İZMİR KATİP ÇELEBİ ÜNİVERSİTESİ
ROMATOLOJİ
2014

Vaskülitlere Yaklaşım ve Sınıflandırma

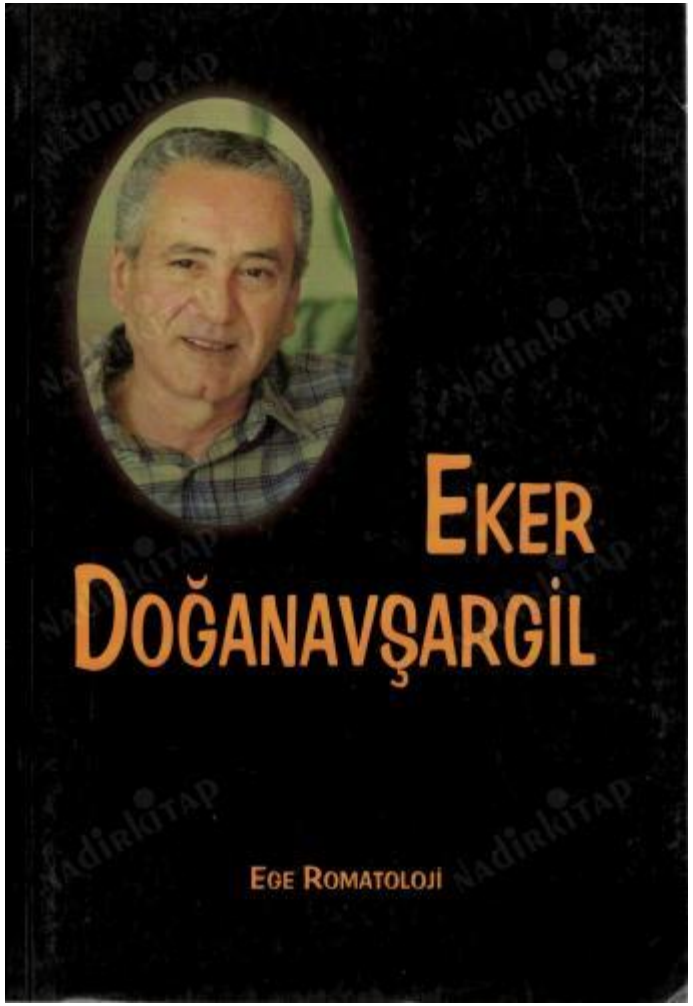
Doç Dr Mustafa Özmen

İKÇÜ Tıp Fakültesi

İç Hastalıkları AD, Romatoloji BD

Sunum planı

- Vaskülit tanımı
- Vaskülitlerin sınıflandırması
- Vaskülitlere yaklaşım
- Özet



ISSN: 1305-385X

Türkiye Klinikleri

DAHİLİ TIP BİLİMLERİ

İMMÜNOLOJİ ROMATOLOJİ

Cilt / Vol : 1 • Sayı / No : 43 • 2005

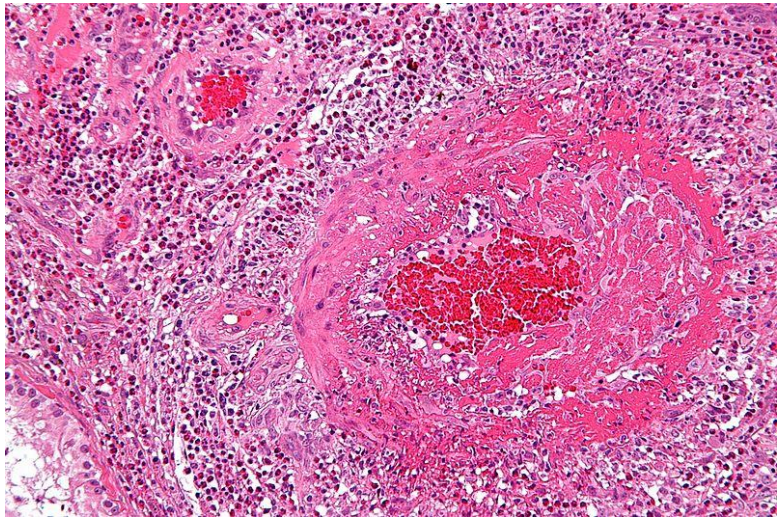
VASKÜLİTLER ÖZEL SAYISI

(Sayı Editörü: Prof.Dr. Eker DOĞANAVŞARGİL)

Türkiye Klinikleri Journal of Internal Medical Sciences

www.turkiyeklinikleri.com

Vaskülit tanımı



Vaskülit tanımı

«Vaskülitler, çeşitli çapta, çeşitli tip ve yerleşimde damar duvarı inflamasyonu ve sonuçta damar duvar nekrozu, lümen daralması ve tıkanması ve bazen anevrizma ve rüptür gelişimi ile organ yetmezliğine yol açan, nadir ama çoğu yaşamsal önemde patolojilerdir»

E Doğanavşargil. Turkiye Klinikleri J Int Med Sci. 2005;1(43):1-15

- **Patogenetik mekanizmalar** kesin olarak bilinmemektedir
- Damar duvarında fibrinoid nekroz;

