Nephropathology Case Presentation

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1. Case presentation

- MS is a 31-y-old male patient who presented to my office for evaluation of incidental finding of proteinuria discovered during employment physical check up 3 months earlier.
- **He is asymptomatic:**
  - No hematuria or lower limb swelling
  - No recent upper respiratory tract infection
  - No recent GI symptoms
  - No arthralgias or arthritis
  - No skin rash or mouth ulcers
  - No history of drug abuse, Over the counter or NSAID
  - No family history of renal diseases. DM or hypertension

Physical examination

- Healthy looking young male patient not in acute distress, but anxious.
- Body weight 78Kg, BP 110/60 mmHg and pulse rate 80/min
- Rest of physical examination was completely normal.
  - No rash, arthritis ,mouth ulcers, jaundice & lower limb edema.

Laboratory Findings

- **CBC:** Hemoglobin 13.5 gm, WBCs 5200, Platelets 243000
  - Both PT, PTT and INR were normal
- **Serum:**
  - Creatinine 0.9 mg/
  - Phosphorous 3.8 mg/dl
  - Total protein 6.5 gram/dl
  - A1C 5.1%
  - Calcium 9.3 mg/dl
  - Bicarbonate 23 Meq/L
  - Albumin 4.3 gram/dl
  - Uric Acid 6.3 mg/dl

Laboratory Findings

- **Urine analysis:**
  - ++ Protein and + hemoglobin and no sugar
  - WBCs 4-8/ hpf and RBCs 16-20/hpf
  - Protein/Creatinine ratio 0.9 gram
  - Albumin/Creatinine ratio 0.65 grams

- **TESTING FOR ORTHOSTATIC PROTEINURIA WAS NEGATIVE**

Laboratory Findings

- **Serology**
  - AS0 titer < 200 & ESR 32
  - ANA & Anti DNA were Negative
  - HBsAg & HCV were negative
  - C3 125 mg/dl & C4 20 mg/dl
  - Anti-PLA2R autoantibody
- Renal US: Normal size kidneys, no hydronephrosis, no stones.
- Chest X-ray Normal

Case summary

- 31-y-old male patient with incidental finding of 0.9 gram protein and Microscopic hematuria.
  - **Albumin/Creatinine ratio 0.65 grams**
- Normal BP and physical examination.
- Normal kidney function.
- All work up is negative.

Differential Diagnosis of Asymptomatic Proteinuria & Hematuria

What is your DD ?

Types of proteinuria

1. **Selective**

(> than 60% of the proteins is Albumin)

2. **Non Selective**

Classification and characterization of proteinuria types

Classification of proteinuria	Clinical setting	Typical level of proteinuria in adults	Predominant protein type
Transient proteinuria	Fever, heavy exercise, vasopressor infusion, albumin infusion	<1 g/day	Albumin
Persistent proteinuria – orthostatic proteinuria	Uncommon over age 30 years, may occur in 2 to 5% of adolescents	<1 to 2 g/day	Albumin
Persistent proteinuria – overflow proteinuria	Myeloma (monoclonal light chains), hemolysis (hemoglobinuria), rhabdomyolysis (myoglobinuria)	Variable, could be nephrotic range	Nonalbumin
Persistent proteinuria – glomerular proteinuria	Primary glomerular diseases, secondary glomerular diseases, diabetic nephropathy, hypertensive nephrosclerosis	Variable, often nephrotic range	Albumin
Persistent proteinuria – tubulointerstitial proteinuria	Heavy metal intoxications, autoimmune or allergic interstitial inflammation, medication-induced interstitial injury	<3 g/day	Nonalbumin
Post-renal proteinuria	Urinary tract infections, nephrolithiasis, genitourinary tumor	<1 g/day	Nonalbumin

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X

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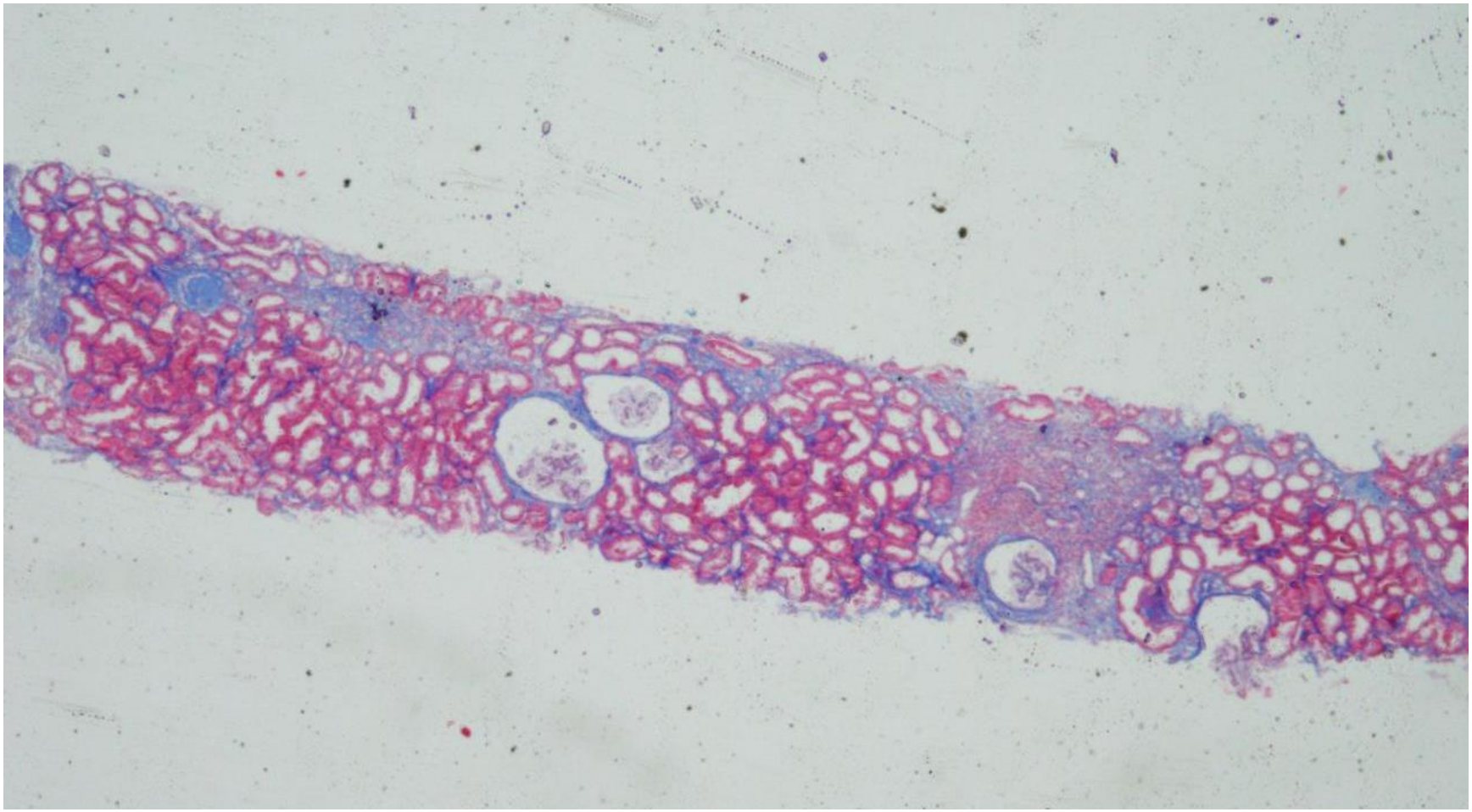
Kidney biopsy X

- Light microscopy: 8 glomeruli; 3 totally sclerosed
- IF Microscopy : 3 glomeruli
- EM : 2 Viable glomeruli



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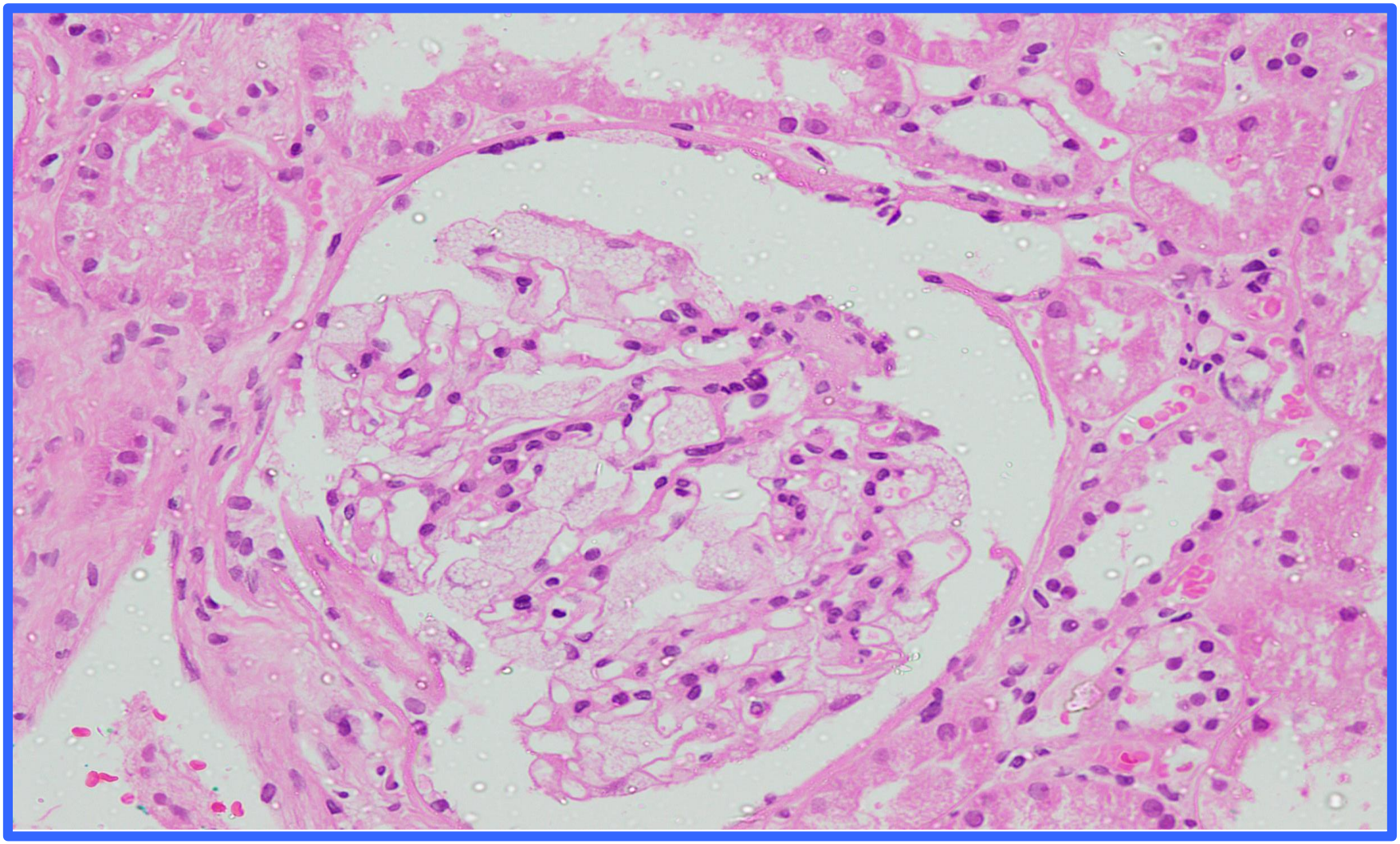

