TAKAYASU'S ARTERITIS

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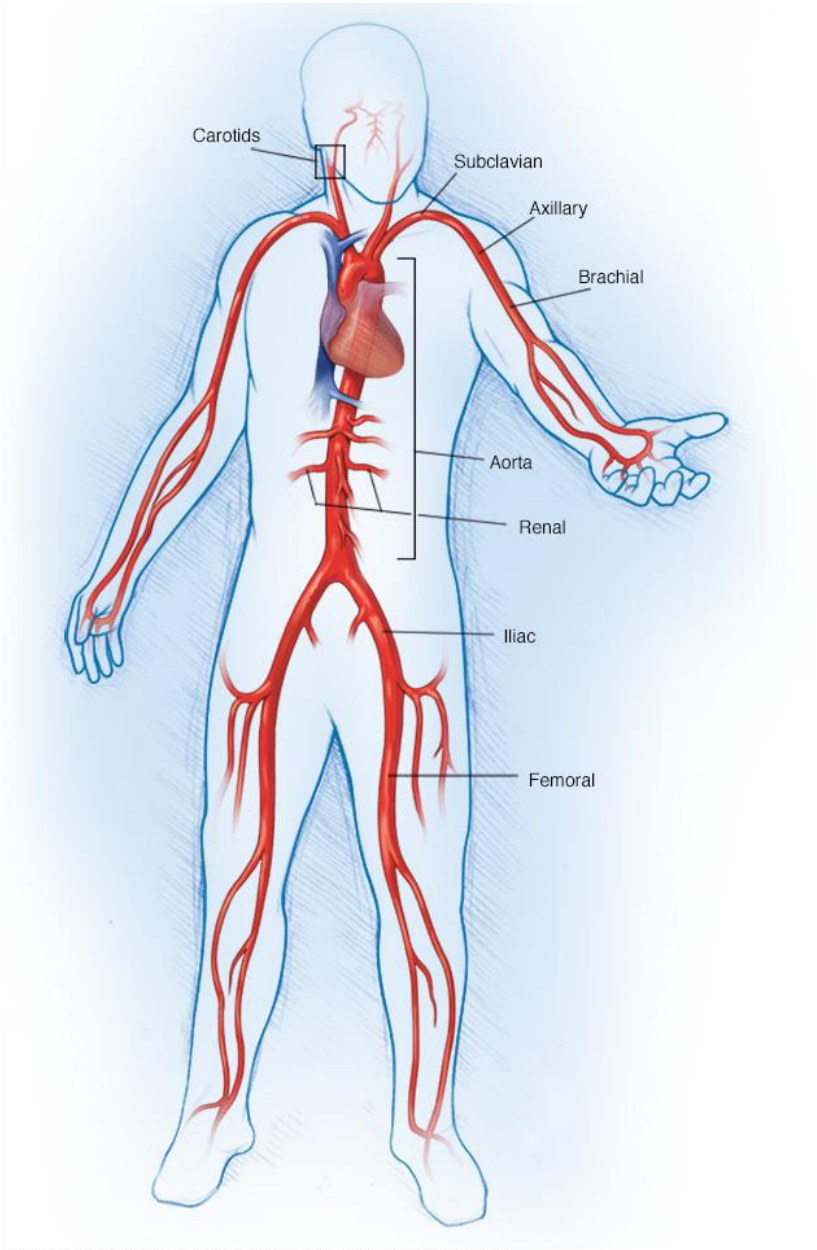
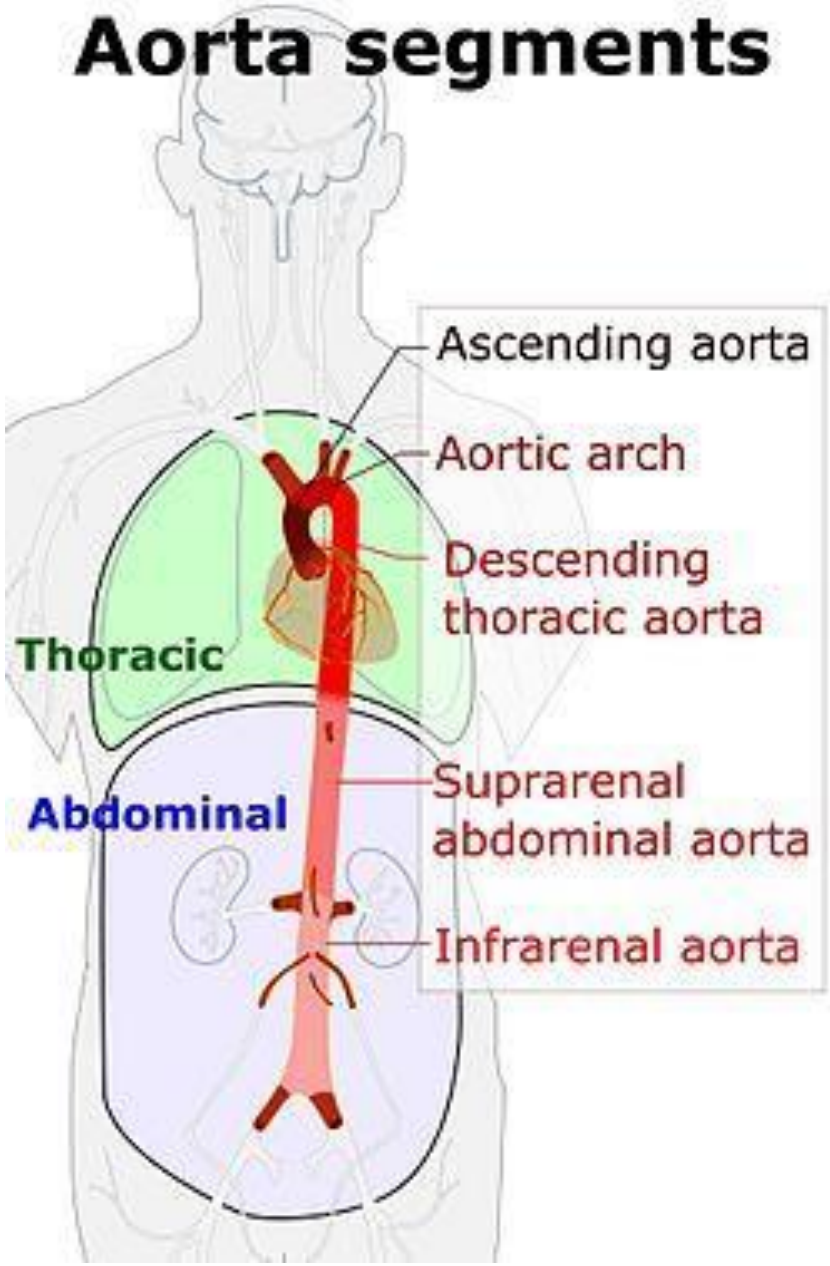
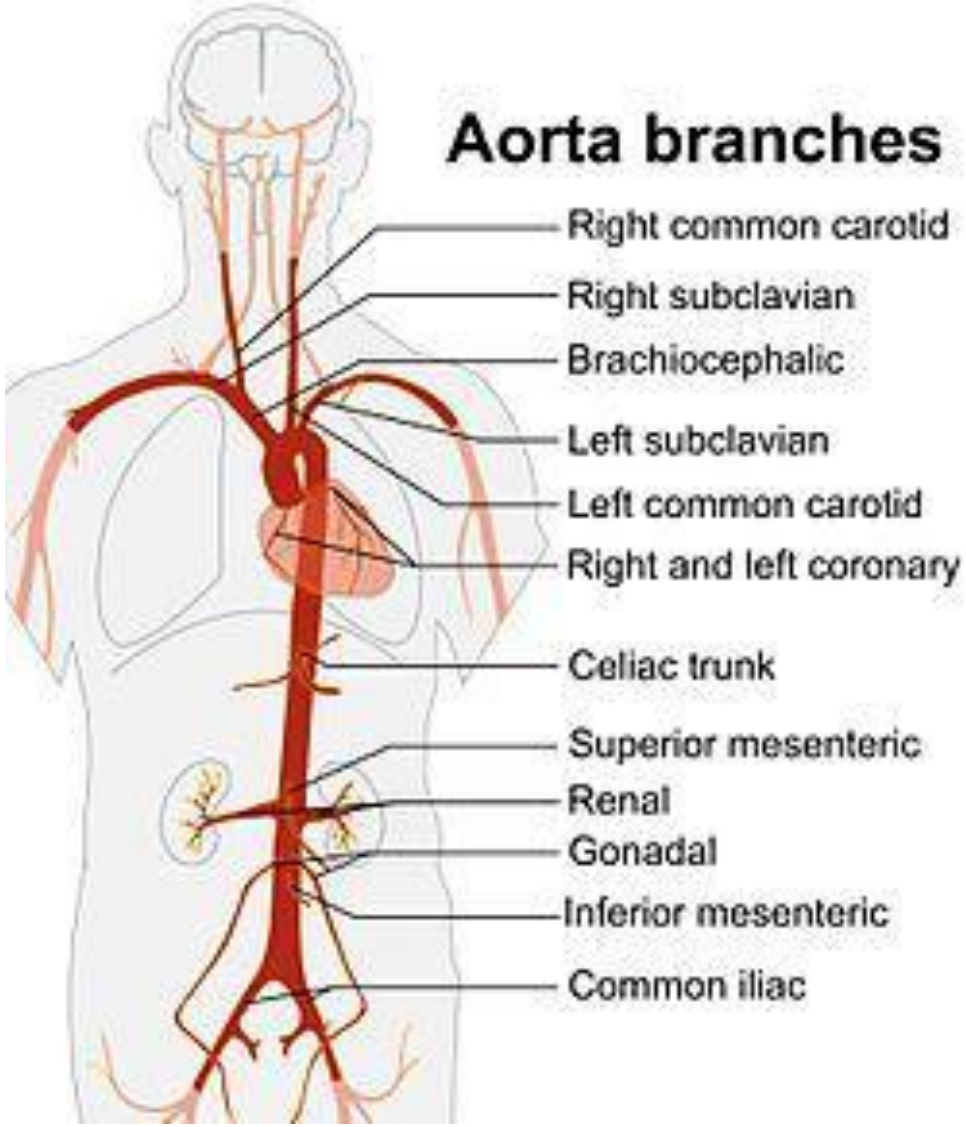
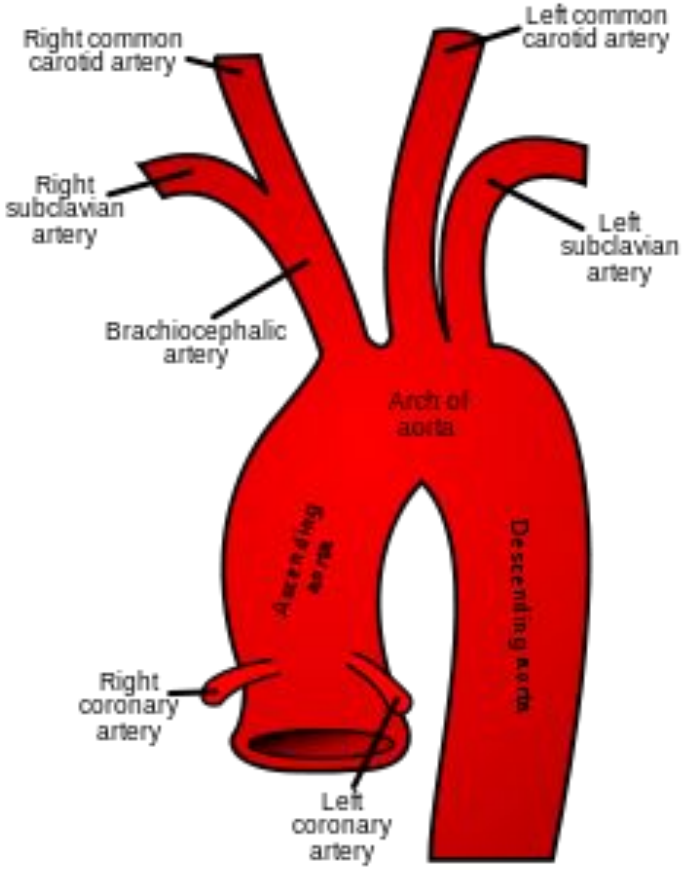
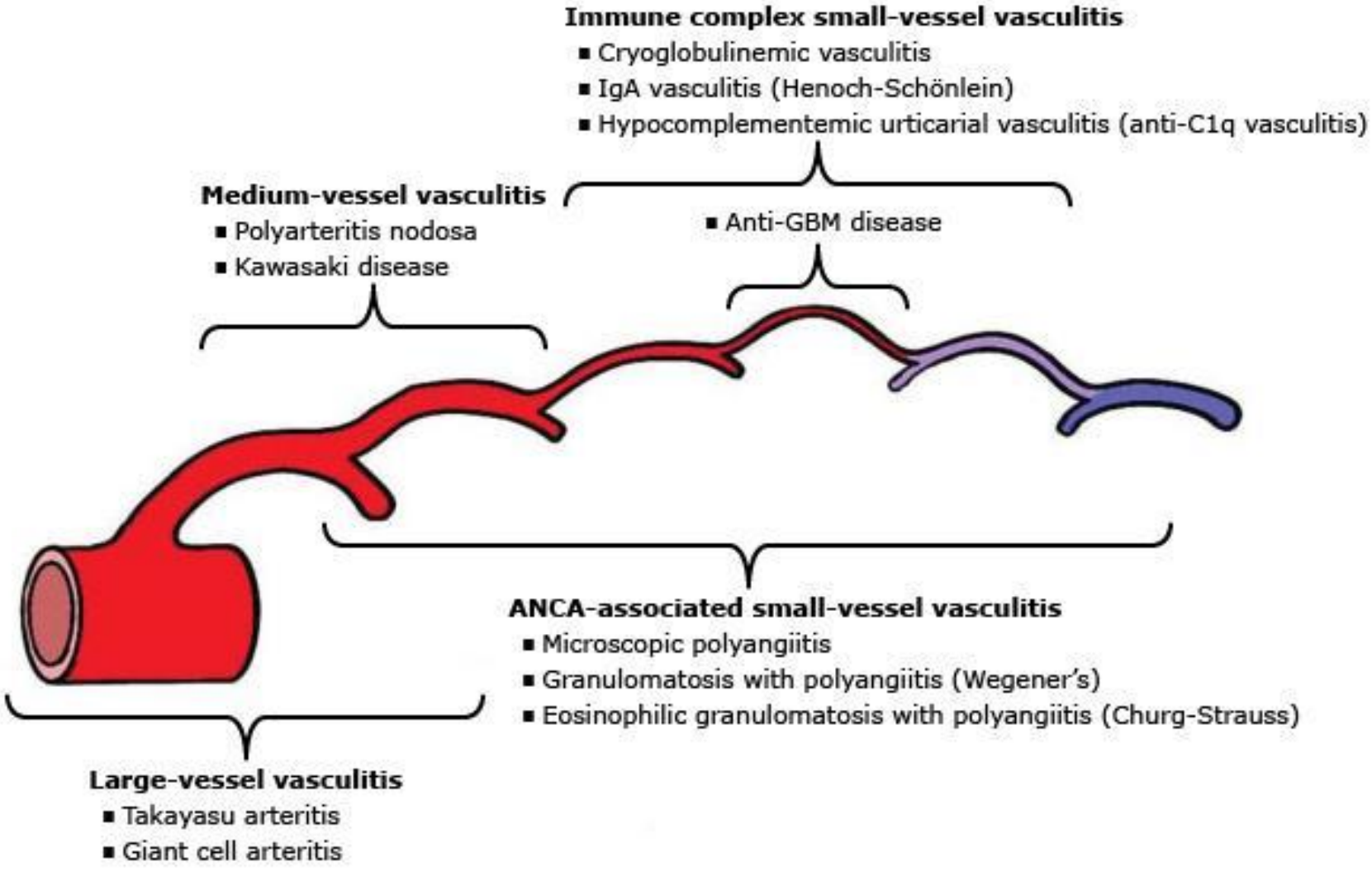


