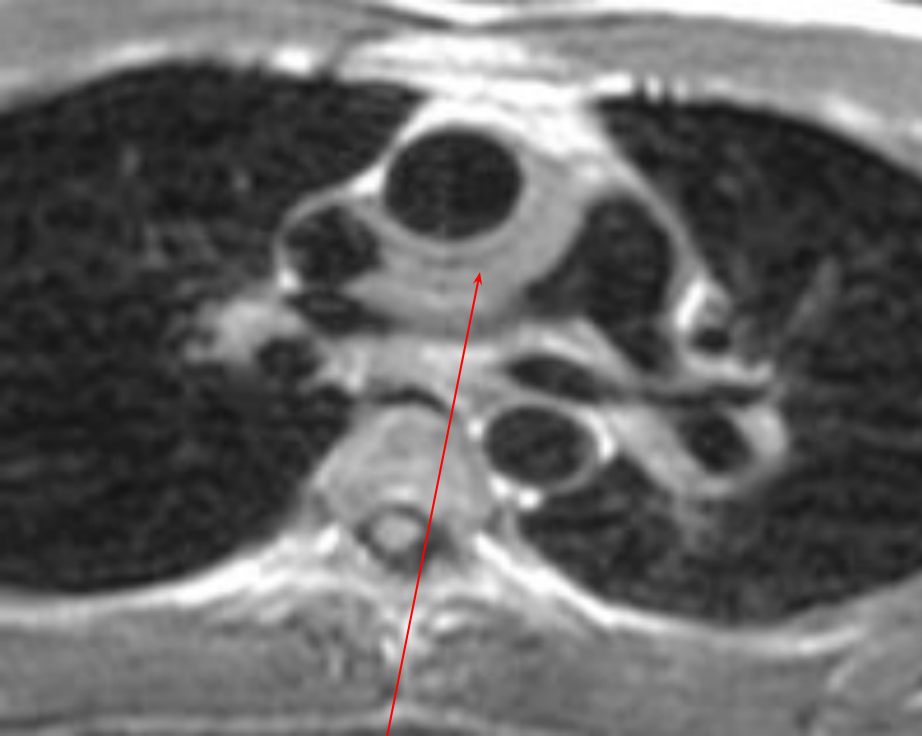




← ostial stenosis of the right renal artery

after deployment of a stent →





a/c phase-Axial T1-weighted image
wall thickening of As aorta and PA

Axial T1-weighted image- improvement of
wall thickening of As Ao and PA after steroid
therapy

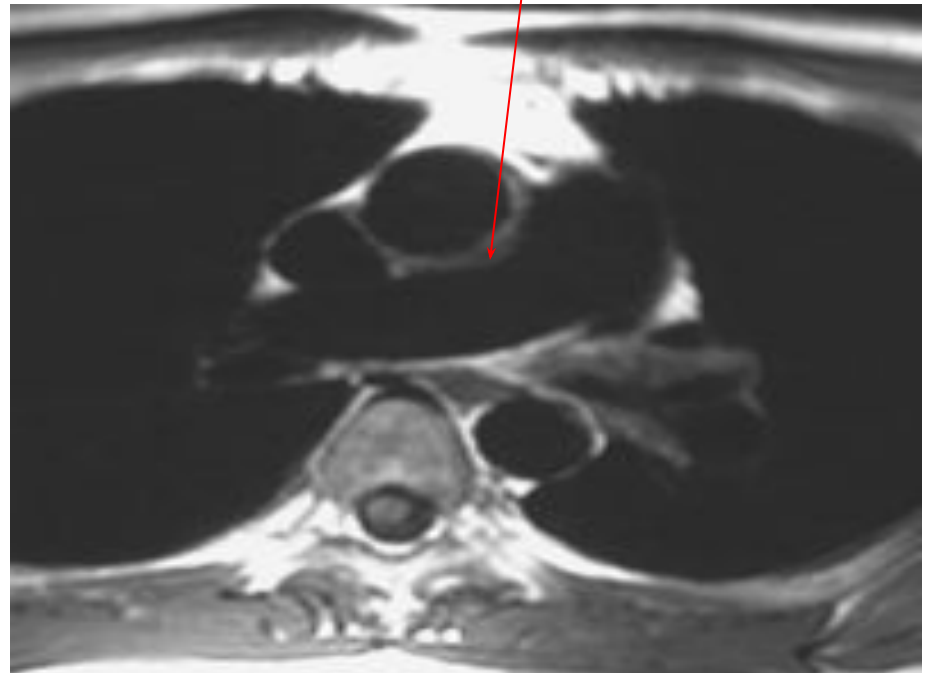


Table 4. American College of Rheumatology Classification Criteria of Takayasu Arteritis*

