When to suspect pulmonary renal Vasculitis? Radiology & Clinical clues

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NRITLD

Vasculitis

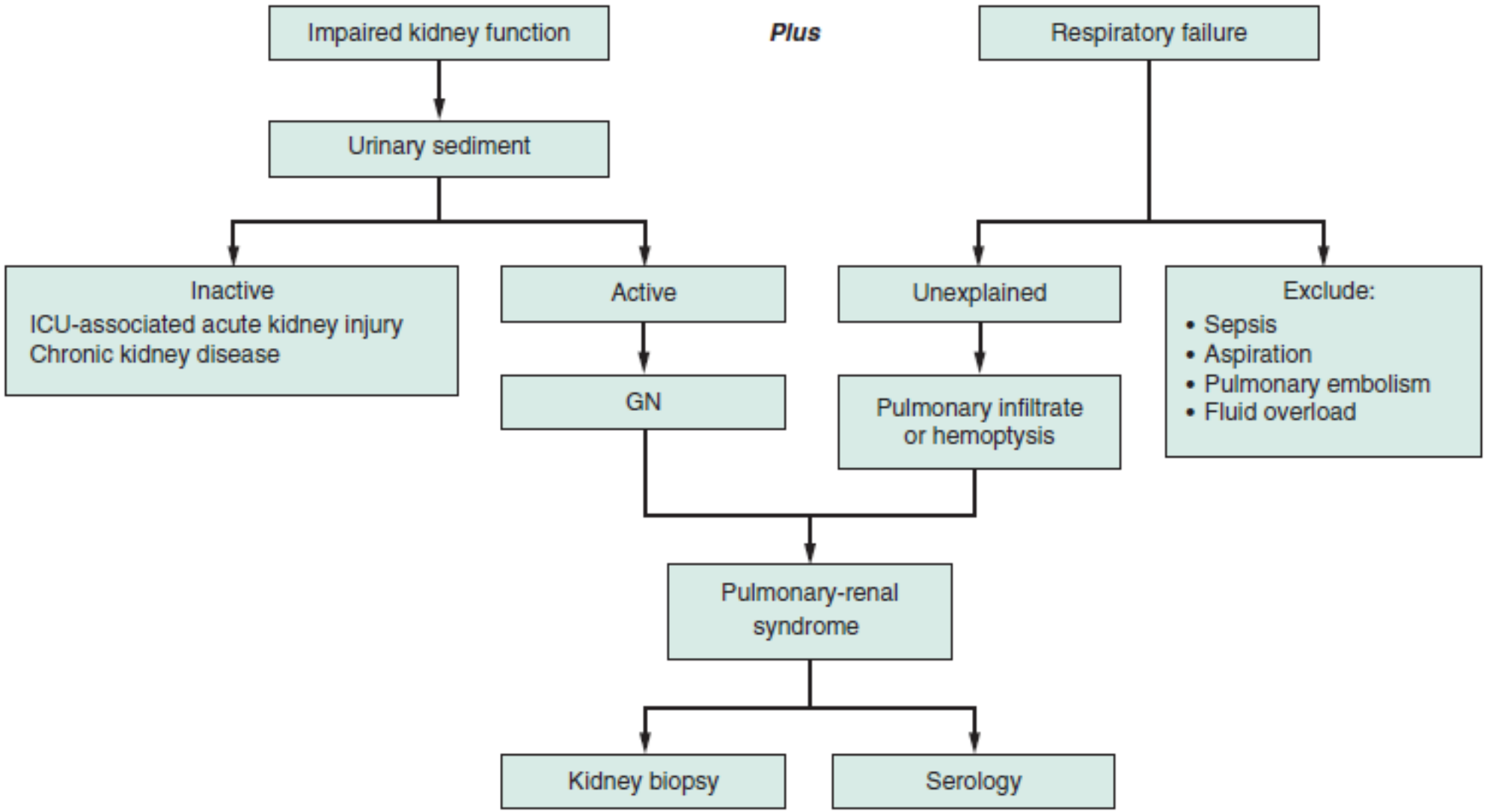
- Vasculitis is an inflammatory destructive process affecting blood vessels.

- Pulmonary vasculitis may be secondary to other conditions or constitute a primary, and in most cases idiopathic, disorder.
- Underlying conditions in the secondary vasculitides are infectious diseases, connective tissue diseases, malignancies, and hypersensitivity disorders

Pulmonary-Renal Syndrome

Elke L. Woodhouse and Richard K.S. Phoon

Diagnosis of pulmonary-renal syndrome



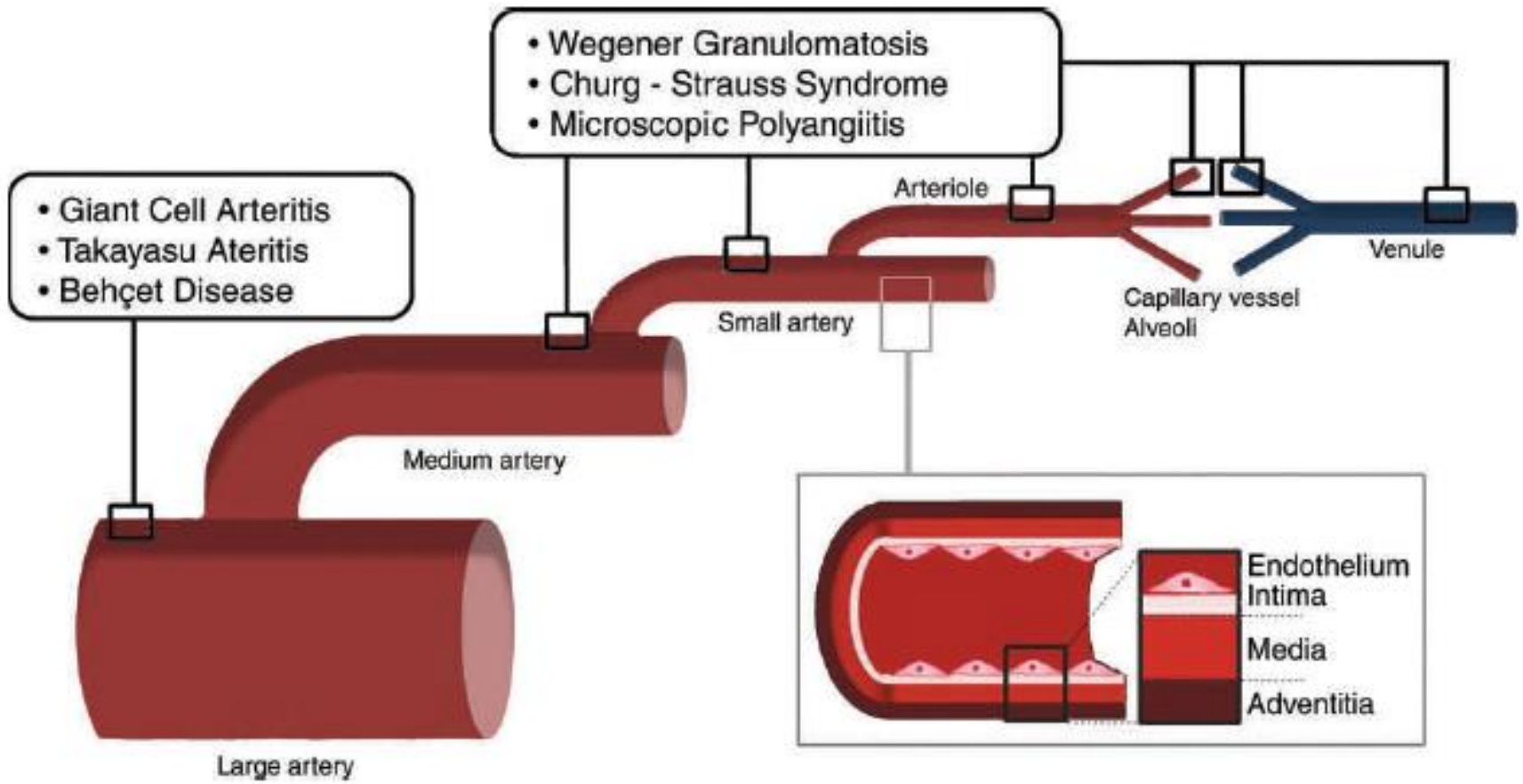

• Wegener Granulomatosis
• Churg - Strauss Syndrome
• Microscopic Polyangiitis
• Giant Cell Arteritis
• Takayasu Ateritis
• Behçet Disease
Arteriole
Venule
Capillary vessel
Alveoli
Small artery
Medium artery
Large artery
Endothelium
Intima
Media
Adventitia

Table 1
Classification of the Vasculitides

Included in the Chapel Hill nomenclature
Large-vessel vasculitis
GCA
Takayasu arteritis
Medium-sized vessel vasculitis
Polyarteritis nodosa
Kawasaki disease
Small-vessel vasculitis
Wegener granulomatosis*
CSS*
Microscopic polyangiitis*
Henoch-Schönlein purpura
Essential cryoglobulinemic vasculitis
Cutaneous leukocytoclastic angiitis
Not included in the Chapel Hill classification
Primary immune complex–mediated vasculitis
Goodpasture syndrome
Behçet disease
Immunoglobulin A nephropathy
Secondary vasculitis
Classic autoimmune disease
Systemic lupus erythematosus
Rheumatoid arthritis
Polymyositis, dermatomyositis
Scleroderma
Antiphospholipid antibody syndrome
Inflammatory bowel disease
Drug induced
Paraneoplastic
Infection

Source.—References 2, 6, and 7.
*ANCA-associated vasculitis.

- ANCAs are antibodies against intracellular antigens found in neutrophils and monocytes.

- The ANCA-associated vasculitides (Wegener granulomatosis, CSS, and microscopic polyangiitis) are grouped together because of common clinical features, histopathologic involvement of small vessels, similar response to immunosuppressive treatment, and ANCA positivity (9).

- ANCA positivity is common in these entities but not universal; thus, ANCA negativity does not completely rule out these diseases

Table 2
Types of ANCA Associated with Primary Small-Vessel Vasculitis

Small-Vessel Vasculitis	Type of ANCA*	Comments
Wegener granulomatosis	c-ANCA (anti-PR3)	85%–90% sensitivity for generalized active Wegener granulomatosis 60% sensitivity for limited pulmonary disease 40% sensitivity for disease in remission
CSS	p-ANCA (anti-MPO)	35%–50% sensitivity
Microscopic polyangiitis	p-ANCA (anti-MPO)	35%–70% sensitivity

Source.—References 9–11.
*anti-MPO = anti-myeloperoxidase, anti-PR3 = anti–proteinase 3, c-ANCA = cytoplasmic ANCA, p-ANCA = perinuclear ANCA.

Differential Diagnosis of the Pulmonary-Renal Syndrome

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Department of Internal Medicine, Division of Nephrology, Robert-Bosch-Hospital, Stuttgart

Disease	Proteinase-3-Antibody	Myeloperoxidase (MPO-)-Antibody	ANCA negative	Anti-GBM-Ab
Wegener`s Granulomatosis	70 %	20 %	10 %	<10%
Microscopic Polyangiitis	30 %	60 %	10 %	<10%
Churg-Strauss-Syndrome	10 %	60 %	30 %	<10%
Goodpasture Syndrome	<10%	<30%	70%	95%

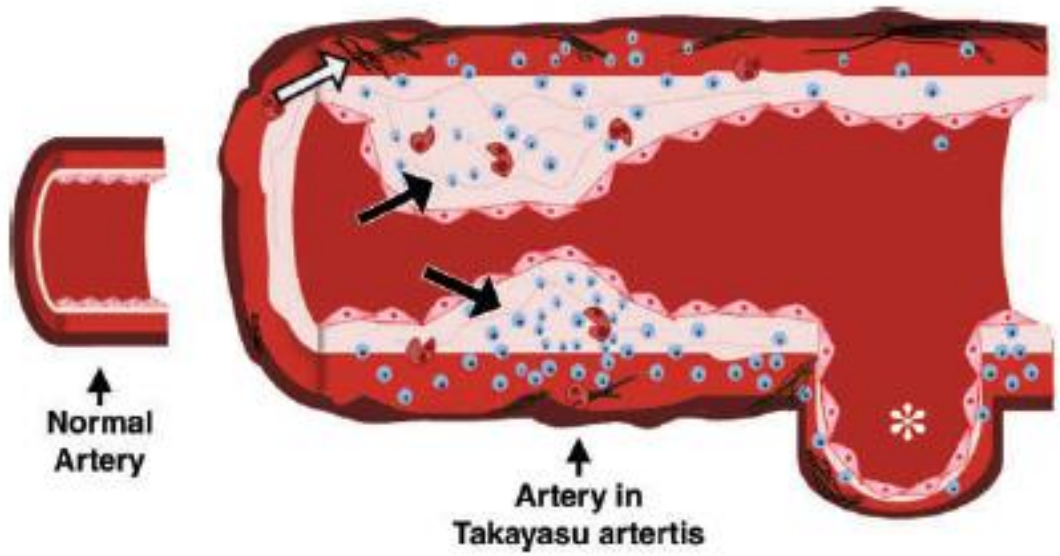


Figure 2. Diagram shows the granulomatous inflammation of the vessel wall that takes place in Takayasu arteritis. Note the marked intimal proliferation (black arrows) and the fibrosis of the media and adventitia (white arrow). These processes lead to segmental stenosis and poststenotic aneurysms (*).

Table 3
Clinical and Radiologic Scenarios Suggestive of Vasculitis

Deforming or ulcerating upper airway lesions
Palpable purpura
Mononeuritis multiplex (peripheral neuropathy)
Rapidly progressive glomerulonephritis
Pulmonary-renal syndrome (DAH and glomerulonephritis)
Chest imaging findings of nodular or cavitary diseases
DAH

Source.—References 2 and 9.