Aorta segments




Aorta branches
Right common carotid
Right subclavian
Brachiocephalic
Left subclavian
Left common carotid
Right and left coronary
Celiac trunk
Superior mesenteric
Renal
Gonadal
Inferior mesenteric
Common iliac


Right common carotid artery
Left common carotid artery
Right subclavian artery
Left subclavian artery
Brachiocephalic artery
Arch of aorta
Ascending aorta
Descending aorta
Right coronary artery
Left coronary artery


Immune complex small-vessel vasculitis
Cryoglobulinemic vasculitis
IgA vasculitis (Henoch-Schönlein)
Hypocomplementemic urticarial vasculitis (anti-C1q vasculitis)
Medium-vessel vasculitis
Polyarteritis nodosa
Kawasaki disease
Anti-GBM disease
ANCA-associated small-vessel vasculitis
Microscopic polyangiitis
Granulomatosis with polyangiitis (Wegener's)
Eosinophilic granulomatosis with polyangiitis (Churg-Strauss)
Large-vessel vasculitis
Takayasu arteritis
Giant cell arteritis

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

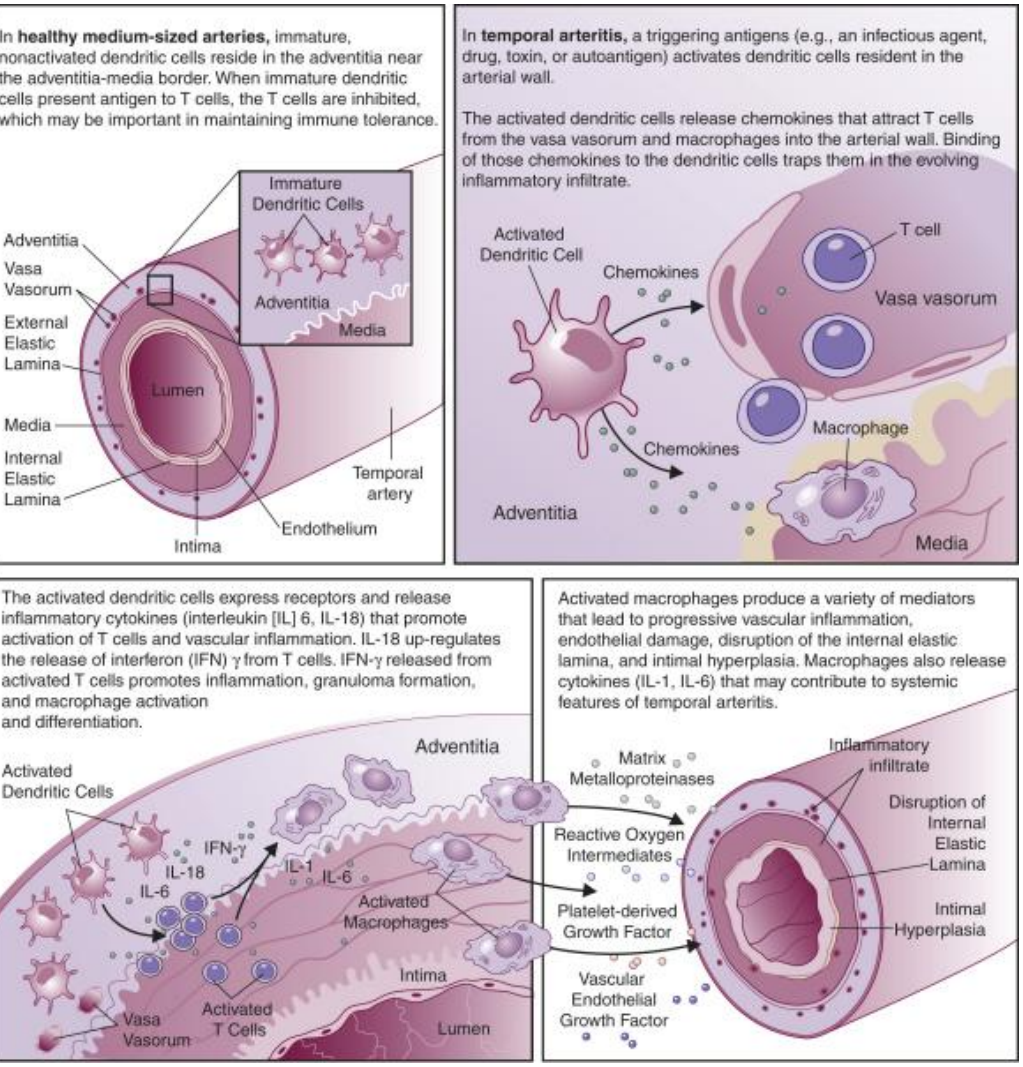
- Japan - HLA-B52 and B39
- Mexican and Colombian patients - HLA-DRB1*1301 and HLA-DRB1*1602
- India- HLA- B 5, -B 21