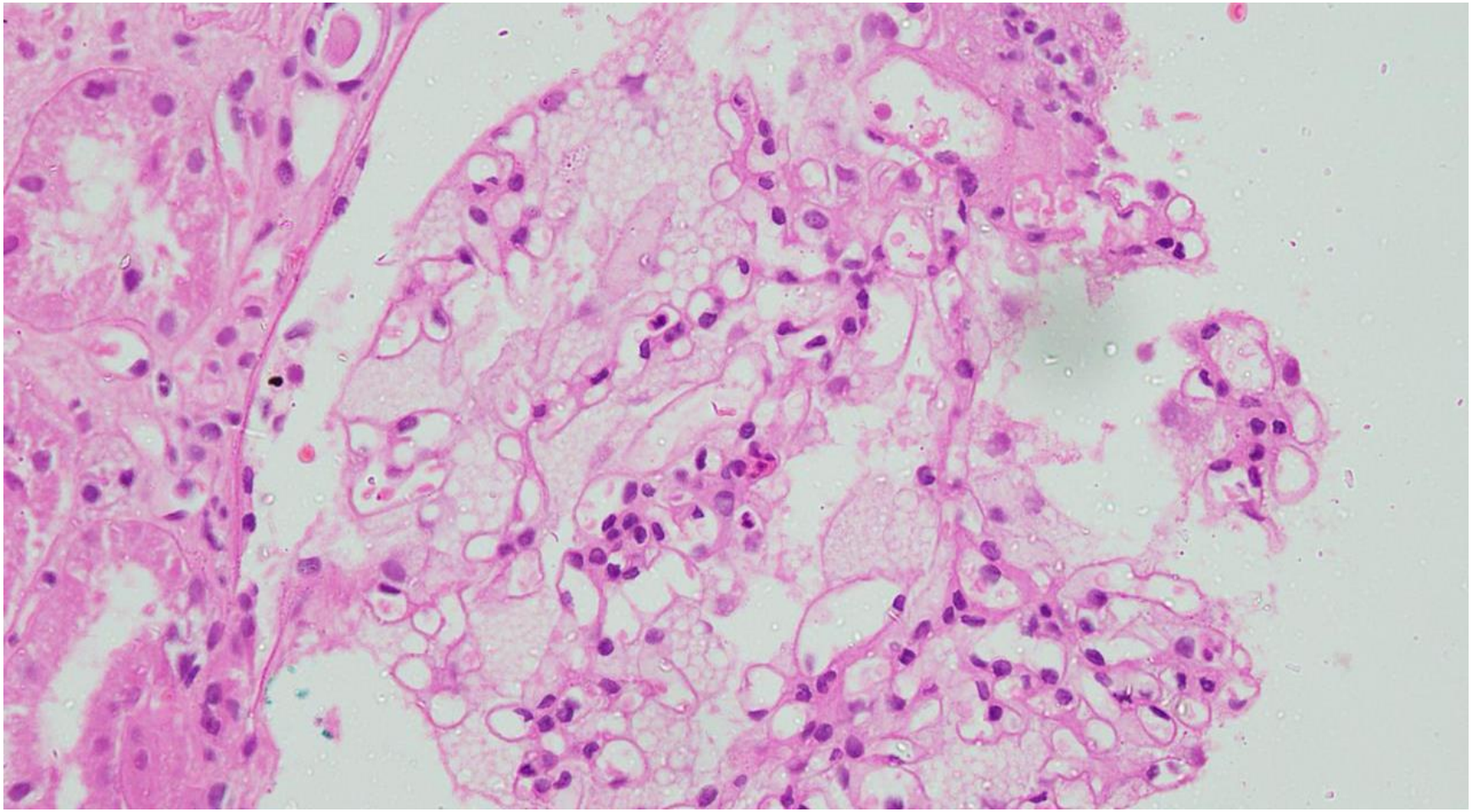

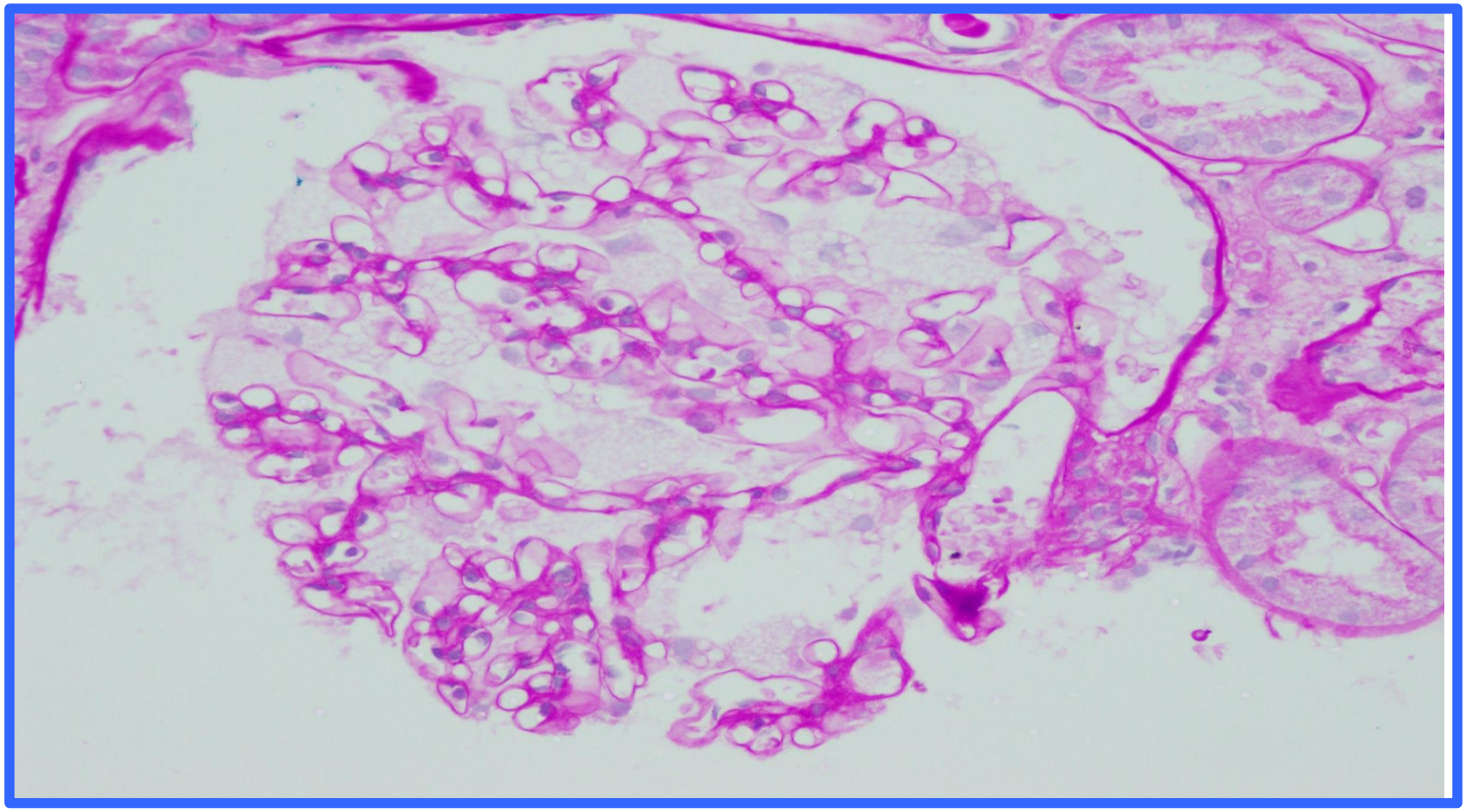

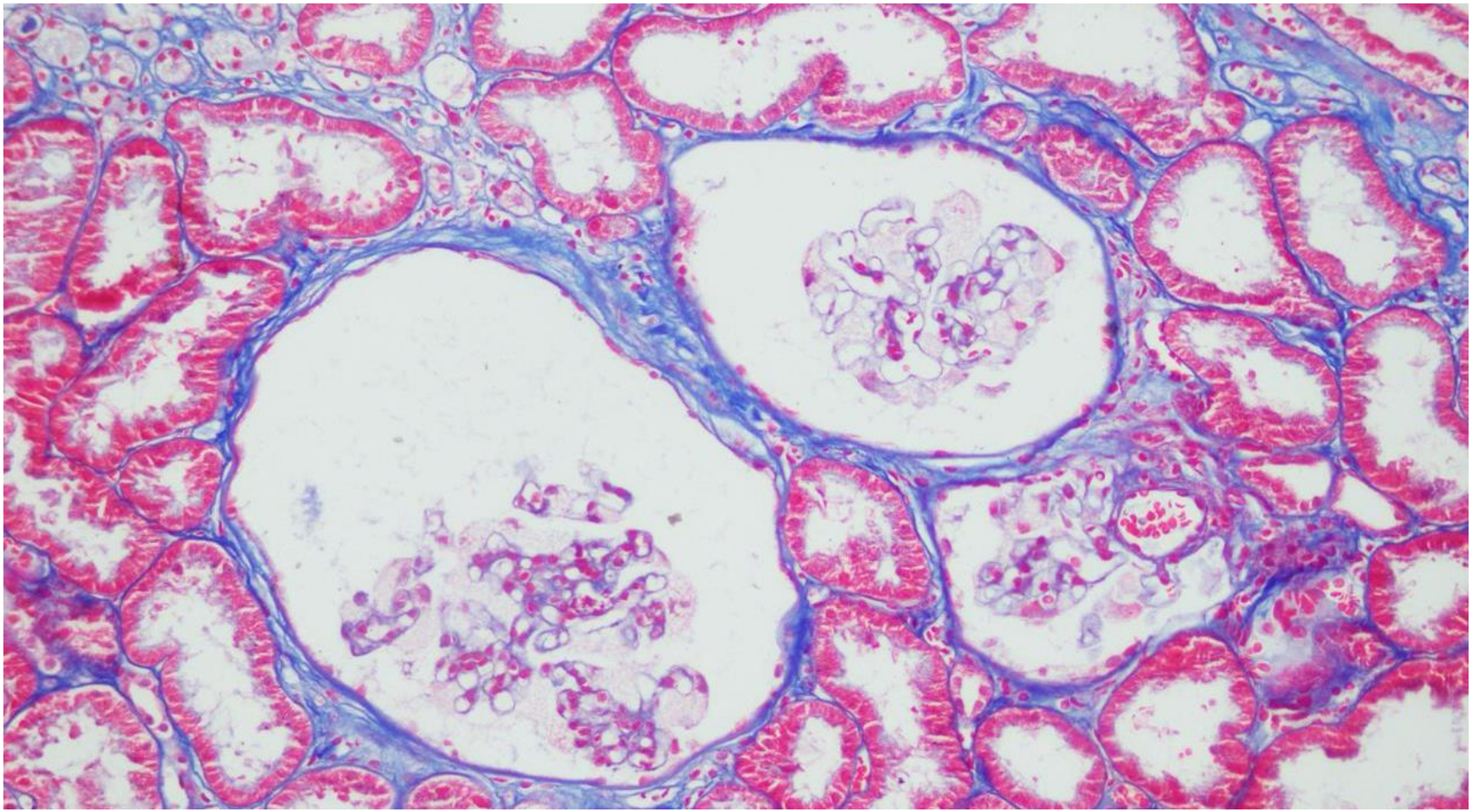

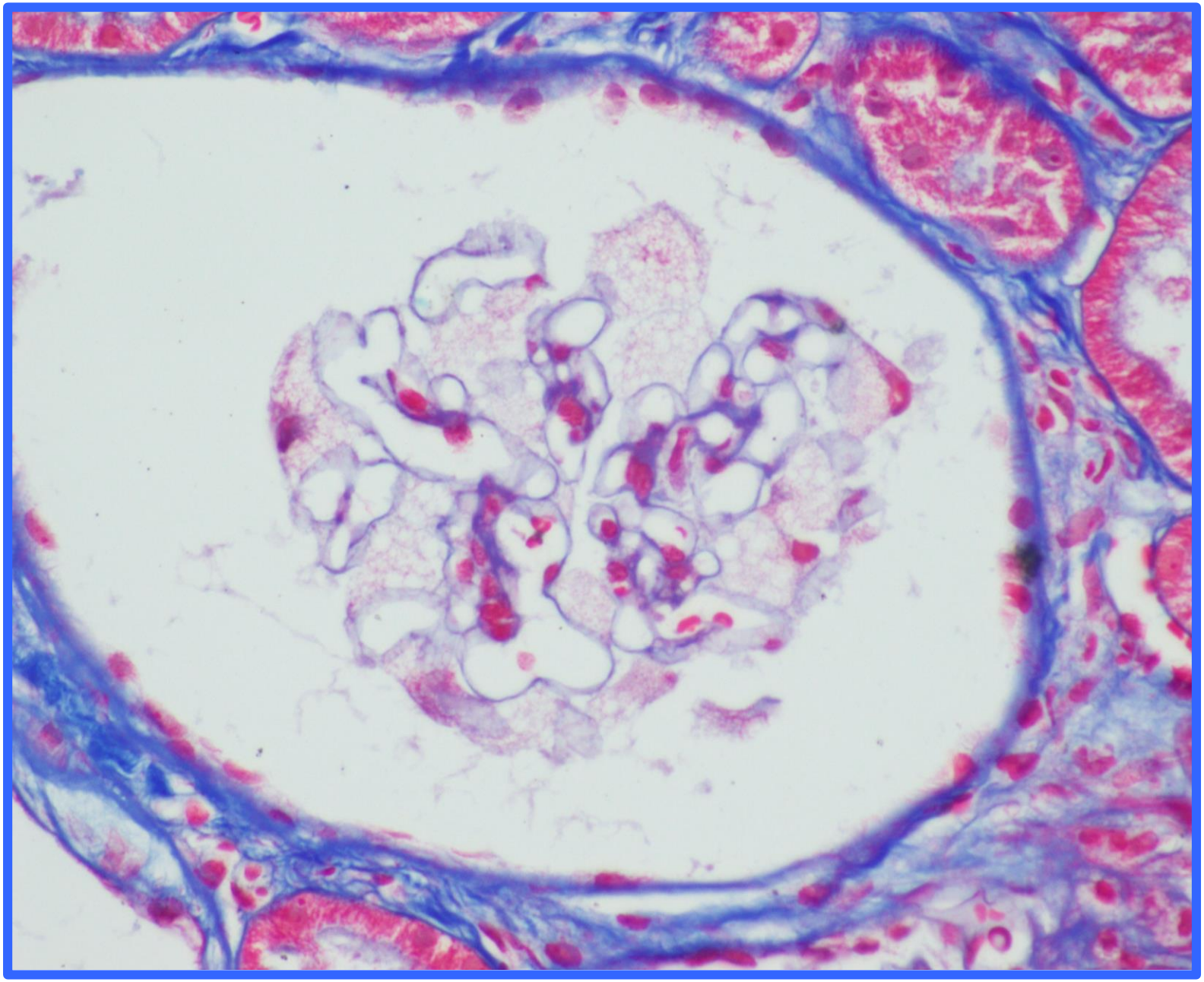

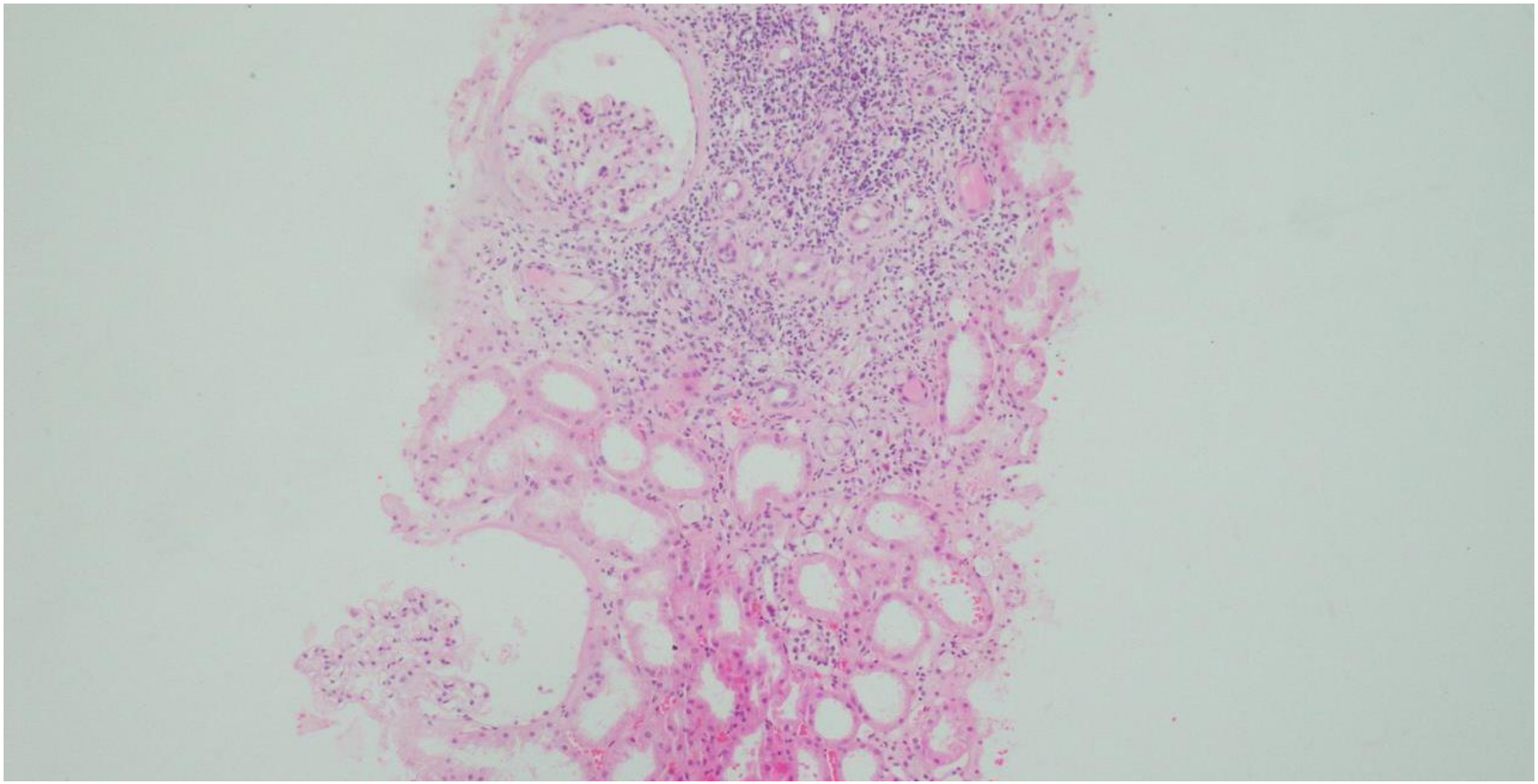

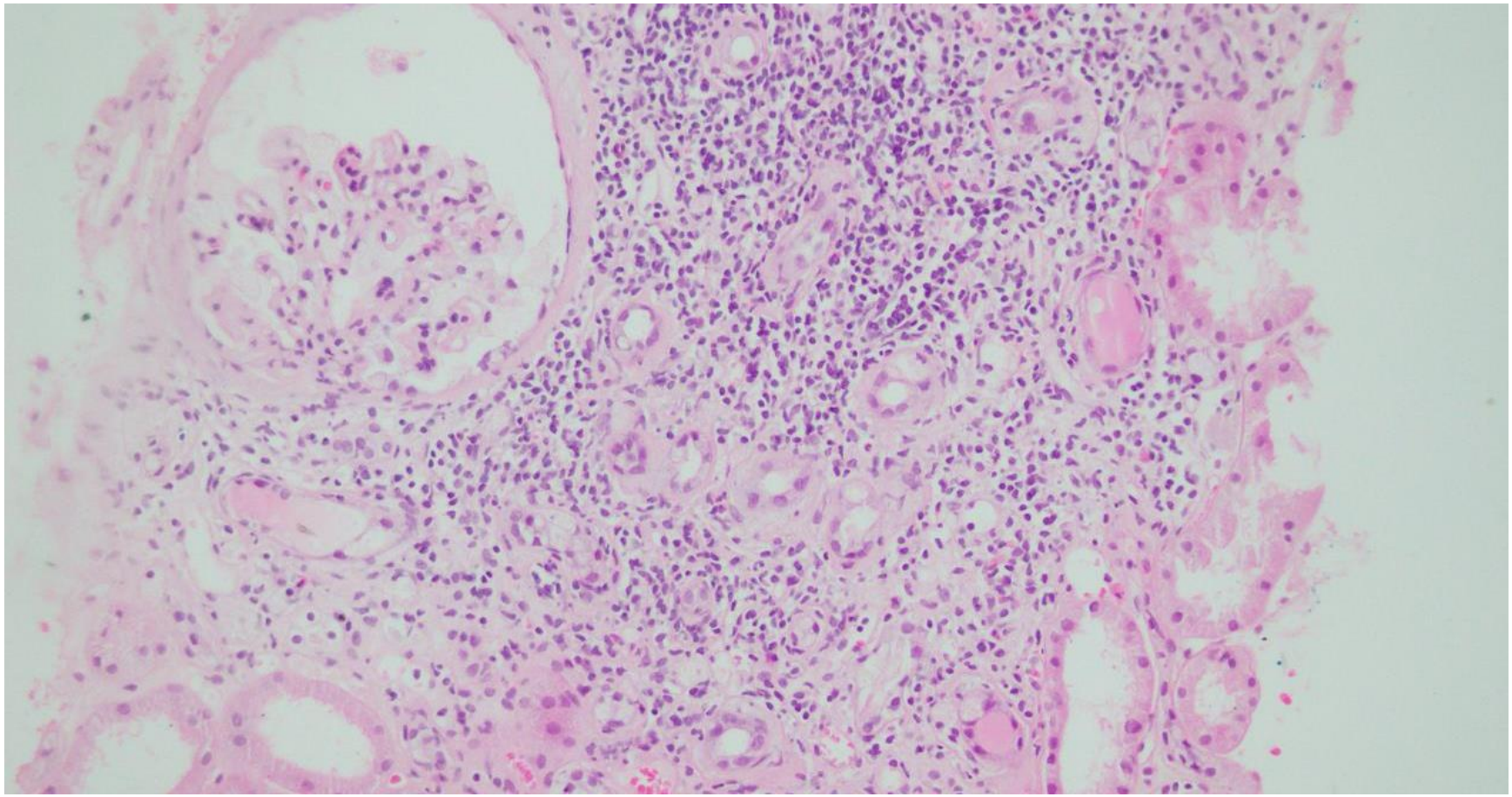

