- S.A , sex masculin, 75 ani
- Antecedente personale: apendicectomie (1992), amigdalectomie, HTA
- Antecedente heredo-colaterale: neaga
- 03. 2019 – Clinica de Medicina Interna Spital Municipal Timisoara

CLINIC

-edeme gambiere masive

-dispnee inspiratorie

-durere toracica

-parestezii la nivelul membrelor inferioare

BIOLOGIC

	Valori normale	26.03.2019
Creatinina serica	0.5 – 1 mg/dl	2.43mg/dl
Uree serica	6 – 20 mg/dl	138 mg/dl
Proteinurie	<150 mg/24h	6 g/ 24h

- Transfer in Clinica de Nefrologie

➢29.03.2019 – *Internare Clinica de Nefrologie SCJUT*

CLINIC:

-edeme generalizate (retromaleolar, gamba, coapsa, scrot)

-dispnee inspiratorie

-parestezii la nivelul membrelor inferioare

-crestere in greutate aproximativ 20 kg in 3 luni

EXAMEN OBIECTIV:

- Stare generala buna
- Tegumente si mucoase: normal colorate, edeme generalizate, albe , moi, pufose, cu godeu persistent
- Stetacustic cardiac: arie precordiala de aspect normal, zgomote cardiace ritmice, bine batute, fara sufluri supraadaugate, TA=130/80mmHg, FC=64bpm
- Stetacustic pulmonar: matitate la ascultatie bazal bilateral, fara raluri decelabile stetacustic, SpO2=97% spontan
- Abdomen destins de volum, nedureros spontan si la palpare

➢PARACLINIC

	Valori normale	30.03.2019
Creatinina serica	0.5-1 mg/dl	2.57 mg/dl
Uree serica	6 -20 mg/dl	171 mg/dl
Proteine totale	6.4 -8.3mg/dl	5.5 g/dl
Albumina serica	3.5 – 5.2mg/dl	2.5 g/dl
Colesterol	< 200mg/dl	307mg/dl
Trigliceride	30-150mg/dl	450 mg/dl
Complement		1.13 g/l
VSH		65 mm/h
CRP		15.9mg/l
Sumar de urina	Hematii (negativ) Cilindrii(negativ) Leucocite(negativ)	24000/min 1500/min 9700/min
Proteinurie (Bioclinica)	< 150mg/dl	6 g/24h

Rg torace : cord cu alungirea arcului inferior stang, opacitate omogena a sinusurilor costodiafragmatice bilateral (de natura lichidiana)

Ecografie abdominala: colecist fara calculi, Vp=6mm, CBP normal, RD=118/50mm, ip=11mm, RS=105/62mm, Ip-14mm, Splina=73mm, lichid de ascita in cantitate medie, pleurezie bilaterala.

EKG: ritm sinusal, fara modificari ischemice acute
Ecocardiografie: HVS (Siv=1.5cm), DD tip 1, R mitrala grII, mici calcificari de cuspe Ao, scleroza Ao, R tricuspidiana gr I/II
Ecografie carotidiana: mici placi de aterom la nivelul carotidei drepte(nesemnificativa hemodinamic)