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

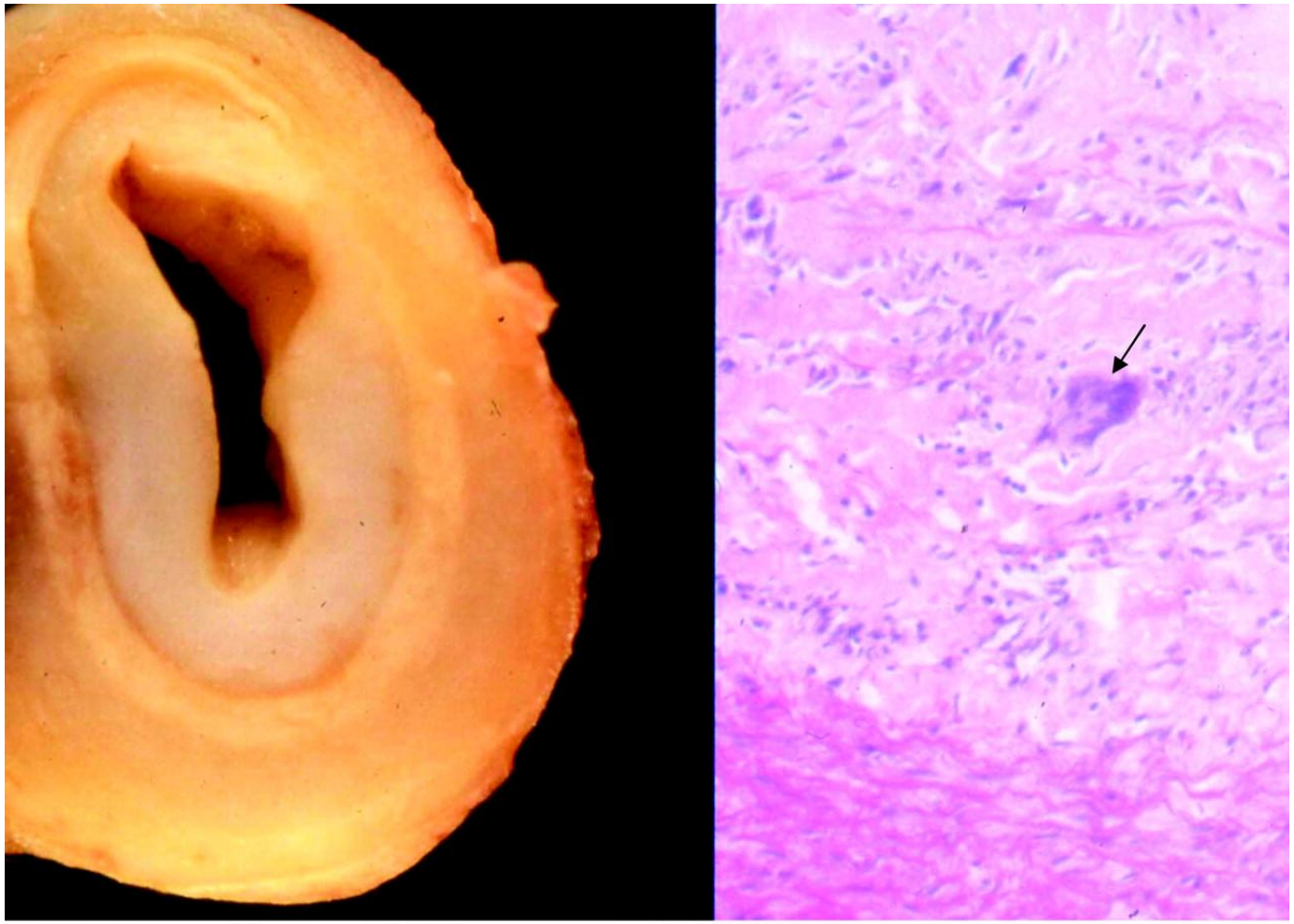
  or diffuse involvement

Pathogenesis



- 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 <u>interferon-γ</u>→ 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