Differential Diagnosis of Pulmonary Hemorrhage and Acute Renal Failure

Wegener's granulomatosis
Goodpasture's syndrome
Systemic lupus erythematosus
Poststreptococcal glomerulonephritis
Henoch-Schönlein purpura
Pulmonary veno-occlusive disease
Drug toxicity (i.e., cocaine, sirolimus)
Severe pulmonary sepsis

Pulmonary Manifestations of Systemic Vasculitis

BRIAN P. O'SULLIVAN AND TED KREMER

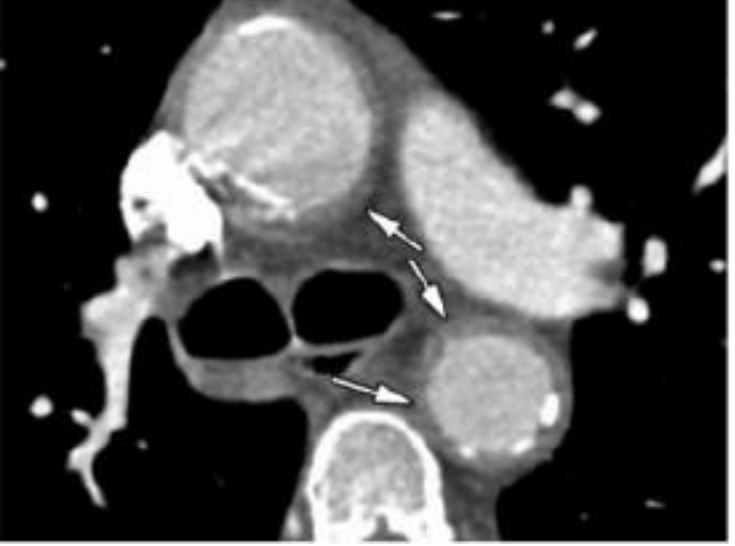
Table 11-2 Clinical and Serologic Findings in Patients with Pulmonary-Renal Syndromes*

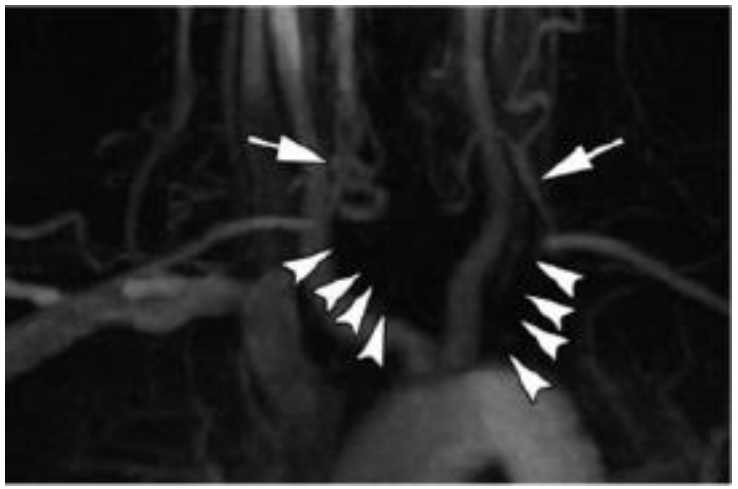
	HSP	GPS	WG	MPA	SLE
Pulmonary hemorrhage	0 to +	++++	+++	+++	+ to ++
Glomerulonephritis	++++	++++	++++	++++	+++ to ++++
Upper airway involvement	0	0	++++	++	+ to ++
Skin rash	++++	0 to +	+++	+++	++++
Arthralgia	++++	0	+++	+++	++++
Elevated ESR	+	0	++++	++++	++++
Abdominal involvement	++++	0	0	0	0
Serology	IgA positive, IgM positive	Anti-GBM (rarely P-ANCA)	C-ANCA (rarely P-ANCA)	P-ANCA, C-ANCA	ANA, anti–double-stranded DNA (rarely P-ANCA)

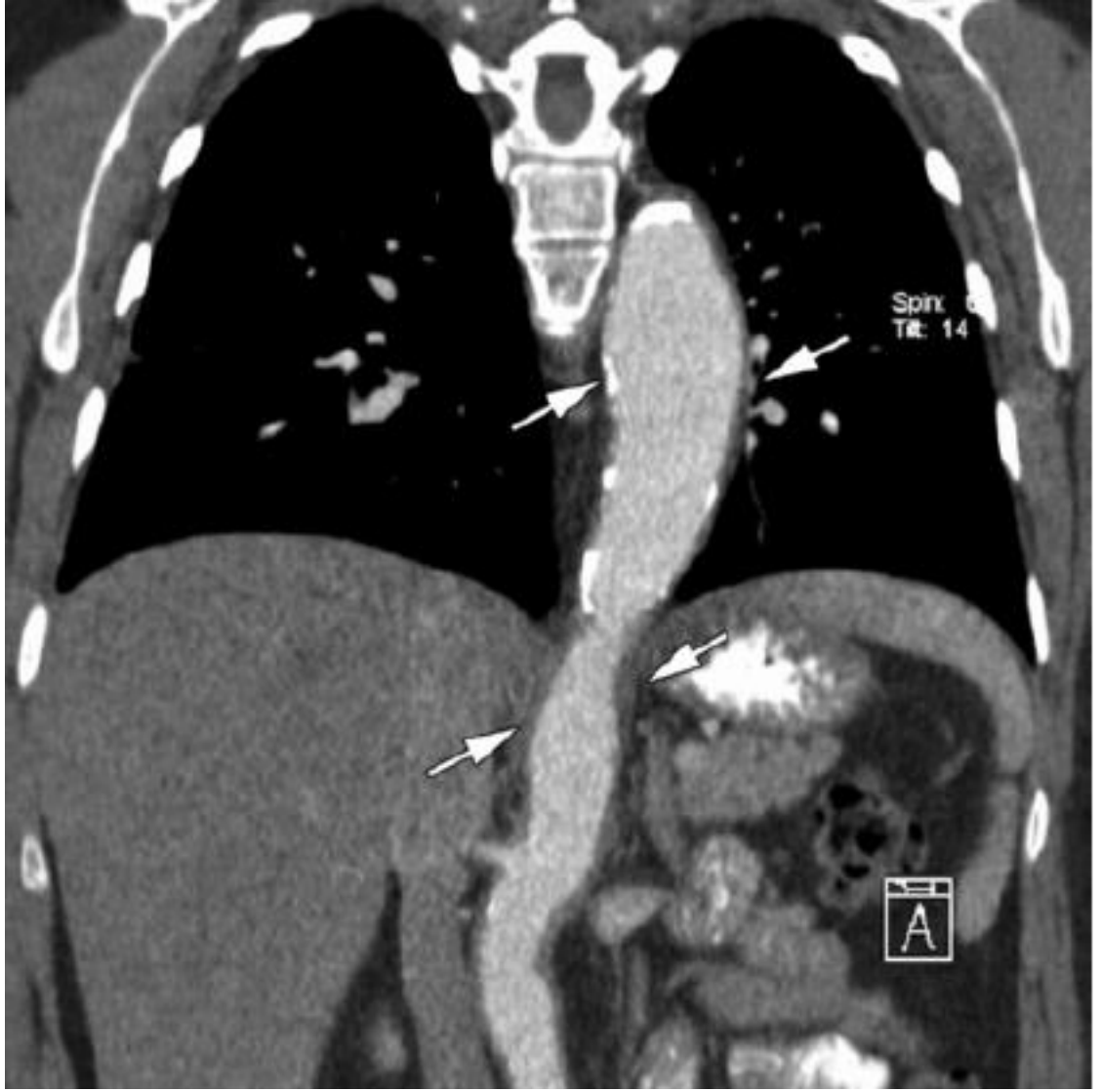
ANA, antinuclear antibody; C-ANCA, cytoplasmic antineutrophilic cytoplasmic antibody; ESR, erythrocyte sedimentation rate; GBM, glomerular basement membrane; GPS, Goodpasture syndrome; HSP, Henoch-Scho¨nlein purpura; MPA, microscopic polyangiitis; P-ANCA, perinuclear antineutrophilic cytoplasmic antibody; SLE, systemic lupus erythematosus; WG, Wegener granulomatosis

Takayasu Arteritis

- The clinical manifestations are usually divided into early and late phases, with a classic triphasic pattern of expression. This consists of an early or prepulseless phase (characterized by nonspecific systemic features, such as low-grade fever, malaise, weight loss, and fatigue), a vascular inflammatory phase, and a late quiescent and occlusive phase; the most common symptom related to vascular stenosis is diminished or absent pulses (96% of patients), typically in association with limb claudication and blood pressure discrepancies

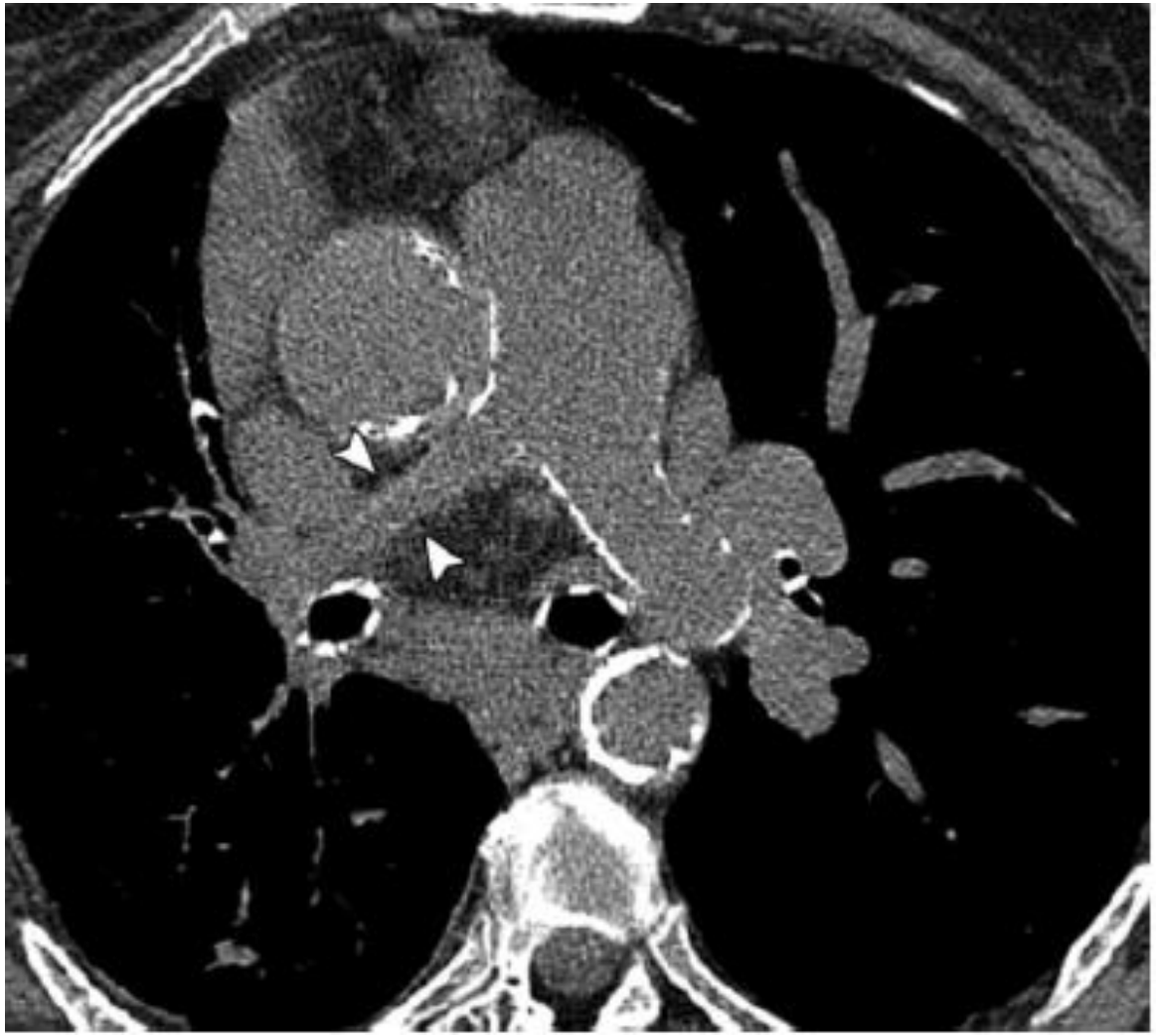






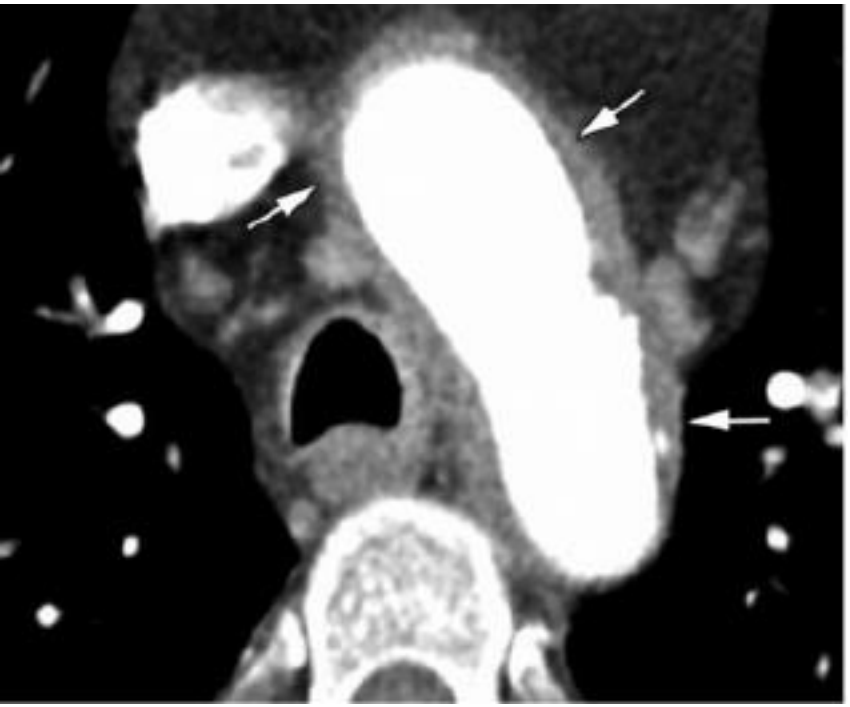
Takayasu arteritis is an idiopathic vascular disorder that may involve the thoracoabdominal aorta and its branches and the pulmonary arteries

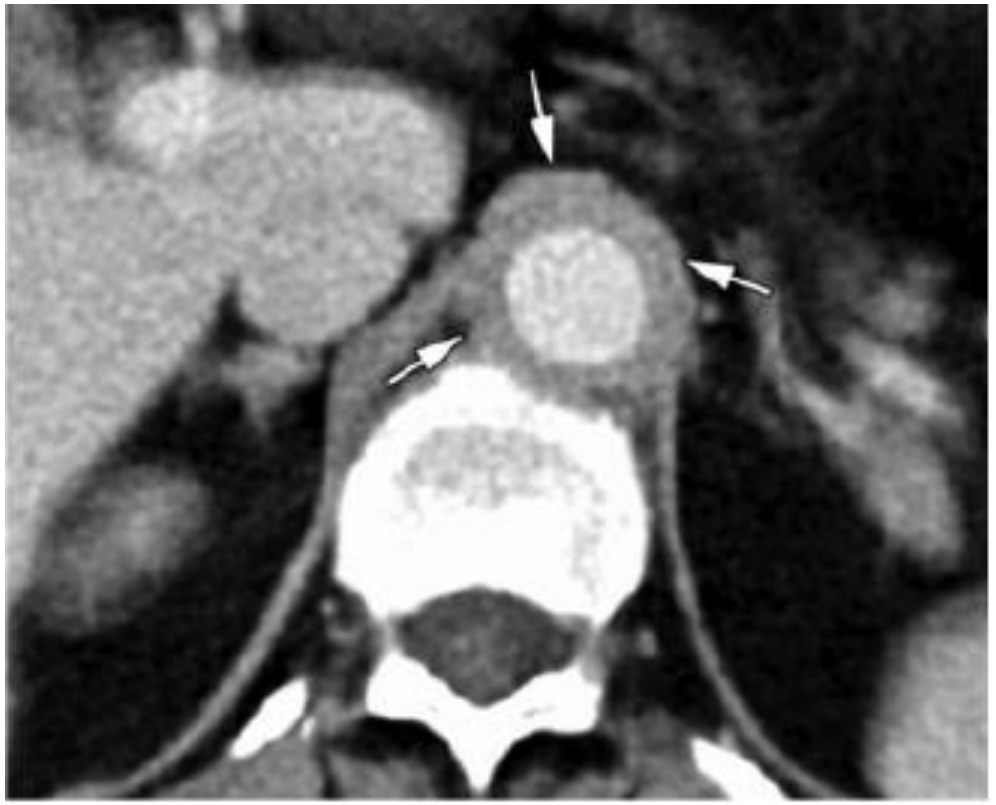
Late-stage Takayasu arteritis with pulmonary artery involvement in a 63-year-old woman. Unenhanced CT image shows marked stenosis of the right pulmonary artery