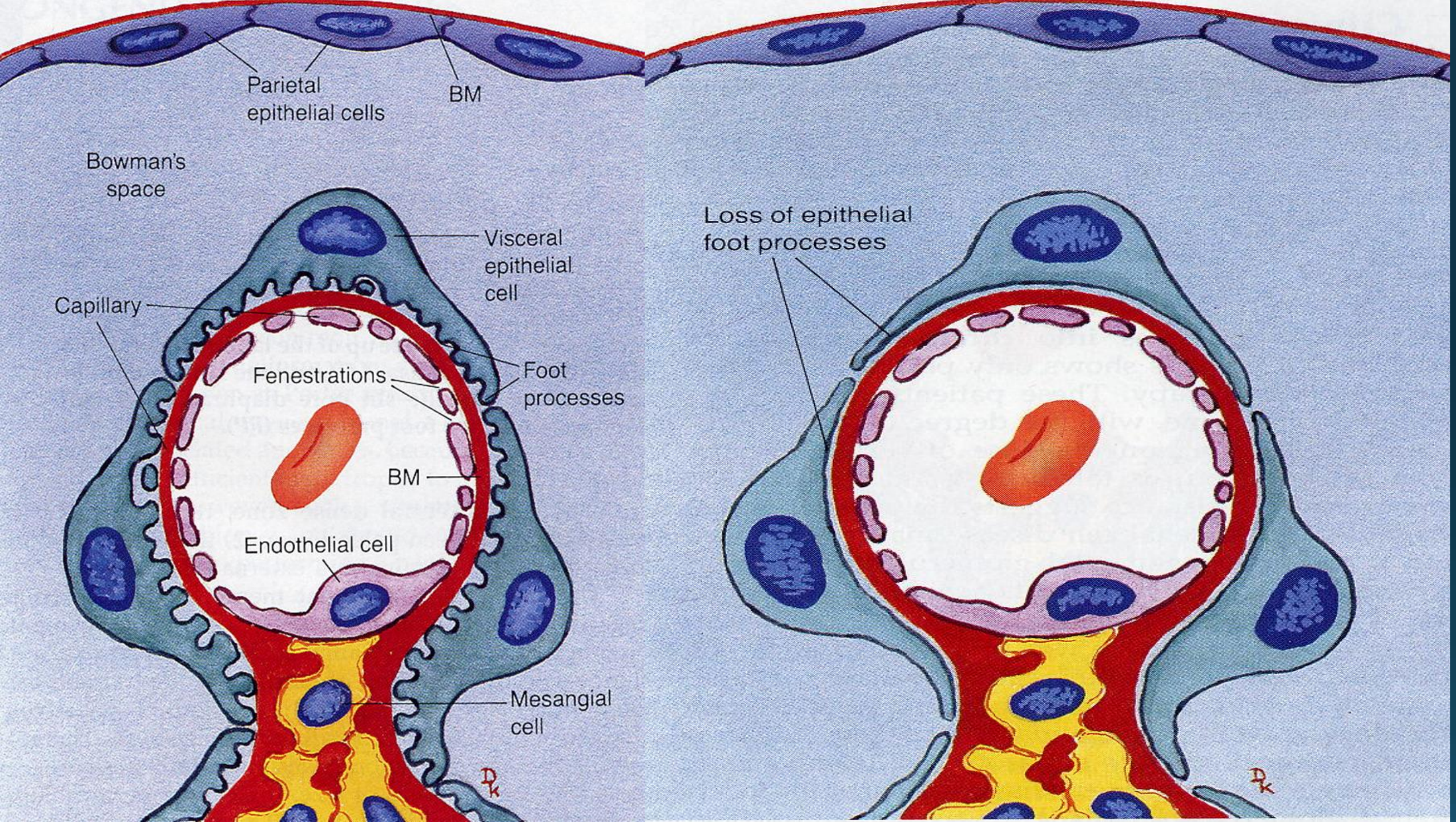
PUNCTIE BIOPSIE RENALA 06.04.2019

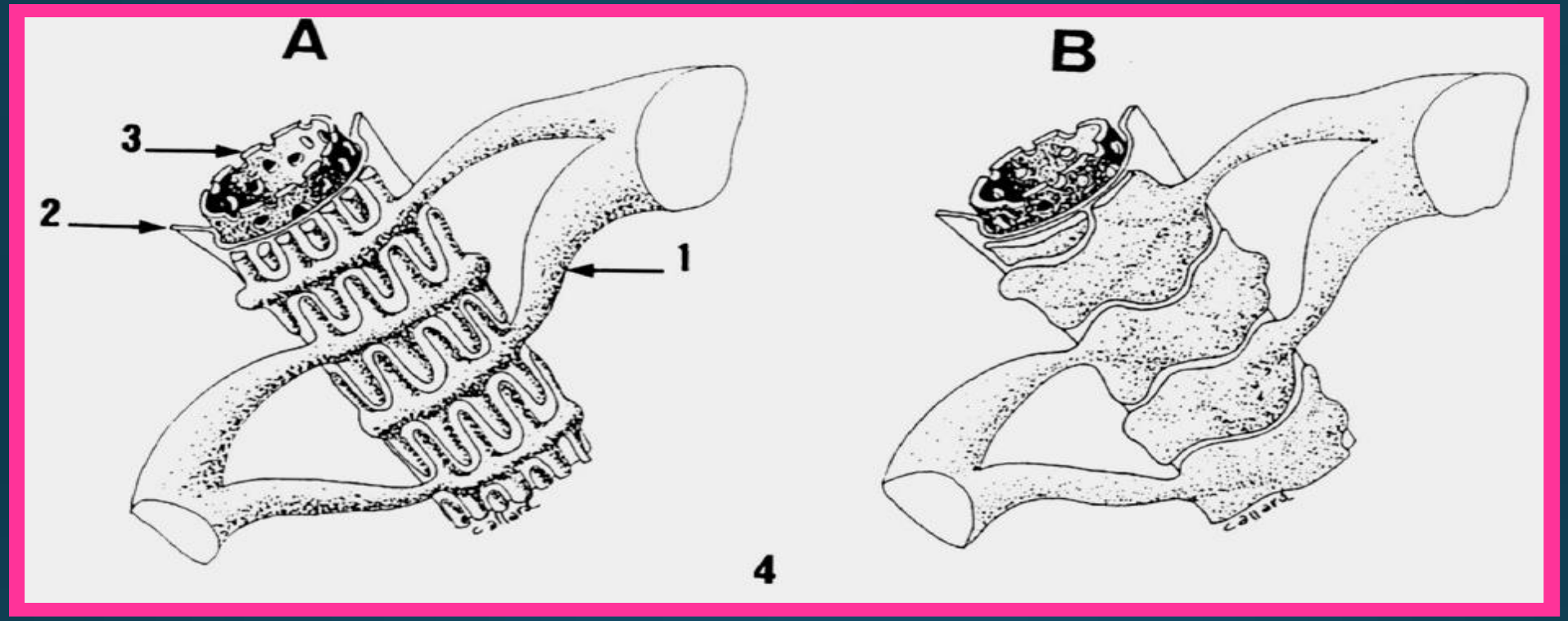
- Antibioterapie profilactica (Biseptol 2x400mg/zi – 4 zile)
- 21 glomeruli
- MO (H.E, tricrom, impregnare argentica):