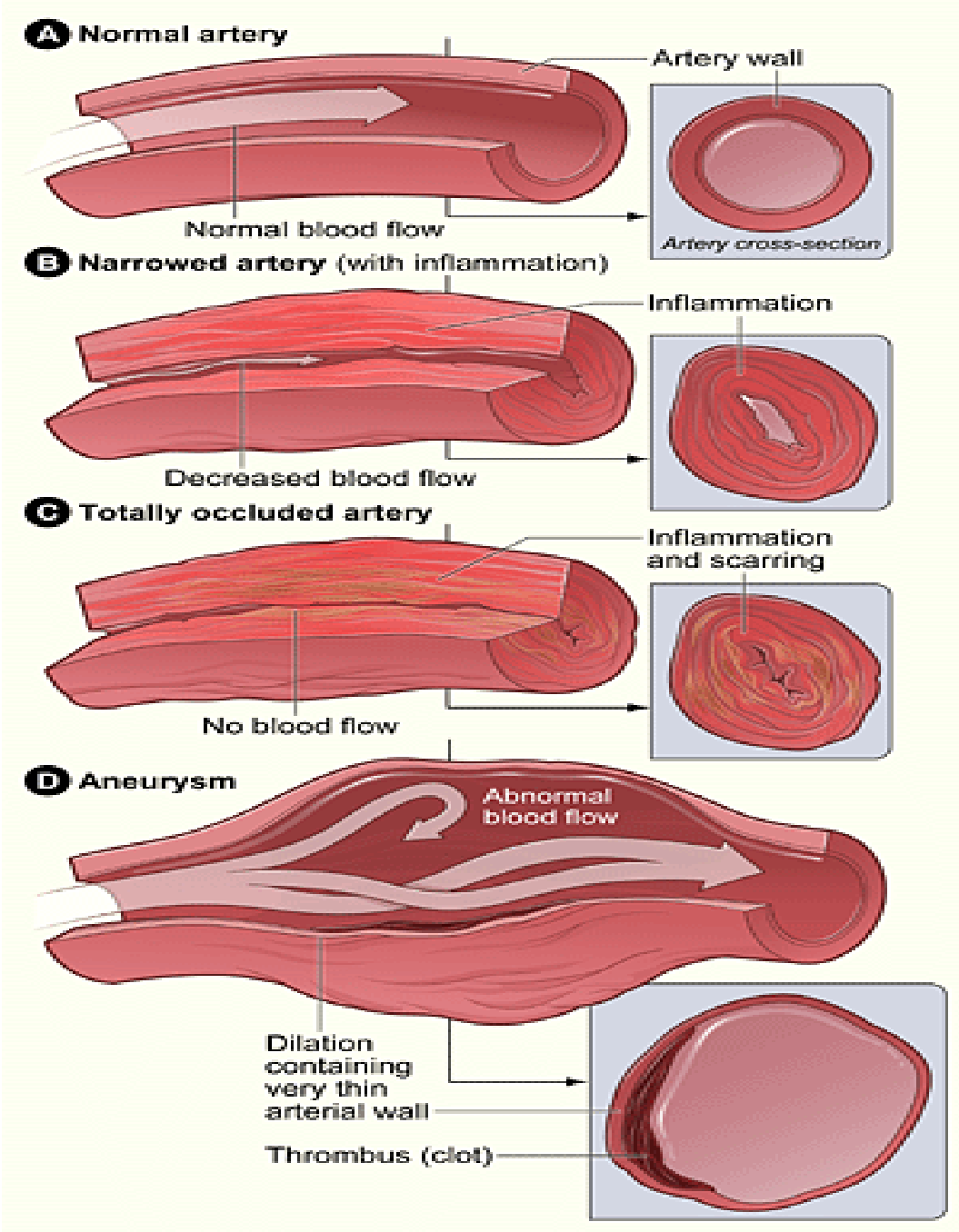
  «nekrotizan vaskülitler»