Giant Cell Arteritis

- GCA (temporal arteritis) is the most common vasculitis of large and medium-sized arteries, affecting almost exclusively individuals over50 years of age
- tender and swollen temporal arteries, temporal headache, jaw claudication, and visual loss

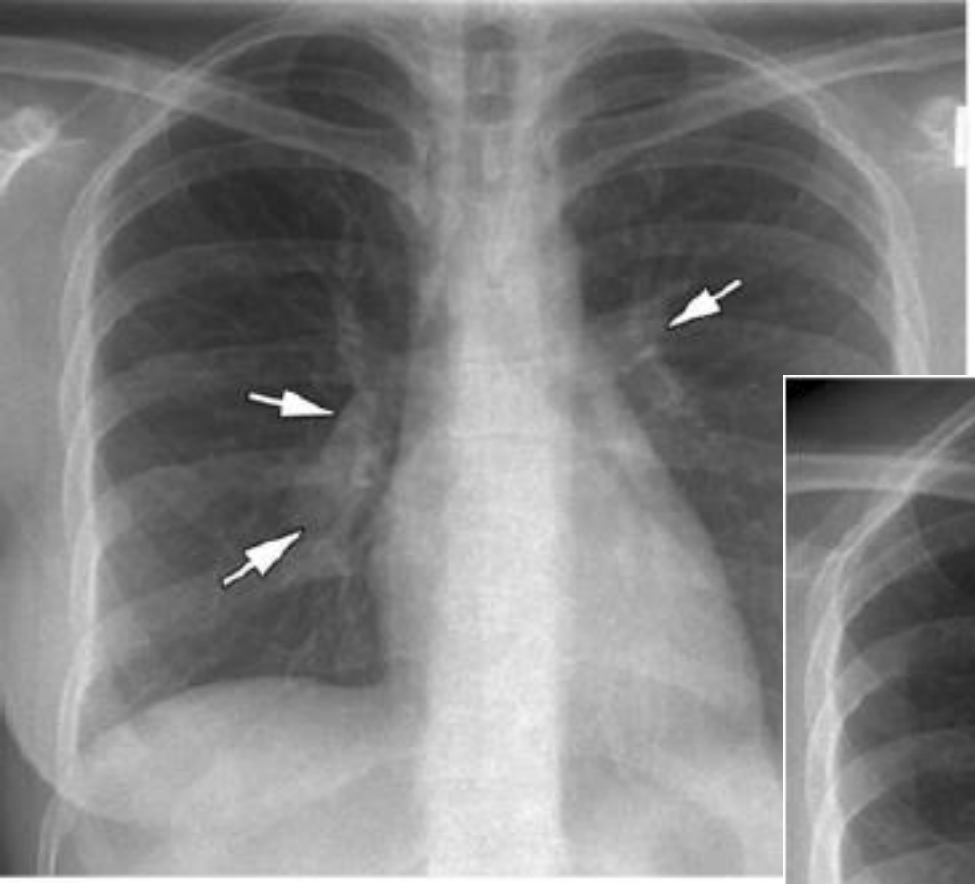


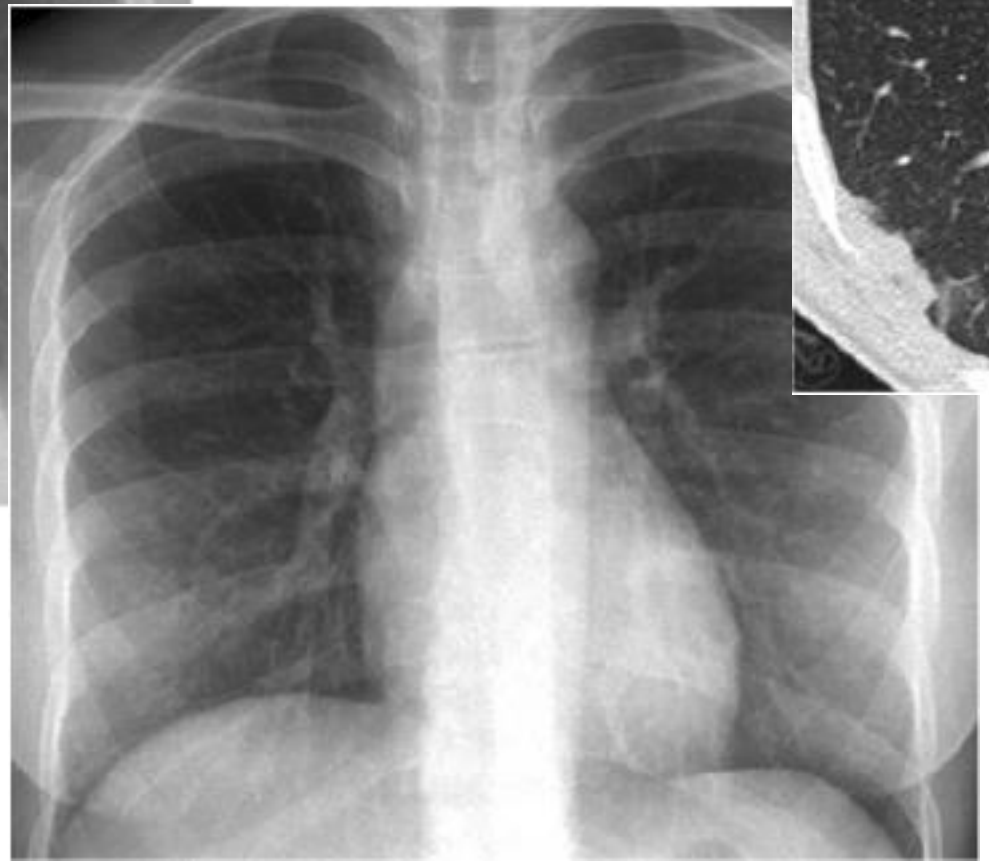


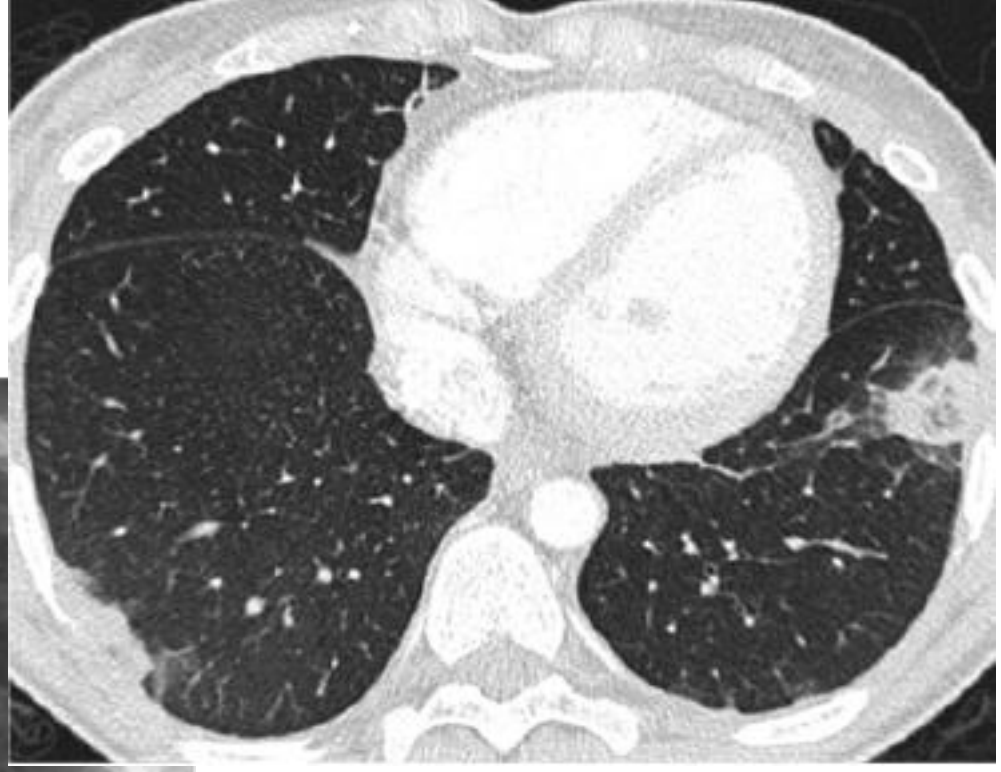
GCA in a 72-year-old woman who presented with jaw claudication. Contrast enhanced CT images show concentric wall thickening (arrows) of the aortic arch And abdominal aorta

Behçet Disease

- Behçet disease is a chronic multisystemic vasculitis.
- It is characterized by recurrent oral and genital ulcerations, ocular anomalies (uveitis), and additional clinical manifestations in multiple organ systems. The disease usually manifests in the second or third decade of life, and the male-to-female ratio is reported to be almost equal
- The reported prevalence of thoracic involvement in Behçet disease ranges from 1% to 8%



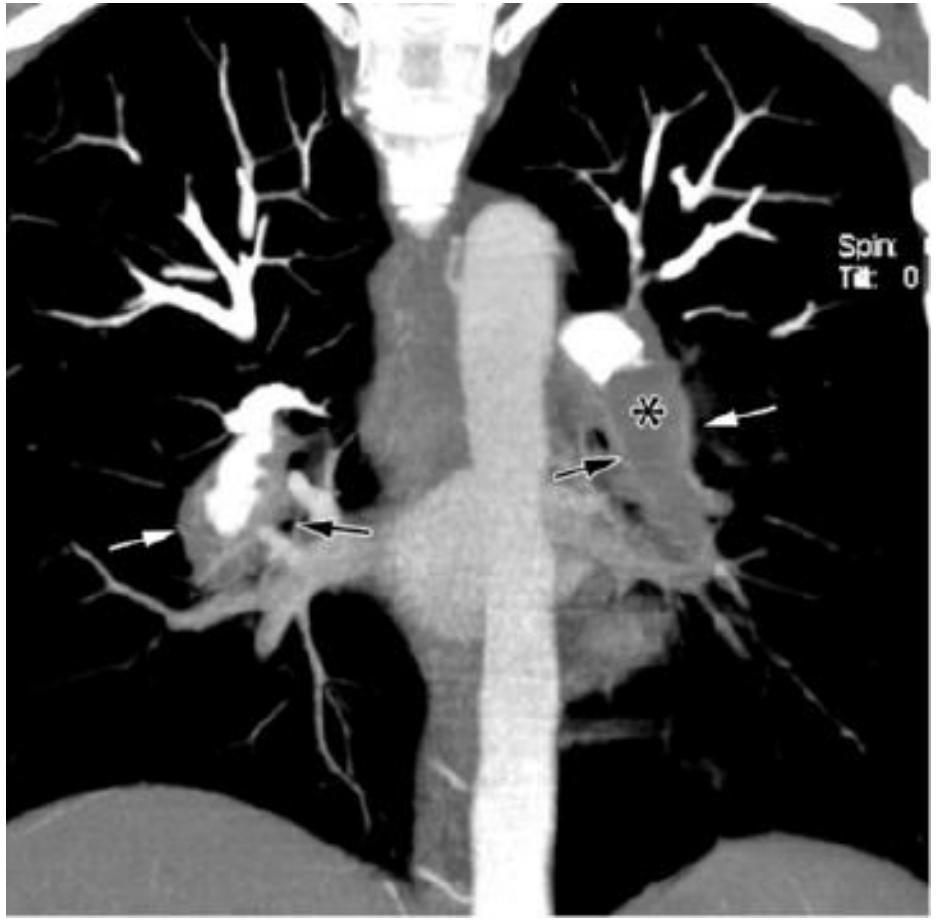


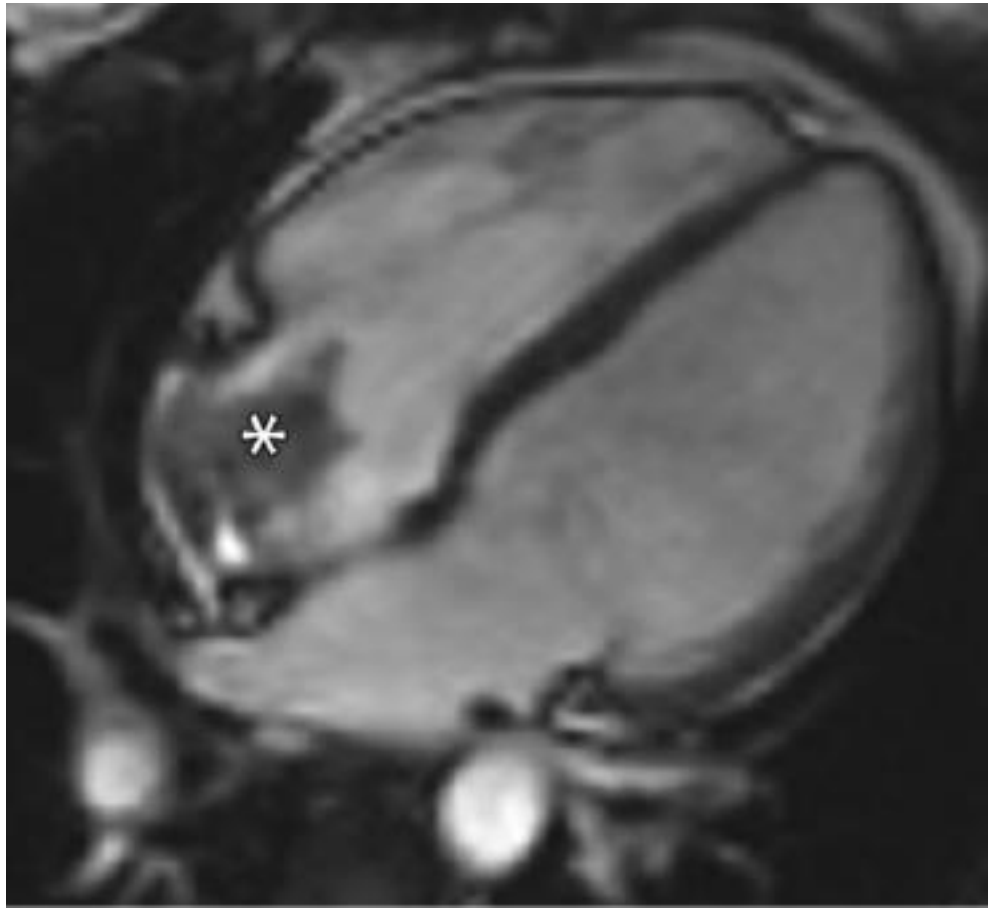


(a) Chest radiograph shows increased size and opacity of the right interlobar and lower lobe pulmonary arteries as well as of the left pulmonary artery (arrows). **(b)** Chest radiograph obtained 6 months earlier shows normal findings. **(d)** CT image (lung window) shows subpleural wedge-shaped areas of increased opacity, which are suggestive of pulmonary infarction associated

- Behçet disease is the most common cause of pulmonary artery aneurysm
- Hemoptysis is the most common presenting symptom and is one of the leading causes of death
- Pulmonary aneurysms in Behçet disease are fusiform to saccular, commonly multiple and bilateral, and located in the lower lobe or main pulmonary arteries
- Frequently, in Behçet disease, aneurysms of the pulmonary arteries are partially or totally thrombosed

(c) Coronal maximum intensity projection CT image, obtained with 10-mm section thickness, shows increased diameter of both interlobar and lower lobe pulmonary arteries. The aneurysms are thrombosed (arrows), with partial thrombosis on the right and complete thrombosis on the left**(e)** T2-weighted MR image (four-chamber view) shows a thrombus in the right atrium (*).