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Macroscopic

Gelatinous plaques-early

White plaques-collagen

Diffuse intimal thickening

⇓

Superficial– deep scarring

⇓

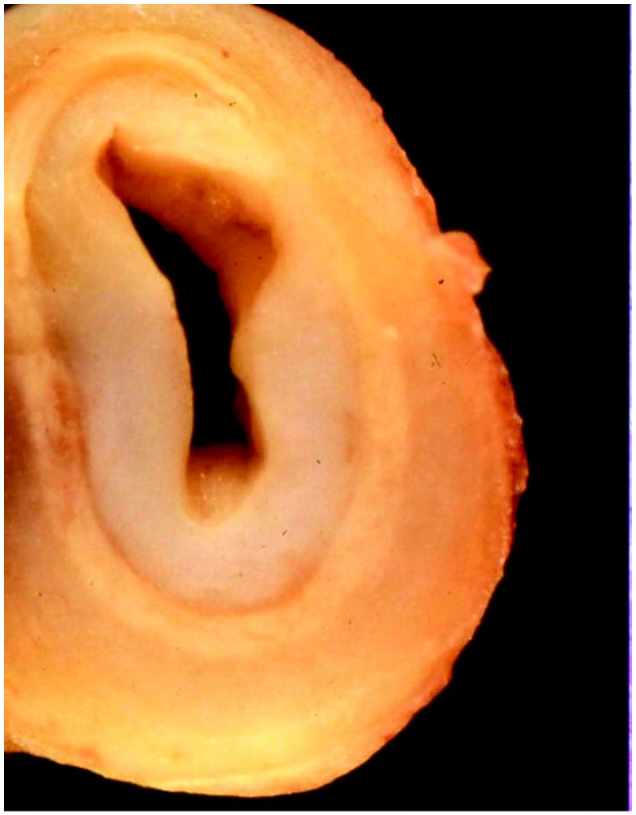
circumferential → stenosis

Mural thrombus

2^0 atheromatous changes

long standing,

HTN

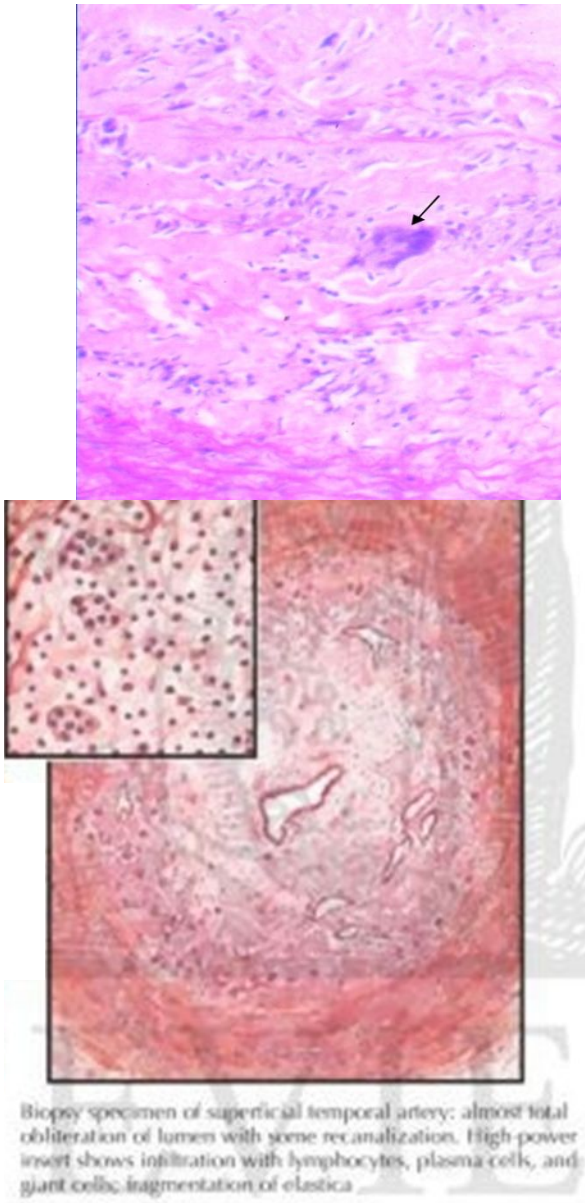


Macroscopic

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

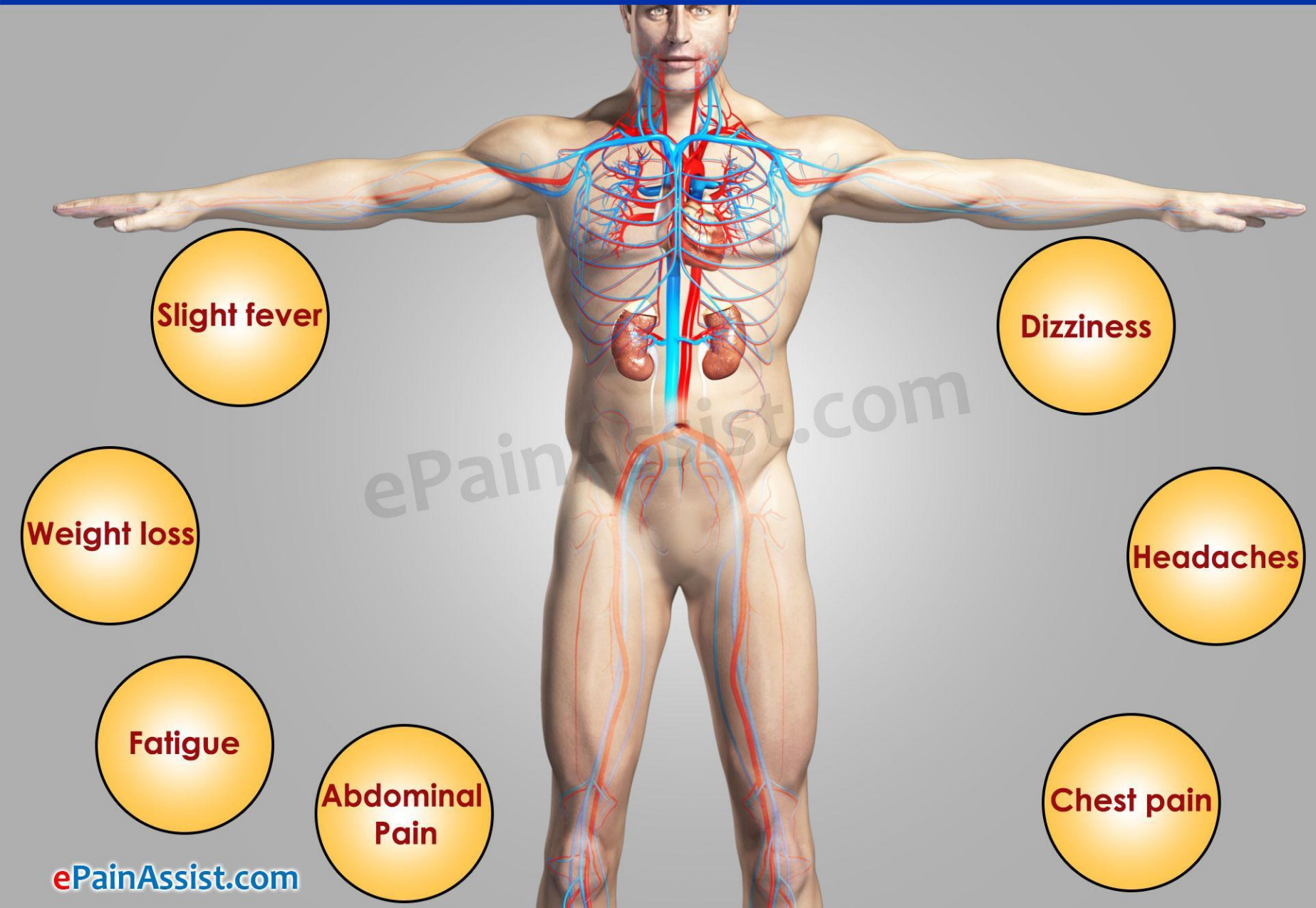
Microscopic

- 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



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	**↓/− pulses (84–96%) -claudication & BP Diff ,Bruits (80–94%) -carotids, subcl & abd vess.** **HTN- (33–83%) –Mcc RAS (28–75%),↓Ao capacitance,atyp CoA, barroreceptor reactivity** **CHF-(28%)- HTN, AR, DCM-5%** **AR-(7-24%) Ao root dil > valve inv, annuloaortic ectasia** **Coronary & vascular involvement**
CNS	Cerebral ischemia 2 ^{0} to obliterative arteritis, seizures etc
RENAL	RAS & Ischemic Nephropathy
SKIN	Erythema nodosum, Raynauds disease, leg& hand ulcers
PULMONARY	15-27%, stenosis/ occlusion of lobar/segmental pul art UL>LL, R> L—INDIA (Panja et al 1997)