- Damar lümen daralması / tıkanması

  → **Doku iskemisi**

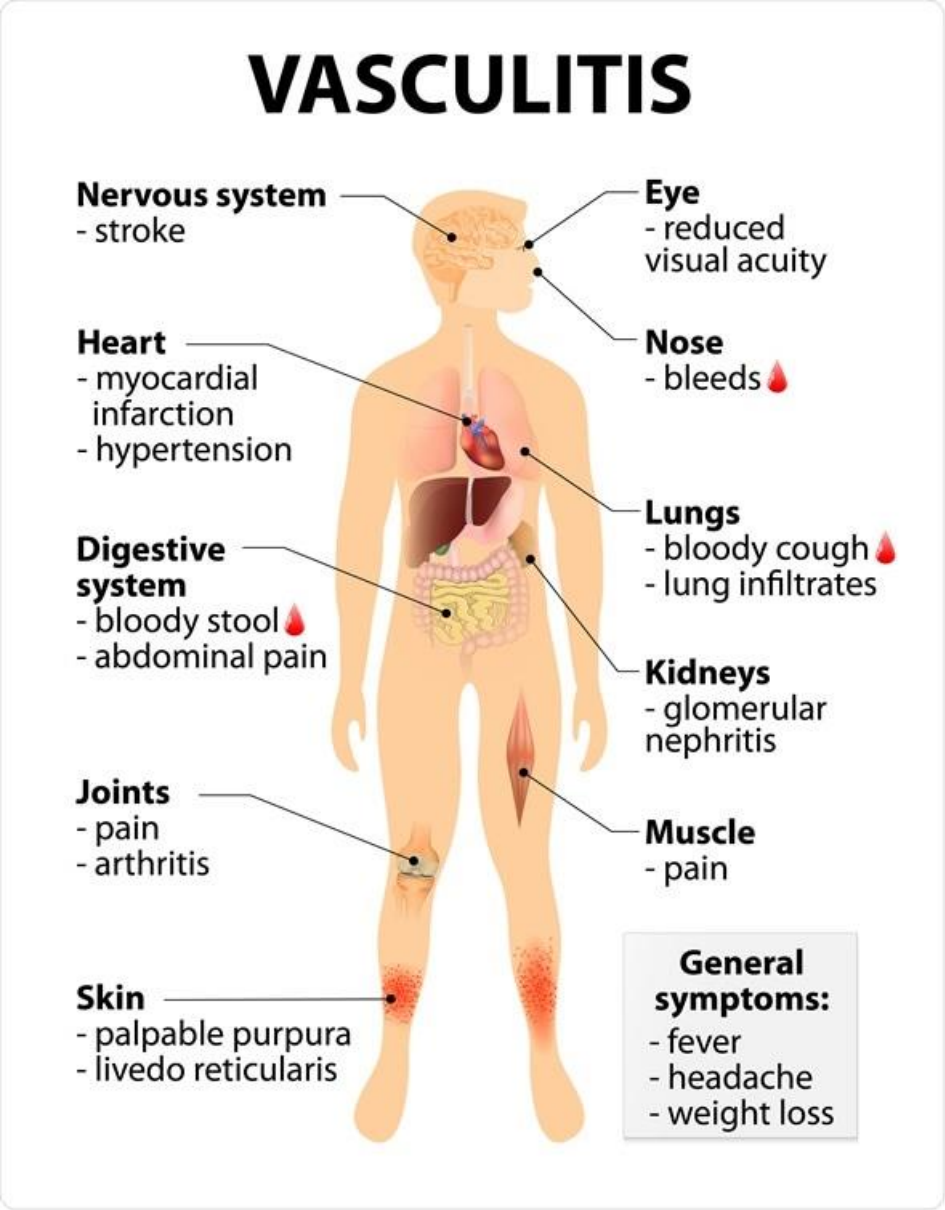
- Damar duvar incelmesi, rüptür

  → **Anevrizma, trombüs, kanama**



- Klinik tablo tutulan damarın yeri, büyüklüğü, tipi, hastalığın hızı ve kişinin immün cevabına bağlıdır;
  - **Her damar tutulabilir!**

- Tek bir organla sınırlı kalabilir, birden fazla organı da etkileyebilir;
  - **Hemen her organ tutulabilir!**



Vaskülitlerin sınıflandırılması

Terimler

Terim	Açıklama	Örnek
İsim (*nomenclature, diagnosis*)	Hastalığın ismi	Poliarteritis nodosa
Tanım (*definition*)	Hastalığa özgü temel **patolojik özelliklerle** bağlantılı standart isim	Glomerülonefrit veya arteriyollerde, kılcal damarlarda veya venüllerde vaskülit olmaksızın, ANCA ile ilişkili olmayan, orta veya küçük arterlerin nekrotizan arteriti
İsimlendirme sistemi (*nomenclature system)*	**İsim & tanım** (tanımlayıcı veya etiyolojiye dayalı isimlendirme)	2012 CHCC
Sınıflandırma kriterleri (*classification criteria*)	Klinik araştırmalar için tek tip bir **hasta grubu** oluşturmak için kullanılan standartlaştırılmış tanımlar	1990 ACR Sınıflandırma kriterleri
Tanı kriterleri (*diagnostic criteria*)	**Bir hastada** hastalığın belirleyici özelliklerinin varlığını gösterir	

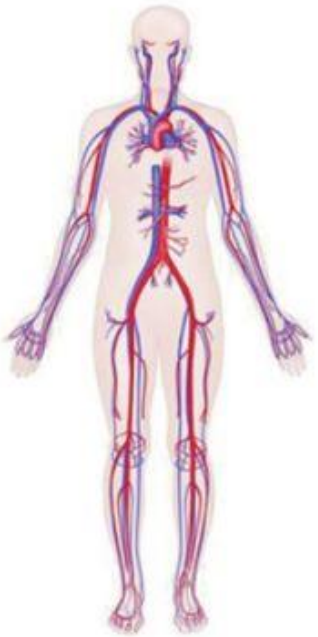
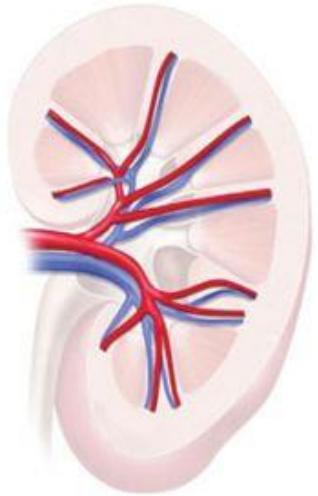
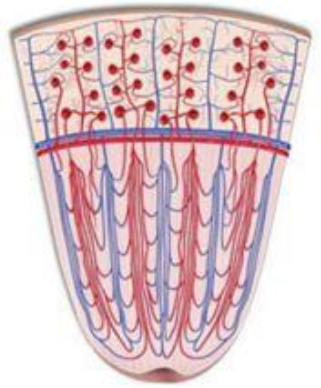
Rheumatology Textbook, 2018