-glomeruli normocelulari sau cu discrete hipercelularitate mezangiala insotita de accentuare matriceala

- 2/21 glomerului sclerozati
- cativa glomeruli cu aspect ischemic cu ratatinarea ghemului de capilare
- fara aspect de proliferare extracapilara
- minima afectare tubulointerstitiala prin fibroza usoara, rari tubi atrofici
- vase fara modificari semificative

CONCLUZIE : aspect histologice sugestive pentru ***Nefropatie glomerulara cu leziuni minime***


Parietal epithelial cells
BM
Bowman's space
Visceral epithelial cell
Capillary
Fenestrations
Foot processes
BM
Endothelial cell
Mesangial cell
Loss of epithelial foot processes

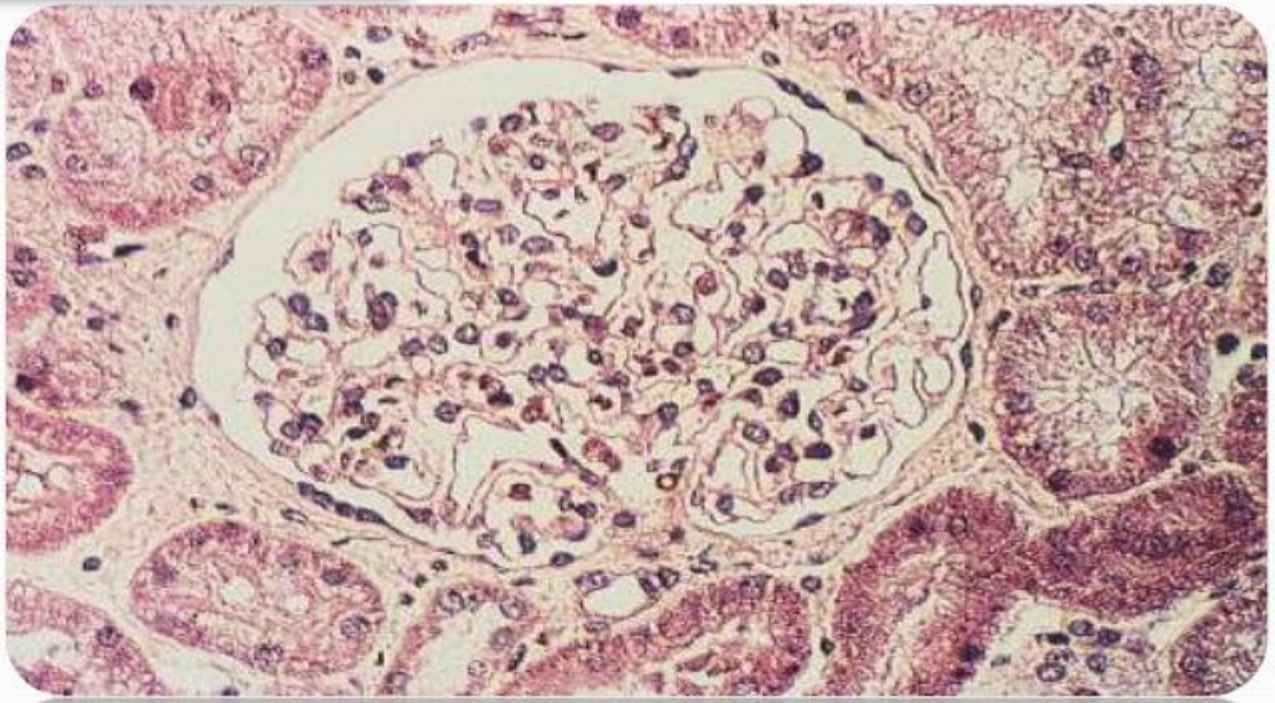


A - aspect normal: 2 pedicele de la 2 podocite diferite delimiteaza o fanta epiteliala
(1) - pedicele
(2) - membrane bazala
(3) - endoteliu
(4) -spatiul de filtare

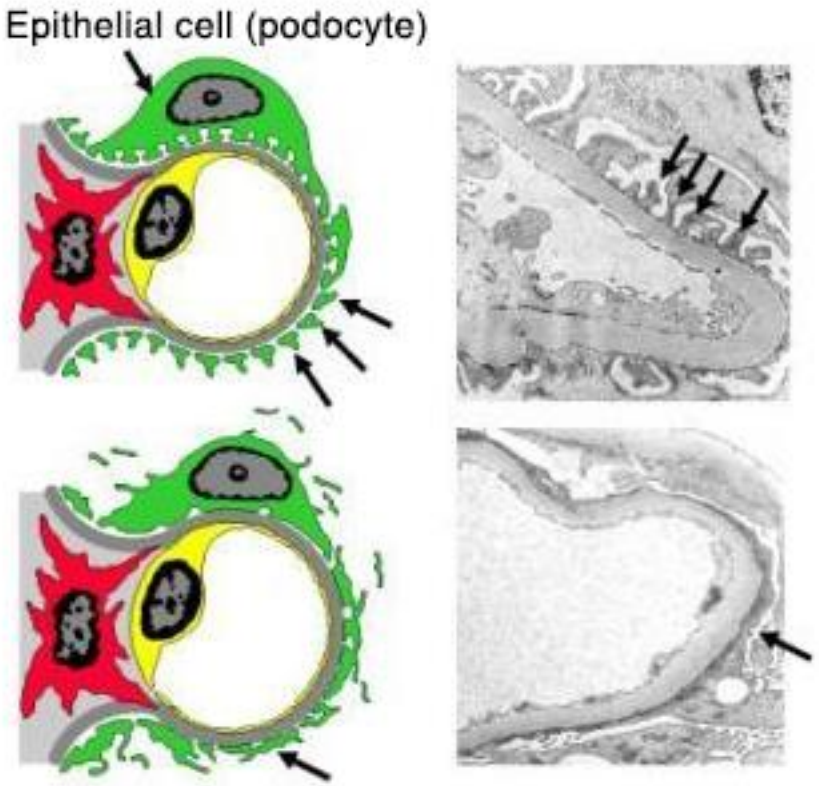
B – aspect de GNLM : stergerea pedicelelor si diminuarea semificativa a fantei de filtrare

MINIMAL CHANGE DISEASE

LIGHT MICROSCOPY



The glomerulus is normocellular, the capillary loops are patent, and the basement membrane is normal in thickness