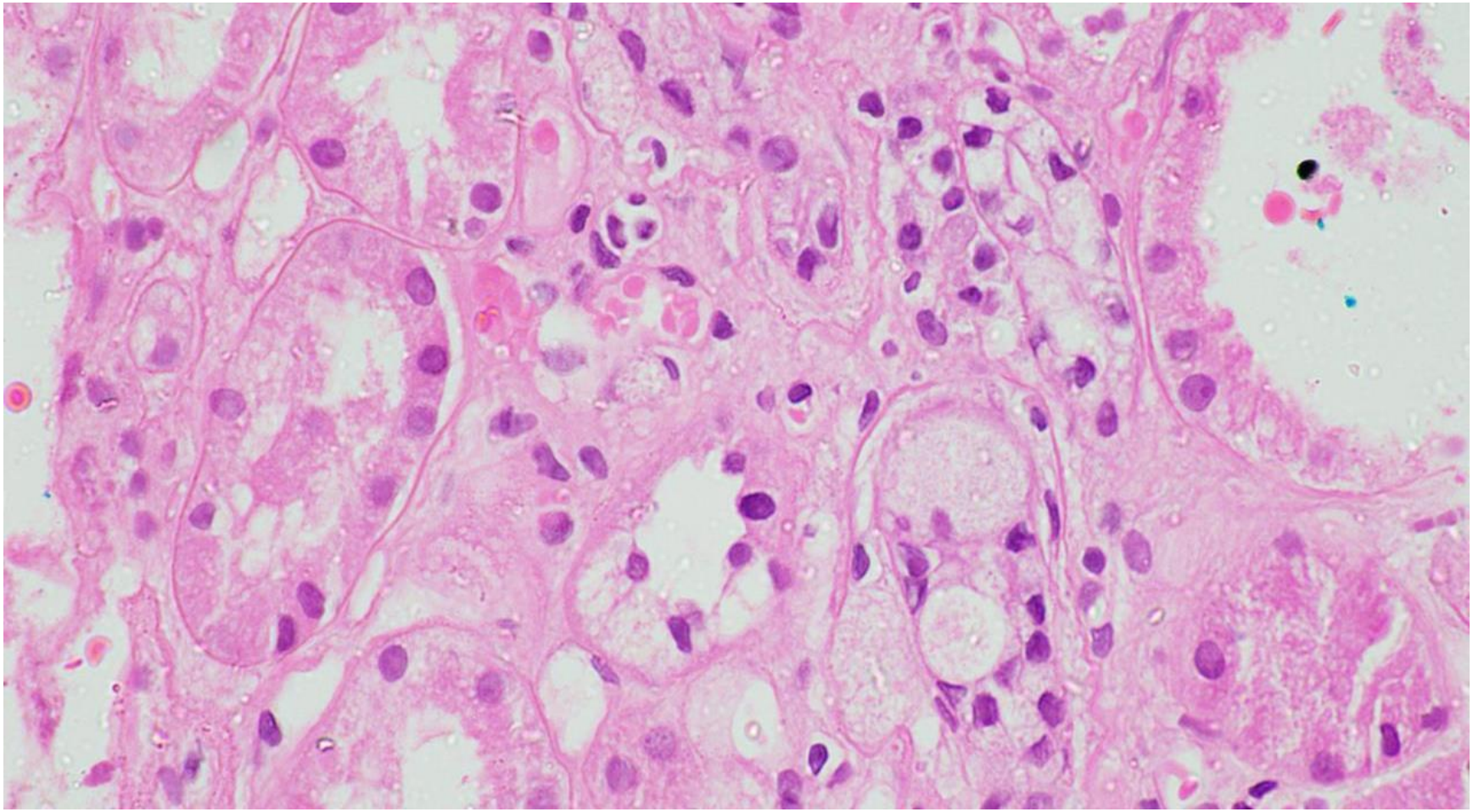

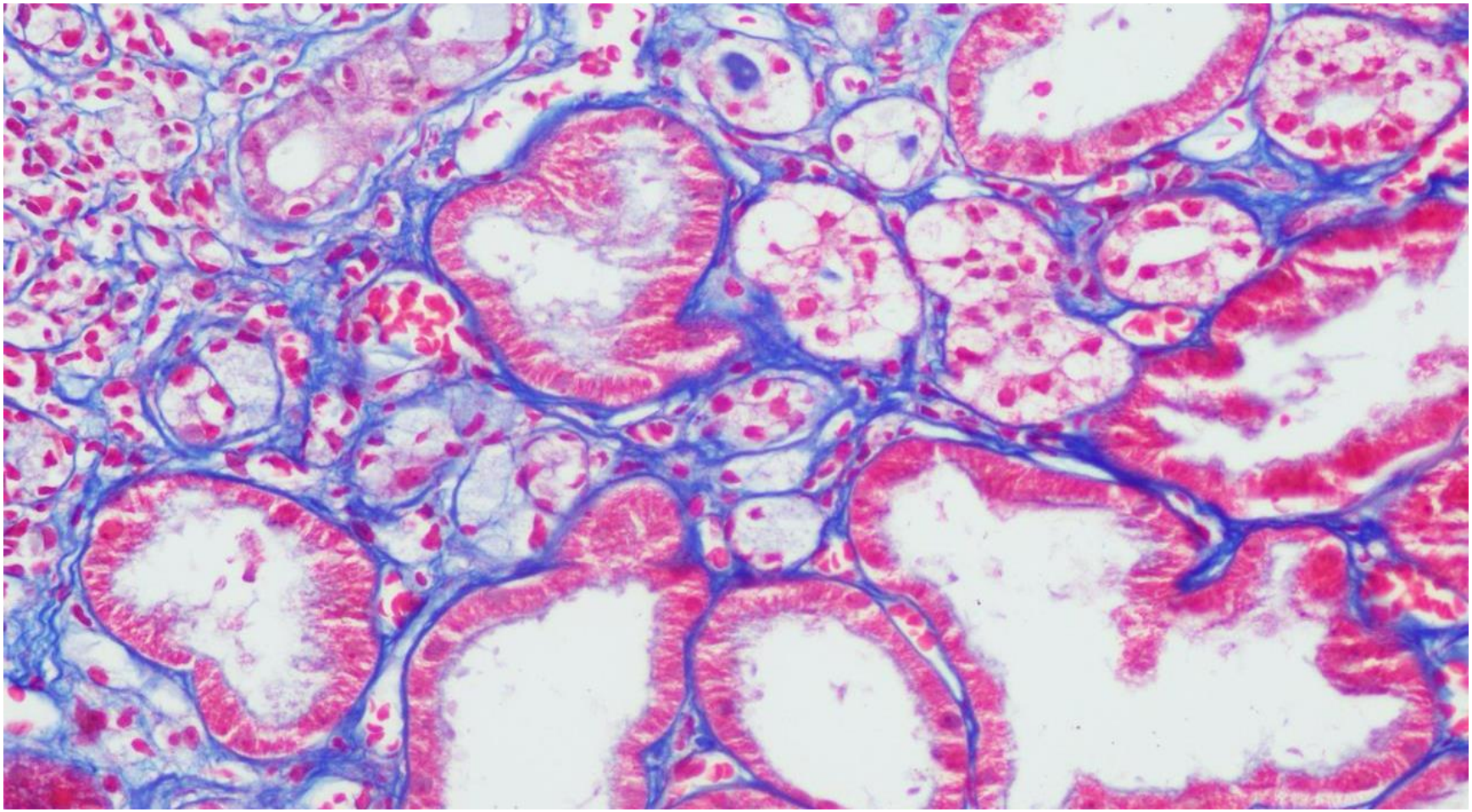

Kidney biopsy

IF Microscopy : 3 glomeruli

- Direct IF microscopy showed granular mesangial deposition of IgM (trace) and it was negative for IgG, IgA, C3, C4, Kappa and Lambda