Jennette JC. Arthritis Rheum. 2013

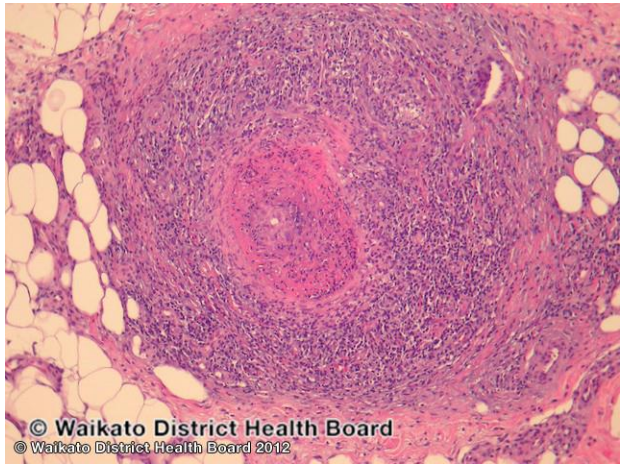
Sistemik vaskülitlerin sınıflandırması

- Damar çapı
- Primer & sekonder
- Patolojik tutulum
  - Granülomatöz & nongranülomatöz
- Patogenez
  - ANCA & İmmunkompleks

Çaplarına göre damar tipleri

Large Vessels	Medium Vessels	Small Vessels
		
✓aorta ✓major branches ✓analogous veins	✓main visceral arteries & veins ✓their initial branches	✓intraparenchymal arteries ✓Arterioles ✓capillaries ✓venules & veins

Jennette JC. Arthritis Rheum. 2013 Jan;65(1):1-11



1866 PAN

1952 Zeek

1990 ACR Sınıflandırma kriterleri

1994 International Chapel Hill Consensus Conference

AMERICAN COLLEGE OF RHEUMATOLOGY

2005 EMA algoritması

UNIVERSITY OF NORTH CAROLINA CHAPEL HILL
LVX
LIBERTAS

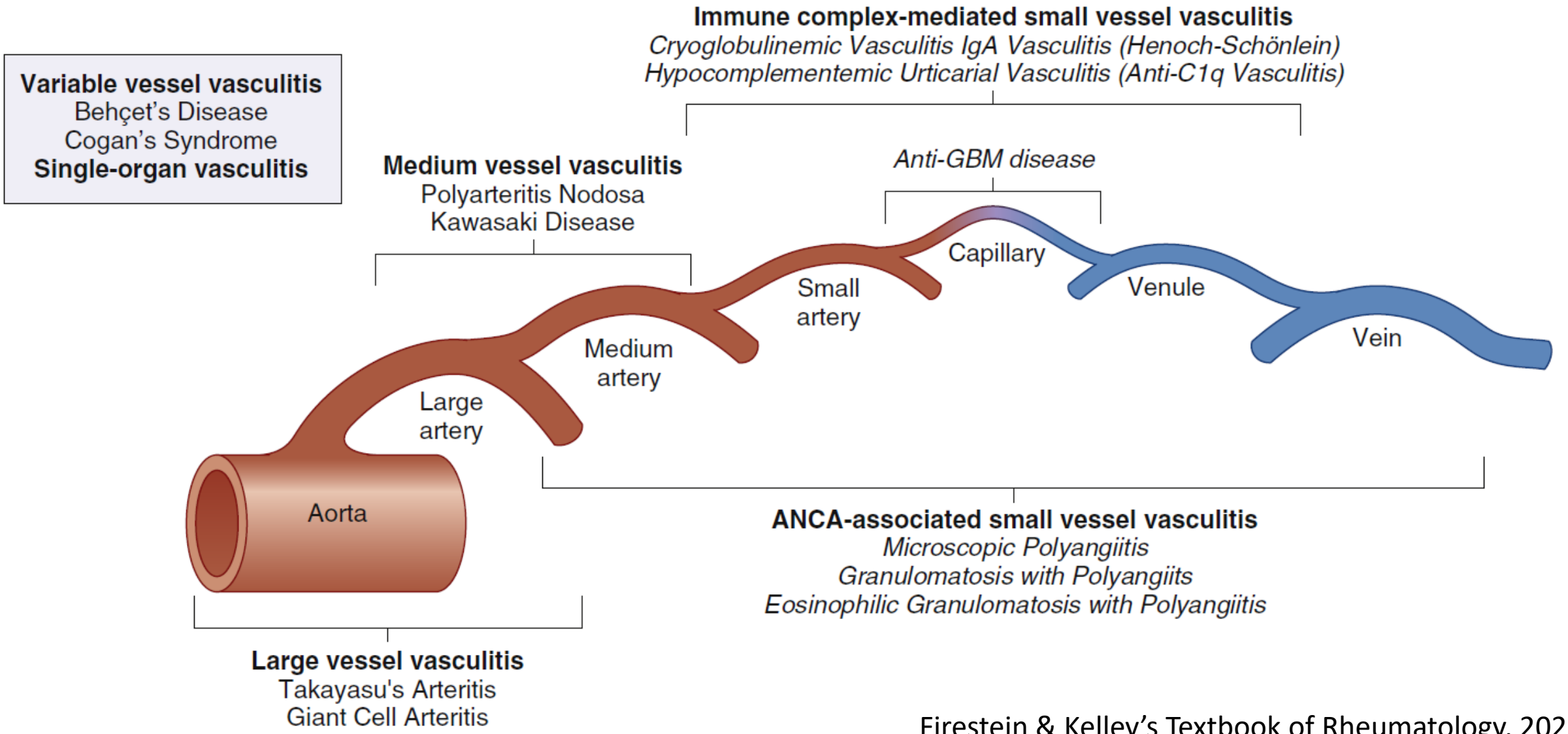
2012 International Chapel Hill Consensus Conference