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

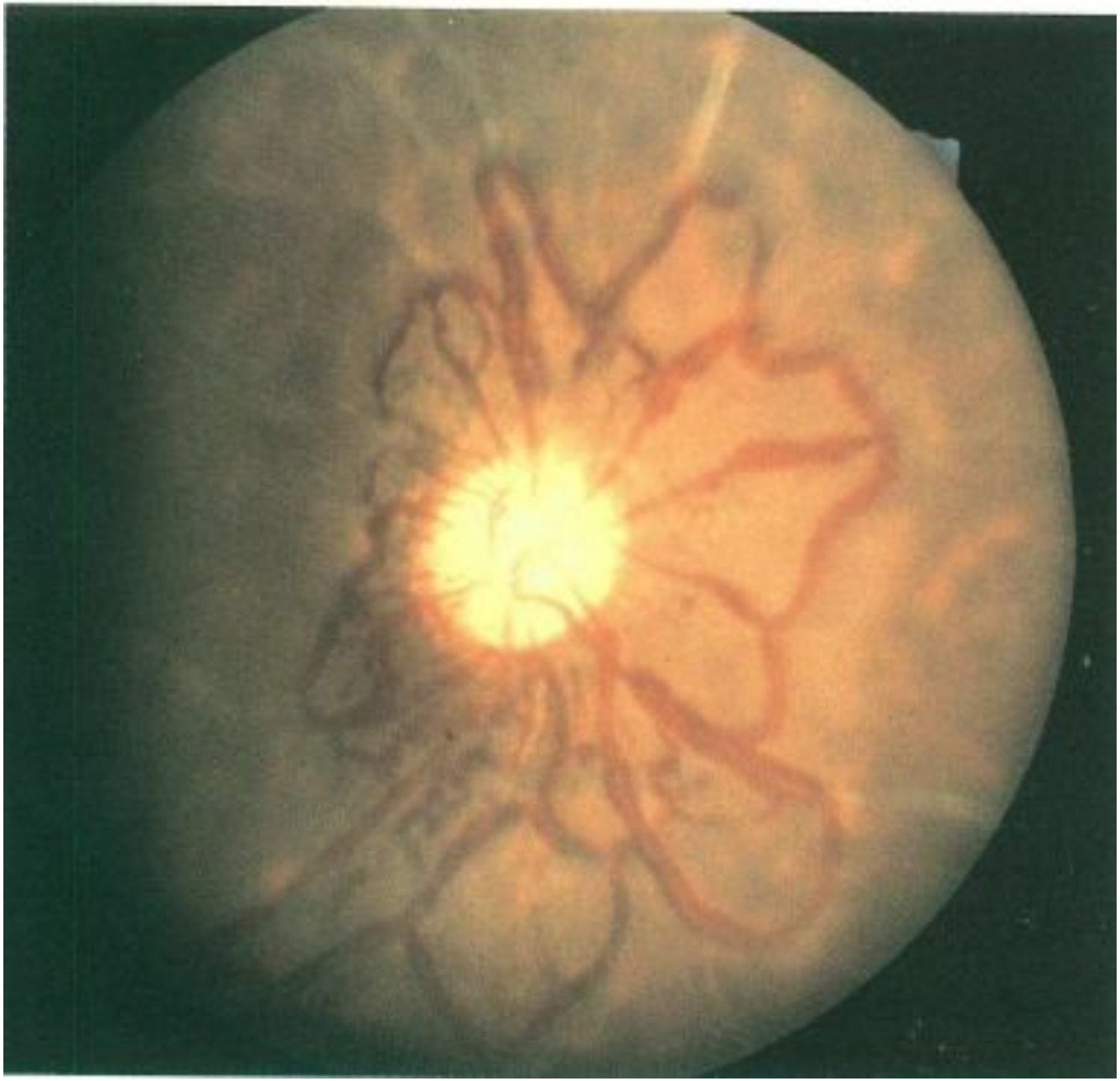
Occular involvement

Hypertensive retinopathy

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

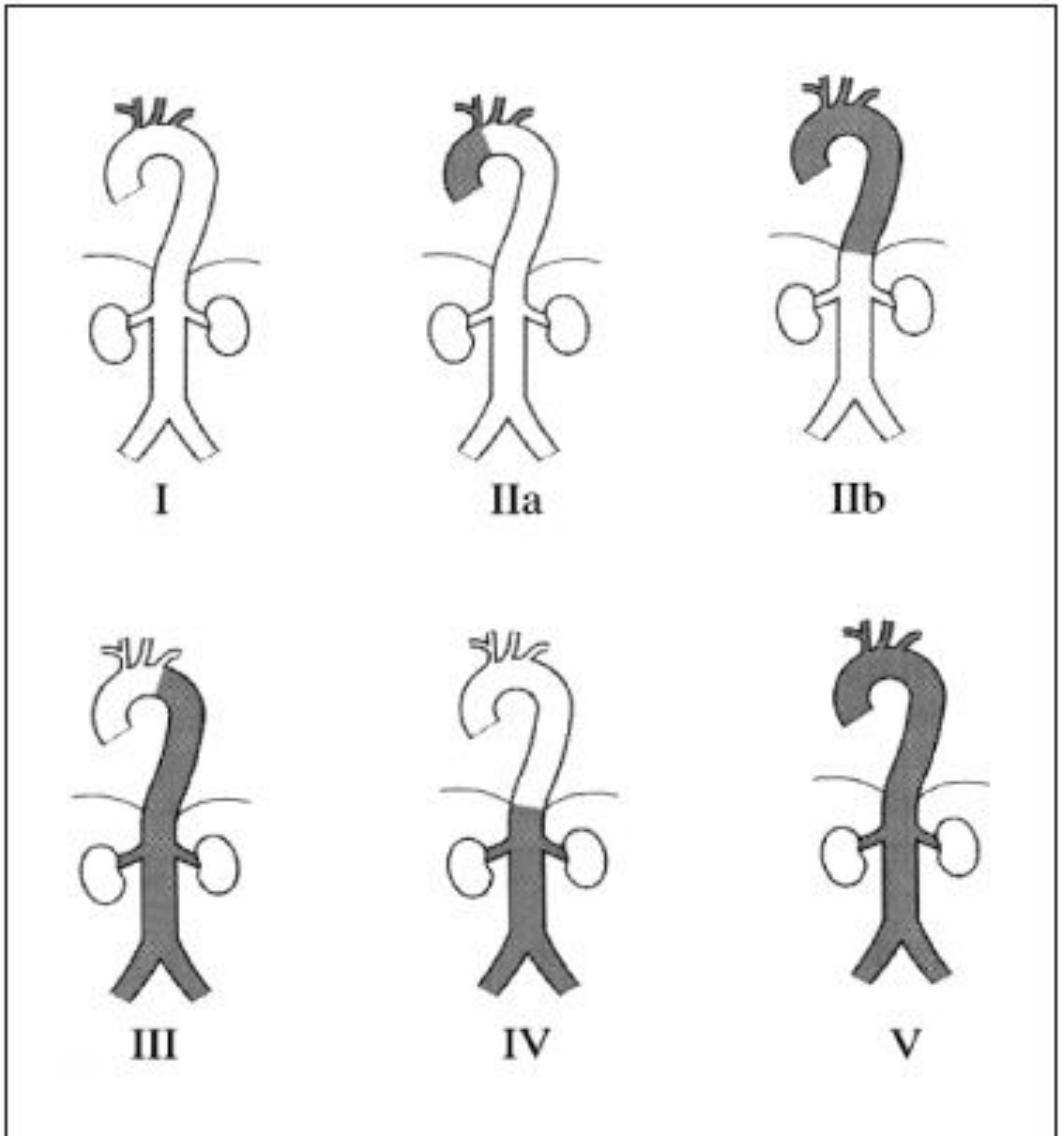
Nonhypertensive retinopathy

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



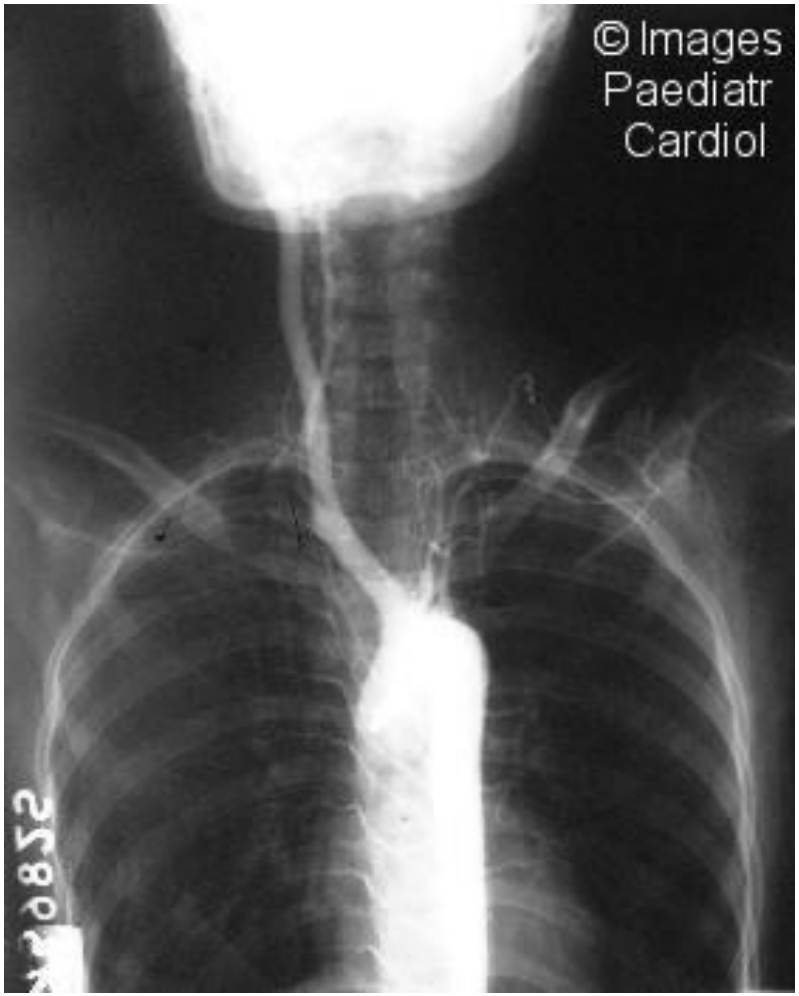
Coronary anastomosis of retinal vessels

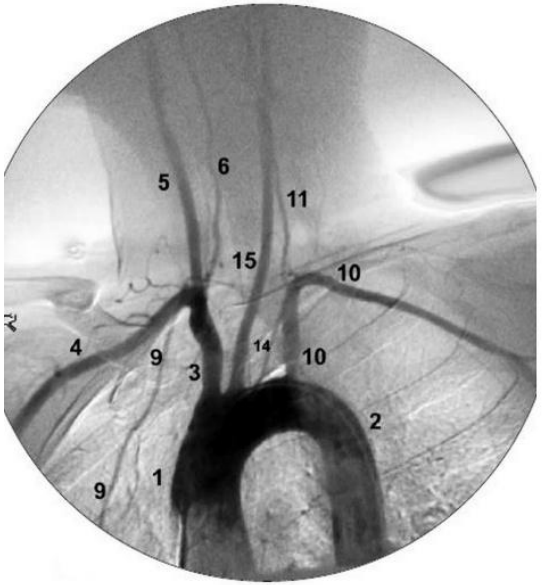
New classification of angiogram International Conference on Takayasu Arteritis, 1994



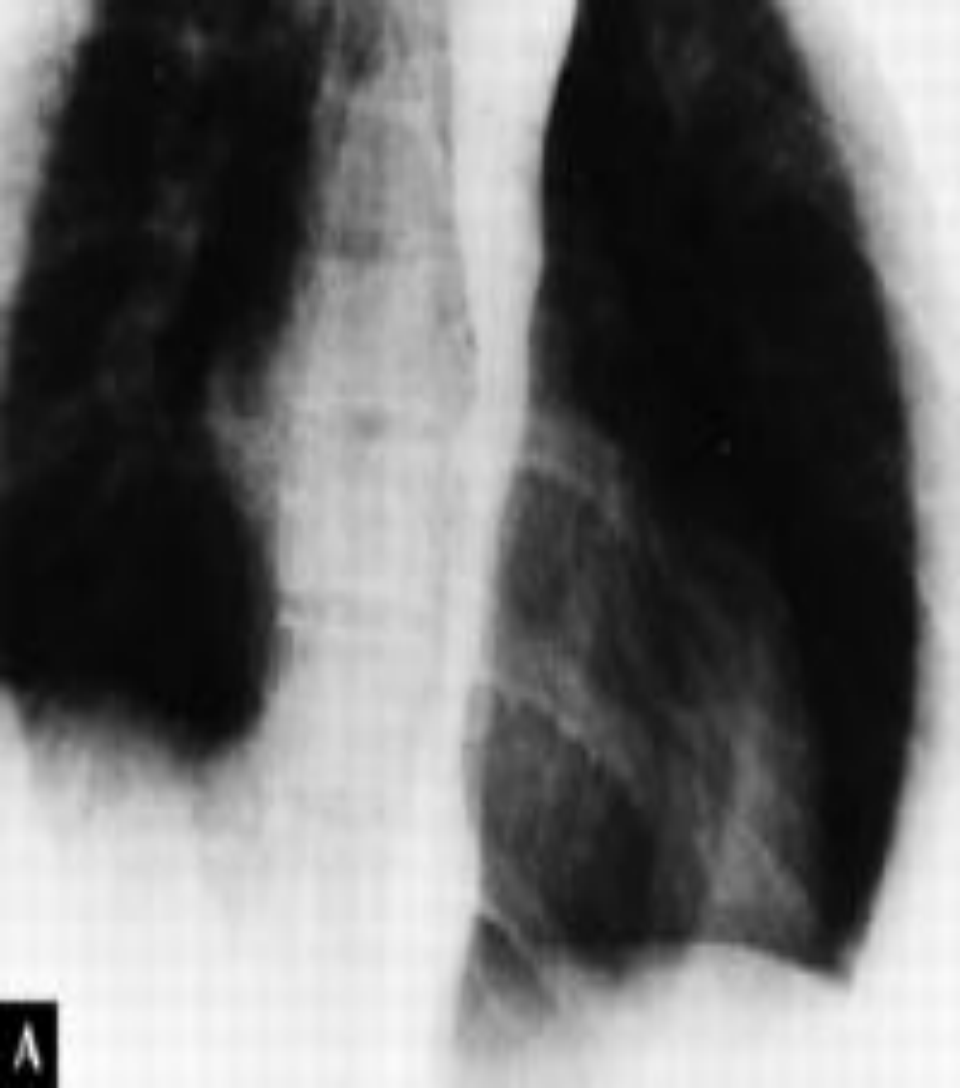
According to this classification system, involvement of the coronary or pulmonary arteries should be designed as C(+) or P(+), respectively.

