Prezentare de caz

Vasculita ANCA pozitiva

Glomerulonefrita rapid progresiva

Istoricul bolii

- GB, sex M, 45 ani, mediu urban
- AHC- mama: diabet zaharat, AVC ischemic, tata: BPOC
- Comportament: fost fumator, fara medicatie cronica, ultimele analize de rutina efectuate in urma cu 5 ani- fara modificari patologice
- Profesie: inginer
- Prezentare initiala la MF: astenie marcata, artralgii bilaterale, fugace, dispnee la eforturi mici, rash purpuric cu debut de aprox.1 saptamana.

Afebril, TA 145/95 mmHg, FC 90bpm, Stetacustic cardio-pulmonar- relatii normale, aparat digestiv-normal, diureza prezenta, scaun normal, examen neurologic- normal.

Se prescriu AINS – Diclofenac 2cp/zi, 5 zile + Omeprazol 20 mg/zi + medicatie antihistaminica Xyzal 1 cp/zi.

Istoricul bolii

- Starea pacientului nu se amelioreaza in urma tratamentului:
  - Persistenta eruptiei, in usoara extindere
  - Instalarea edemelor declive cu godeu persistent
  - Dispnee agravată

  → internare in Clinica de Medicina Interna

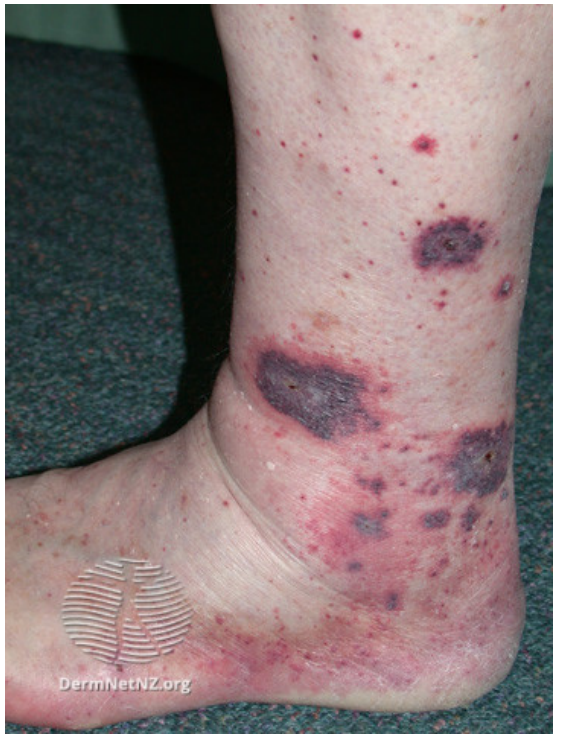
E.O.:

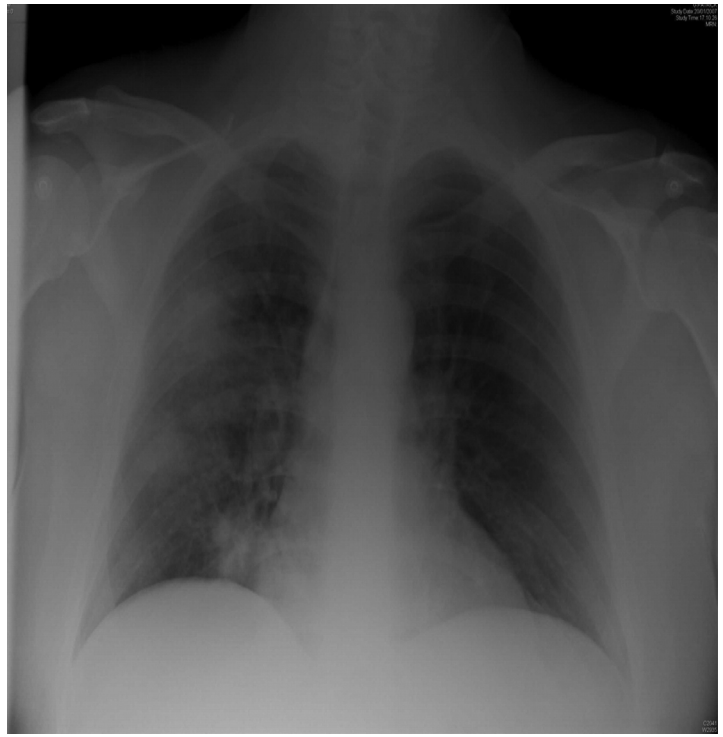
TA 150/100 mmHg, FC 95 bpm, SpO2 94% spontan, diureza aprox 1500 ml/24h, scaun normal, stetacustic pulmonar- MV innasprit bilateral, stetacustic cardiac: relatii normale, aparat digestiv-normal

EKG: ritm sinusal, ax QRS intermediar, FC 100 b/min, fara modificari patologice.