Wegener Granulomatosis

- Wegener granulomatosis is the most common of the ANCA-associated vasculitides. It is characterized clinically by the triad of upper airway disease (nasal, oral, or sinus inflammation),lower respiratory tract disease (airway or lung), and glomerulonephritis
- Pulmonary symptoms include hemoptysis, cough, chest pain, anddyspnea. Tracheobronchial involvement is seen in 10%–55% of patients and causes stridor, dyspnea, and postobstructive pneumonia

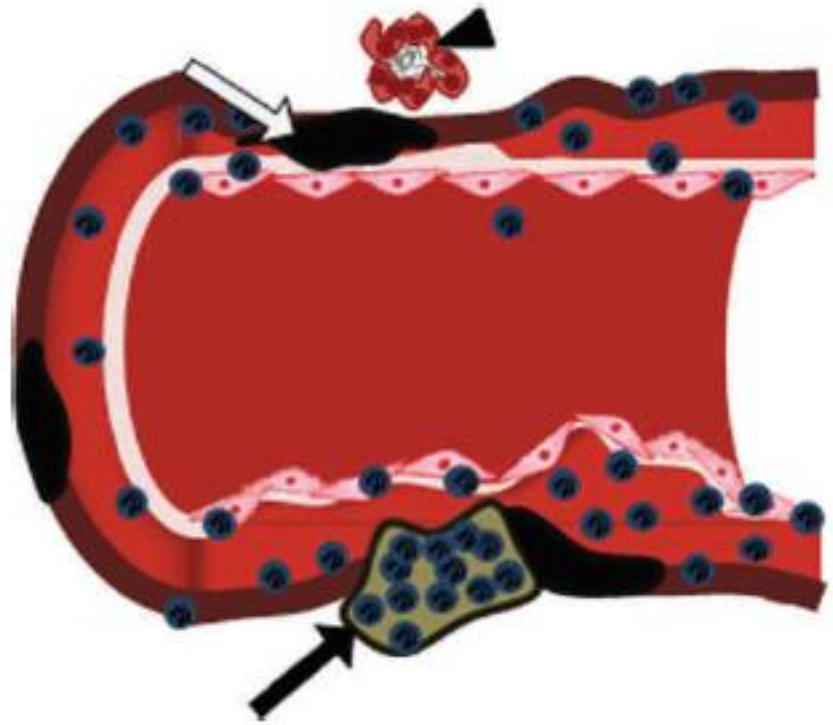


Figure 7. Diagram shows the three major histologic features that characterize Wegener granulomatosis: *(a)* vasculitis with inflammation of medium-sized and small arteries, capillaries, and venules, which are frequently located within inflammatory nodules; *(b)* areas of necrosis (white arrow); and *(c)* necrotizing and nonnecrotizing granulomatous inflammation (arrowhead). In association with the vasculitis, neutrophilic infiltration and microabscess formation (black arrow) may be present.

Pulmonary Manifestations of Systemic Vasculitis

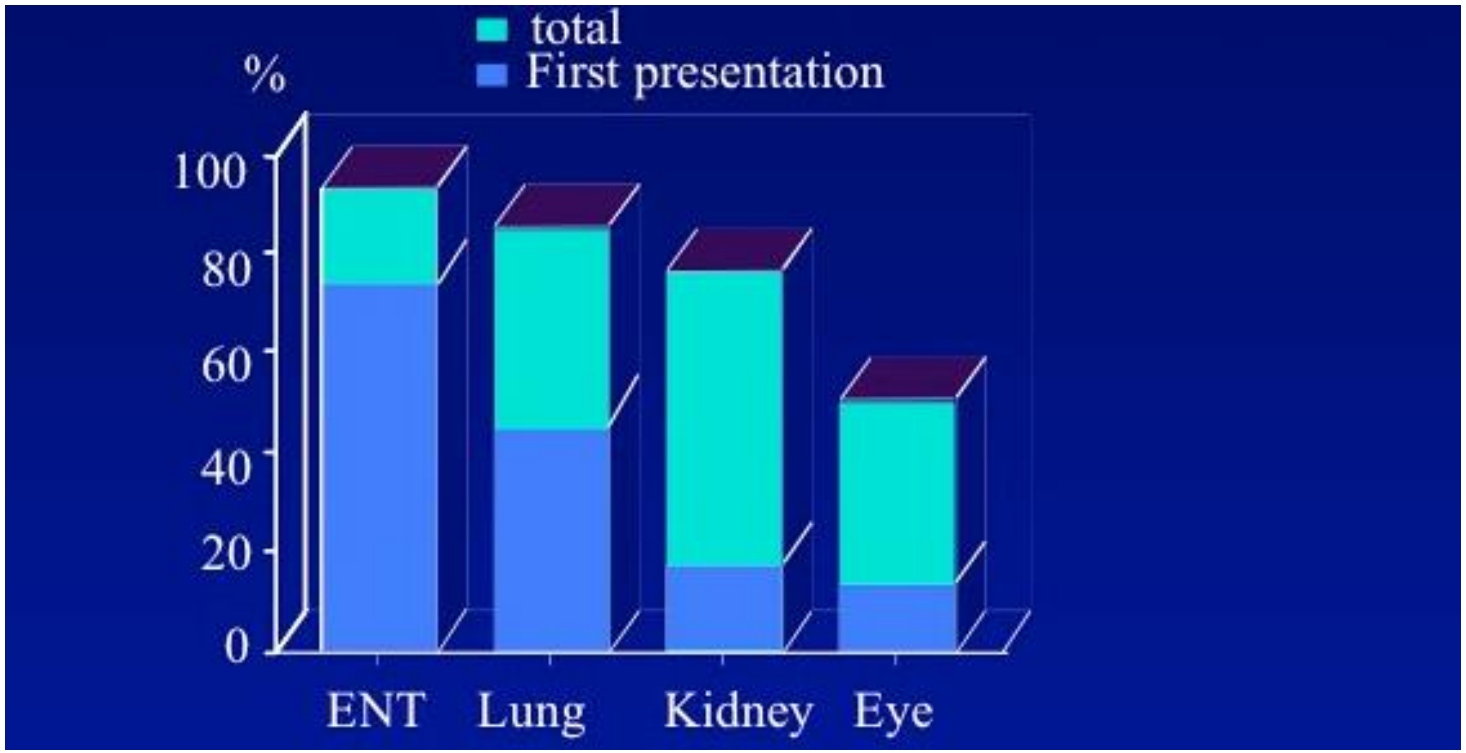
Brian P. O'Sullivan and Ted Kremer

Table 11-4 Classification Criteria for Wegener Granulomatosis

Three of the following six conditions should be present

- Abnormal urinalysis*
- Granulomatous inflammation on biopsy specimen
- Nasal-sinus inflammation
- Subglottic, tracheal, or endobronchial stenosis
- Abnormal chest x-ray or CT scan of the chest
- High titer of proteinase-3 or positive C-ANCA staining

Organ involvement in Wegener's granulomatosis



Differential Diagnosis of the Pulmonary-Renal Syndrome

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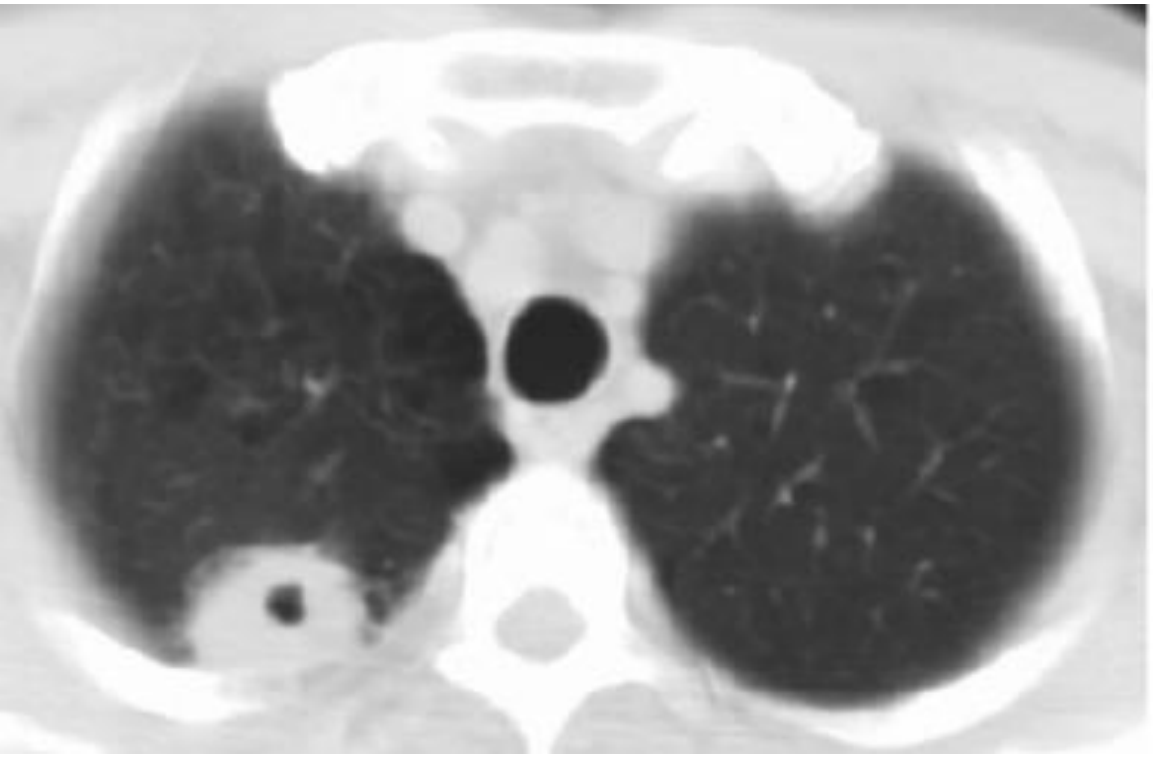
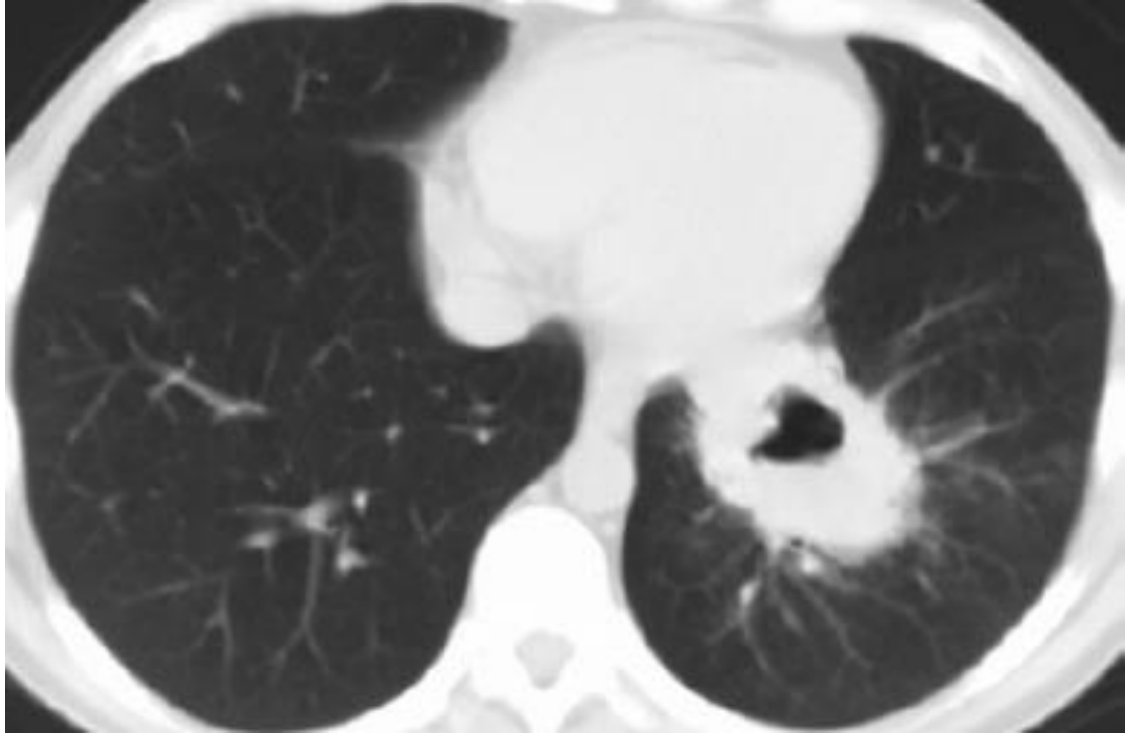
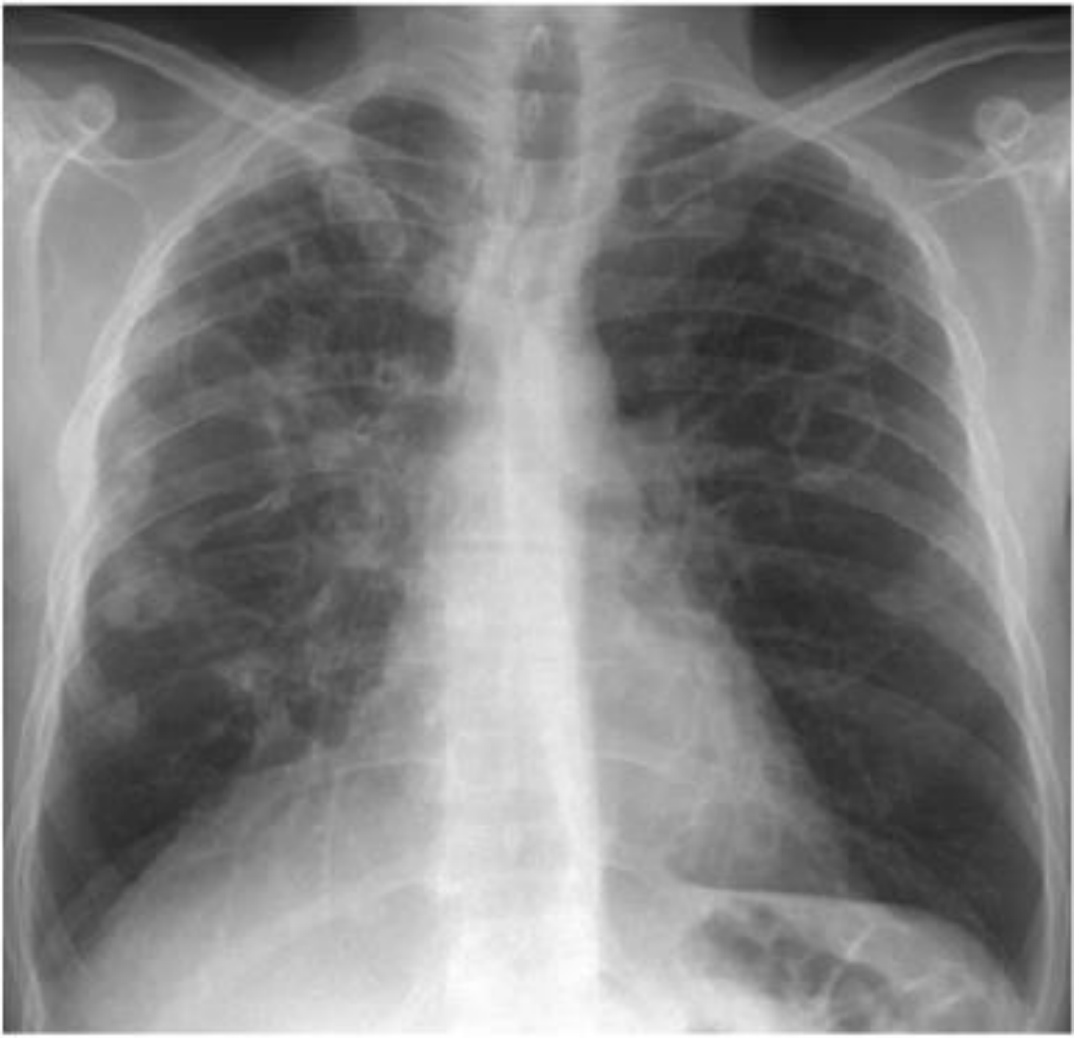
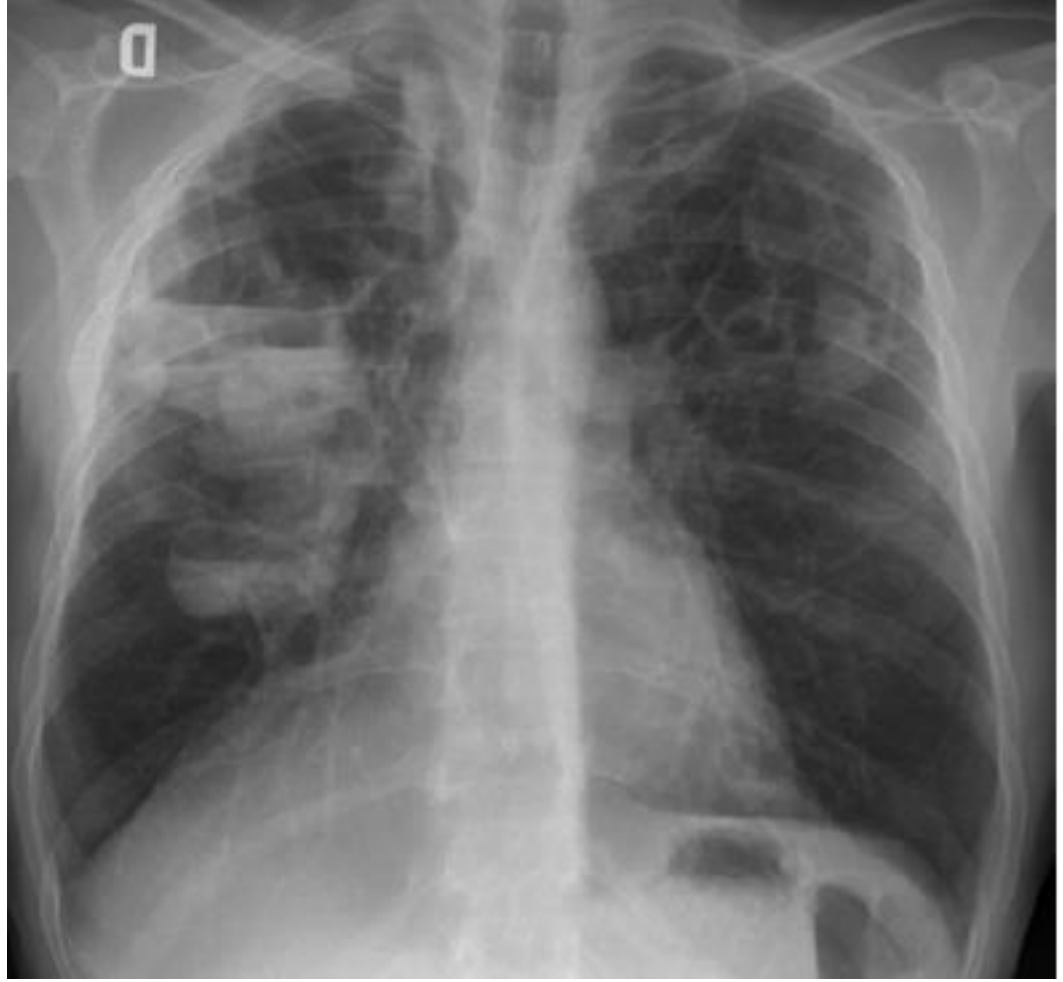