Kidney biopsy

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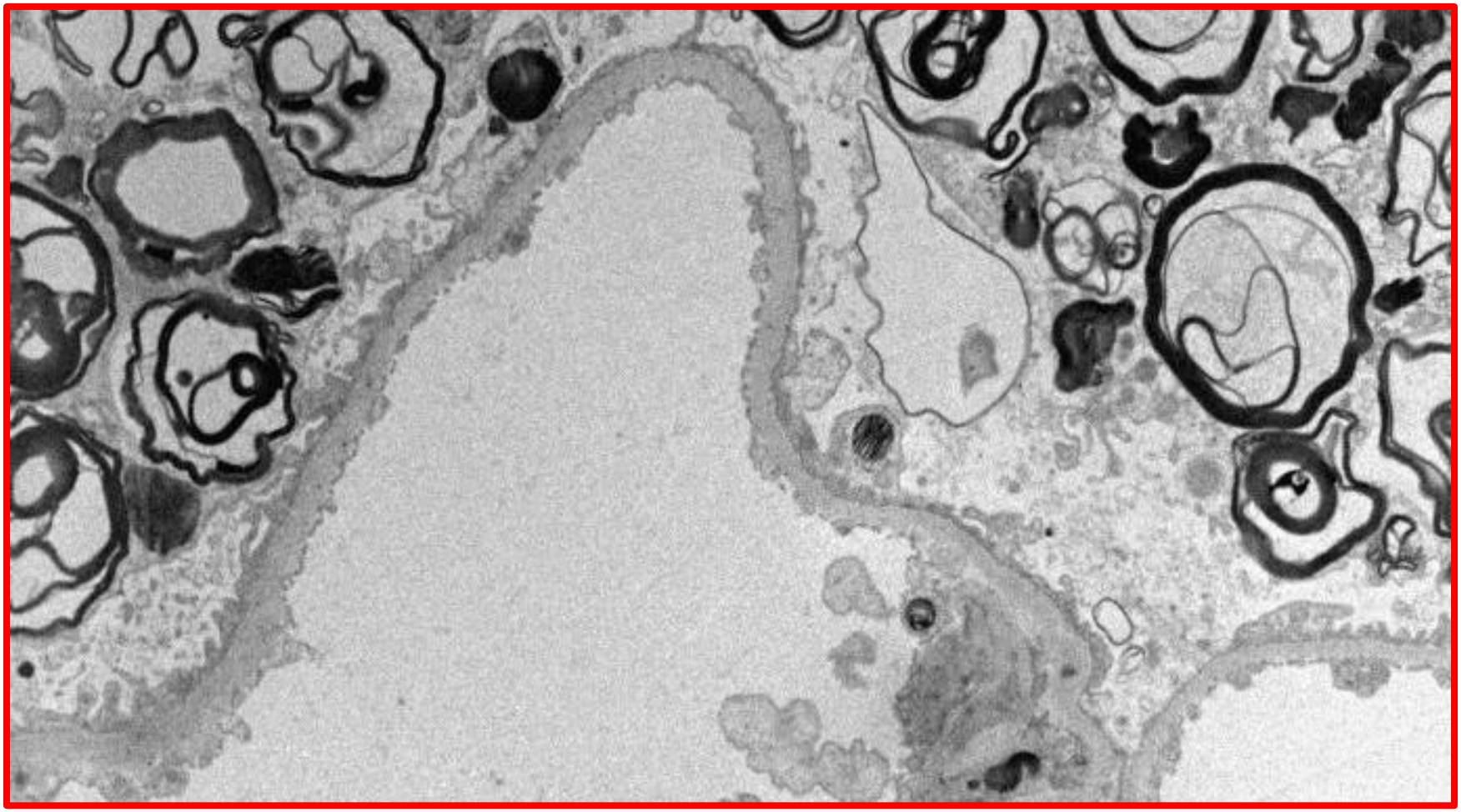
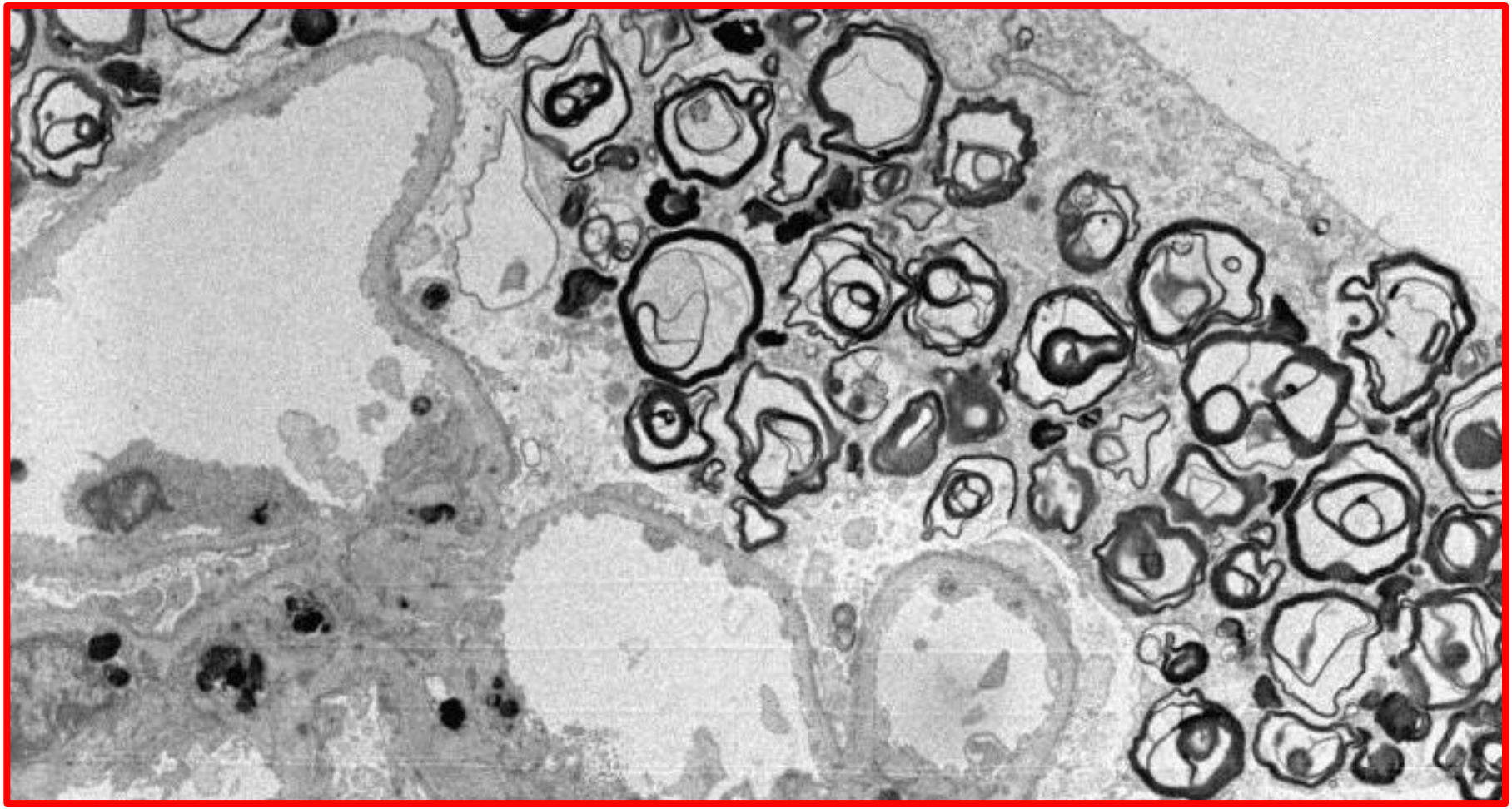
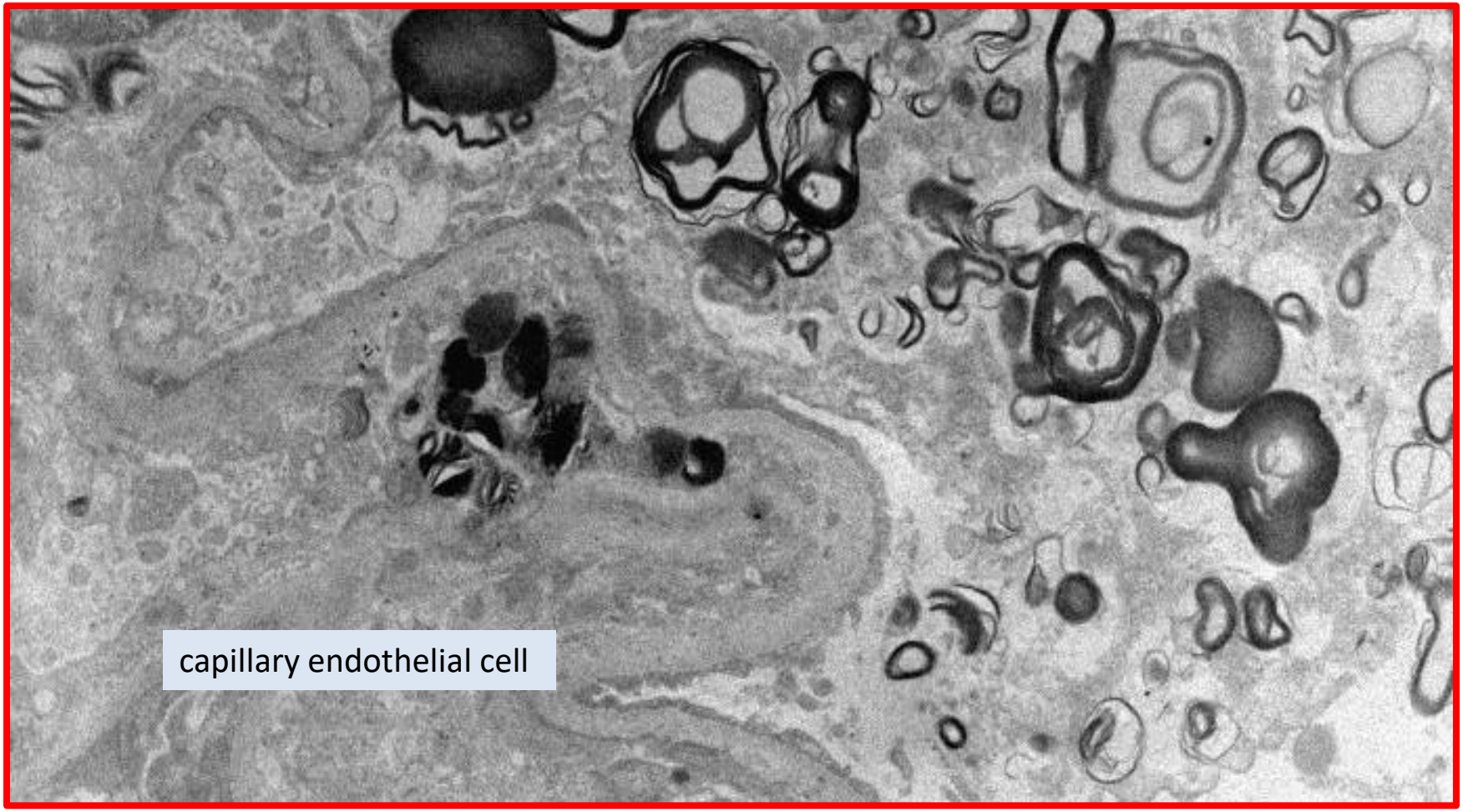
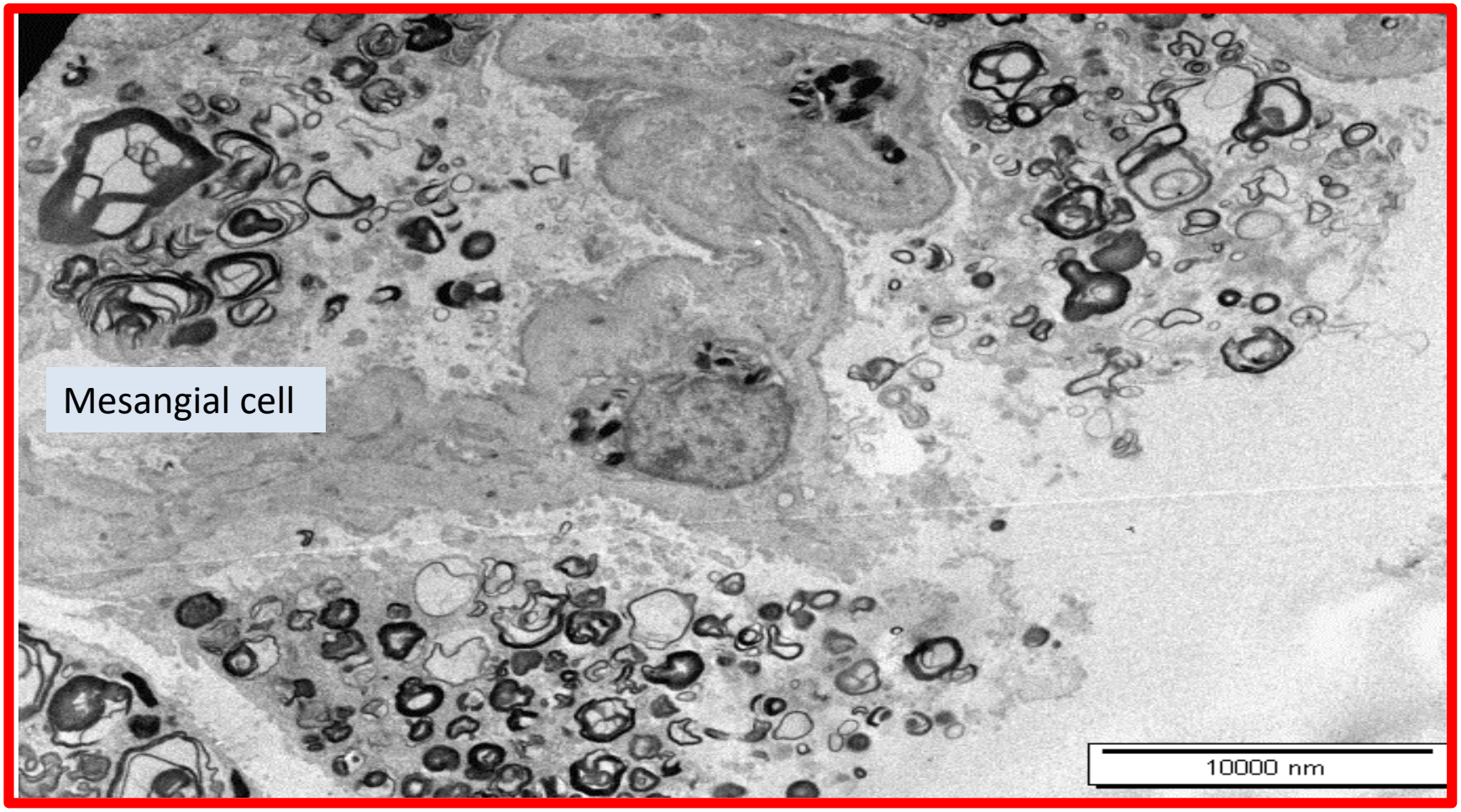
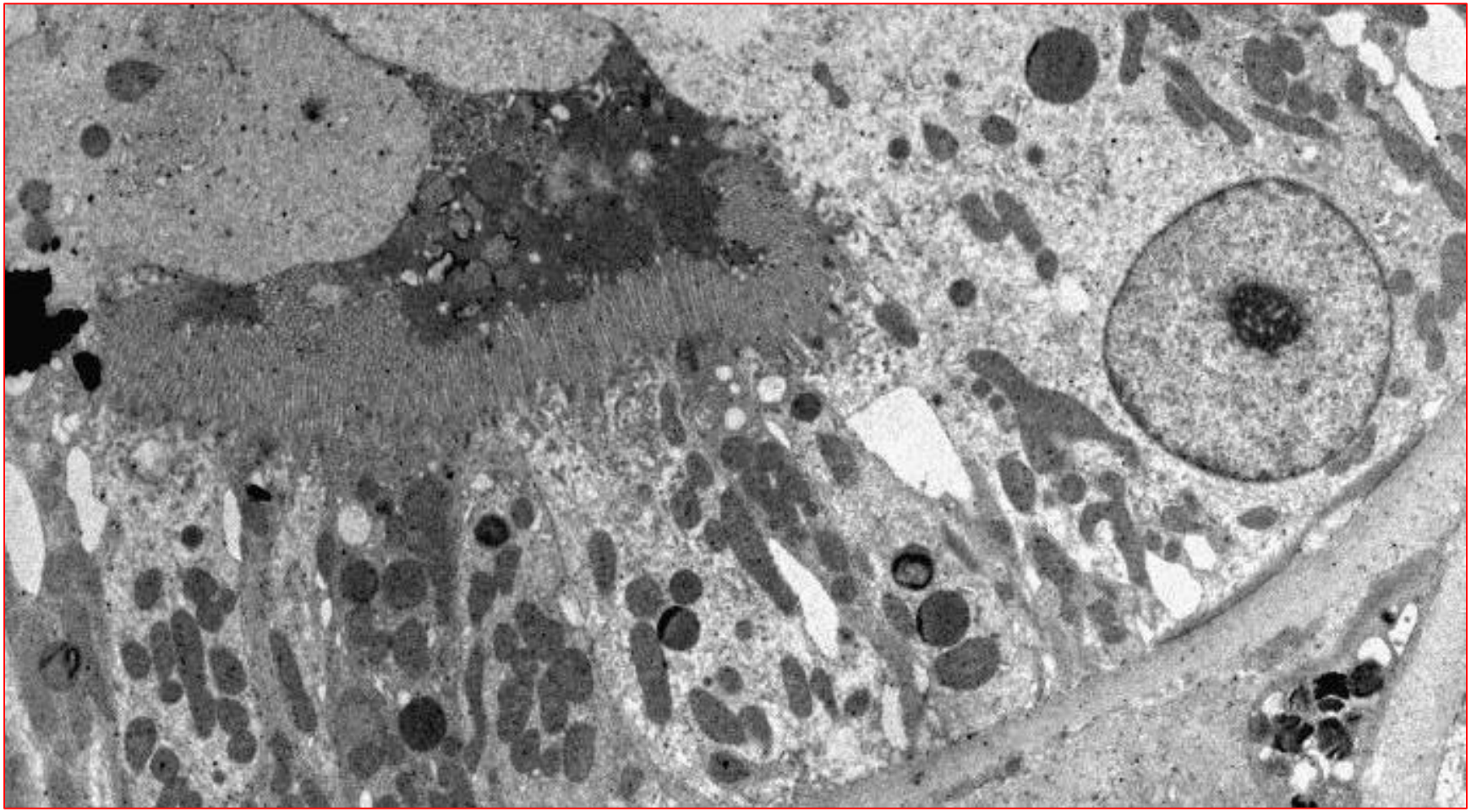
- EM : 2 Viable glomeruli ?

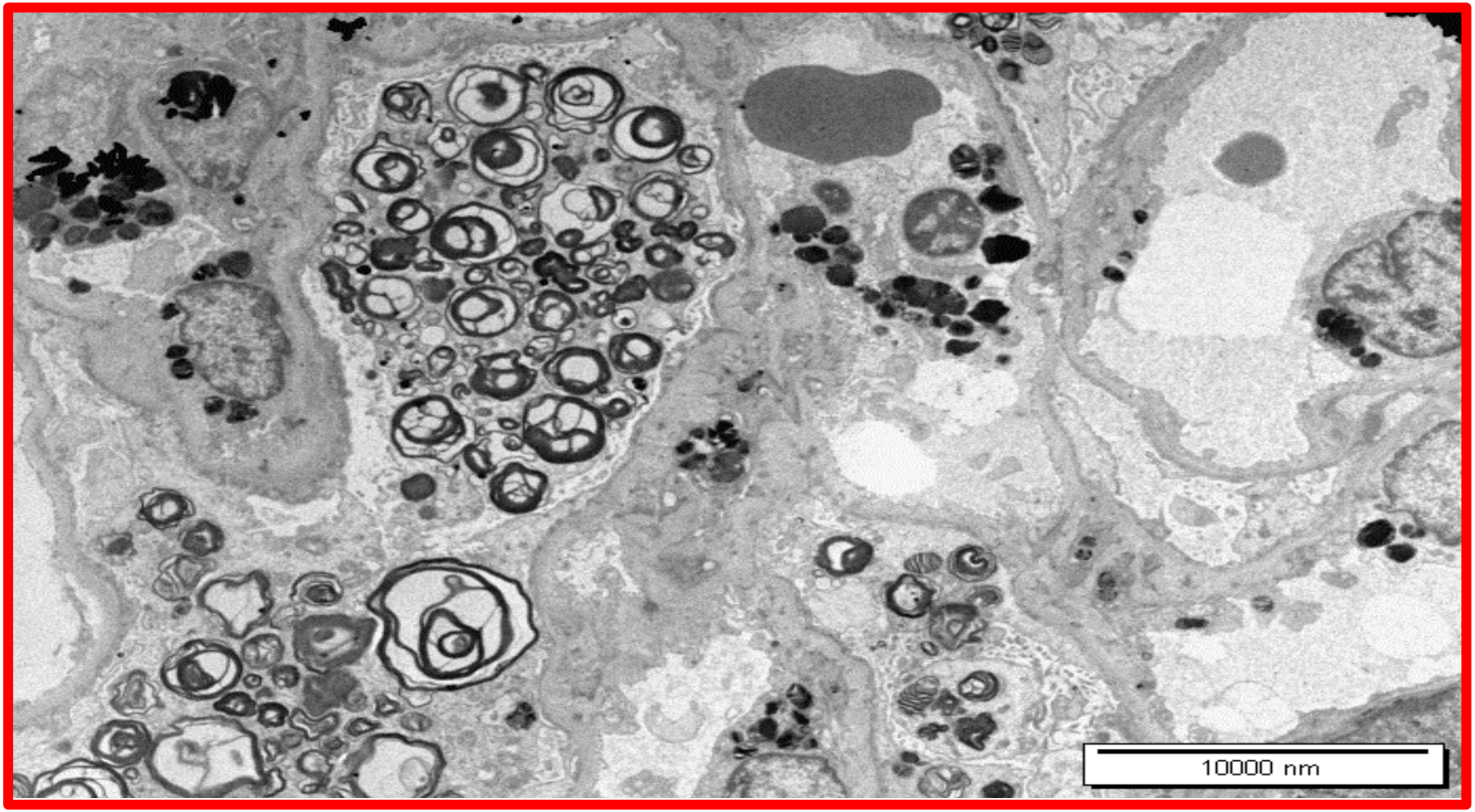





capillary endothelial cell


Mesangial cell
10000 nm




10000 nm

Kidney biopsy

EM Microscopy

These ultra structural features are CONSISTANT WITH FABRY DISEASE

Fabry Disease

- Fabry disease,(an X-linked inborn error of metabolism) also called Anderson-Fabry disease, is the second most prevalent lysosomal disease after Gaucher disease.