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

2012 International Chapel Hill Consensus Conference

Large vessel vasculitis	**Single-organ vasculitis**
Takayasu arteritis	Cutaneous leukocytoclastic angiitis
Giant cell arteritis	Cutaneous arteritis
Medium vessel vasculitis	Primary central nervous system vasculitis
Polyarteritis nodosa (PAN)	Isolated aortitis
Kawasaki disease	Others
Small vessel vasculitis	**Vasculitis associated with systemic disease**
ANCA associated vasculitis (AAV)	Lupus vasculitis
Microscopic polyangiitis (MPA)	Rheumatoid vasculitis
Granulomatosis with polyangiitis (GPA)	Sarcoid vasculitis
Eosinophilic granulomatosis with polyangiitis (EGPA)	Others
Immune complex vasculitis	**Vasculitis associated with probable etiology**
Anti-glomerular basement membrane (anti-GBM) disease	Hepatitis C virus-associated cryoglobulinemic vasculitis
Cryoglobulinemic vasculitis	Hepatitis B virus-associated vasculitis
IgA vasculitis (Henoch-Schönlein)	Syphilis-associated aortitis
Hypocomplementemic urticarial vasculitis (anti-C1q vasculitis)	Drug-associated immune complex vasculitis
Variable vessel vasculitis	Drug-associated ANCA-associated vasculitis
Behçet's disease	Cancer-associated vasculitis
Cogan's syndrome	Others

Jennette JCl. Arthritis Rheum 65:1-11, 2013



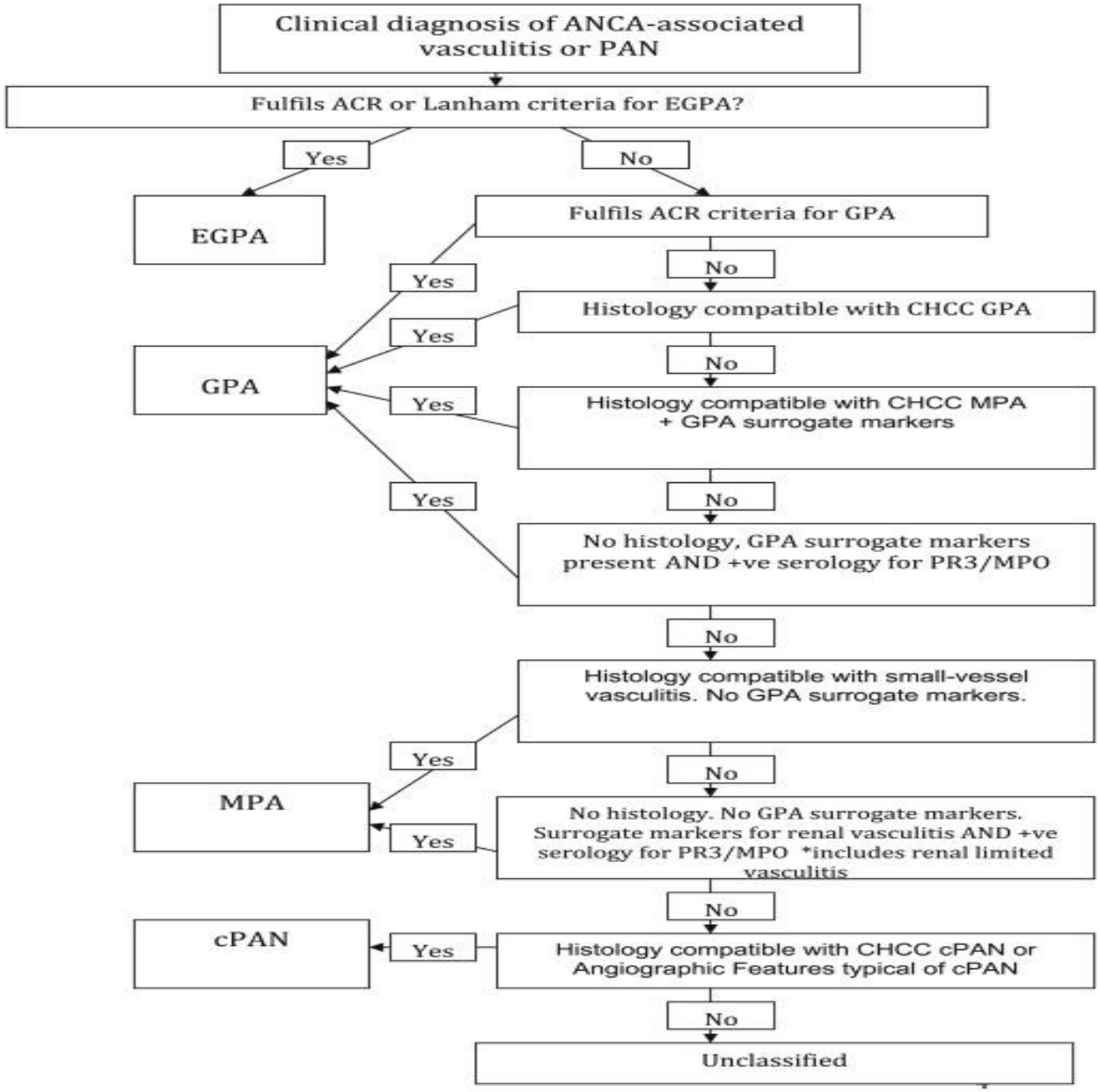
Firestein & Kelley's Textbook of Rheumatology, 2021

Definitions for vasculitides adopted by the 2012 International Chapel Hill Consensus Conference on the Nomenclature of Vasculitides (CHCC2012)