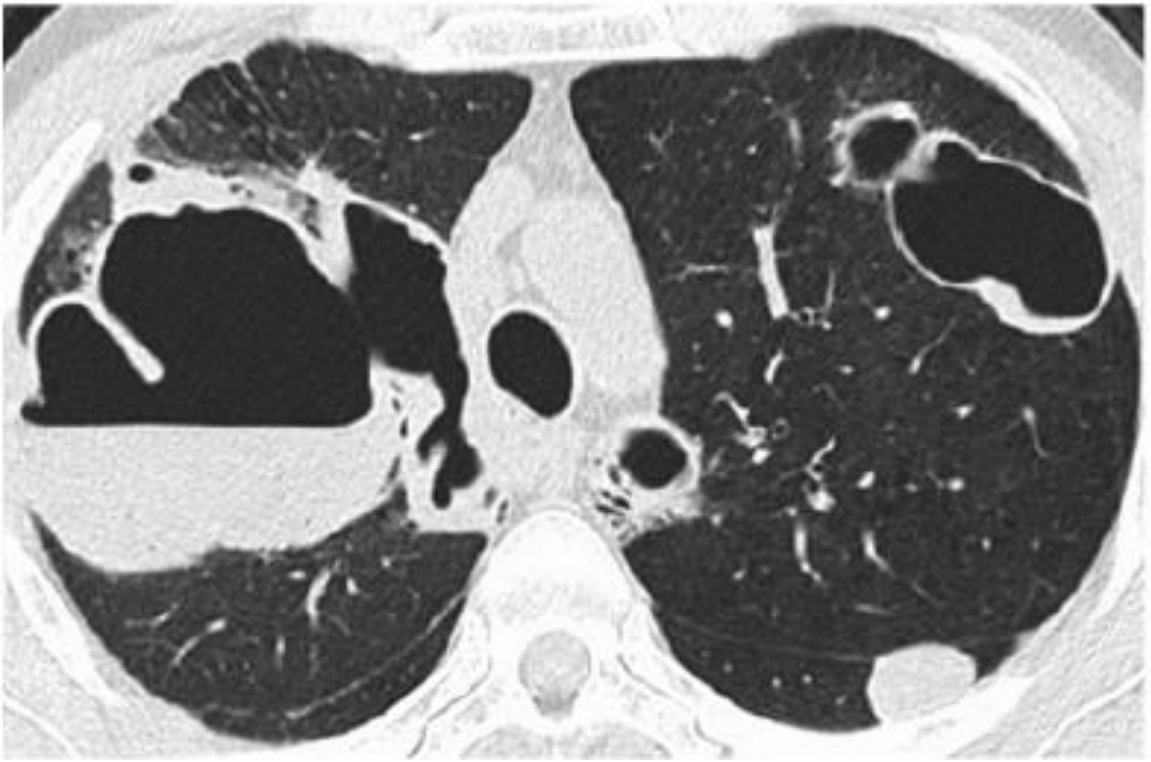


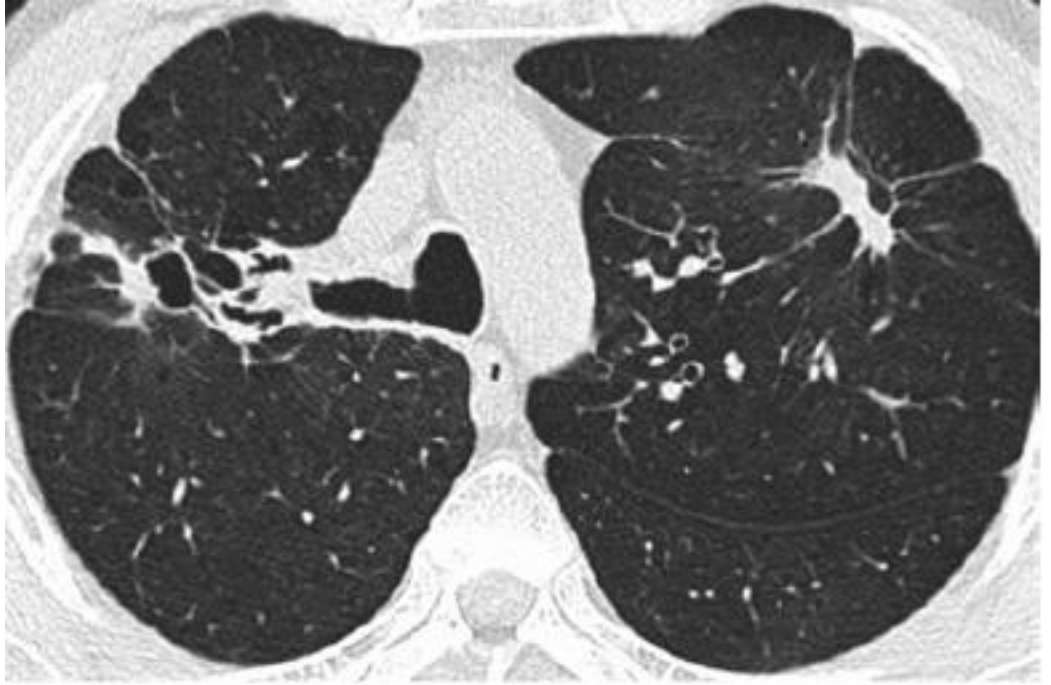
Relapsing Wegener granulomatosis in a 57-year-old man who initially presented with malaise and recurrent episodes of epistaxis.**(a, b)** CT images (lung window) show irregular, thick-walled, cavitatedmasses in the right upper lobe **(a)** and left lower lobe **(b)**. The patient responded satisfactorily to treatment,with complete resolution of the pulmonary masses. Two years later, the patient presented with arthralgias and hemoptysis.





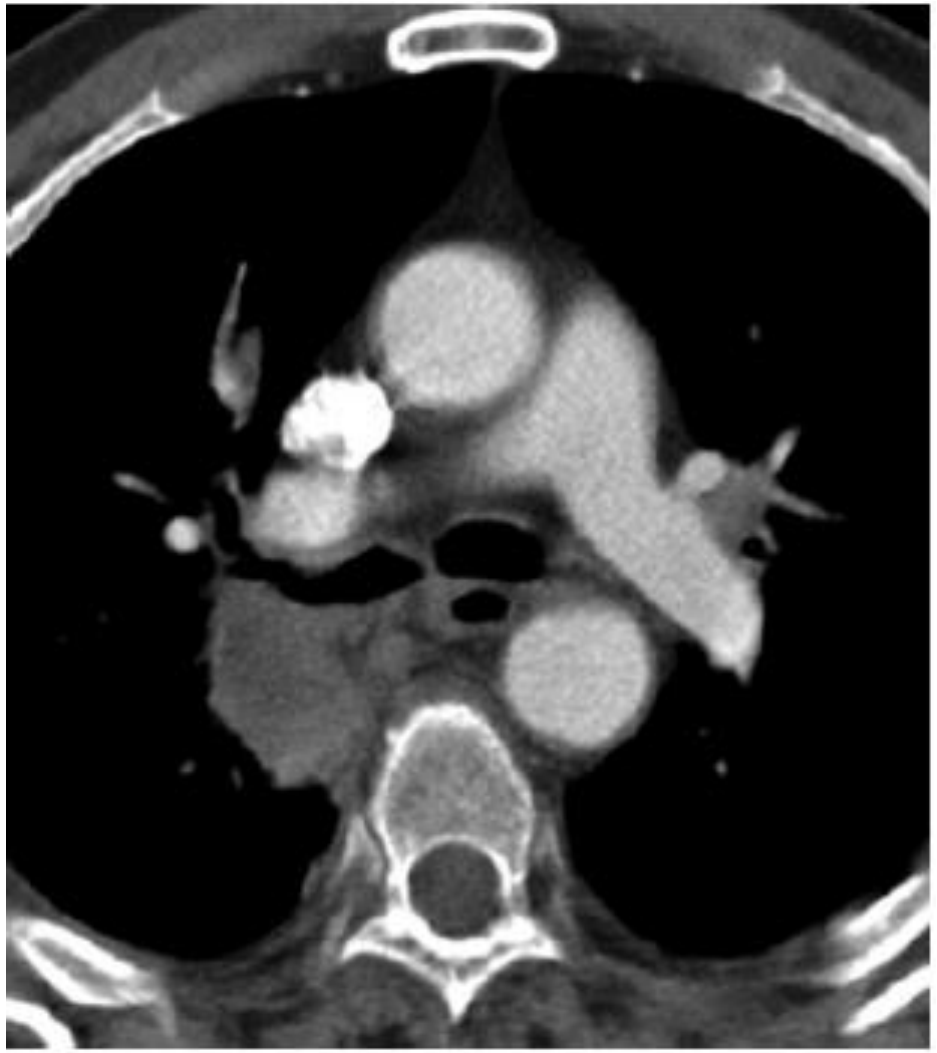
(c) Posteroanterior chest radiograph shows well-defined multiple bilateral nodules, some of which are cavitated, affecting predominantly the upper lobes. Despite immunosuppressive treatment, 3 months later the patient presented with acute shortness of breath and a cough. **(d)** Chest radiograph shows coalescence of the cavitated lesions, some of which demonstrate an air-fluid level secondary to infection