- The metabolic defect in Fabry disease is deficiency of the lysosomal hydrolase alpha-galactosidase A (alpha-Gal A), which primarily catalyzes the hydrolytic cleavage of the terminal galactose from alpha D-galactosyl moieties of glycolipids such as globotriaosylceramide (Gb3) and glycoproteins.

Fabry Disease

- The accumulation of glycosphingolipids, especially (Gb3) in a wide variety of cells, thereby leading to the protean manifestations of the disease

- The threshold level of alpha-Gal A activity below which clinically significant Fabry disease occurs is thought to be 30 - 35 % of the mean normal control

- In this patient the serum Alpha - Galactosidase activity was < than 10 %.

Clinical Manifestations

Clinical manifestations begin in childhood or adolescence and include:

- Severe neuropathic or limb pain (acroparesthesias) ~~ 75% of patients
- Telangiectasias and angiokeratomas > 70% of patients
- Gastrointestinal symptom between 20-70%
- Corneal opacities (cornea verticillata)
- Cardiac disease,
- Kidney manifestations.

Fabry disease: Kidney manifestations

- Proteinuria
  - Proteinuria, one of the initial kidney findings, occurs in approximately 50 % of untreated males with classic Fabry disease by the age of 35 years
  - The prevalence of proteinuria in males increases with age, reaching approximately 90% by the age of 50 years.
- Isosthenuria and Fanconi syndrome
- Renal sinus cysts
- Chronic kidney disease and ESRD

Recurrent disease after kidney transplantation

- Kidney transplantation can be performed in appropriately selected patients with ESKD due to Fabry disease.
- In general, Fabry kidney disease does not recur in the allograft, although some transplant recipients may manifest Gb3 deposition within vascular endothelial cells without compromise to graft function

.

- These cells are likely of recipient origin .

Treatment of Fabry Disease

There is no cure for Fabry disease

- Goals of therapy in patients with Fabry disease are:
  - To slow down or prevent progression to irreversible tissue damage,
  - To prevent organ failure,
  - To prevent premature death,
  - To Improve quality of life.

- Types of treatment:
  - Fabry-specific therapy.
  - Non-Fabry-specific therapies.

Treatment of Fabry Disease

Fabry-specific Treatment

- **Enzyme replacement therapy (ERT)**
  - Recombinant alpha-galactosidase A (alpha-Gal A), the enzyme that is deficient in patients with Fabry disease:
    - agalsidase alfa (Replagal)
    - agalsidase beta (Fabrazyme),

      Fabry disease: IV: 1 mg/kg every 2 weeks.

      5 mg (per each): $1,341.62

      35 mg (per each): $9,392.96
- **Chaperone therapy:**
  - Migalastat hydrochloride, an oral pharmacologic chaperone that corrects folding of mutated alpha-Gal A in patients with Fabry disease and amenable alpha-Gal A mutations.

Treatment of Fabry Disease

Non-Fabry-specific therapies:

- Non-Fabry-specific therapies include adjunctive therapies for complications such as chronic kidney disease (CKD), cardiac disease, neurologic disease, gastrointestinal disease, and other clinical manifestations.

2. Case History

- RB is a 22-y-old single female patient S/P LRKT from her 50-y- old mother on September 21st,2021 at Jordan hospital.
- Her primary renal disease is Alport's Syndrome
- Initial graft function was excellent with serum creatinine of 0.6-0.75 mg/dl on discharge on day 6th, post operative day.
- BP was 120/75 mmHg ; weight 57 kg.
- **IS Medications**:
  - **No Induction therapy ; (she received 1 gram solumedrol IV intraoperative)**
  - Advagraf 7mg daily
  - MMF 1 gram BID
  - Prednisone 15 mg daily

Case History

Laboratory data upon discharge were as follows:

- **CBC:** Hemoglobin 11.3 gram; WBCs 8400; Platelets 278.000
- **Serum:**
  - **Creatinine 0.7 mg /dl**
  - **Blood sugar 95 mg/dl**
  - **Total protein 6.4gm/dl with serum Albumin of 3.8 gm/dl**
  - **Normal liver enzymes**
- **Porgraf Blood level was 8.3 mg/dl (dose; 7 mg Advagraf daily) .**
- **Urine analysis:**
  - **Few WBCs, and 30-40 RBCs / hpf (DJ still in place)**
  - **Proteinuria ~ 300 mg / day**
- **Doppler US of transplanted kidney was perfect wit RI 0.6**

Case history

- Seen regularly in the clinic and she was doing well with an average serum creatinine of 0.7-0.8 mg /dl and a prograf level ~~ 6.5-7.5 mg/dl on a dose of Advagraf 7 mg daily and Dilzem 90 mg BID.

- **Progressive raising serum creatinine over several months**.

Laboratory data: follow Up

Transplant date: September 21st,2021

	30/10/21	20/11/21	24/1/22	5/3/22	2/4/22	18/4/22
Serum Creatinine (mg/dl)	0.8	1.0	1.1	1.34	**1.56**	1.55
Prograf level (mg/dl)	6.5	10	8.7	9.4	**8.6**	10.2
Advagraf (mg/day)	7	8	8	8	**7**	7
Prednisone (Mg/day)	5	5	5	5	**5**	**5**
Cellcept	1 gm X2	0.5 gmX2	0.5 gmX2	0.5 gmX2	**0.5 gmX2**	0.5 gmX2
		US TX			**US TX**	
Urine analysis	RBCs 10-20 Proteinuria 0.3-0.4 gram			RBCs 30 Proteinuria 0.2 gram		

Case Summary

- 22- y-old female S/P LRKT from her mother on September 21th, 2021 with excellent initial graft function.
- Primary kidney disease ;Alport's syndrome
- Progressive worsening of kidney function 6 months later.
- Microscopic Hematuria and mild proteinuria
- Normal BP
- Normal US of transplanted kidney

What is your DD ??

Allograft Dysfunction during the First Year following Transplantation

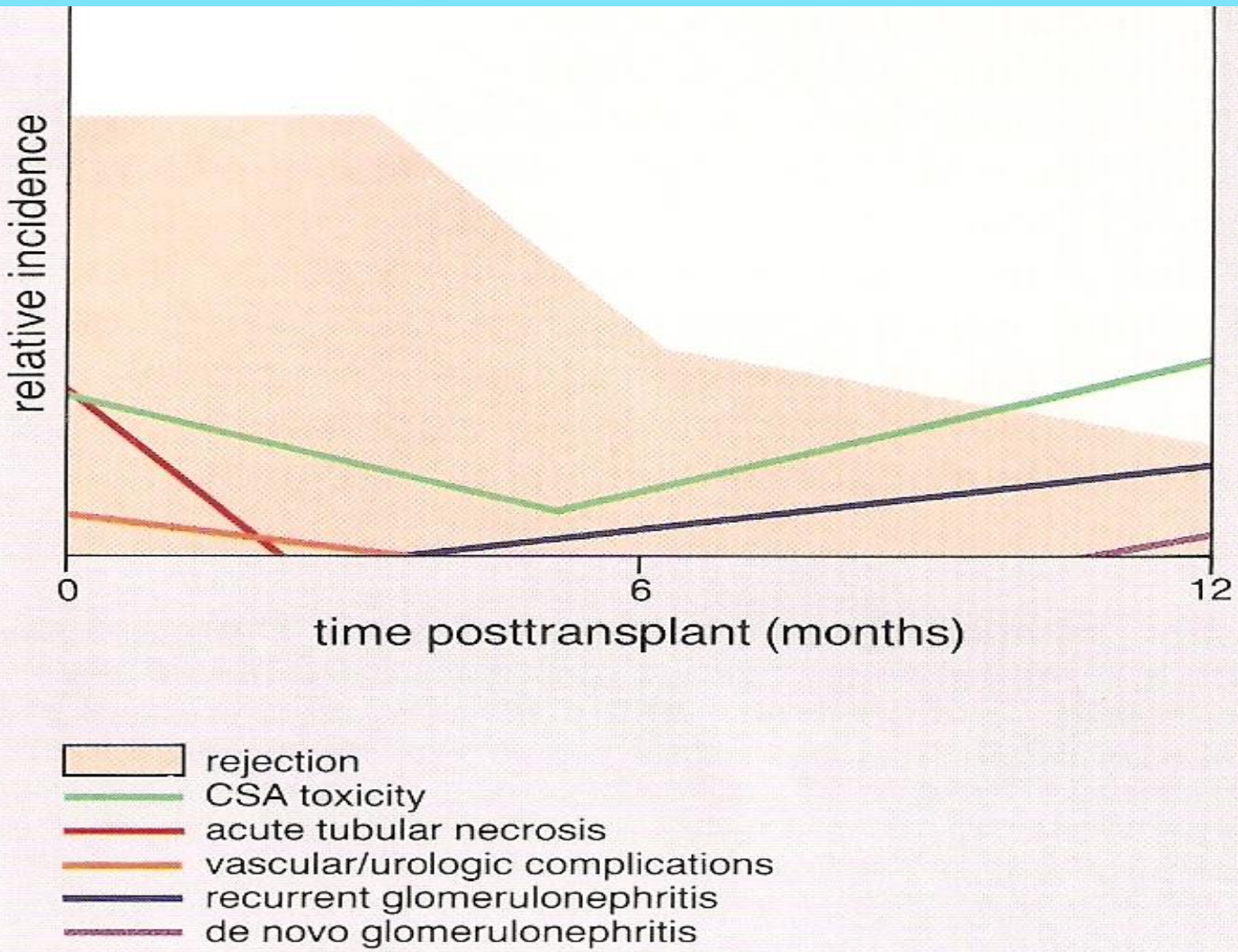


Fig. 11.39 Relative incidence of causes of allograft dysfunction during the year following transplantation.

Common transplant-specific causes of AKI

Diagnosis	Immediate 0–1 week	Early 1–12 weeks	Late >12 weeks
Pre-renal			
Volume depletion, hypotension	xx	x	x
Calcineurin inhibitor effects	xx	x	x
Renal			
Delayed graft function **(Hyperacute Rejection, Vascular catastrophy)**	xx		
Acute rejection			
Cellular	x	xx	xx
Antibody-mediated	xx	x	x
Recurrent primary kidney disease		x	xx
Infection			
Urinary tract infection	xx	xx	x
Polyoma virus (BK)		x	xx
Post-renal			
Obstruction (lymphocele, ureteral stricture, urine leak, hematoma, abscess)	xx	x	x

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The Primary kidney disease is Alport's Syndrome

What is your DD ??

Case Summary

What is your DD ??

1. **Rejection**
2. **Prograf Toxicity**
3. **Anti-GBM antibody disease**
4. **BK Nephropathy**

Case Summary

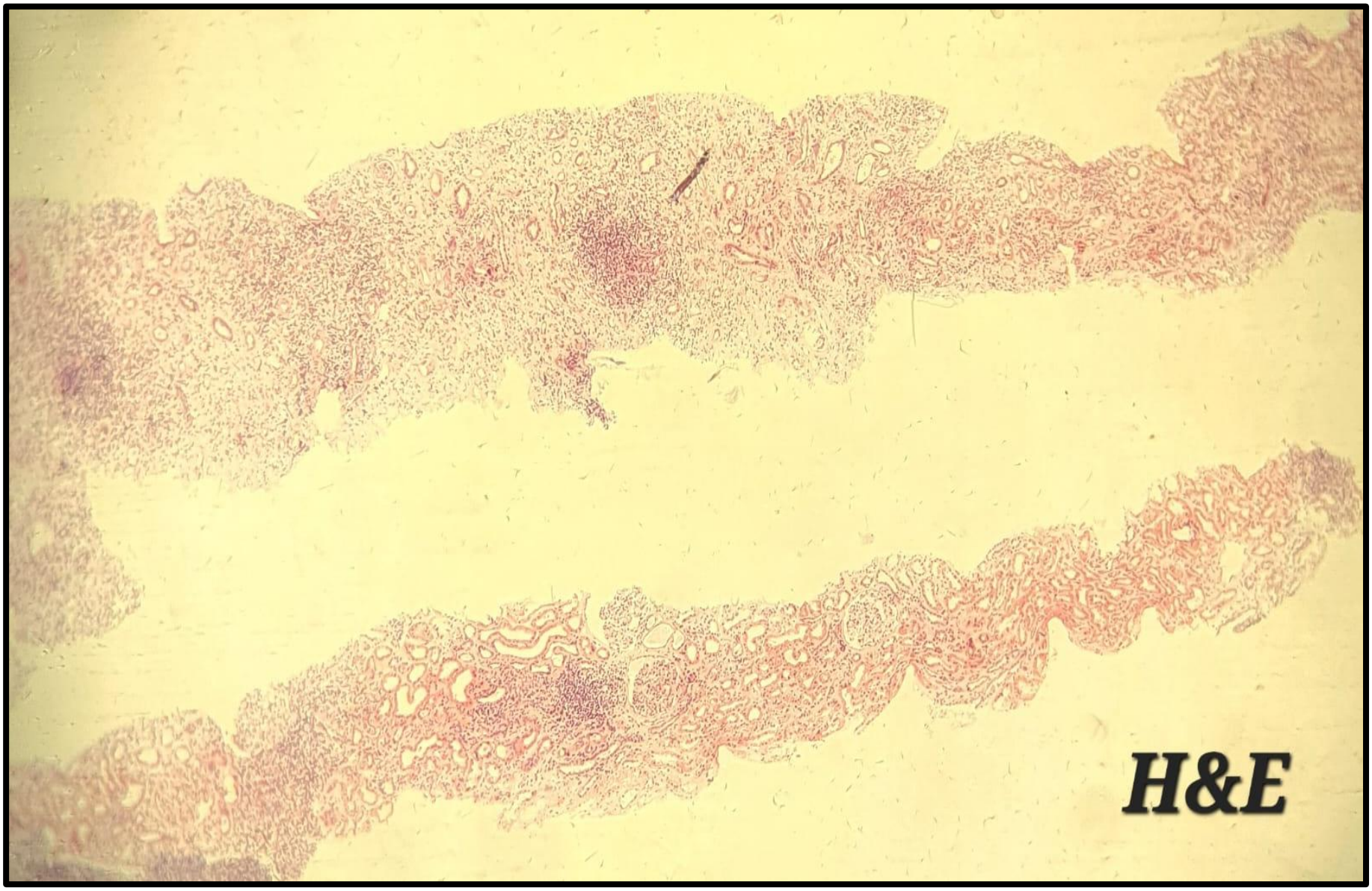
What is your Next step ??