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

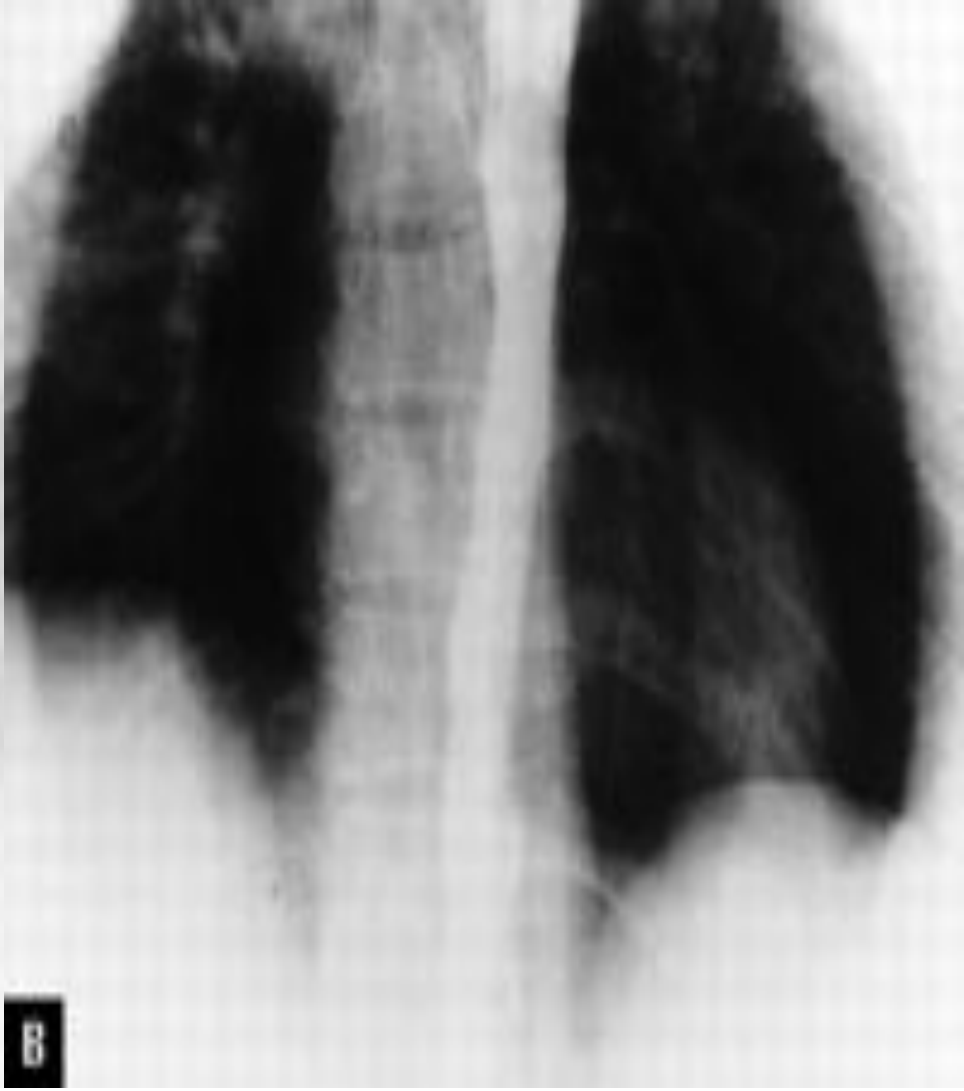




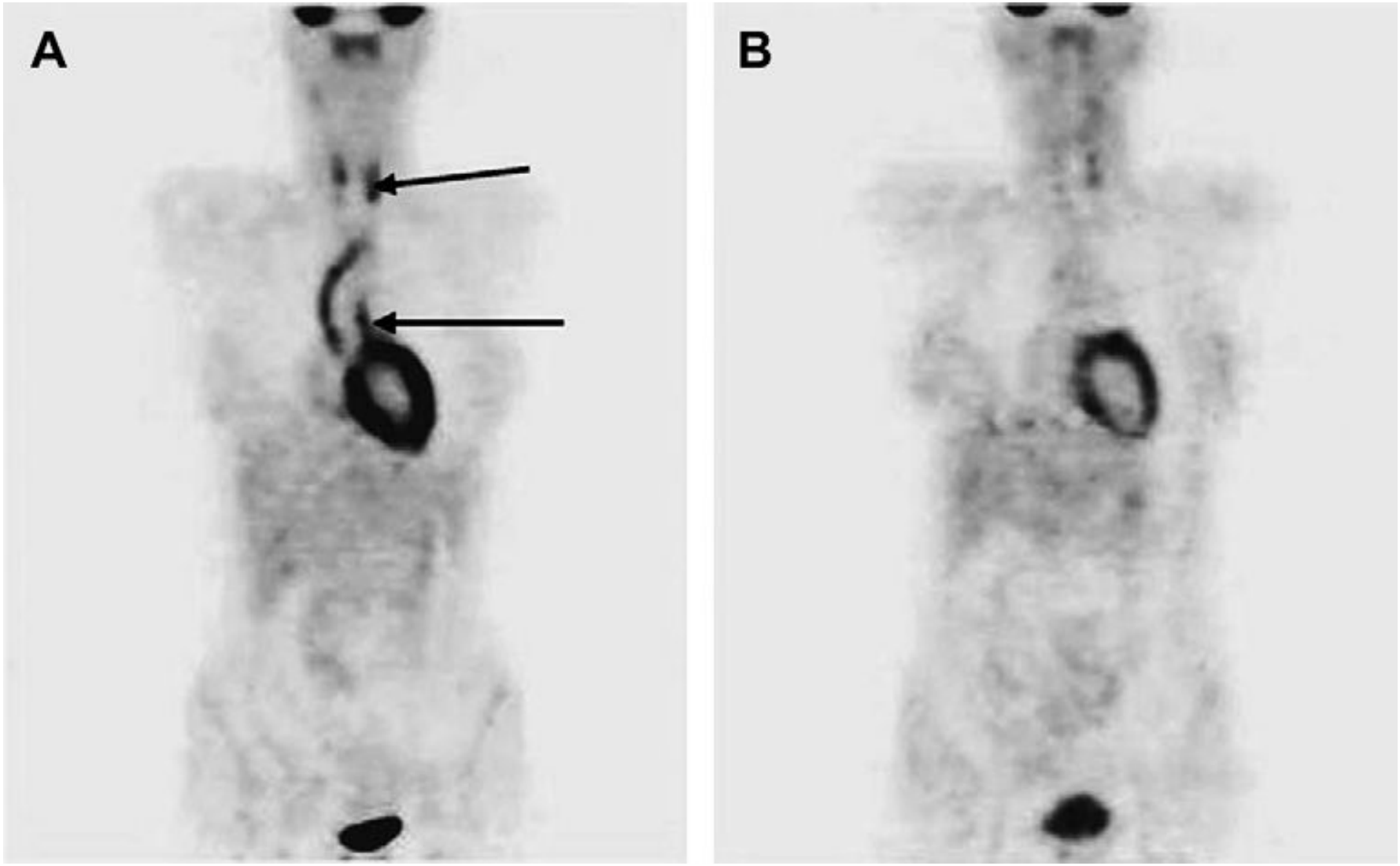
1 ascending thoracic aorta
2 descending thoracic aorta
3 innominate artery
4 right subclavian artery
5 right common carotid artery
6 right vertebral artery
9 right internal mammary artery
10 left subclavian artery
11 left vertebral artery
12 left thyrocervical trunk
14 left internal mammary artery
15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



long-segment diffuse stenotic involvement of the DTA



after deployment of stents.



remission after treatment

Figure 4. Takayasu arteritis involving the coronary ostia.

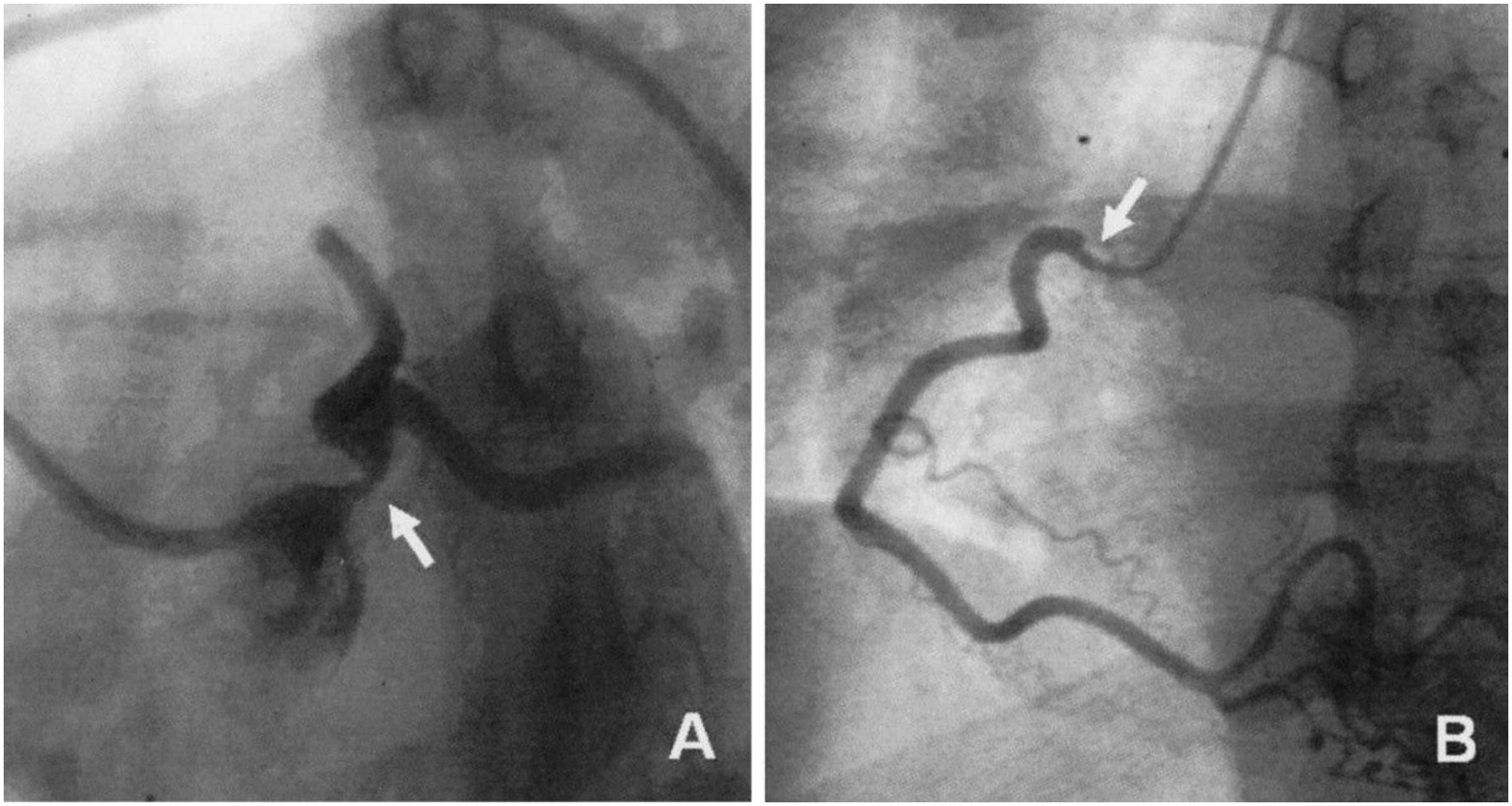


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Figure 3. Aortic occlusive disease in a patient with Takayasu arteritis and bilateral leg claudication.