CHCC2012 name	CHCC2012 definition
Large-vessel vasculitis	Vasculitis affecting large arteries more often than other vasculitides. Large arteries are the aorta and its major branches. Any size artery may be affected.
Takayasu arteritis (TAK)	Arteritis, often granulomatous, predominantly affecting the aorta and/or its major branches. Onset usually in patients younger than 50 years.
Giant cell arteritis (GCA)	Arteritis, often granulomatous, usually affecting the aorta and/or its major branches, with a predilection for the branches of the carotid and vertebral arteries. Often involves the temporal artery. Onset usually in patients older than 50 years and often associated with polymyalgia rheumatica.
Medium-vessel vasculitis	Vasculitis predominantly affecting medium arteries defined as the main visceral arteries and their branches. Any size artery may be affected. Inflammatory aneurysms and stenoses are common.
Polyarteritis nodosa (PAN)	Necrotizing arteritis of medium or small arteries without glomerulonephritis or vasculitis in arterioles, capillaries, or venules, and not associated with antineutrophil cytoplasmic antibodies (ANCAs).
Kawasaki disease (KD)	Arteritis associated with the mucocutaneous lymph node syndrome and predominantly affecting medium and small arteries. Coronary arteries are often involved. Aorta and large arteries may be involved. Usually occurs in infants and young children.
Small-vessel vasculitis	Vasculitis predominantly affecting small vessels, defined as small intraparenchymal arteries, arterioles, capillaries, and venules. Medium arteries and veins may be affected.
ANCA-associated vasculitis (AAV)	Necrotizing vasculitis, with few or no immune deposits, predominantly affecting small vessels (ie, capillaries, venules, arterioles, and small arteries), associated with myeloperoxidase (MPO) ANCA or proteinase 3 (PR3) ANCA. Not all patients have ANCA. Add a prefix indicating ANCA reactivity, eg, MPO-ANCA, PR3-ANCA, ANCA-negative.
Microscopic polyangiitis (MPA)	Necrotizing vasculitis, with few or no immune deposits, predominantly affecting small vessels (ie, capillaries, venules, or arterioles). Necrotizing arteritis involving small and medium arteries may be present. Necrotizing glomerulonephritis is very common. Pulmonary capillaritis often occurs. Granulomatous inflammation is absent.
Granulomatosis with polyangiitis (Wegener's) (GPA)	Necrotizing granulomatous inflammation usually involving the upper and lower respiratory tract, and necrotizing vasculitis affecting predominantly small to medium vessels (eg, capillaries, venules, arterioles, arteries and veins). Necrotizing glomerulonephritis is common.
Eosinophilic granulomatosis with polyangiitis (Churg-Strauss) (EGPA)	Eosinophil-rich and necrotizing granulomatous inflammation often involving the respiratory tract, and necrotizing vasculitis predominantly affecting small to medium vessels, and associated with asthma and eosinophilia. ANCA is more frequent when glomerulonephritis is present.
Immune complex vasculitis	Vasculitis with moderate to marked vessel-wall deposits of immunoglobulin and/or complement components predominantly affecting small vessels (ie, capillaries, venules, arterioles, and small arteries). Glomerulonephritis is frequent.
Anti-glomerular basement membrane (anti-GBM) disease	Vasculitis affecting glomerular capillaries, pulmonary capillaries, or both, with GBM deposition of anti-GBM autoantibodies. Lung involvement causes pulmonary hemorrhage, and renal involvement causes glomerulonephritis with necrosis and crescents.
Cryoglobulinemic vasculitis (CV)	Vasculitis with cryoglobulin immune deposits affecting small vessels (predominantly capillaries, venules, or arterioles) and associated with serum cryoglobulins. Skin, glomeruli, and peripheral nerves are often involved.
IgA vasculitis (Henoch-Schönlein) (IgAV)	Vasculitis, with IgA1-dominant immune deposits, affecting small vessels (predominantly capillaries, venules, or arterioles). Often involves skin and gastrointestinal tract, and frequently causes arthritis. Glomerulonephritis indistinguishable from IgA nephropathy may occur.
Hypocomplementemic urticarial vasculitis (HUV) (anti-C1q vasculitis)	Vasculitis accompanied by urticaria and hypocomplementemia affecting small vessels (ie, capillaries, venules, or arterioles), and associated with anti-C1q antibodies. Glomerulonephritis, arthritis, obstructive pulmonary disease, and ocular inflammation are common.
Variable-vessel vasculitis	Vasculitis with no predominant type of vessel involved that can affect vessels of any size (small, medium, and large) and type (arteries, veins, and capillaries).
Behçet's syndrome	Vasculitis occurring in patients with Behçet's syndrome that can affect arteries or veins. Behçet's syndrome is characterized by recurrent oral and/or genital aphthous ulcers accompanied by cutaneous, ocular, articular, gastrointestinal, and/or central nervous system inflammatory lesions. Small-vessel vasculitis, thromboangiitis, thrombosis, arteritis, and arterial aneurysms may occur.
Cogan's syndrome	Vasculitis occurring in patients with Cogan's syndrome. Cogan's syndrome is characterized by ocular inflammatory lesions, including interstitial keratitis, uveitis, and episcleritis, and inner ear disease, including sensorineural hearing loss and vestibular dysfunction. Vasculitic manifestations may include arteritis (affecting small, medium, or large arteries), aortitis, aortic aneurysms, and aortic and mitral valvulitis.
Single-organ vasculitis	Vasculitis in arteries or veins of any size in a single organ that has no features that indicate that it is a limited expression of a systemic vasculitis. The involved organ and vessel type should be included in the name (eg, cutaneous small-vessel vasculitis, testicular arteritis, central nervous system vasculitis). Vasculitis distribution may be unifocal or multifocal (diffuse) within an organ. Some patients originally diagnosed as having single-organ vasculitis will develop additional disease manifestations that warrant redefining the case as one of the systemic vasculitides (eg, cutaneous arteritis later becoming systemic polyarteritis nodosa, etc).
Vasculitis associated with systemic disease	Vasculitis that is associated with and may be secondary to (caused by) a systemic disease. The name (diagnosis) should have a prefix term specifying the systemic disease (eg, rheumatoid vasculitis, lupus vasculitis, etc).
Vasculitis associated with probable etiology	Vasculitis that is associated with a probable specific etiology. The name (diagnosis) should have a prefix term specifying the association (eg, hydralazine-associated microscopic polyangiitis, hepatitis B virus-associated vasculitis, hepatitis C virus-associated cryoglobulinemic vasculitis, etc).