Ecografie abdominala:

Ficat cu structura omogena, colecist fara calculi, CBP, VP normale, splina 11 mm, pancreas-aspect normal, RD, RS –simetrici, aprox 105/60 mm cu IP 15 mm, fara staza/calculi, VU contur regulat, fara lichid in sp. Douglas





Sursa: Alan D. Salama, H. Terence Cook, Charles D. Pusey and Ruth J. Pepper
CJASN March 2008, 3 (2) 637-645; DOI: https://doi.org/10.2215/CJN.05071107

Rx torace efectuata la prezentare: infiltrat interstitial predominant medio-bazal dreapta, fara leziuni bacilare/

- **Intrebarea 1**
- Ce analize de laborator recomandati si de ce?
- Ce consulturi interdisciplinare vi s-ar parea utile si de ce?

Istoricul bolii

- Analize in dinamica
- Diagnostic prezumtiv initial: pneumonie interstitiala
- Se incepe tratament antibiotic cu ceftriaxon 1 g/12h + perfuzabil 1500 ml NaCl 0,9%/24h

Dupa 4 zile de tratament antibiotic, starea pacientului nu se amelioreaza, diureza scade la 800 ml/24h.

Pacientul prezinta primul episod de hemoptizie.

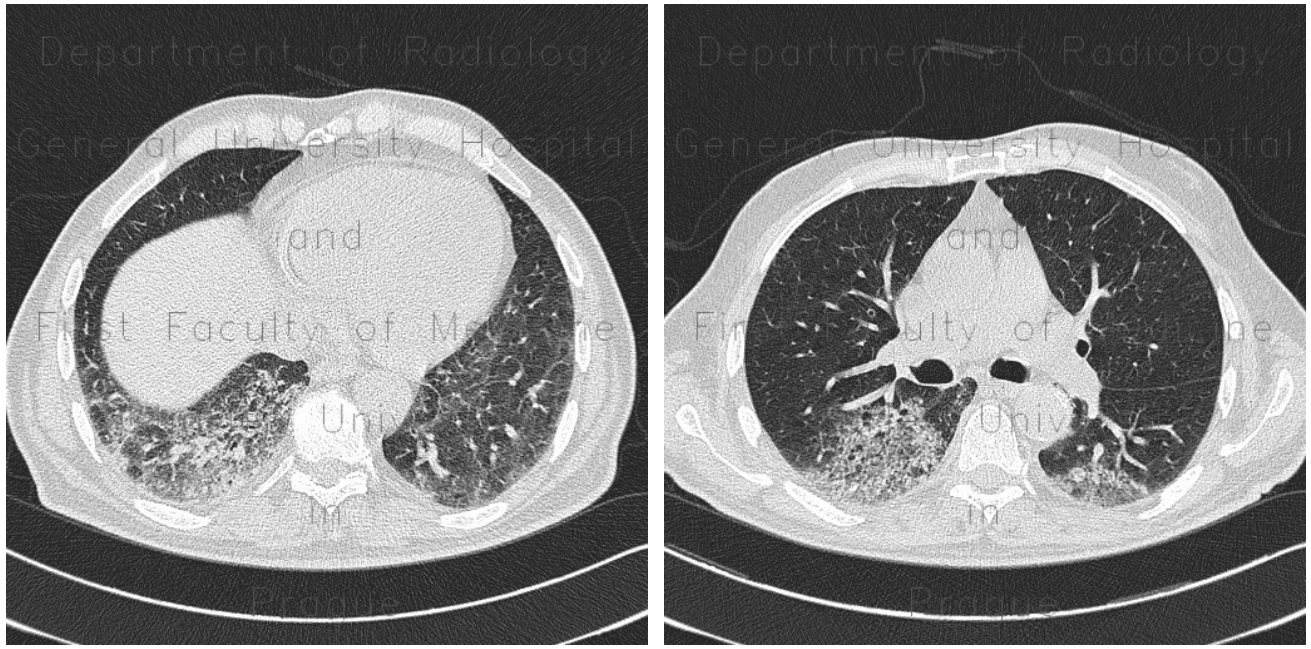
	La internare	Dupa 4 zile de antibiotic
Hb	12 g/dl	9,5 g/dl
Leucocite Neutrofile	14000/mm3 85%	17400/mm3 89%
CRP	232 mg/l	350 mg/l
Proteine serice Albumine serice	6,1 g/l 2,8 g/l	6 g/l 2,5 g/l
Creatinina Uree	2,4 mg/dl (antecedent de creatinina in urma cu 5 ani- 0,9 mg/dl) 110 mg/dl	5,8mg/dl 190mg/dl
TGO TGP	49 u/l 23 u/l	43 u/l 24 u/l
K seric Na seric Bicarbonat seric	4,8 138 22	5,3 136 17
Sumar de urina	Proteine ++ Hematii 15-20/camp nitriti absenti, flora microbiana nedecelabila	Proteine +++ Hematii peste 40/camp