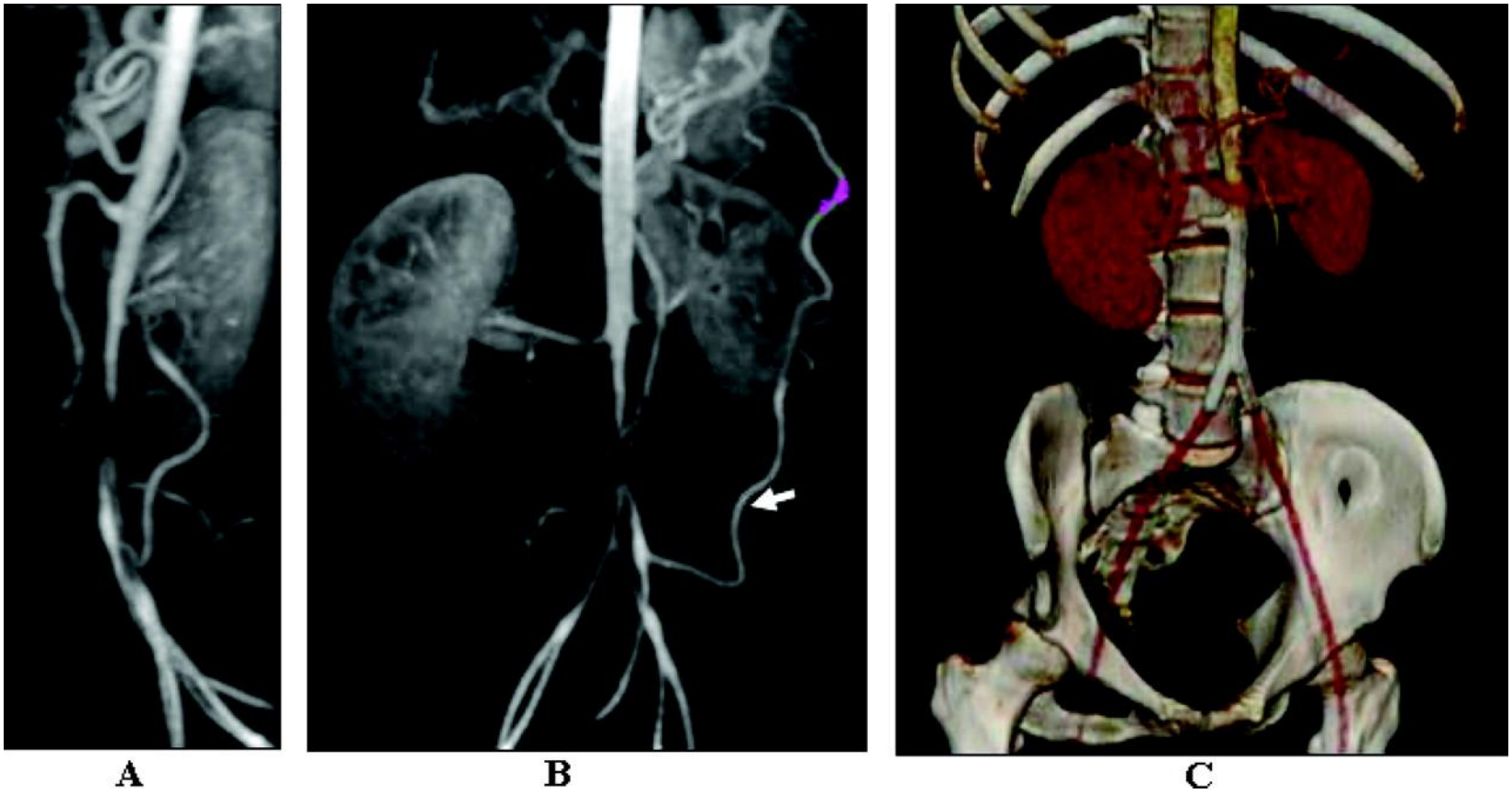

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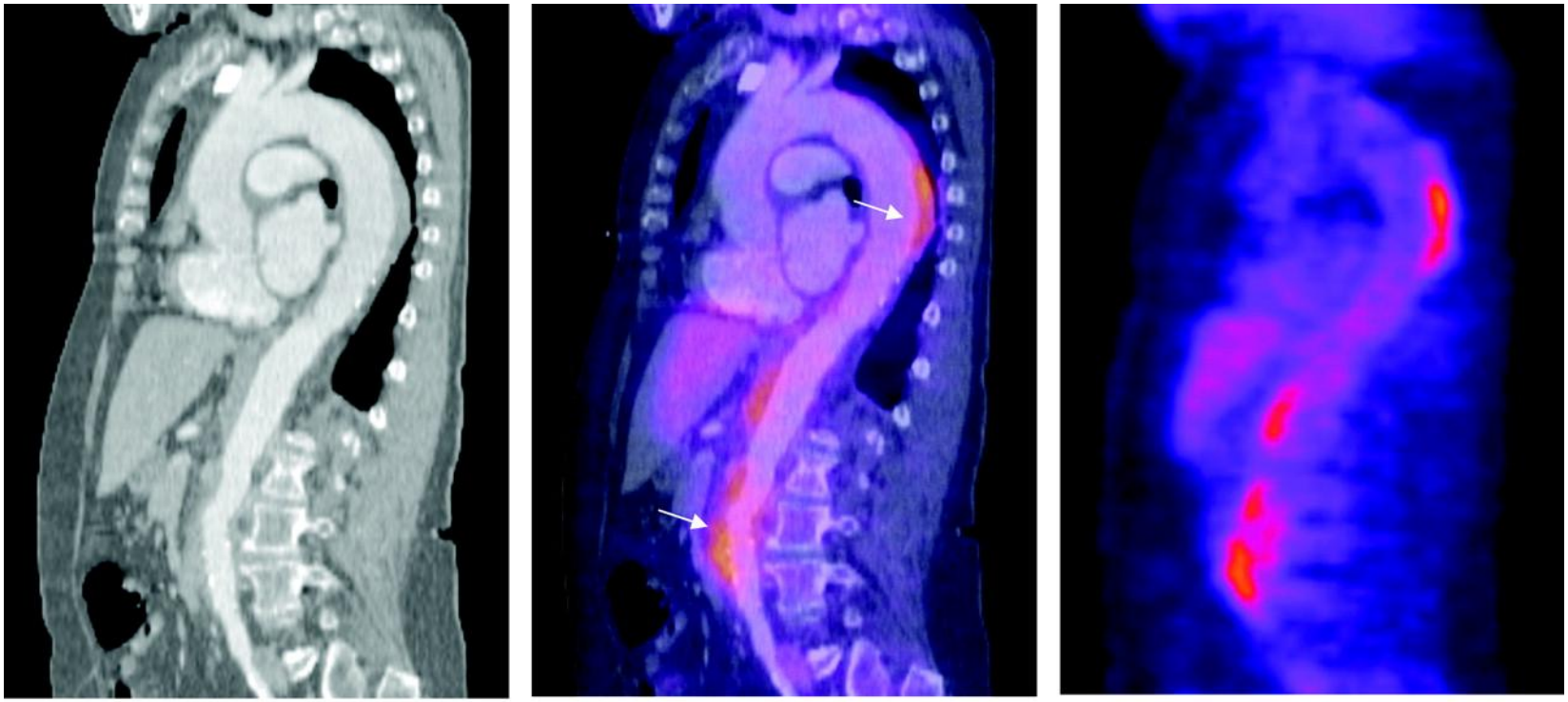
Figure 7. Combination of 18F-FDG PET and CTA for assessment of Takayasu arteritis.