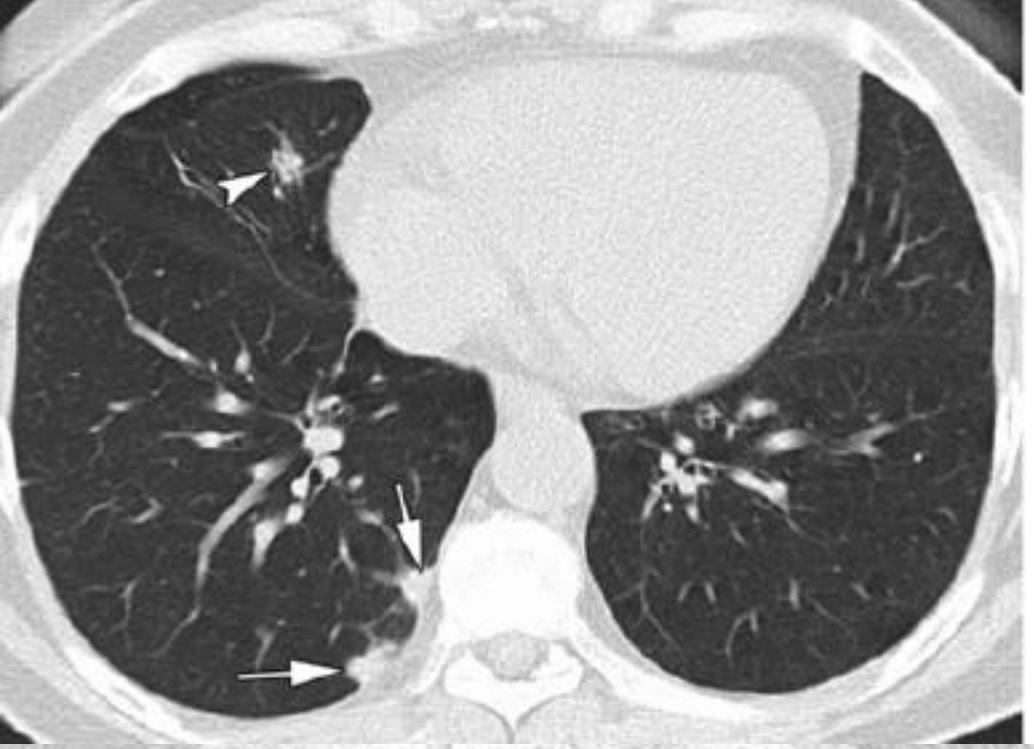


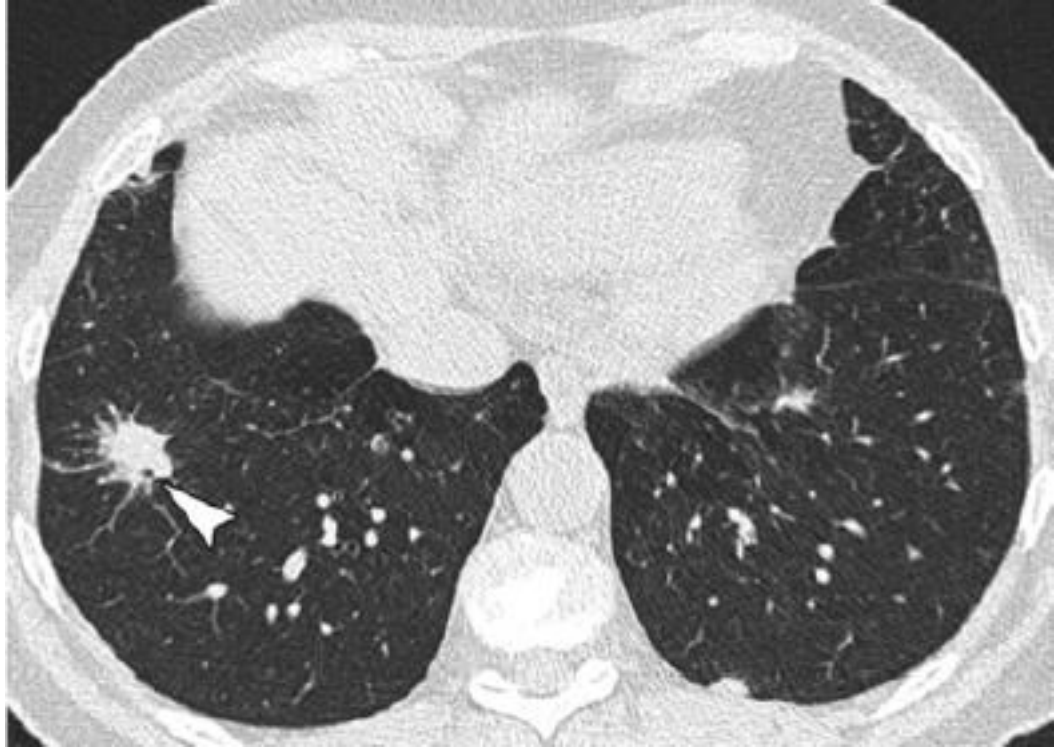


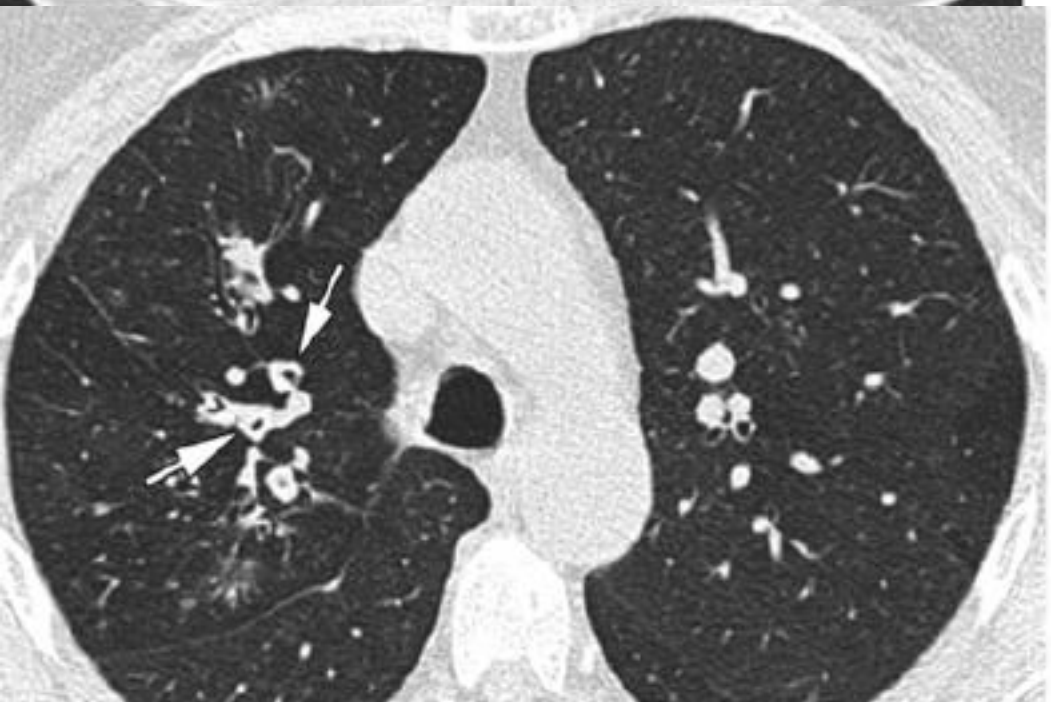
(e) CT image (lung window) shows bilateral fairly well-defined nodules and masses. Some lesions are cavitated and demonstrate air-fluid levels. Some of the cavities are thin walled. **(f)** CT image (lung window) obtained 1 year later shows a favorable response to treatment, with marked fibrotic reaction around the healing residual lesions

Wegener granulomatosis in a 76-year-old man who presented with otitis and arthralgias. Contrast-enhanced CT image shows a mass in the right lower lobe with a central low-attenuation area. The patient also had other bilateral noncavitated masses (not shown).







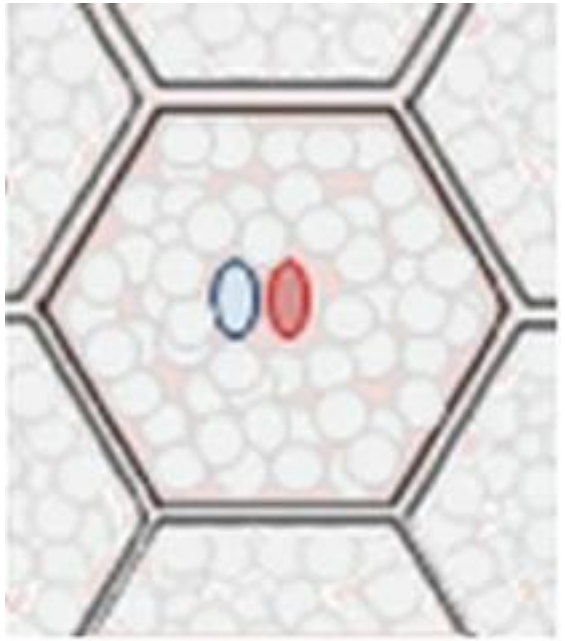


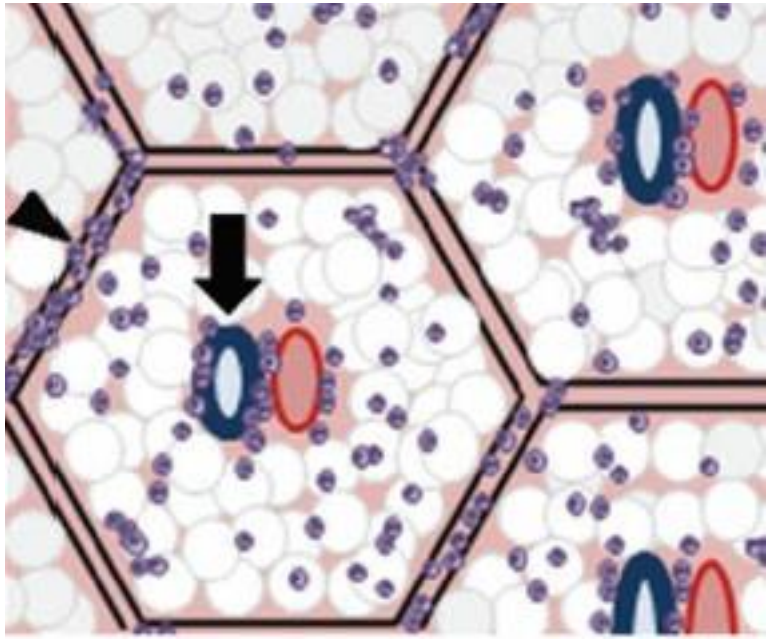
Wegener granulomatosis in a 56-yearold woman who presented with malaise, fever, and chronic sinusitis. **(a, b)** CT images (lung window) show patchy airspace consolidations. Some consolidations in the right lower lobe are wedge shaped and pleura based (arrows in **a**), mimicking pulmonary infarcts. Note the peribronchial distribution of some of the consolidations (arrowhead). **(c)** CT image (lung window) shows marked wall thickening of the right upper lobe bronchi (arrows).

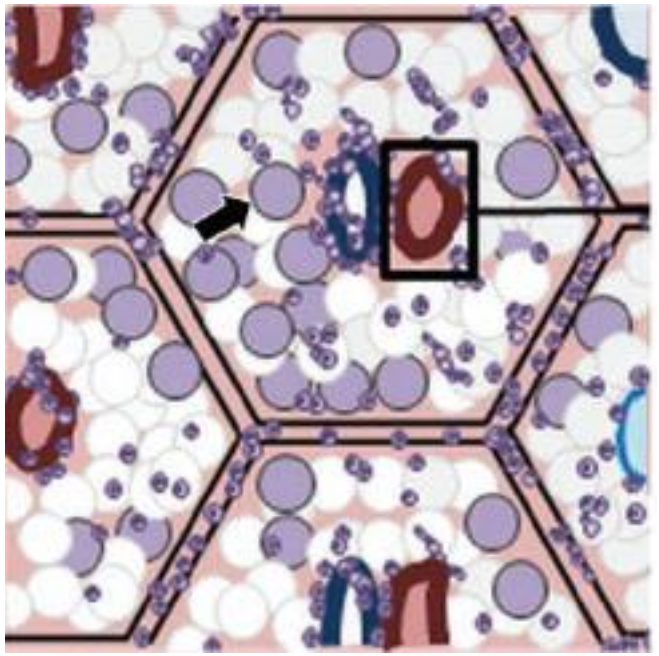
Churg-Strauss Syndrome

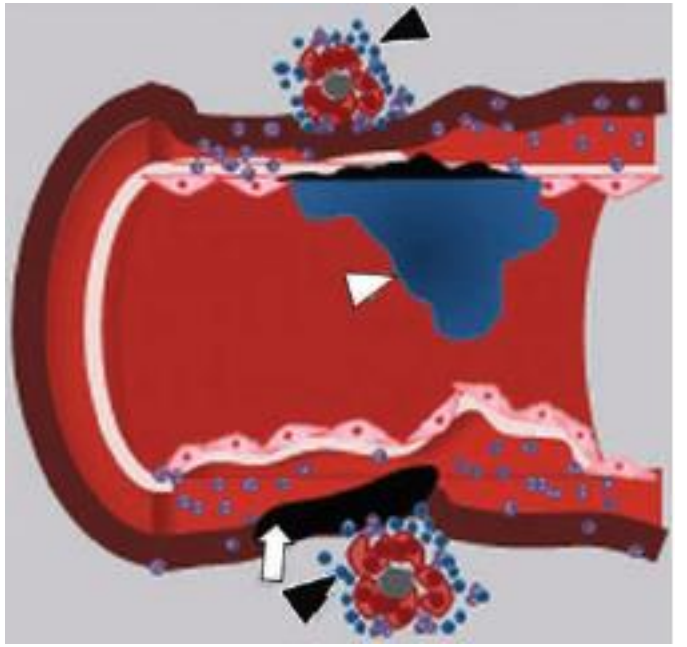
- Asthma
- more than 10% eosinophilia in a differential white blood cell count
- mononeuropathy or polyneuropathy attributable to systemic vasculitis
- migratory or transient pulmonary opacities
- paranasal sinus abnormalities
- extravascular eosinophils in a biopsy specimen

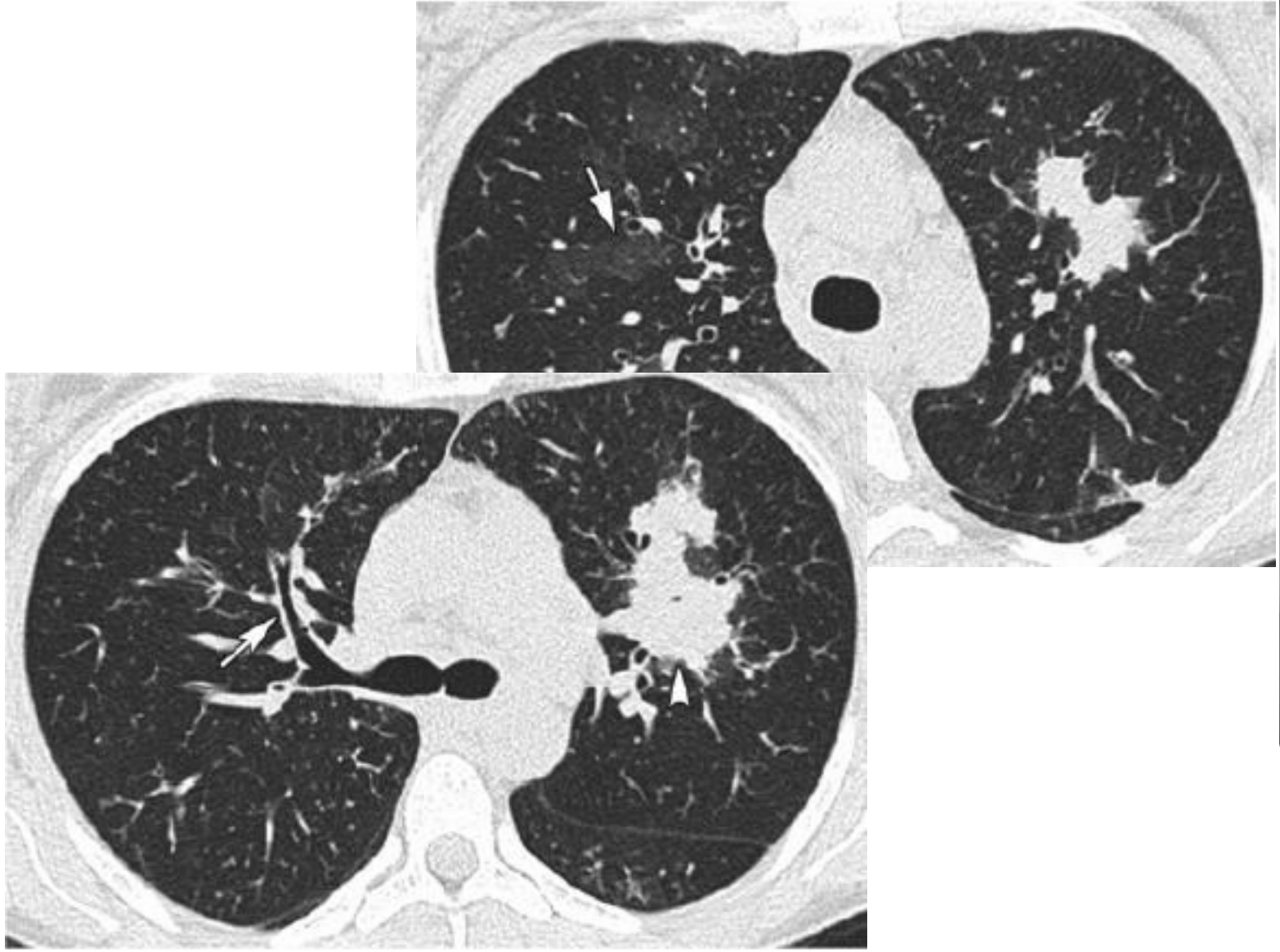
Main histologic features of CSS. Diagrams show the normal secondary pulmonary lobule **(a)**, the secondary pulmonary lobule in the prodromal stage **(b)**, eosinophilic infiltration of the alveoli (arrow in **c**), and the vasculitic phase **(d)**. In **a–c**, the bronchus (blue oval) and artery (red oval) are seen in the middle of the lobule; the white circles represent the alveoli.
In the prodromal stage, bronchiolitis with eosinophilic and neutrophilic infiltration of the bronchial wall (arrow in **b**) and septal infiltration by eosinophils (arrowhead in **b**) can be seen. Once the vasculitic phase is established, granulomatous necrosis of medium-sized arteries, veins, and capillaries is apparent. Extravascular granulomas (black arrowheads in **d**), fibrinoid necrosis (arrow in **d**), and thrombosis (white arrowhead in **d**) are common findings