Istoricul bolii

- Se efectueaza CT pulmonar nativ
- Se solicita consult nefrologic

  → **transfer Sectia de Nefrologie**

Proteinurie/24h	**4,3 g/24h**
Sediment Addis + morfologie eritrocitara	Hematii 74000/min, 100% dismorfe Leucocite 7000/min
Profil ANA	Negativ
ANCA	Pozitiv PR3 – titru 240 UI/ml
Ag HBs, Atc HCV, atc HIV	Negativ
Crioglobuline	Negativ
C3,C4	Normal
Anti MBG	negativ



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Aspecte CT sugestive pentru o vasculita cu determinare pulmonara:

- Granuloame si noduli cu margini neregulate, cu distributie peribronhovasculara
- Hemoragie intraalveolara
- Modificari ”in geam mat”
- Ingrosari ale peretilor traheo-brosici (Aspect de ”crazy pavement”)
- Atelectazii segmentale

Punctie biopsie renală

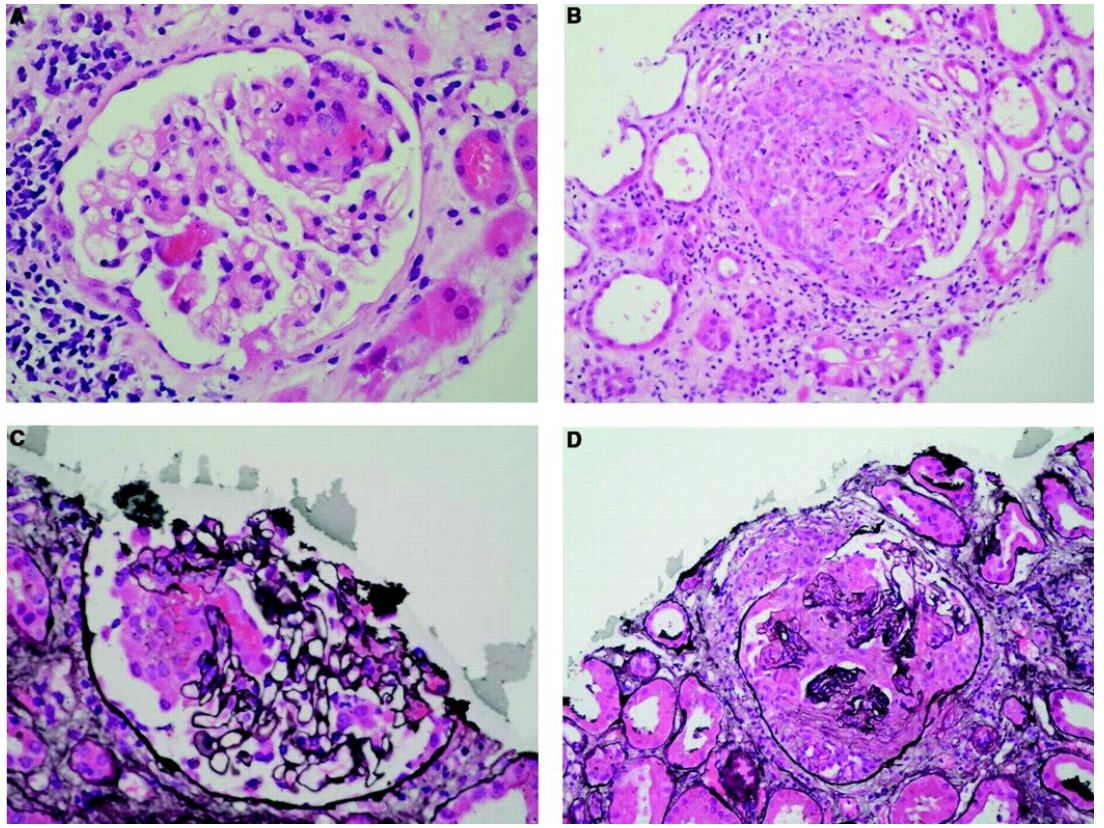
- Se efectueaza punctie-biopsie renala:

Rezultat:

Microscopie Optica: 22 glomeruli, 8 cu semilune celulare, 12 cu semilune fibro-celulare, 2 cu scleroza globala. In compartimentul tubular- infiltrat inflamator difuz, necroze si atrofii tubulare.