Kidney Biopsy

Kidney Biopsy

Light Microscopy: 9 glomeruli

Immunoflourescence: 2 glomeruli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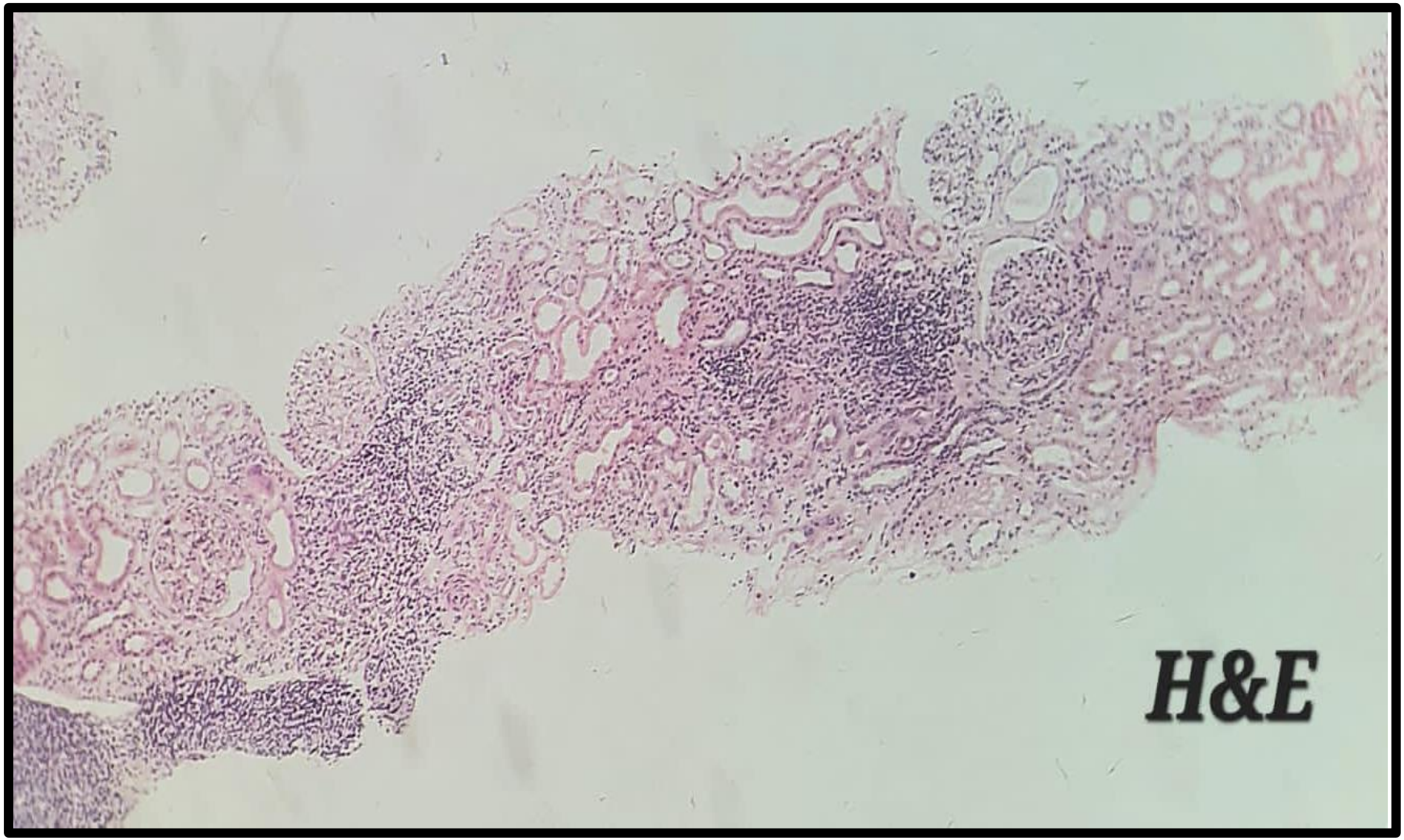
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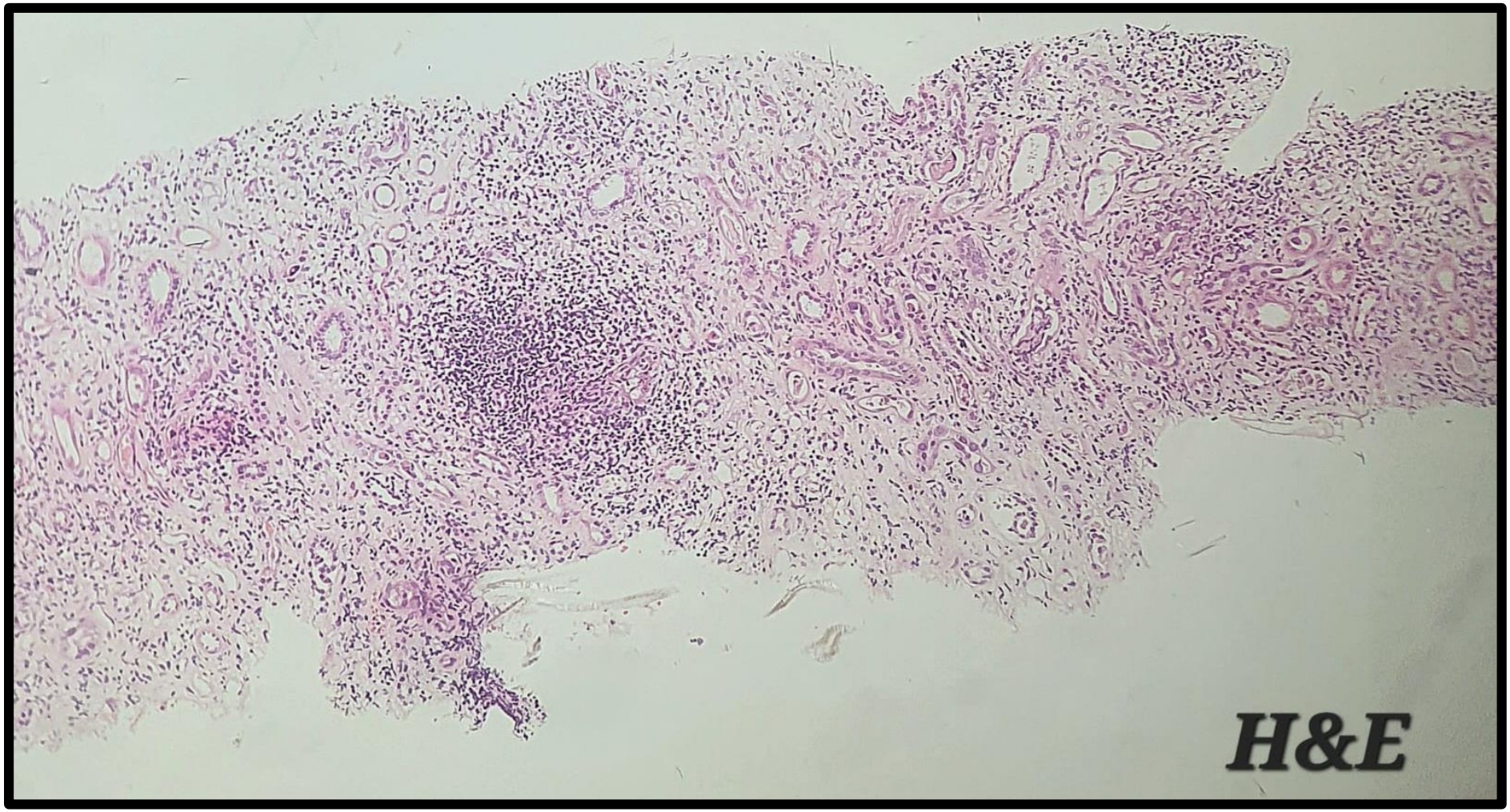
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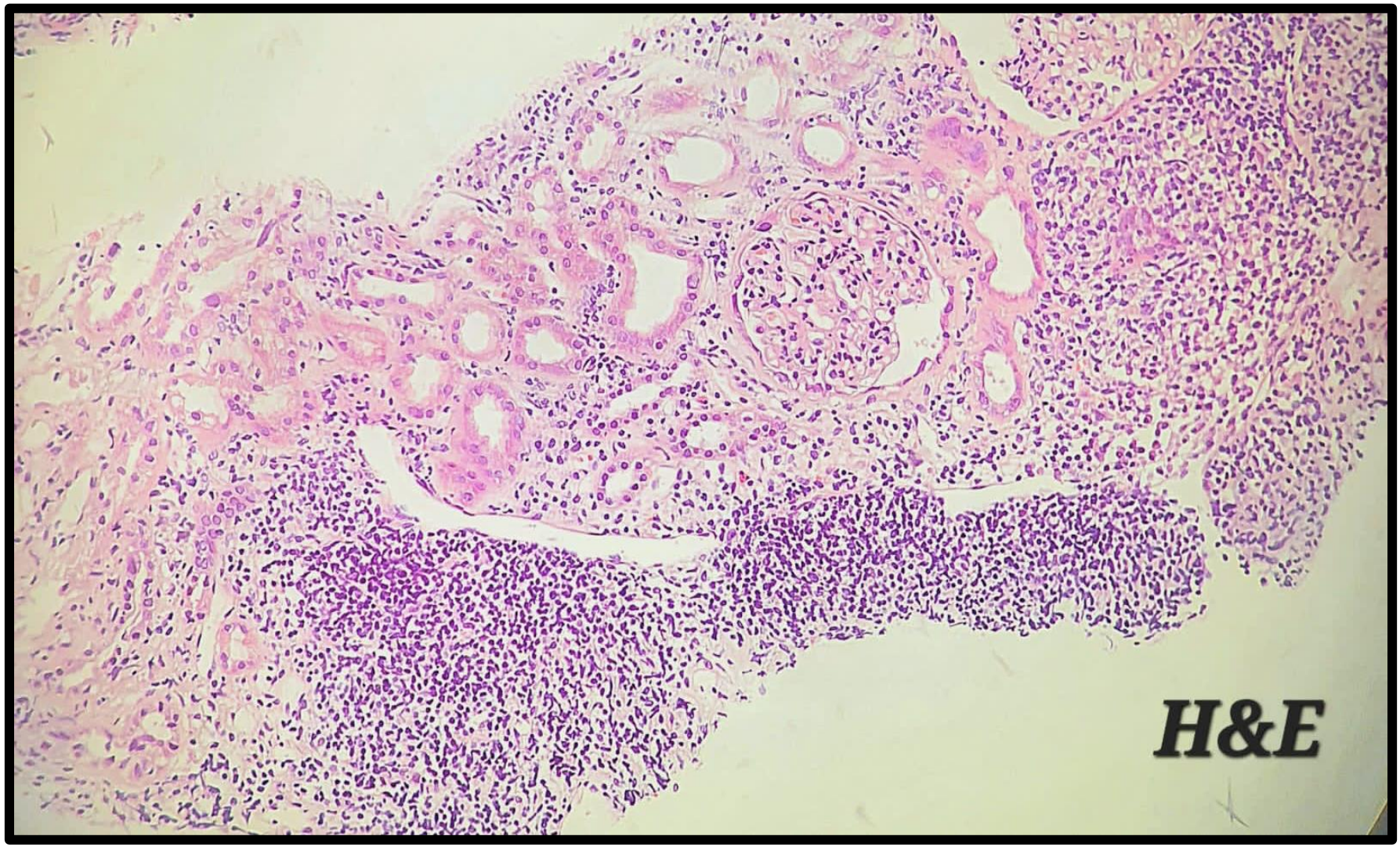