By electron microscopy, a normal glomerular capillary has separate foot processes (arrows).

A minimal change disease glomerular capillary has fused foot processes (arrow).

[UNC Kidney Center]

- 11.04.2019 – scaune diareice moi, apoase, verzui
  - Toxina Clostridium Difficile A si B pozitiva
  - tratament cu Vancomicina 1g oral(4x125mg) -15zile
    - Saprosan
    - Smecta
    - Levurin
  - BIOLOGIC

	Valori normale	30.03.2019	11.04.2019	15.04.2019	26.04.2019
Creatinina serica	0.5-1 mg/dl	2.57 mg/dl	6.35mg/dl	4.07mg/dl	2.58mg/dl
Uree serica	6 -20 mg/dl	171 mg/dl	254mg/dl	250mg/dl	121mg/dl

DIAGNOSTIC DE ETAPA

- Edeme generalizate
- Ascita
- Pleurezie bilaterala

ANASARCA

+

PROTEINURIE = 6g/24h
+ hipolabuminemie
+ hipercolesterolemie

SINDROM NEFROTIC

PBR : glomeruli optic normali, fara leziuni la nivelul vaselor, sumar de urina cu hematuria minima

→ ***GLOMERULONEFRITA CRONICA PRIMITIVA CU LEZIUNI GLOMERULARE MINIME***

DIAGNOSTIC DE ETAPA

- LEZIUNE ACUTA DE RINICHI AKIN III

  - cresterea valorilor creatininei serice 3x valoare de baza cu revenirea la valoarea de baza in 14 zile.