Imunofluorescenta: absenta depozitelor pe intreg campul.

→ glomerulonefrita crescentica pauci-imuna



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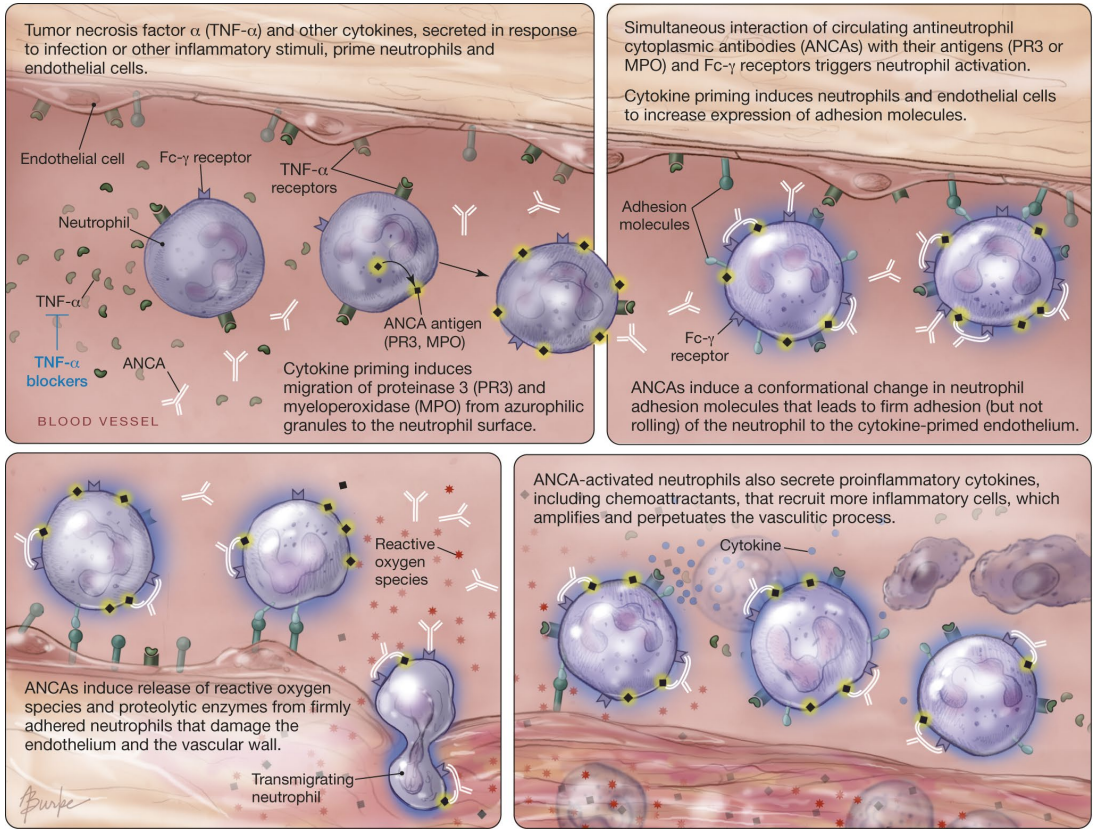
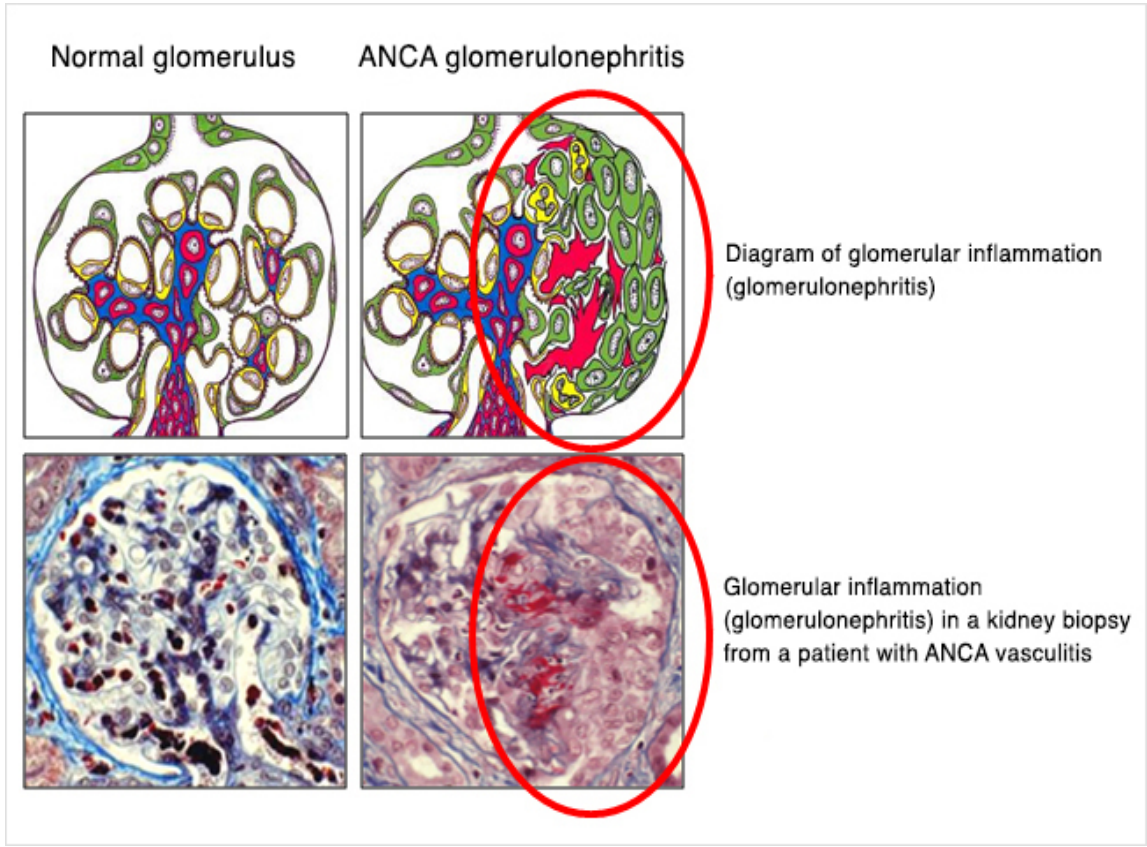
Patogeneza leziunilor vasculitice