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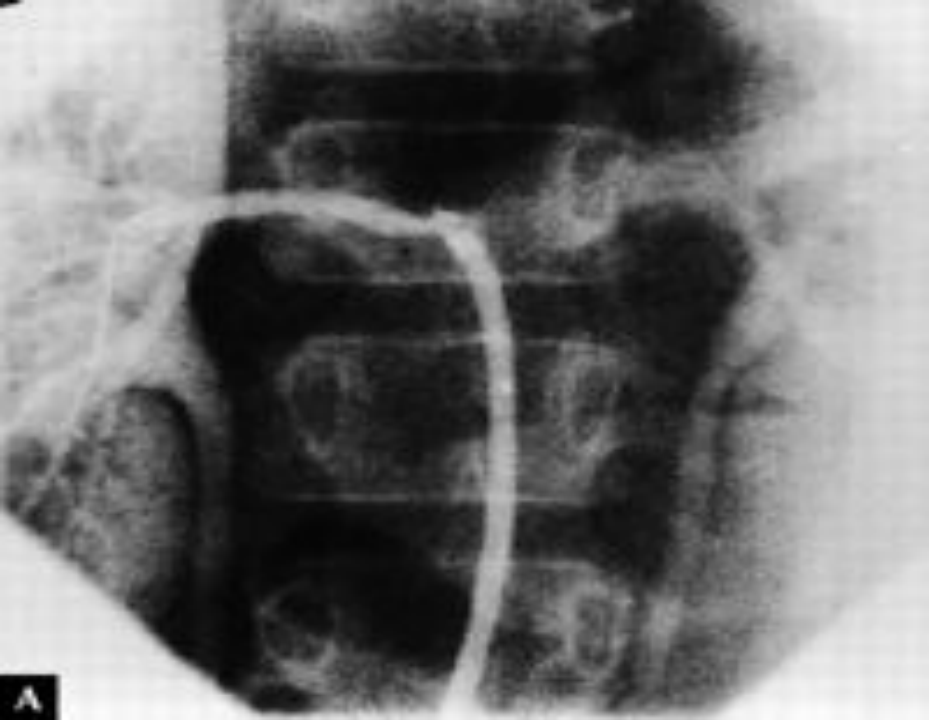
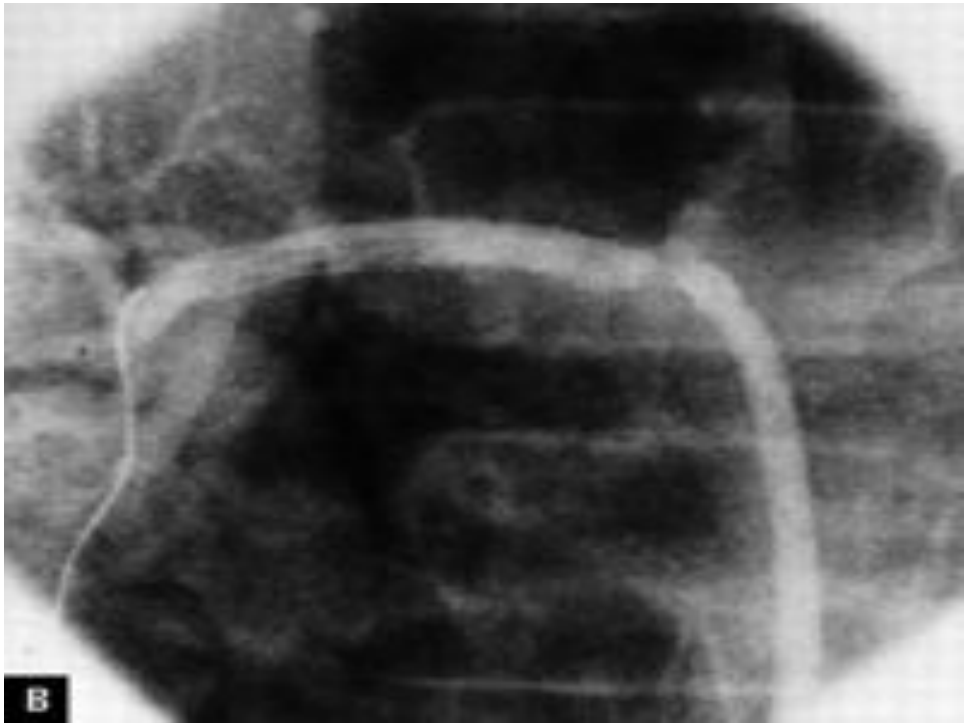
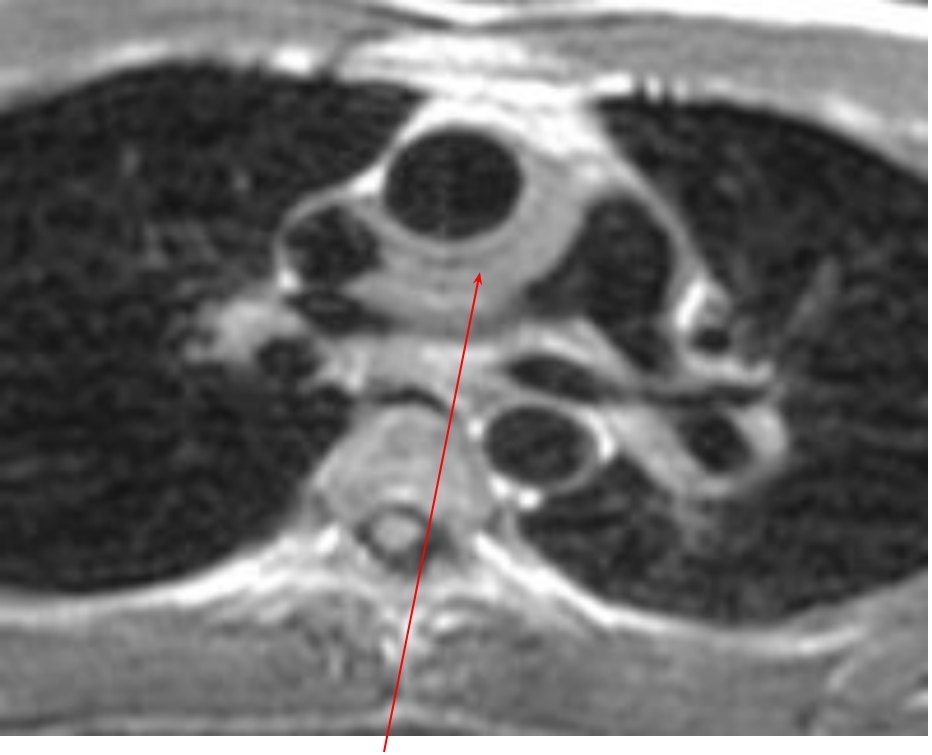


ostial stenosis of the right renal artery

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

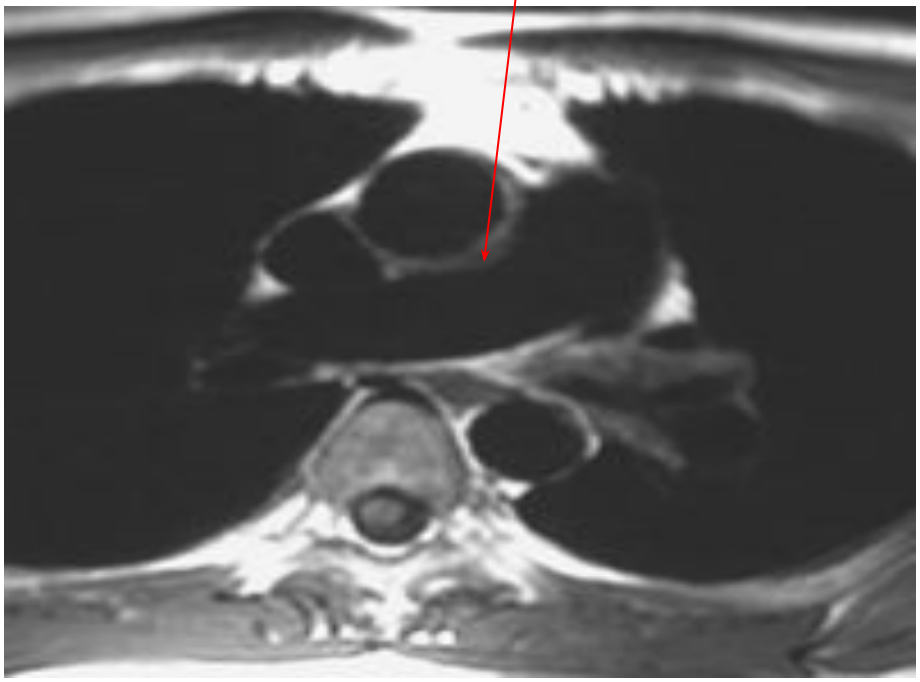


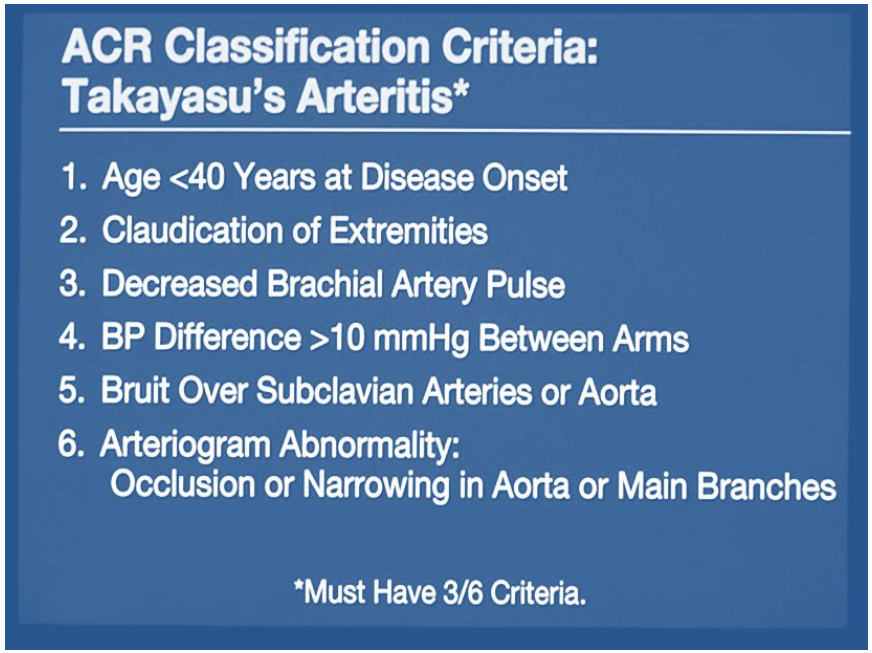
Table 4. American College of Rheumatology Classification Criteria of Takayasu Arteritis*

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 al[47] with permission of Wiley-Liss, Inc, a subsidiary of John Wiley and Sons, Inc.

Diagnosis



- 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)