  - cauze: hipoperfuzie renala-in cadrul sindromului nefrotic

    episode infectios(Enterocolita cu clostridium difficile))

- ENETROCOLITA ACUTA CU CLOSTRIDIUM DIFFICILLE

  -pe baza simptomatologiei clinice: scaune diareice moi, apoase, verzui

  -paraclinic: toxina Clostridium Difficille pozitiva

- HIPERTENSIUNE ARTERIALA ESENTIALA GRADUL I RISC FOARTE INALT

  - HVS la ecocord

  - placi de aterom pe carotide

DIAGNOSTIC DIFERENTIAL

- Nefropatie glomerulara cu leziuni minime – alte GN primitive (excluse prin biopsie)

  GSFS : evolutie asemanatoare (LAR, hematurie) DAR aspectul biopsiei actuale pledeaza pentru NGLM + HTA esentiala

  debutul GSFS - la nivelul glomerulilor juxtamedulari(posibil ca biopsia sa nu fi fost suficient de profunda)

- GNC primitive – GNC secundare

  excluse cauze secundare: -infectioase – AgHbs, Ac anti HCV negative

  -boli autoimmune: fara manifestari clinice caracteristice

  -neoplazii : marker tumorali N

  -medicamentoase: nega consum AINS, bifosfonati, ATB

DIAGNOSTIC POZITIV - initial

- *BOALA CRONICA DE RINICHI STADIUL G4 KDIGO(RFG=24ml/min)*
- *LEZIUNE ACUTA DE RINICHI AKIN III REMISA*
- *GLOMERULONEFRITA CRONICA PRIMITIVA CU LEZIUNI MINIME ACTIVA*
- *HIPERTENSIUNE ARTERIALA ESENTIALA GRADUL I RISC CARDIOVASCULAR FOARTE INALT*
- *REGURGITARE MITRALA GRADUL I DEGENERATIVA*
- *REGURGITARE TRICUSPIDIANA GRADUL I/II*
- *ATEROSCLEROZA CAROTIDIANA*
- *HIPOALBUMINEMIE MODERATA*
- *DISLIPIDEMIE MODERATA*
- *PLEUREZIE BILATERALA*
- *ASCITA IN CANTITATE MEDIE*
- *ENTEROCOLITA ACUTA CU CLOSTRIDIUM DIFFICILE IN TRATAMENT CU VANCOMICINA*

TRATAMENT

- KDIGO 2012 Clinical Practice Guideline for Glomerulonephritis
- ►Treatment of initial episode of adult MCD
- ●corticosteroids be given for initial treatment of nephrotic syndrome.
- - prednisone or prednisolone be given at a daily single dose of 1 mg/kg (maximum 80 mg) or alternate-day single dose of 2 mg/kg (maximum 120 mg).
- - the initial high dose of corticosteroids, if tolerated, be maintained for a minimum period of 4 weeks if complete remission is achieved, and for a maximum period of
- 16 weeks if complete remission is not achieved. In patients who remit, we suggest that corticosteroids be tapered slowly over a total period of 6 months

TRATAMENT

- **for patients with relative contraindications or intolerance to high-dose corticosteroids (e.g., uncontrolled diabetes, psychiatric conditions, severe osteoporosis), we suggest oral cyclophosphamide or CNIs as discussed in frequently relapsing MCD.**
- **the same initial dose of corticosteroids for infrequent relapses as in Recommendation 5.1.2 until remission is achieved, followed by at least 2 months of tapering steroids.**

[KDIGO Clinical Practice Guideline for Glomerulonephritis. *Kidney Int* 2012; Suppl 2: 139–274]

TRATAMENT

- **Frequent Relapses/Steroid Dependent MCD**

●oral cyclophosphamide 2-2.5 mg/kg/d for 8 weeks.

●CNI (cyclosporine 3-5 mg/kg/d or tacrolimus 0.05-0.1 mg/kg/d

in divided doses) for FR/SD MCD patients who have relapsed despite cyclophosphamide, and for people who wish to preserve fertility.