Sursa: https://unckidneycenter.org/kidneyhealthlibrary/glomerular-disease/anca-vasculitis/
https://jamanetwork.com/journals/jama/fullarticle/208292

Diagnostic pozitiv

Granulomatoza cu poliangeita Vasculita ANCA-PR3 pozitiva cu determinare renala, pulmonara, articulara, cutanata

Glomerulonefrita rapid progresiva pauci-imuna tip 3 forma cu sindrom nefrotic impur

Leziune acuta de rinichi AKIN 3

Hiperpotasemie usoara

Acidoza metabolica

Hipoalbuminemie secundara

Hipertensiune arteriala secundara

→ diagnostic argumentat pe pozitivitatea ANCA + manifestări clinice specifice

→ afectarea renală se screeneaza prin dozarea proteinuriei/24h + evidentierea hematuriei microscopice/macroscoice DISMORFE. Dupa aceste teste este NECESARA biopsia renala

→ LAR AKIN 3 prin mecanism renal intrinsec

Stage	Serum creatinine	Urine output
1	1.5–1.9 times baseline OR $\geq$ 0.3 mg/dL ($\geq$ 26.5µmol/L) increase	<0.5ml/kg/h for 6–12 hours
2	2.0–2.9 times baseline	<0.5ml/kg/h for $\geq$ 12 hours
3	3.0 times baseline OR Increase in serum creatinine to $\geq$ 4.0mg/dL ($\geq$ 353.9 µmol/L) OR Initiation of renal replacement therapy OR, in patients <18 years, decrease in eGFR to < 35 mL/min per 1.73m^2	<0.3ml/kg/h for $\geq$ 24 hours OR Anuria for $\geq$ 12 hours

Vasculite sistemice- scor de activitate

VASCULITIS ACTIVITY SCORE 2003

☐ Tick box **only** if abnormality represents active disease [use the Vasculitis Damage Index, VDI to score items of damage]. If there are no abnormalities in a system, please tick the "None" box

○ **If all** the abnormalities recorded represent smouldering/low grade/grumbling disease, and there are no new/worse features, please remember to tick the box at the bottom right corner