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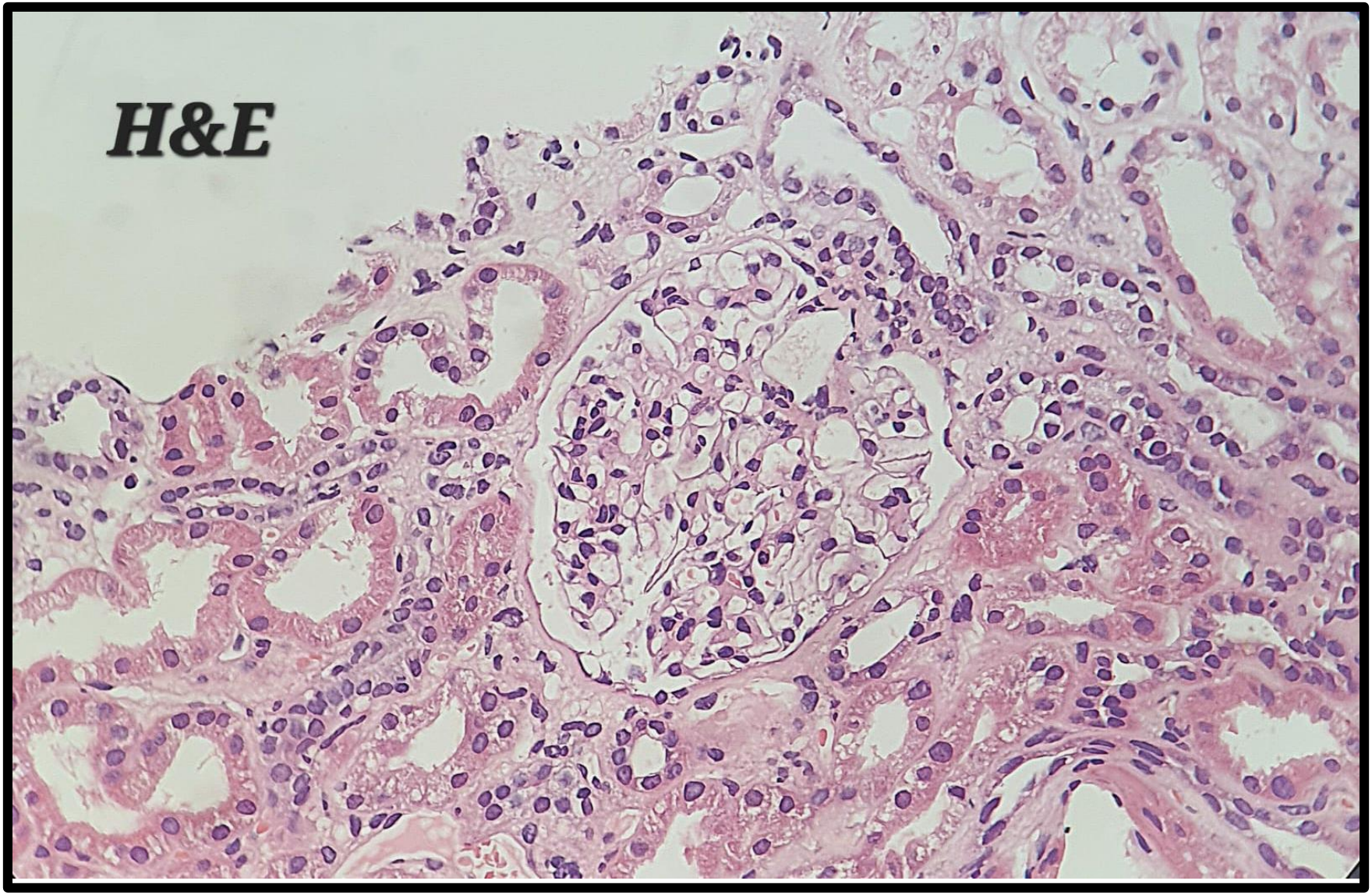
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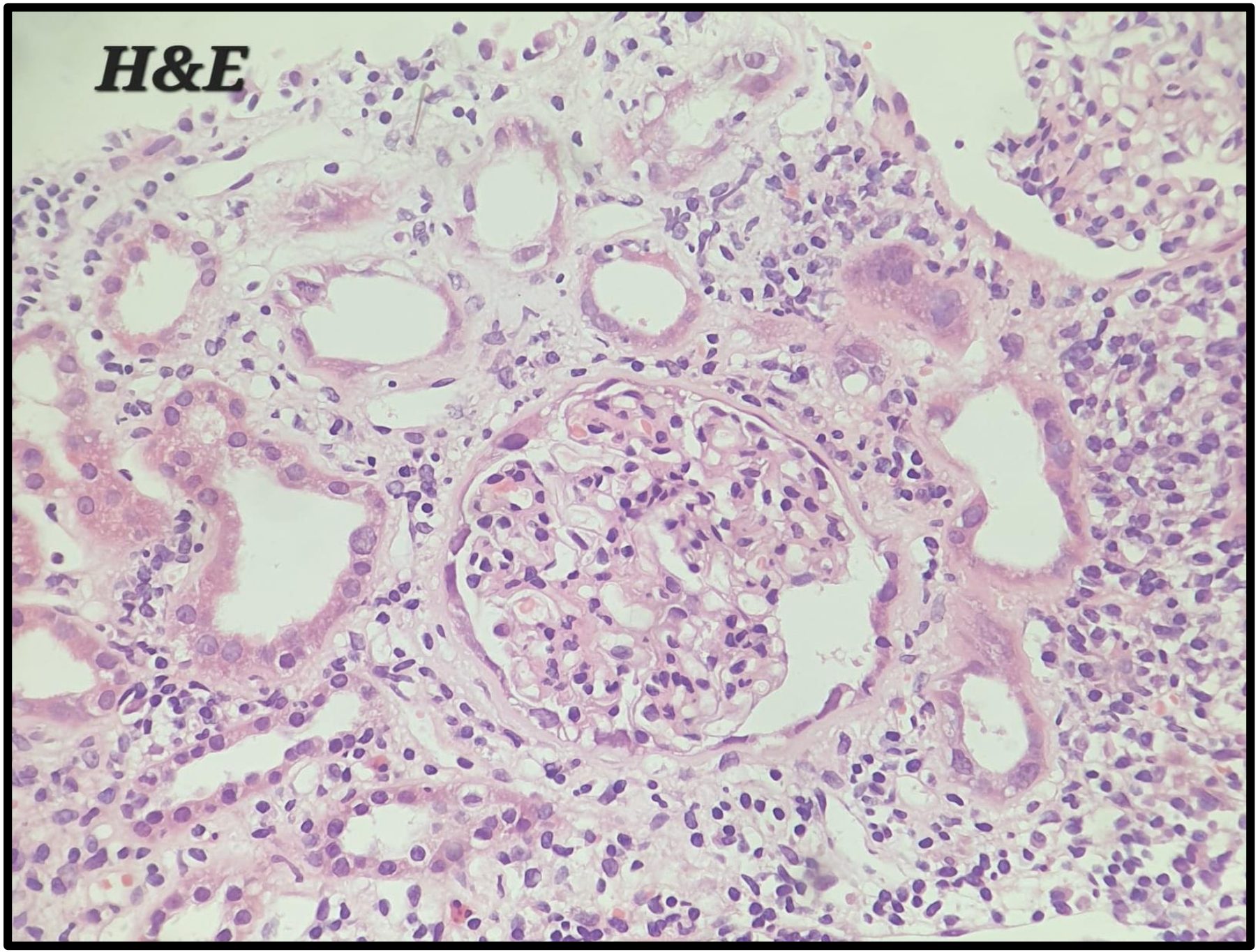
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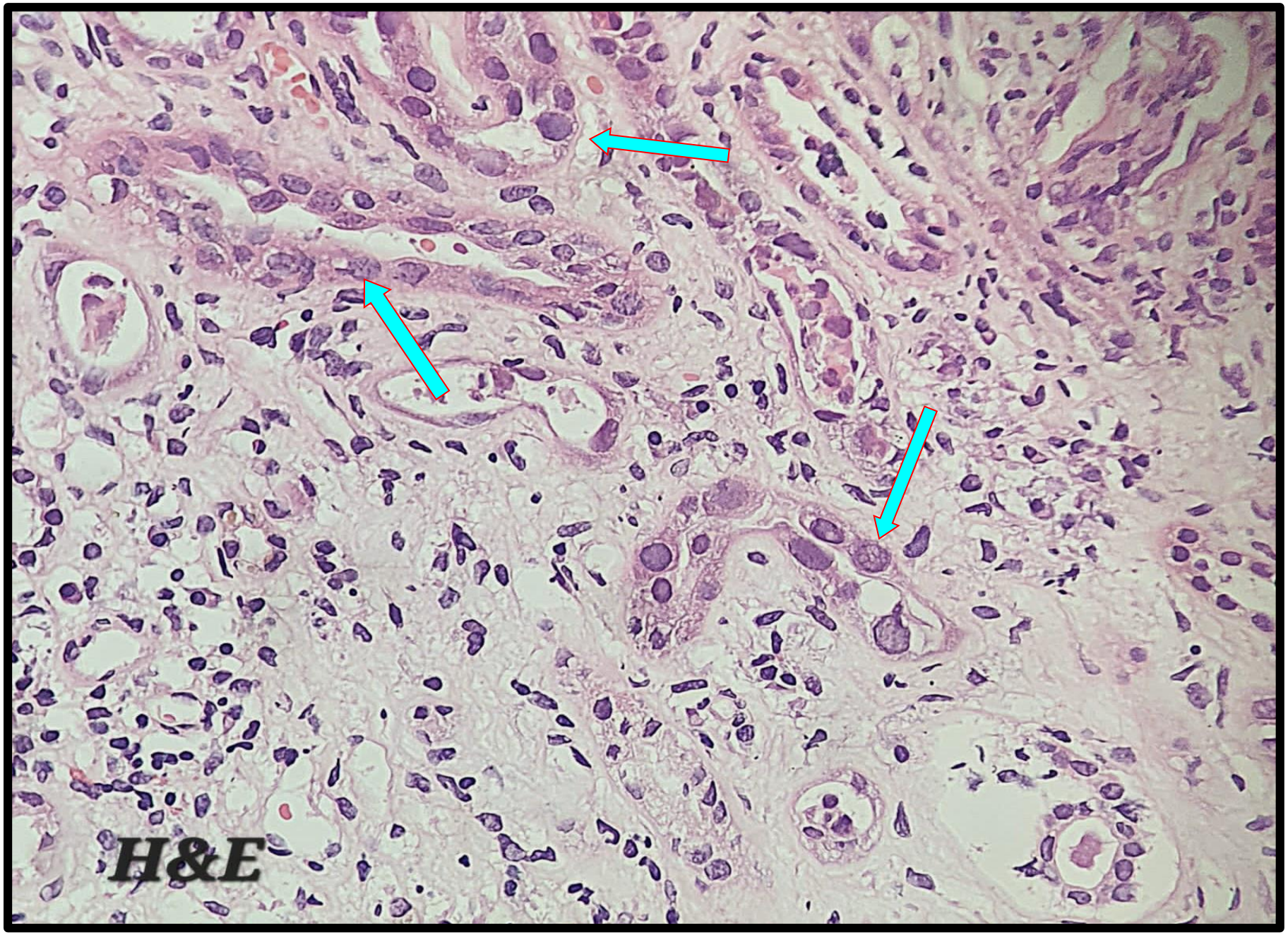
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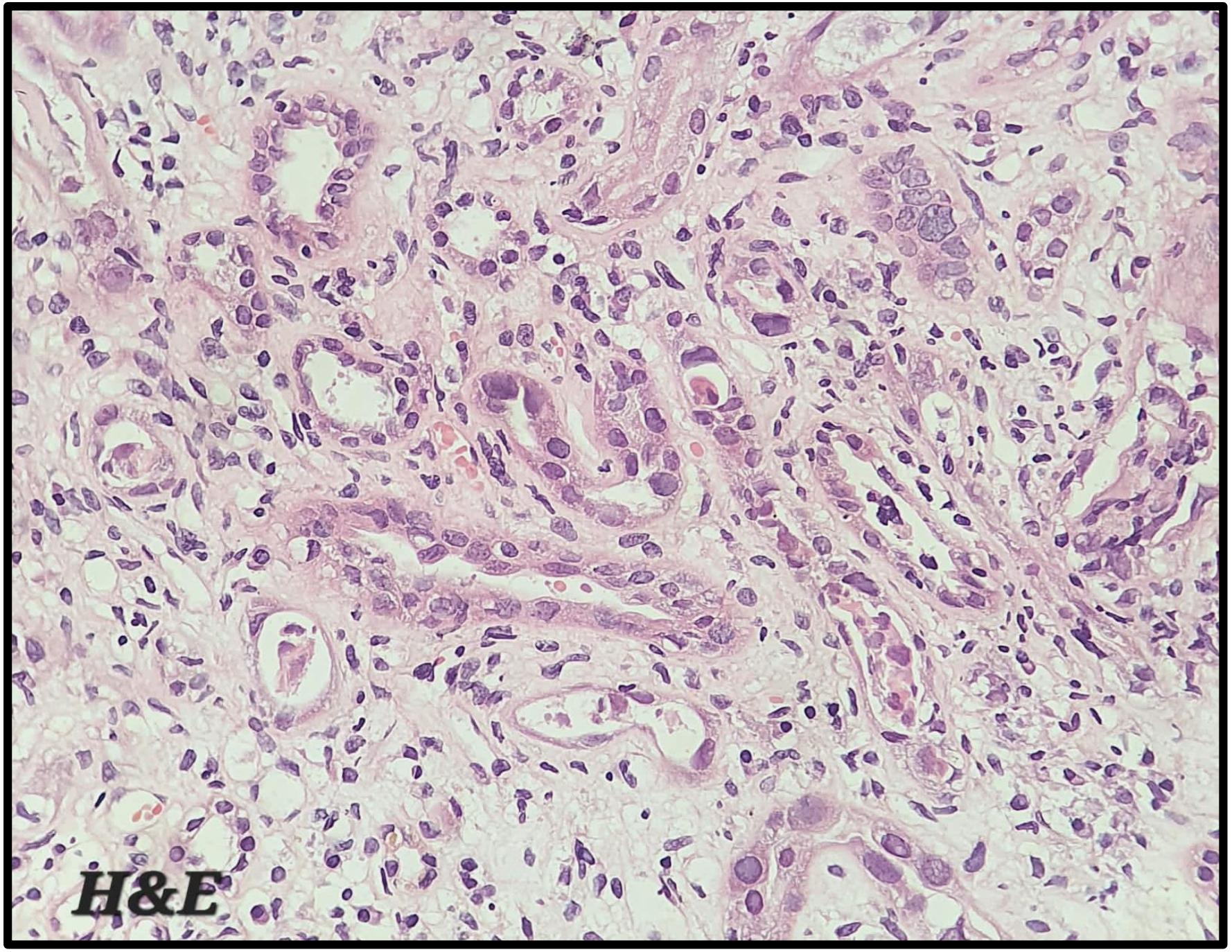
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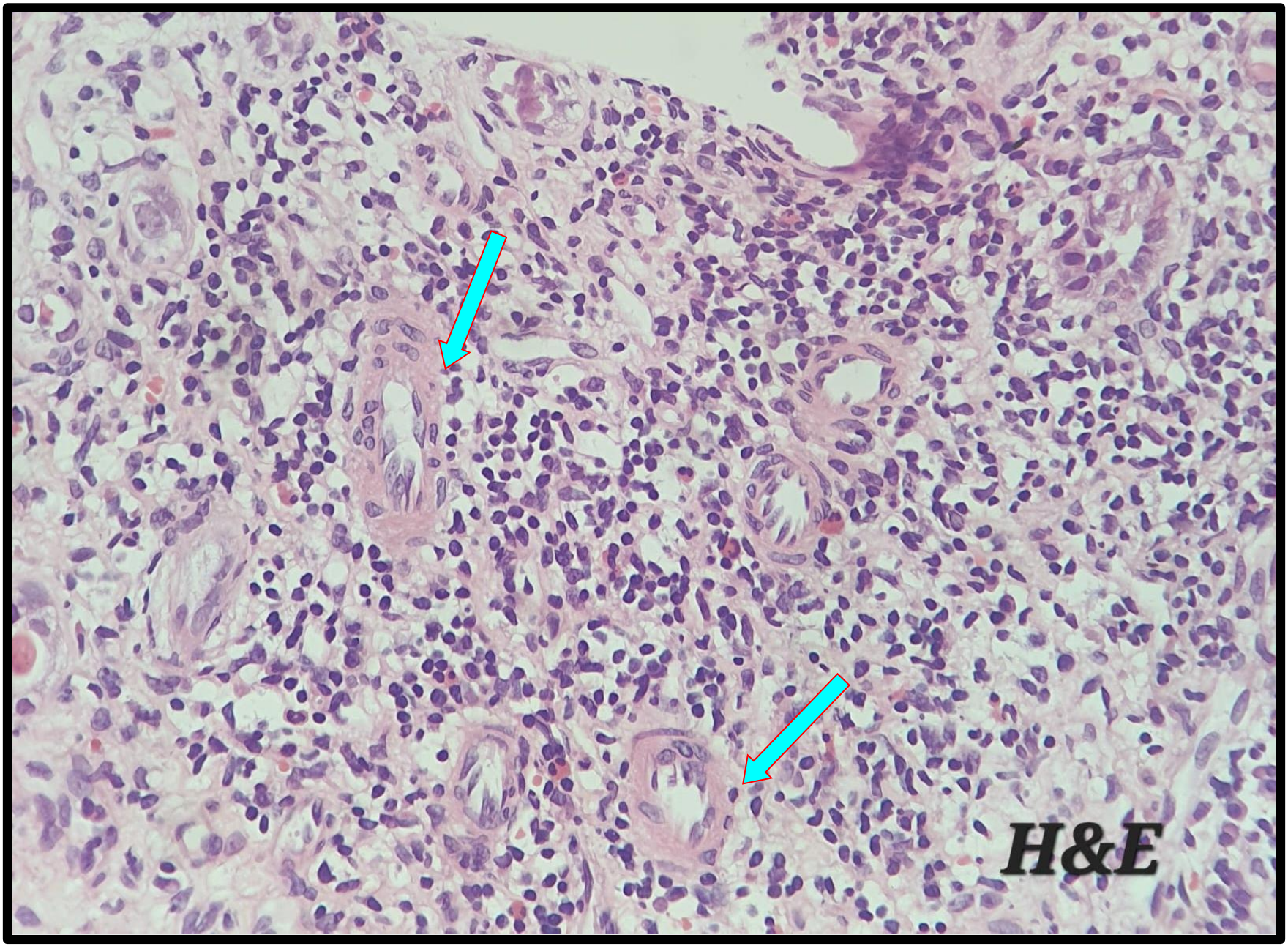