Jennette JC, Falk RJ, Bacon PA, et al. 2012 revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides. Arthritis Rheum 2013; 65:1.

EMA algorithm for vasculitis classification



Sınıflandırmada gelinen nokta…

- Patogenez konusundaki bilgilerimiz arttıkça gelişmeye devam etmektedir
- MPO-ANCA & PR3-ANCA
  - Klinik ve prognoz ile ilişkili
- Kesin tanı kriterleri henüz geliştirilmemiştir
  - «Diagnostic and Classification Criteria in Vasculitis Study» (DCVAS) Projesi

Vaskülitlere yaklaşım

- Genellikle **ciddi** & bazen **ölümcül** hastalıklar; hemen tanı ve tedavi!
- Hafif / lokalize ←→ yaşam / organ tehditi
- **Heterojen klinik & nadir** → zor tanı ve yönetim
- Genellikle **tanı gecikmesi**+

«**yaşamsal** değerde bir zaman kaybı olabileceği için hekim tanı koyma çabası yanında mantıklı bir **tedavi** yaklaşımını da formüle etmelidir»

- **Yapısal semptomlarla** + tek ve/veya çoklu **organ disfonksiyonu**

  → **Vaskülit**?!

- Sistematik ve kapsamlı bir **öykü** ve **muayene**

  → Belirli vaskülitik patolojilere özgü belirti ve bulgular

- Vaskülitler arasında «**çakışmalar»**

Vaskülit düşündüren belirti ve bulgular

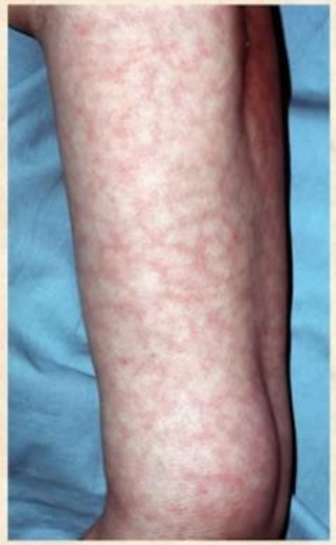
Sistem	Belirti & bulgu
Yapısal	Açıklanamayan ateş, kilo kaybı, anoreksi, halsizlik, terleme
Cilt	**Palpabl purpura**, Raynaud fenomeni, **livedo retikülaris**, dijital gangren, ürtiker, zımba ile delinmiş gibi ülser, hemorajik makül, sc nodül, splinter hemoraji, saçlı deri hassasiyeti
KBB	Kalıcı nazal kurutlanma, epistaksis, kanlı burun akıntısı, kulak akıntısı, işitme kaybı
Solunum sistemi	Hemoptizi, astım, nefes darlığı
KVS	HT, ekstremite kladikasyosu, periferik nabız değişiklikleri, periferik üfürüm ve kan basıncı uyumsuzlukları, Çene ve/veya dilde klaudikasyo, göğüs ağrısı
Sinir sistemi	Düşük ayak veya düşük bilek, Periferik SS (duysal ve/veya motor NP (**MNM**, PNP)), SSS (baş ağrısı, görme bozuklukları, nöbet, inme, bilinç bulanıklığı)
Genitoüriner sistem	GN (**pulmonorenal sendrom**), testiküler ağrı
Kas-iskelet sistemi	Artralji, kas ağrısı
Göz	Sklerit, görme kaybı, ağrılı kırmızı göz
GİS	Karın ağrısı, diare, hematemez, melena, hematokezya
Diğer	İlaç, hepatit veya başka sistemik hastalık (SLE) hikayesi

M Hng. Clinical Medicine 2020 Vol 20, No 6: 572–9

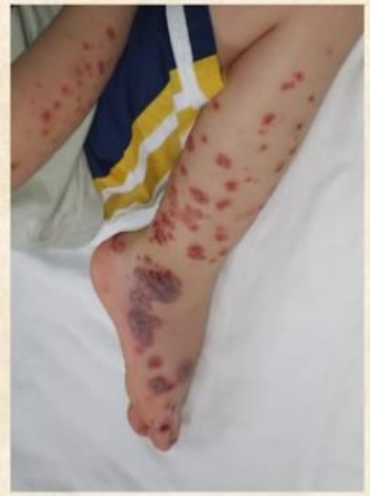
Vasküliti yüksek olasılıkla düşündüren klinik özellikler

Mononeuritis Multiplex

Pulmonary-Renal Pattern



Livedo Reticularis



Palpable Purpura

<u>Diğer</u>:

Baş ağrısı, HT, pulmoner kanama, karın ağrısı, anormal idrar sedimenti, EN, artralji, kladikasyo