	None	Active disease
1. General	☐	
Myalgia		○
Arthralgia or arthritis		○
Fever>38.0 °C		○
Weight loss>2 kg		○
2. Cutaneous	☐	
Infarct		○
Purpura		○
Ulcer		○
Gangrene		○
Other skin vasculitis		○
3. Mucous membranes/eyes	☐	
Mouth ulcers/granulomata		○
Genital ulcers		○
Adnexal inflammation		○
Significant proptosis		○
Red eye (Epi)scleritis		○
Red eye conjunctivitis/ blepharitis/keratitis		○
Blurred vision		○
Sudden visual loss		○
Uveitis		○
Retinal vasculitis/retinal vessel thrombosis/retinal exudates/ retinal haemorrhages		○
4. ENT	☐	
Bloody nasal discharge/nasal crusts/ulcers and/or granulomata		○
Paranasal sinus involvement		○
Subglottic stenosis		○
Conductive hearing loss		○
Sensorineural hearing loss		○
5. Chest	☐	
Wheeze		○
Nodules or cavities		○
Pleural effusion/pleurisy		○
Infiltrate		○
Endobronchial involvement		○
Massive haemoptysis/alveolar haemorrhage		○
Respiratory failure		○

	None	Active disease
6. Cardiovascular	☐	
Loss of pulses		○
Valvular heart disease		○
Pericarditis		○
Ischaemic cardiac pain		○
Cardiomyopathy		○
Congestive cardiac failure		○
7. Abdominal	☐	
Peritonitis		○
Bloody diarrhoea		○
Ischaemic abdominal pain		○
8. Renal	☐	
Hypertension		○
Proteinuria>1+		○
Haematuria>10 rbc/hpf		○
Creatinine 125-249 µmol/l		○
Creatinine 250-499 µmol/l		○
Creatinine>500 µmol/l		○
Rise in creatinine>30% or creatinine clearance fall>25%		○
9. Nervous system	☐	
Headache		○
Meningitis		○
Organic confusion		○
Seizures (not hypertensive)		○
Stroke		○
Cord lesion		○
Cranial nerve palsy		○
Sensory peripheral neuropathy		○
Motor mononeuritis multiplex		○
10. Other	☐	
		○
		○
		○
		○

Persistent disease only:

Tick here if **all** the above abnormalities are due to low grade grumbling disease and not due to new/worse disease ☐

Pentru stabilirea activității și severității bolii, se calculeaza scorul BVAS.

Diagnostic diferential

1) Cu alte tipuri de vasculite. Manifestarile clinica ale vasculitelor cu vase mici →

Clasificarea vasculitelor:

Table 1. Classification of Primary Systemic Vasculitis (Chapel Hill Consensus Conference Nomenclature)

Vasculitis	*Description*
Small vessel	
Churg-Strauss syndrome	Eosinophil-rich and granulomatous inflammation involving the respiratory tract; necrotizing vasculitis of small to medium vessels; associated with asthma
Cutaneous leukocytoclastic angiitis	Isolated cutaneous leukocytoclastic angiitis without systemic vasculitis or glomerulonephritis
Essential cryoglobulinemic vasculitis	Vasculitis, with cryoglobulin immune deposits, affecting capillaries, venules, or arterioles; associated with serum cryoglobulins; skin and glomeruli are often involved
Henoch-Schönlein purpura	Immunoglobulin A–dominant immune deposits, affecting capillaries, venules, or arterioles; typically involves skin, gut, and glomeruli; associated with arthralgias or arthritis
Microscopic polyangiitis	Necrotizing vasculitis, with few or no immune deposits, affecting capillaries, venules, or arterioles, but may involve small and medium arteries; necrotizing glomerulonephritis is very common; pulmonary capillaritis often occurs
Wegener granulomatosis	Granulomatous inflammation involving the respiratory tract, and necrotizing vasculitis affecting capillaries, venules, arterioles, and arteries; necrotizing glomerulonephritis is common
Medium vessel	
Kawasaki disease	Arteritis involving coronary arteries, but aorta and veins may be involved; associated with mucocutaneous lymph node syndrome
Polyarteritis nodosa	Necrotizing inflammation of medium or small arteries without glomerulonephritis or vasculitis in arterioles, capillaries, or venules
Large vessel	
Giant cell (temporal) arteritis	Granulomatous arteritis of the aorta and its major branches, with a predilection for the extracranial branches of the carotid artery; often involves the temporal artery; associated with polymyalgia rheumatica
Takayasu arteritis	Granulomatous inflammation of the aorta and its major branches

Adpated with permission from Jennette JC, Falk RJ, Andrassy K, et al. Nomenclature of systemic vasculitides. Proposal of an international consensus conference. Arthritis Rheum. *1994;37(2):189.*