●MMF 750-1000 mg twice daily for patients who are intolerant of corticosteroids, cyclophosphamide, and CNIs.

- **►Corticosteroid-resistant MCD**

●re-evaluate patients who are corticosteroid-resistant for other causes of nephrotic syndrome.

[KDIGO Clinical Practice Guideline for Glomerulonephritis. *Kidney Int* 2012; Suppl 2: 139–274

TRATAMENT INITIAL(2019)

- ***MPDN*** **puls 500mg 3 zile consecutiv**
- **HHC 2x100mg/zi 10zile**
- **26.04.2019 –** ***PDN oral*** **8tb/zi (40mg) cu reducerea progresiva a dozelor :**

  01.07.2019 – 3tb/zi

  13.07.2019 - 1tb/zi
- **Ranitidina 2x20mg/zi**
- **Metoprolol 100mg/zi**
- **Furosemid 40mg 2-1-0 tb/zi**
- **Vancomicina oral 500mg/zi -1 saptamana**

EVOLUTIE

- **13.07.2019 – stare generala alterata, fatigabilitate**
  - **edeme masive**
  - **proteinuria =4g/24h**

INTERNARE CLINICA DE NEFROLOGIE (PRIMA RECADERE)

- **HHC 200mg/zi – 6 zile urmat de PDN oral 12tb/zi**
- **Spironolactona 50mg/zi**
- **Prestarium 2x10mg/zi**
- **anticoagulare cu Fraxiparina pe perioada internarii**

Raspuns favorabil : REMISIUNE : *sept 2019 – proteinuria 200mg/24h (2 determinari)*

EVOLUTIE

- **01.10.2019 – astenie , fatigabilitate, edeme gambiere massive, dispnee**
- **18.10.2019 – *proteinuria = 24g/24h* (a II a RECADEREA)**

INTERNARE IN CLINICA DE NEFROLOGIE

- HHC 200mg/zi – 9 zile urmat
  - ***PDN oral* 8tb/zi din 02-10.11.2019 apoi sevrare cu 10mg/sapt**
  - ***CICLOSPORINA* 50mg 3cpr/zi din 03.11.2019**

- Asociat tratamentul cronic + anticoagulare cu Fraxiparina pe perioada internarii

- **13.11.2019 – *proteinuria = 12g/24h***

EVOLUTIE

- **01.2020 – proteinuria = 5g/24h**
- **02.2020 – edeme gambiere moderate, dispnee**

INTERNARE NEFROLOGIE

	Valori normale	28.07.2020
Creatinina serica	0.5-1 mg/dl	2.8mg/dl
Uree serica	6 -20 mg/dl	111 mg/dl
Proteine totale	6.4 -8.3mg/dl	6.2 g/dl
Albumina serica	3.5 – 5.2mg/dl	1.6 g/dl
Colesterol	< 200mg/dl	364mg/dl
Trigliceride	30-150mg/dl	285 mg/dl
Sumar de urina	Hematii (0-1/camp) Leucocite(1-2/camp)	5-10 5-10
Proteinurie	< 150mg/dl	20 g/24h

DIAGNOSTIC POZITIV FINAL

- ***BOALA CRONICA DE RINICHI STADIUL G 4 KDIGO(RFG=)***
- ***GLOMERULONEFRITA CRONICA PRIMITIVA CU LEZIUNI MINIME CU RECADERI MULTIPLE IN TRATAMENT CU PREDNISON SI CICLOSPORINA***
- ***HIPERTENSIUNE ARTERIALA ESENTIALA GRADUL II RISC FOARTE INALT***
- ***REGURGITARE MITRALA GRADUL I DEGENERATIVA***
- ***REGURGITARE TRICUSPIDIANA GRADUL I/II***
- ***ATEROSCLEROZA CAROTIDIANA***
- ***HIPOALBUMINEMIE SEVERA***
- ***DISLIPIDEMIE MODERATA***

TRATAMENT ACTUAL

- **PDN 5mg 6tb/zi**
- **Ciclosporina 50mg 3tb/zi**
- **Albumina umana 100ml/24h**
- **Furosemid 2fi la 12h**
- **Omeprazol 40mg/zi**
- **Sortis 20mg/zi**
- **Espumisan 2x1tb/zi**
- **Leridip la nevoie**

PROGNOSTIC

- **NEFAVORABIL atat pe termen scurt cat si pe termen lung (varsta inaintata, GNLM corticodepnedenta, efecte adverse ale ciclosporinei)**
- **Posibil transformare in GSFS**