Age at disease onset <40 y

Development of symptoms or findings related to Takayasu arteritis <40 y of age

Claudication of extremities

Development and worsening of fatigue and discomfort in muscles of ≥ 1 extremity while in use, especially the upper extremities

Decreased brachial artery pulse

Decreased pulsation of 1 or both brachial arteries

Blood pressure difference >10 mm Hg

Difference of >10 mm Hg in systolic blood pressure between arms

Bruit over subclavian arteries or aorta

Bruit audible on auscultation over 1 or both subclavian arteries or abdominal aorta

Arteriogram abnormality

Arteriographic narrowing or occlusion of the entire aorta, its primary branches, or large arteries in the proximal upper or lower extremities not due to arteriosclerosis, fibromuscular dysplasia, or similar causes; changes usually focal or segmental

*The presence of ≥ 3 criteria is consistent with a diagnosis of Takayasu arteritis with a sensitivity of 91% and a specificity of 98%.

Adapted from Arend et al⁴⁷ with permission of Wiley-Liss, Inc, a subsidiary of John Wiley and Sons, Inc. Copyright © 1990, John Wiley and Sons.

Diagnosis

ACR Classification Criteria: Takayasu's Arteritis*

1. Age <40 Years at Disease Onset
2. Claudication of Extremities
3. Decreased Brachial Artery Pulse
4. BP Difference >10 mmHg Between Arms
5. Bruit Over Subclavian Arteries or Aorta
6. Arteriogram Abnormality:
Occlusion or Narrowing in Aorta or Main Branches

*Must Have 3/6 Criteria.

- The diagnosis of Takayasu's arteritis should be suspected strongly in a young woman who develops a decrease or absence of peripheral pulses, discrepancies in blood pressure, and arterial bruits.
- The diagnosis is confirmed by the characteristic pattern on arteriography, which includes irregular vessel walls, stenosis, poststenotic dilation, aneurysm formation,

Treatment

- Disease-related mortality most often occurs from congestive heart failure, cerebrovascular events, myocardial infarction, aneurysm rupture, or renal failure.
- The course of the disease is variable, and although spontaneous remissions may occur, Takayasu's arteritis is most often chronic and relapsing.
- Glucocorticoid therapy for acute signs and symptoms.
- An aggressive surgical and/or arterioplastic approach to stenosed vessels. Unless it is urgently required, surgical correction of stenosed arteries should be undertaken only when the vascular inflammatory process is well controlled with medical therapy.
- In individuals who are refractory to or unable to taper glucocorticoids, methotrexate in doses up to 25 mg per week has yielded encouraging results.
- Anti-TNF therapies have encouraging results

Treatment of TA

Control of vasculitis

Steroids



If uncontrolled

immunosuppressants :
Cyclosporine, Cyclophosphamide,
Mtx, Mycophenolate mofetil

Symptomatic occlusion

angioplasty/surgery

thrombosis

Anti-platelet therapy (low-dose Aspirin)

Pharmacological treatment

0.7-1 mg/kg/day –prednisone for 1-3 months

common tapering regimen once remission

↓ pred by 5 mg/week → 20 mg/day.

Thereafter, ↓by 2.5 mg/week → 10 mg/day

↓1 mg/day each week, as long as disease does not become more active

Pulse iv corticosteroids - CNS symptoms- no data to support

- Steroids → 50% response
- Methotrexate → further 50% respond
- 25% with active disease will not respond to current treatments
- resistant to steroids/ recurrent disease once corticosteroids are tapered
 - cyclophosphamide (1-2 mg/kg/day),
 - azathioprine (1-2mg/kg/day), or
 - methotrexate (0.3 mg/kg/week)
 - Mycophenolate mofetil/ anti TNF α agents

- Critical issue is in trying to determine whether or not disease is active
- During Rx- regular clinical examination and ESR+ CRP initially - every few days
- CT or MRA - 3 to 12 months - (active phase of Rx), and annually thereafter
- Criteria for active disease

1. Systemic features (fever, musculoskeletal symptoms, etc.)

2. Elevated erythrocyte sedimentation rate

3. Features of vascular ischaemia or inflammation (claudication, vascular pain as carotodynia, diminished or absent pulse, vascular bruit), asymmetric blood pressure in either upper or lower limbs or both

4. Typical angiographic features

New onset or worsening of two or more features indicates "active disease".

Invasive treatment

- HTN with critical RAS
- Extremity claudication limiting daily activities
- Cerebrovascular ischaemia or critical stenoses of ≥ 3 cerebral vessels
- Moderate AR
- Cardiac ischaemia with confirmed coronary involvement
- Aneurysms

Recommended at quiescent state - avoids complications

(restenosis, anastamotic failure, thrombosis, haemorrhage, infection)