Finding	Pulmonary	Nonpulmonary	Laboratory findings	Lung pathology
Small vessel vasculitis				
ANCA associated				
Microscopic polyangiitis	Alveolar hemorrhage, pulmonary fibrosis, pleural effusion, VTE	Glomerulonephritis	50%–75% ANCA positive; most have pANCA+ MPO-ANCA	Capillaritis, arteriolitis, venulitis
Necrotizing granulomatous vasculitis	Lung nodules, cavitary masses, alveolar hemorrhage, airway stenosis, pleural effusion, VTE	Glomerulonephritis, otitis media, nasal deformity, skin involvement, central nervous system involvement	90% ANCA positive with active systemic; 50%–75% ANCA positive with pulmonary involvement limited; most have cANCA+PR3-ANCA	Capillaritis, arteriolitis, venulitis, necrosis, granulomas
Churg-Strauss syndrome	Pulmonary infiltrates, asthma, alveolar hemorrhage, eosinophilic pleural effusion, VTE	Eosinophilia, glomerulonephritis, central nervous system involvement, skin involvement, gastrointestinal involvement	30%–50% ANCA positive; pANCA+MPO-ANCA	Eosinophilic infiltrate, granulomatous inflammation, capillaritis, arteriolitis, venulitis
Non–ANCA associated				
Goodpasture's syndrome	Alveolar hemorrhage	Glomerulonephritis	Antiglomerular basement membrane antibody (~ 90%)	Capillaritis, linear antibody deposition on basement membrane
Large vessel vasculitis				
Behcet's syndrome	PAA, thrombosis	Aphthous ulcers, genital ulcers, uveitis, retinal occlusion, skin lesions, positive pathergy test	None diagnostic	Mononuclear infiltrate, thrombus, recanalization, small vessel proliferation, breakdown of lamina elastica
Takayasu's arteritis	Pulmonary artery stenosis	Aortitis, great vessel occlusion	None diagnostic	Stenosis/recanalization of pulmonary elastic arteries, cellular infiltration of muscular arteries

ANCA antineutrophil cytoplasmic antibodies, *cANCA* cytoplasmic ANCA, *MPO* myeloperoxidase, *PAA* pulmonary artery aneurysm, *pANCA* perinuclear ANCA, *PR3* proteinase-3, *VTE* venous thromboembolism

Sursa:https://www.semanticscholar.org/paper/Pulmonary-Vasculitis%3A-Clinical-Presentation%2C-and-Ramsey-Amari/c96471e146d5efcc38edabecde6d6f5559ff4d0a

Diagnostic diferential

- Vasculite in context LES →
- Vasculite in context infectios:

Hepatita B, Hepatita C,

- Vasculite asociate consumului medicamentos
- Vasculite localizate (vasculita leucocitoclastica cutanata)
- Vasculite paraneoplazice

→Necesare criteriile clinice si imunologice de LES

→ necesar screening infectios

→ necesara anamneza amanuntita a consumului de medicamente

→ nu asociaza alte simptome

→ necesar screening malign

Diagnostic diferential

2) Altă glomerulopatie primitivă cronică – se exclude ca urmare a debutului brusc, simptomatologiei intricate, si a ***aspectului pe biopsia renală***

Intrebarea 2: Reamintiti-va tipurile de GNC primitive (tablou clinic + aspect PBR)

3) Diagnosticul diferential al leziunii acute de rinichi →

Tratament

- *Tratament de inductie a remisiunii*
- dieta : **hiposodată, hipoproteică**
- corticosteroizi:
  - **“puls-terapie”-** metilprednisolon **:1g/zi, I.V., 3 zile**
  - **urmat de corticoterapie orală**
  - ●prednison- **1 mg/kg/zi,**
- imunosupresoare -**ciclofosfamidă**

- **-1.5-2mg/kg/zi (max 200mg),oral-3-6 luni**
- **-500-700mg/m^2,iv-la 3-4 sapt- 3-6luni (500mg- >60ani)**
- **Doze ajustate pt mentinere leucocite>3,000/mmc**
- imunosupresoare -**rituximab**
- **- Eficacitate similara in inducerea remisiunii**
- **Evenimente adverse- similar**
- **375mg/mp/sapt**

- *Tratament de mentinere a remisiunii*
- **corticoterapie doza mica (12.5- 7.5 mg)**
- **azatioprină – 1.5mg/kg/zi,oral- 12-24 luni**
- **mycophenolat mofetil- 1gx2/zi (alternativa la AZA)**
- **rituximab (alternativa)**
- **metotrexat (rata mare de recadere, neindicat la afectare renala/ pumonara)**
- **asociere Co-trimoxazol- profilaxia infectiilor**