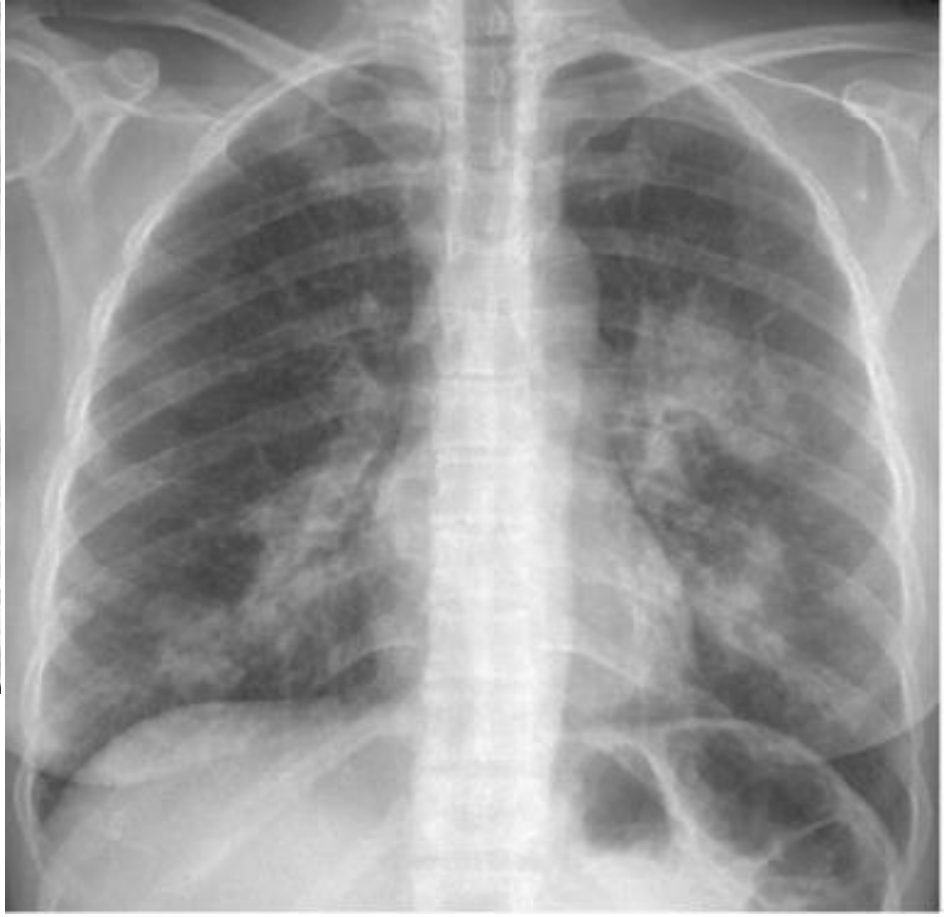




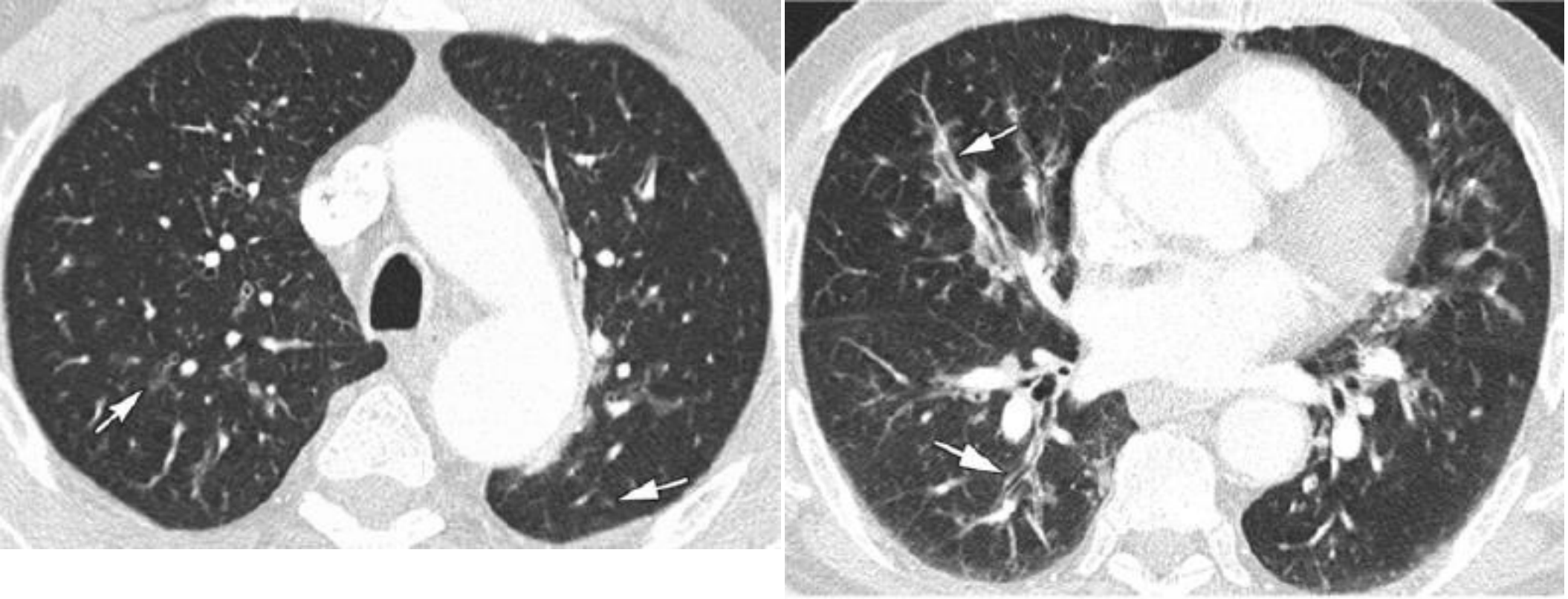








CSS in a 38-year-old woman with asthma diagnosed 7 years before who presented with a 2-month history of fever and cough. She had a history of persistent eosinophilia and sinusitis. **(a)** Chest radiograph shows opacities in both lungs; the opacities spare the apices and costophrenic angles. **(b)** CT image (lung window) shows patchy areas of groundglass opacity in the right upper lobe (arrows) and dense consolidation in the left upper lobe

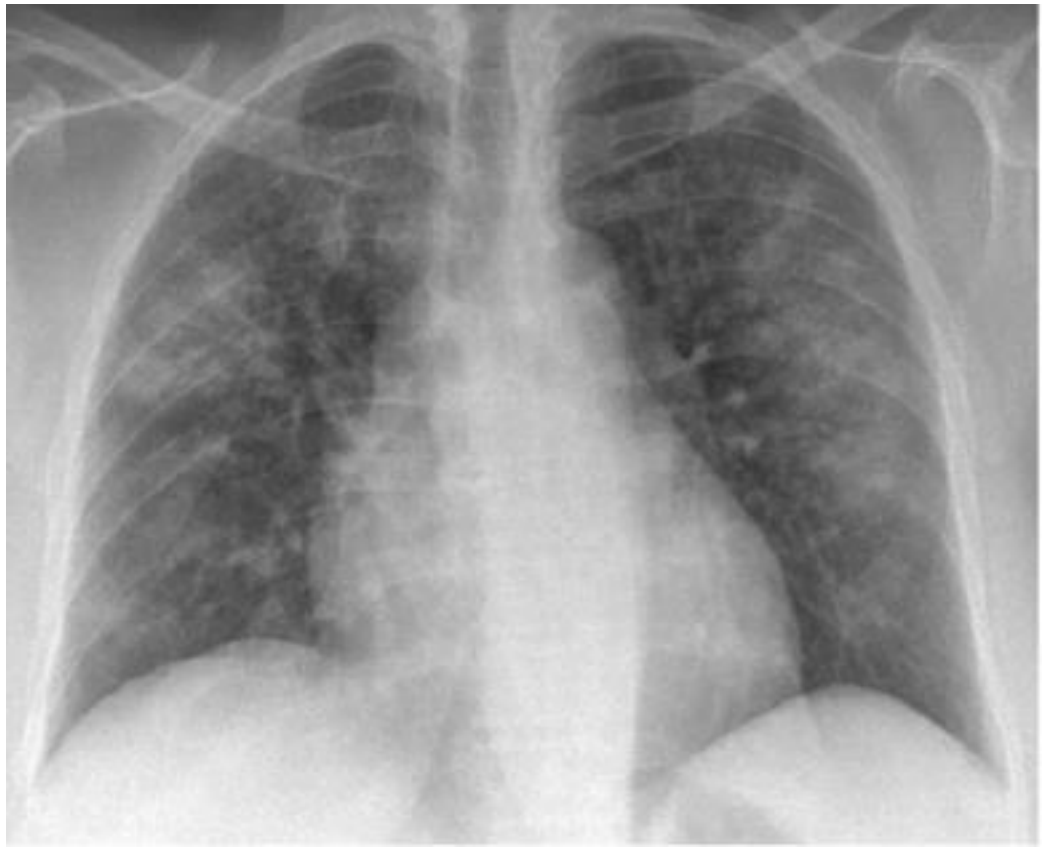


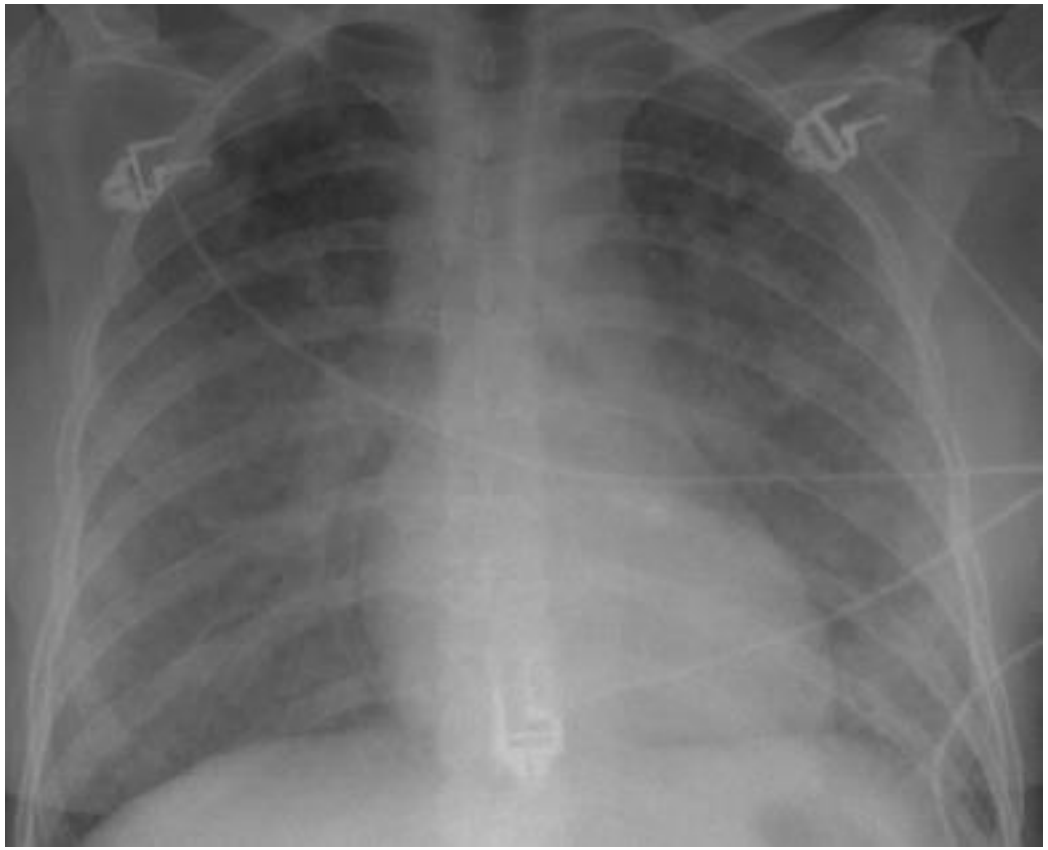
CSS in a 72-year-old asthmatic man who presented with chronic cough and dyspnea. He had a history of persistent eosinophilia and sinus polyposis. CT images (lung window) show small centrilobular nodules (arrows in **a**) and diffuse bronchial wall thickening (arrows in **b**), with some areas of tree-in-bud pattern.