Vaskülitlerde farklı damar tutulumlarına göre gelişmesi olası klinik bulgular

Büyük damar	Orta çaplı damar	Küçük damar
Ekstremitelerde kladikasyo	Cilt nodülleri/ülserleri	Palpe edilen purpura
Nabızsızlık, iki kol arası tansiyon farkı	Dijital ülser/gangren	Vezikülobüllöz lezyonlar
Aort dilatasyonu	Livedo retikülaris	Ürtiker
Üfürüm	Mononöritis mültipleks	Glomerülonefrit
Renovasküler HT	Mezenter iskemi	Mononöritis mültipleks
	Mikroanevrizmalar	Alveolar kanama
	Renovasküler HT	Splinter kanama
		Üveit, episklerit, sklerit

Kelley's textbook 2013

Patterns of Symptoms/Signs

		Size of Vessels		
		Small	Medium	Large
Organ System	Skin	Palpable purpura	Erythema nodosum Livedo reticularis	Cyanosis Discoloration of extremities
	Gastrointestinal	Mucositis GI bleeding	Abdominal pain Bowel perforation	Bowel infarction
	Renal	Hematuria without RBC casts Proteinuria	Hematuria with RBC casts Flank pain	Hypertension No hematuria
	Neuro	Polyneuropathy	Mental status Δ's Strokes	Strokes
	Muscles	Myalgias	Myositis	Claudication

Eric Strong, 2014

Vaskülit tanısı için tanısal işlemler

Table 3. Laboratory investigations useful in the evaluation of suspected vasculitides

Preliminary investigations	More specific investigations
Full blood count	Perinuclear ANCA (pANCA) and cytoplasmic ANCA (cANCA)
Urinalysis, urine protein:creatinine ratio	Antiproteinase 3 (antiPR3) and antimyeloperoxidase (antiMPO) antibody
Renal profile	Antiglomerular basement membrane antibody
Liver function test	Serum cryoglobulins
Creatinine kinase	Immunoglobulin E level
Fasting lipid profile, fasting blood sugar	Appropriate tissue biopsy
C-reactive protein, erythrocyte sedimentation rate	Bronchoscopy, bronchoalveolar lavage
Procalcitonin level	Angiographic examinations
Blood culture	Magnetic resonance angiography / magnetic resonance imaging
Hepatitis B and hepatitis C screening	Positron emission tomography
HIV test	Nerve conduction studies or electromyography
Other serology such as parvovirus B19, cytomegalovirus or specific fungal serology test	
Antinuclear antibody, antidouble stranded deoxyribonucleic acid (antidsDNA), extractable nuclear antigen	
Antiphospholipid antibodies	
Rheumatoid factor	
Complements level	
Urine toxicology screening	
Chest X-ray or computed tomography of the thorax	
Sinus X-ray or computed tomography	
Electrocardiography, echocardiography	
Serum protein electrophoresis, serum free light chains, urine Bence Jones protein	

M Hng. Clinical Medicine 2020 Vol 20, No 6: 572–9

Vaskülit tanısı için tanısal işlemler

- **Laboratuvar testleri**, vaskülit tipini, organ tutulum derecesini veya başka bir hastalığı (taklitçiler, sekonder hastalıklar) tanımlamaya yardımcı olabilir
- Vaskülitin kesin tanısı **doku tanısı**dır
- **Görüntüleme yöntemleri**
  - Anjiografi, PET, vb

→ **Vaskülitlerin tanısı**; genellikle organ hasarı paternlerine, etkilenen damarların boyutuna, serolojik ve histopatolojik özelliklere ve tanısal görüntülemedeki karakteristik bulgulara dayanır

Ayırıcı tanı

- Vaskülit taklitçileri;
  - Enfeksiyon, malignansi!
    - Tanı gecikmesi
    - İmmSuprTdv!

Table 1. Vasculitis mimics

Vasculitis mimics	Example
Infections	Infective endocarditis Bacteria eg meningococcaemia or gonococcaemia Spirochetes Fungi Mycobacteria Viruses
Drugs/therapy	Ergotamine Cocaine Phenylpropanolamine Warfarin Radiation therapy
Malignancy	Leukaemia cutis Plasma cell dyscrasia Metastatic carcinoma Paraneoplastic syndrome Lymphoma, especially involving nasal or paranasal cavity
Thromboembolic disorders	Atrial myxoma Cholesterol emboli from an atheroma Antiphospholipid syndrome Thrombotic thrombocytopenic purpura Sickle cell disease Procoagulant states Calciphylaxis
Other vasculopathy	Fibromuscular dysplasia Amyloid angiopathy Neurofibromatosis type I Coarctation of the aorta Chronic ergotism Scurvy Sweet's syndrome Köhlmeier–Degos disease

M Hng. Clinical Medicine 2020 Vol 20, No 6: 572–9

Vaskülit tedavisi

- Gecikmeden doğru **tanı** konulmalı
- Hastalığın **şiddeti ve yaygınlığı** belirlenmeli!
  - Hangi organ / organlarda **tutulum** var?
  - Organı / hayatı **tehdit** ediyor mu?
- Tedavi = **İmmSuprTdv**

Özet

Vaskülit düşündüren şikayet ve bulgular

Vaskülit taklitçilerini dışla

Sekonder vaskülit nedenlerini dışla

Vaskülit tanısını doğrula

Vaskülitin şiddetini & yaygınlığını belirle

Uygun tedaviye başla

E Doğanavşargil. Turkiye Klinikleri J Int Med Sci. 2005;1(43):1-15

Teşekkür ederim