Asociat corticoterapiei → IPP, alfa D3

La nevoie in caz de ciclofosfamida iv: Ondansetron, Uromitexan

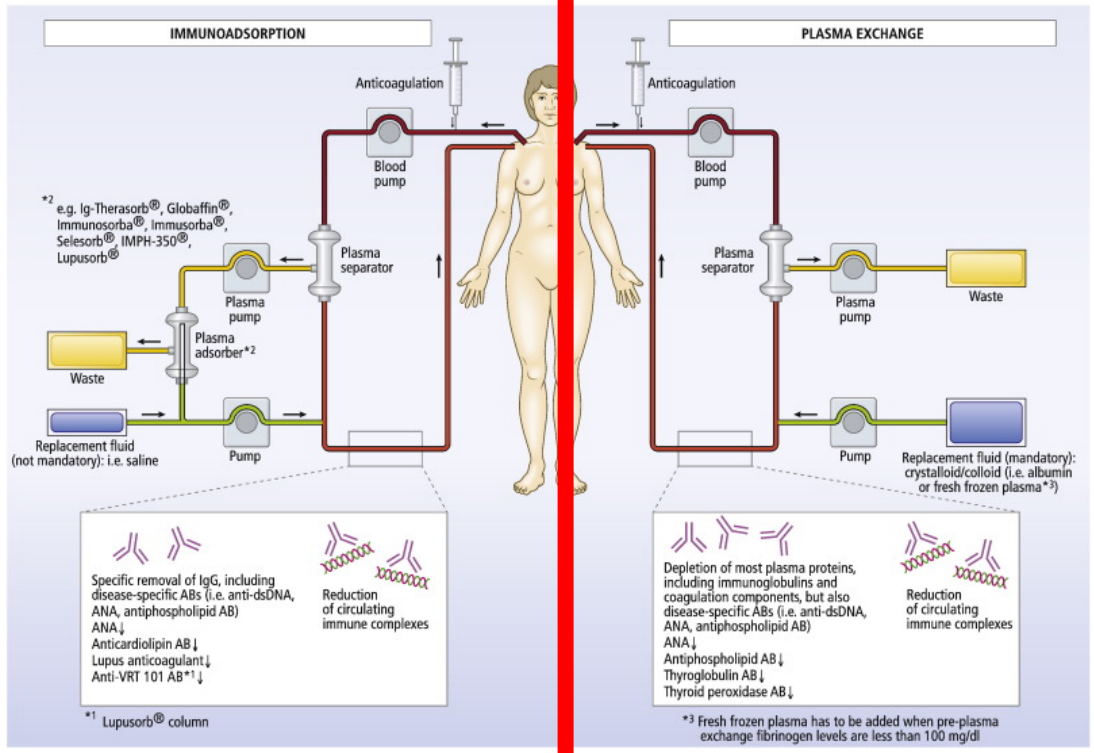
Tratamentul symptomatic al HTA → blocant de canal Ca, beta blocant

Tratamentul hipoalbuminemiei → albumina umana 20%, 100 ml/zi

Tratamentul edemelor → atentie la titrarea dozei de furosemid! Risc de deshidratare

Plasmafereza –indicatii

- Vasculite ANCA +, Sd. Goodpasture : 7 sedinte in 14 zile asigura un clearance de anticorpi > 80%
- Purpura trombocitopenica trombotica
- Sindrom hemolitic uremic atipic
- Sindrom de hipervascozitate (paraproteinemii severe)
- Crioglobulinemii severe
- Sindrom Guillain Barre
- Miastenia gravis



SURSA: https://www.sciencedirect.com/science/article/abs/pii/S1568997215001858

Complicații

1. Instalarea anuriei si necesitatea dializei acute

In cazul in care nu se reia functia renala → dependenta de dializa cronica

Asociere cu hiperhidratare (edem pulmonar acut, anasarca), tulburari hidro-electrolitice (hiperK severa) si acido-bazice (acidoza metabolica severa)

2. Suprainfectii pulmonare, necrozarea +ulcerarea leziunilor cutanate

3. Insuficienta respiratorie acuta in caz de hemoragie intraalveolara severa

- 4. Complicatiile tratamentului

Intrebarea 3: Reamintiti-va efectele adverse ale corticoterapiei si a tratamentului imunosupresor (farmacologie)

Prognostic

- Mortalitate mare (peste 80%) in cazul absentei tratamentului
- Prognostic rezervat datorita complicatiilor bolii si a tratamentului agresiv
- Poate recidiva pe rinichi transplantat