Table 4
Causes of DAH

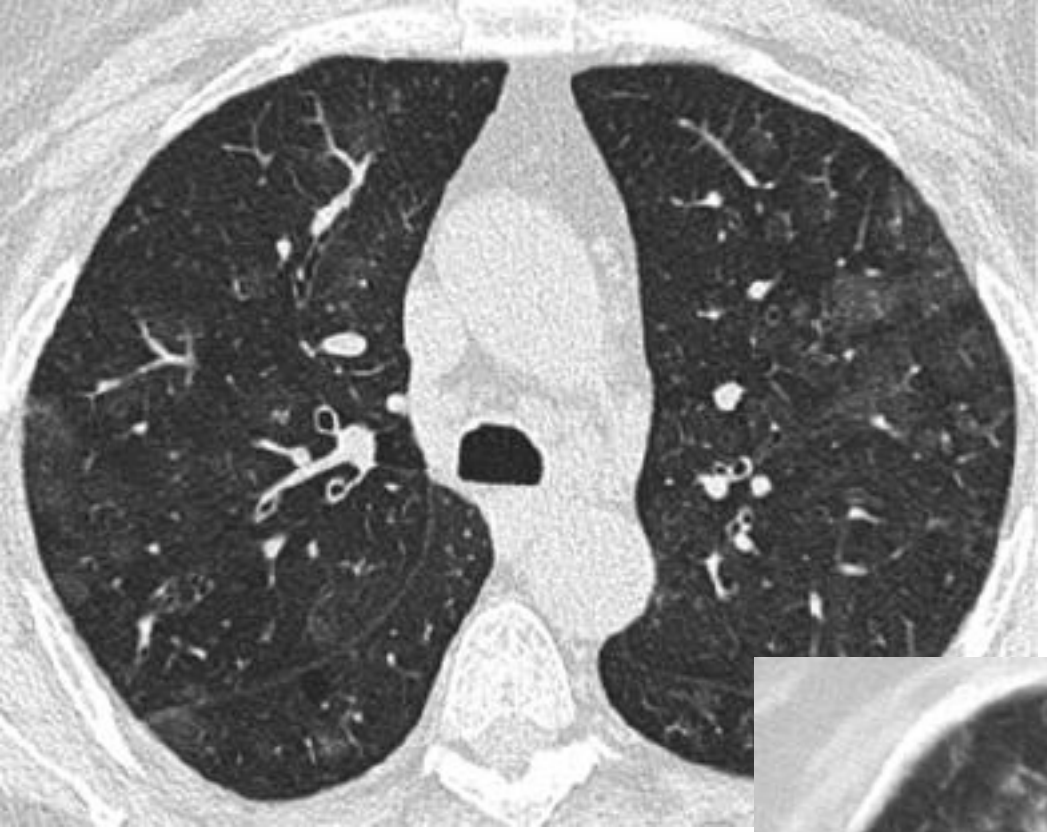
With pathologic capillaritis
Primary idiopathic small-vessel vasculitis
Wegener granulomatosis
CSS
Microscopic polyangiitis
Primary immune complex–mediated vasculitis
Goodpasture syndrome
Henoch-Schönlein purpura
Secondary vasculitis
Classic autoimmune disease
Systemic lupus erythematosus
Rheumatoid arthritis
Antiphospholipid antibody syndrome
Mixed connective tissue disease
Polymyositis, dermatomyositis
Essential cryoglobulinemic vasculitis
Behçet disease
Lung transplantation
Bone marrow transplantation
Drug induced (eg, chemotherapy)
Infection
Without pathologic capillaritis
Idiopathic pulmonary hemosiderosis
Coagulopathy
Mitral stenosis
Inhalation injury
Goodpasture syndrome
Systemic lupus erythematosus
Bone marrow transplantation
Drug-associated disease (eg, chemotherapy)

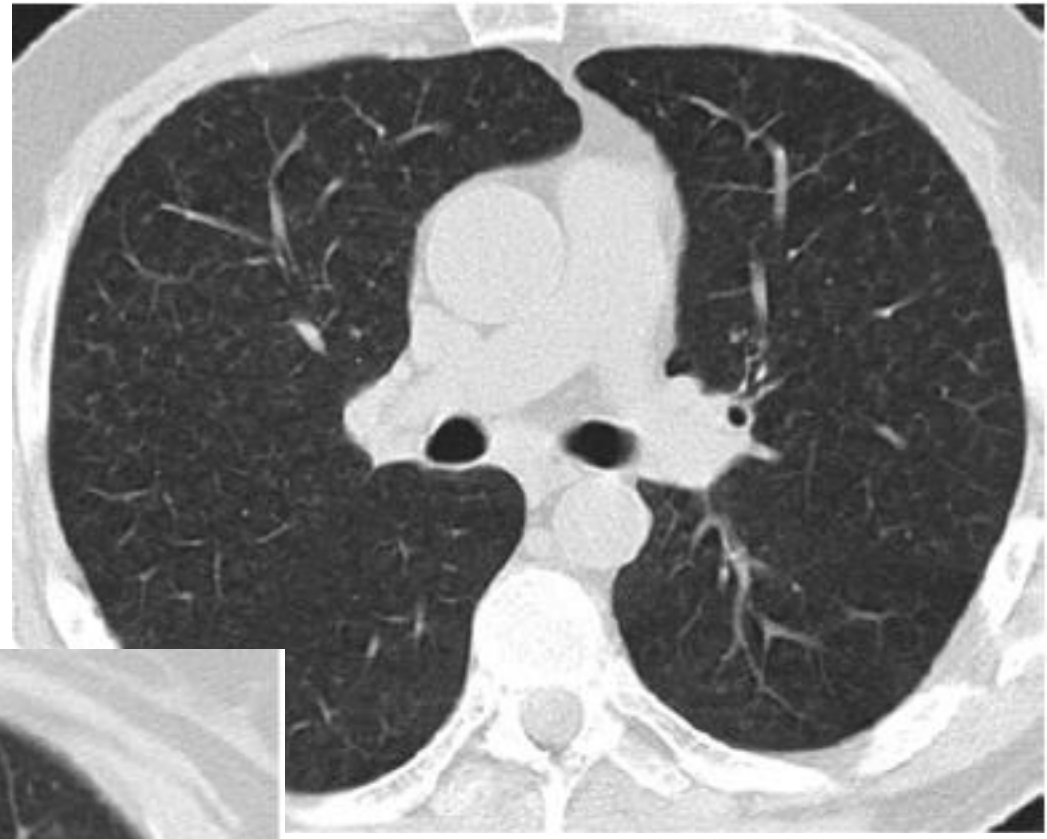
Source.—References 2 and 7.

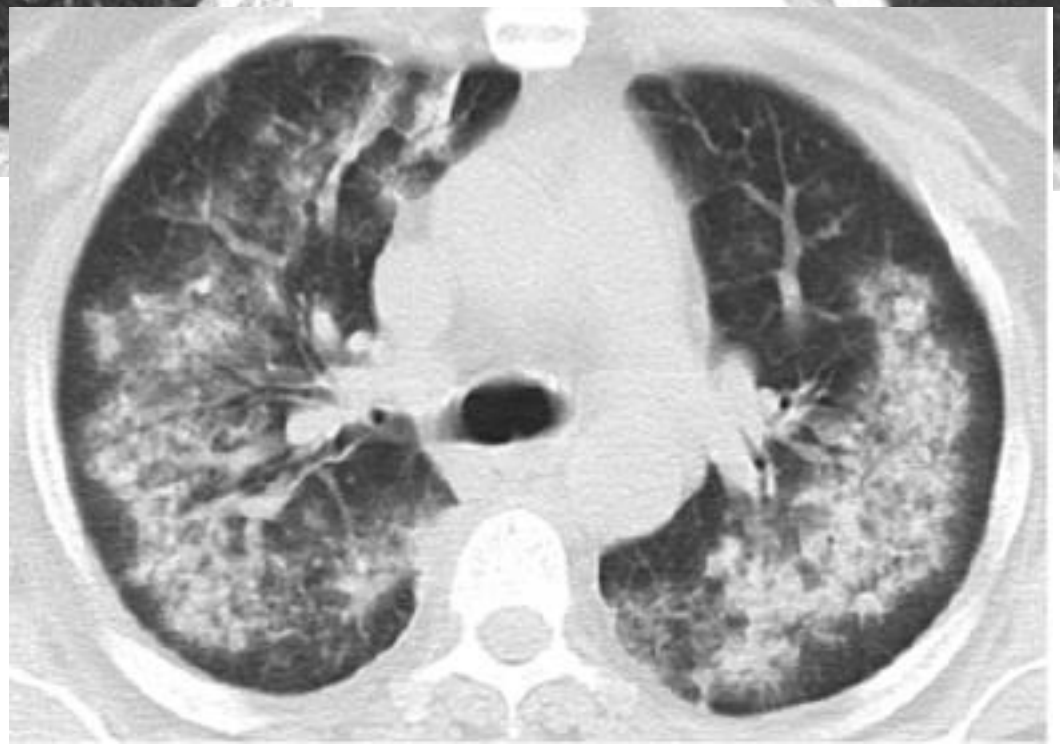




Variety of chest radiographic features that can be found in DAH. **(a)** Wegener granulomatosis in a 62-year-old woman who presented with malaise and hemoptysis and had a positive test result for cytoplasmic ANCA. Chest radiograph shows bilateral hazy areas of increased opacity and areas of consolidation that are more prominent in the perihilar regions. **(b)** Systemic lupus erythematosus in a 35-year-old woman who presented with sudden dyspnea, coughing, hemoptysis, and anemia. Chest radiograph shows diffuse bilateral areas of consolidation.







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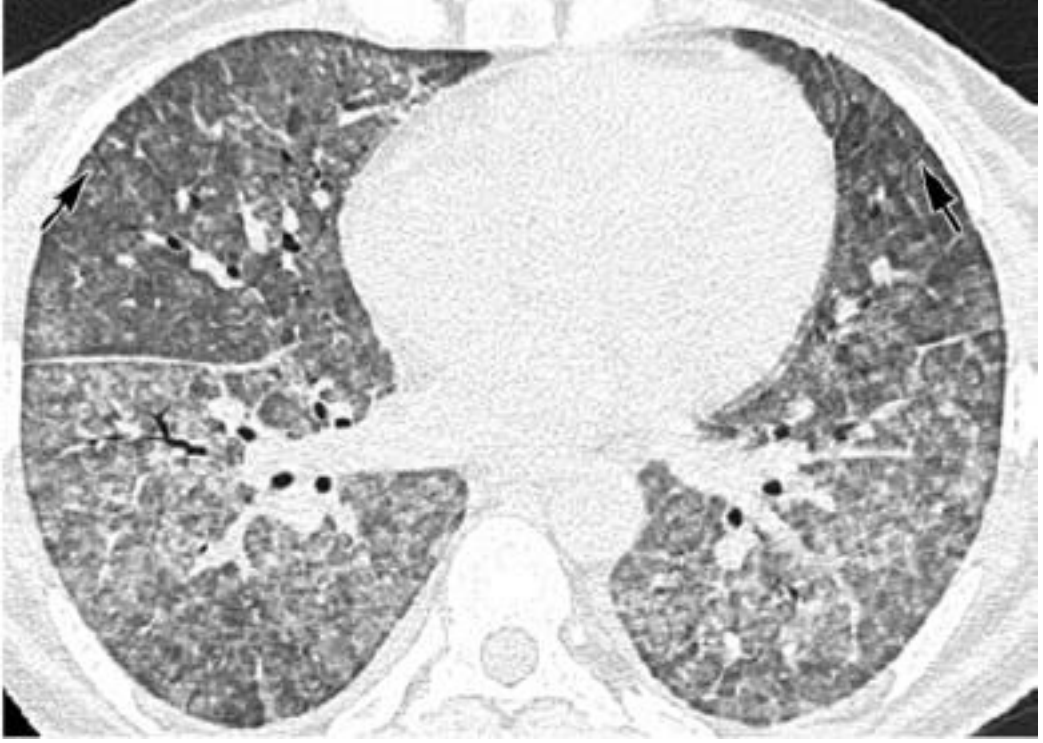
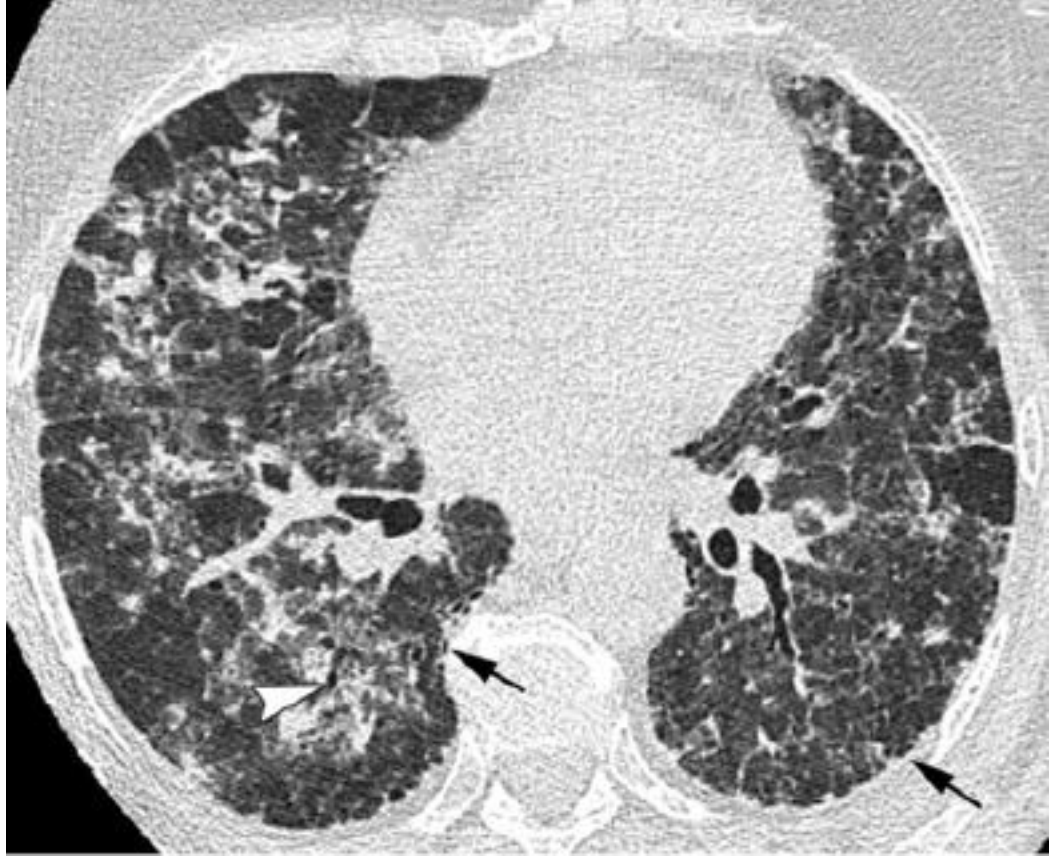
- Variety of high-resolution CT patterns that can be found in DAH.
- **(a)** Microscopic polyangiitis in a 41-year-old man. CT image shows patchy areas of ground-glass opacity.
- **(b)** Microscopic polyangiitis in a 50-year-old woman who presented with cough and dyspnea. Results of bronchoalveolar lavage were positive for alveolar hemorrhage. CT image shows diffuse centrilobular nodules with no other abnormalities.
- **(c)** Wegener granulomatosis in a 62-year-old woman (same patient as in Fig 14a). CT image shows extensive areas of consolidation in a predominantly perihilar distribution





(d) Systemic lupus erythematosus in a 35-year-old woman (same patient as in Fig 14b). CT image shows diffuse ground-glass opacities, ill-defined centrilobular nodules, and septal thickening (arrows).
(e) Microscopic polyangiitis in a 72-year-old woman. CT image obtained
after recurrent episodes of pulmonary hemorrhage shows a fine reticular pattern on a background of ground-glass attenuation, signs of pulmonary fibrosis with a peripheral honeycombing pattern (arrows), and traction bronchiectasis (arrowhead).

Table 1 Causes of pulmonary-renal syndromes.

ANCA-positive vasculitis
- Granulomatosis with polyangiitis (Wegener's)
- Microscopic Polyangiitis
- Churg–Strauss syndrome

Anti-glomerular basement membrane antibodies (Anti-GBM) – Goodpasture's syndrome

Autoimmune connective tissue disease
- Systemic lupus erythematosus
- Polymyositis
- Scleroderma

ANCA-negative vasculitis
- Henoch Schonlein Purpura
- Mixed cryoglobulinaemia
- IgA nephropathy
- Behcet's disease

Drug-induced vasculitis – Hydralazine
- Propylthiouracil
- D-penicillamine

Idiopathic pulmonary-renal syndrome