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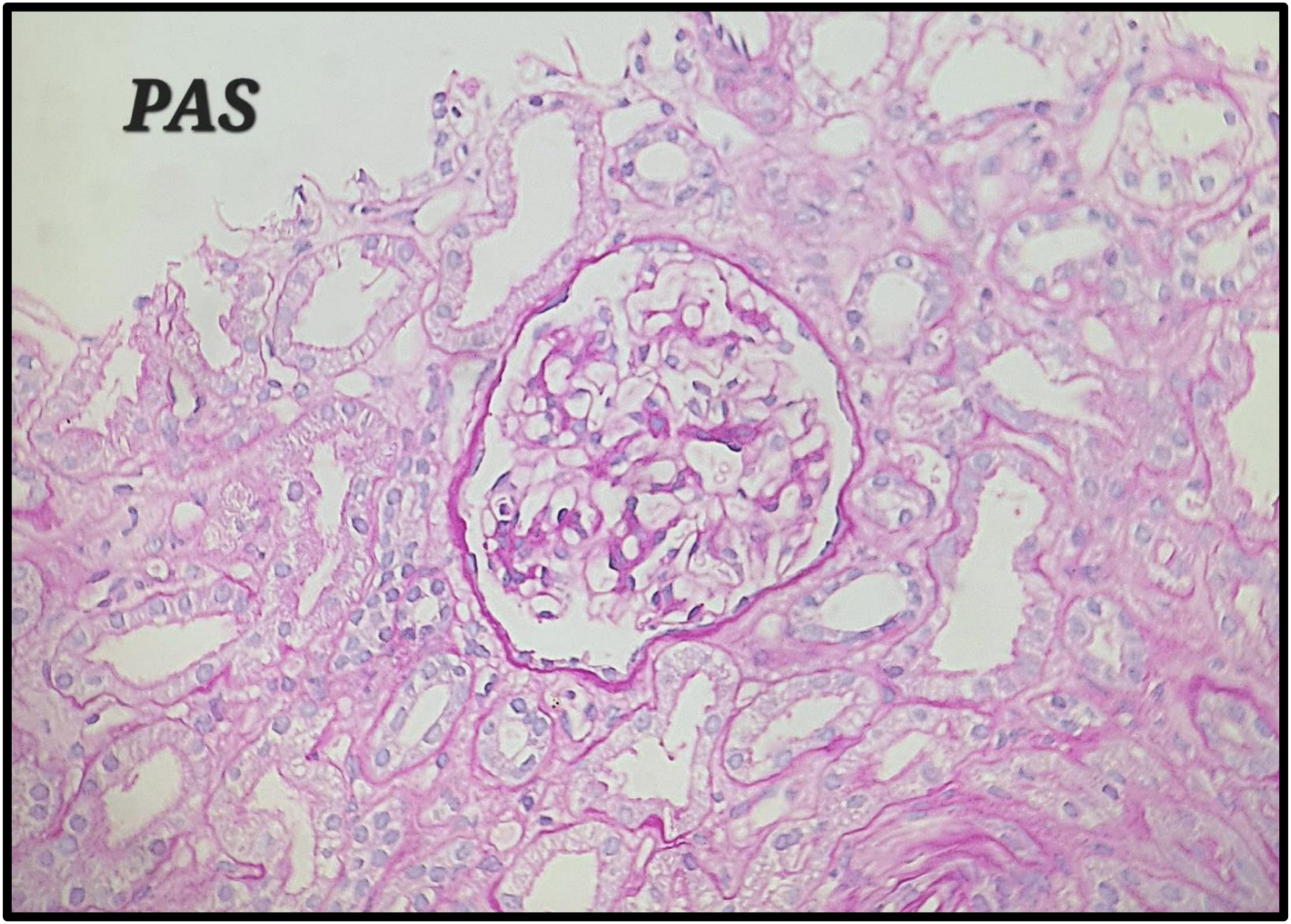
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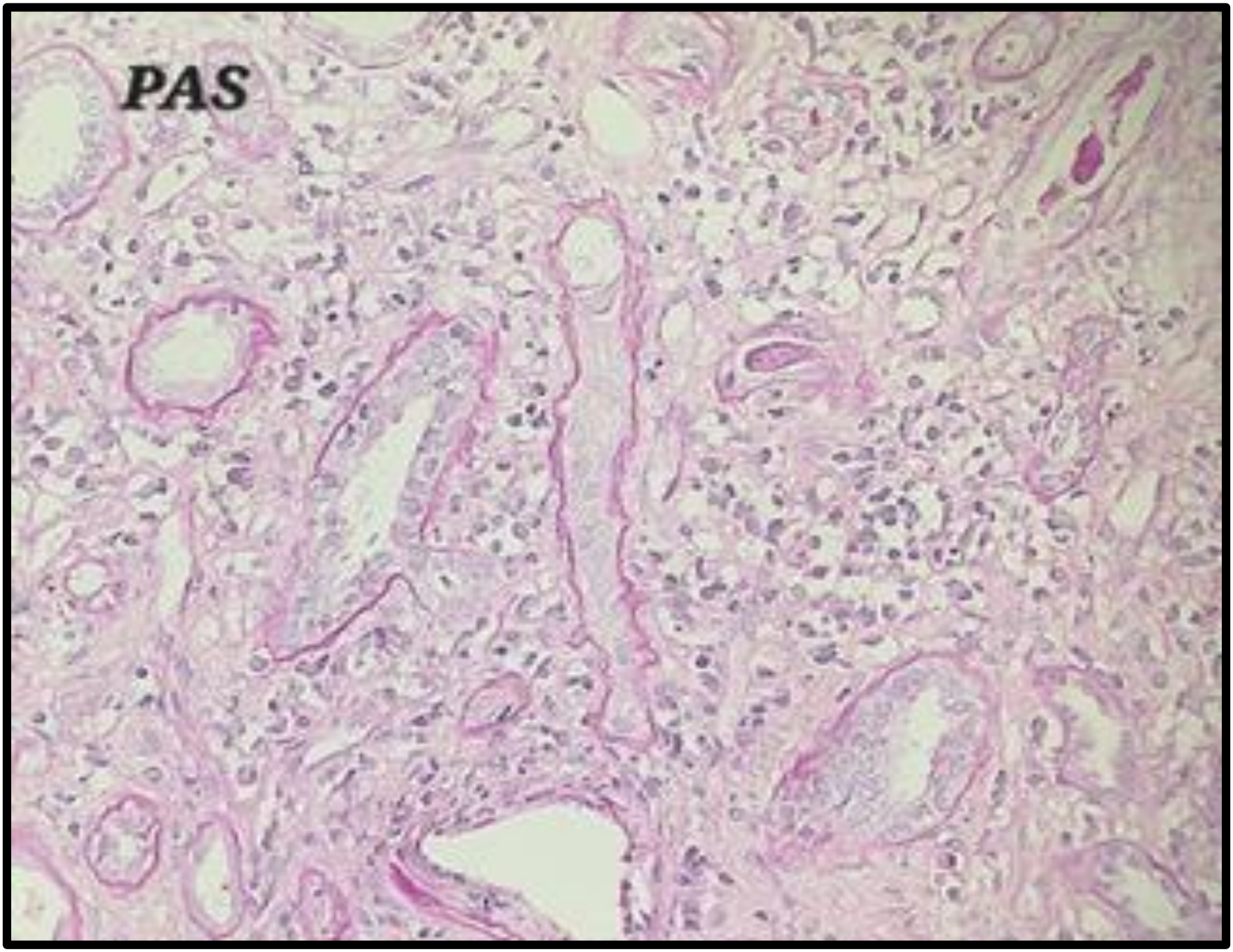
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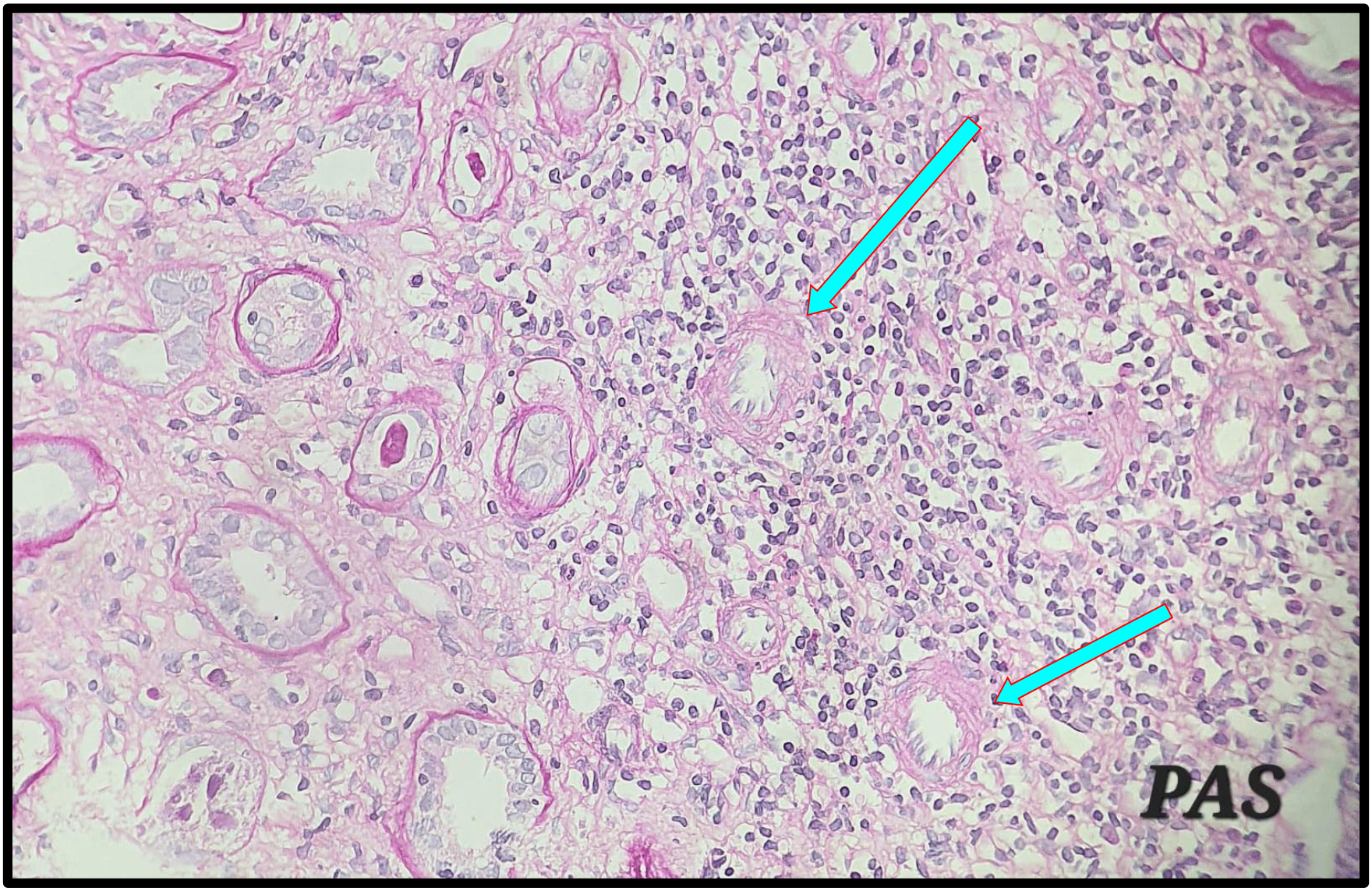
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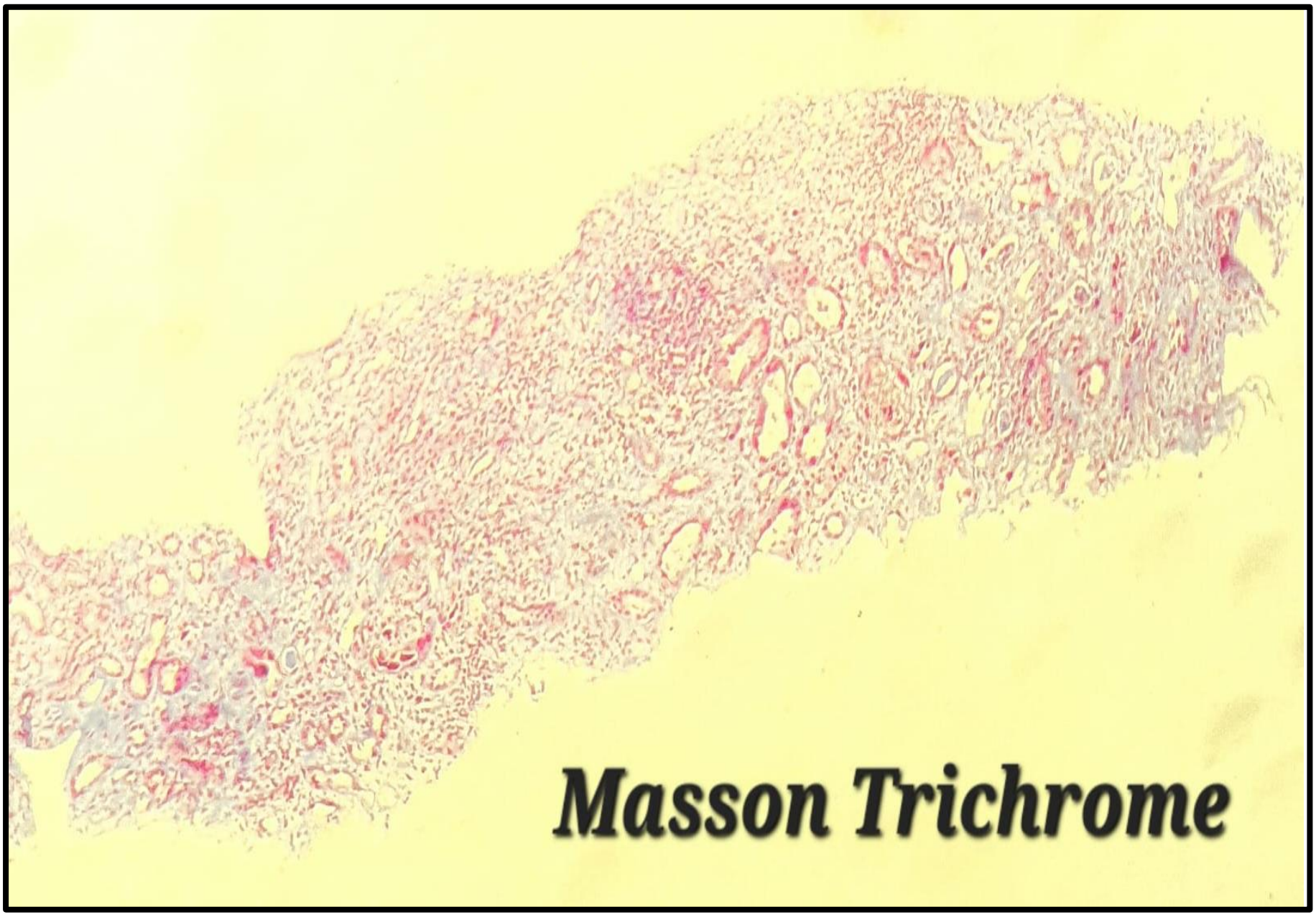
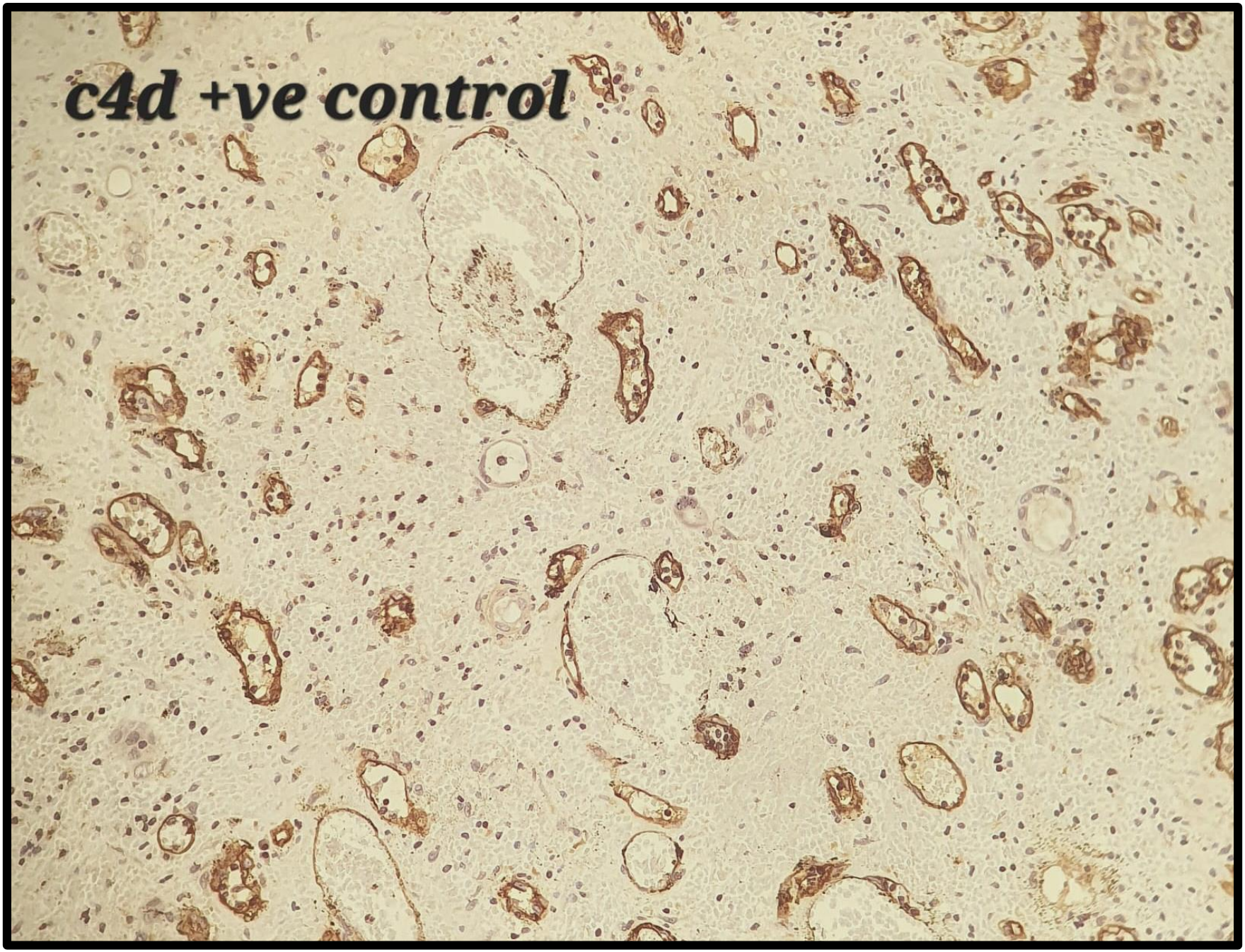
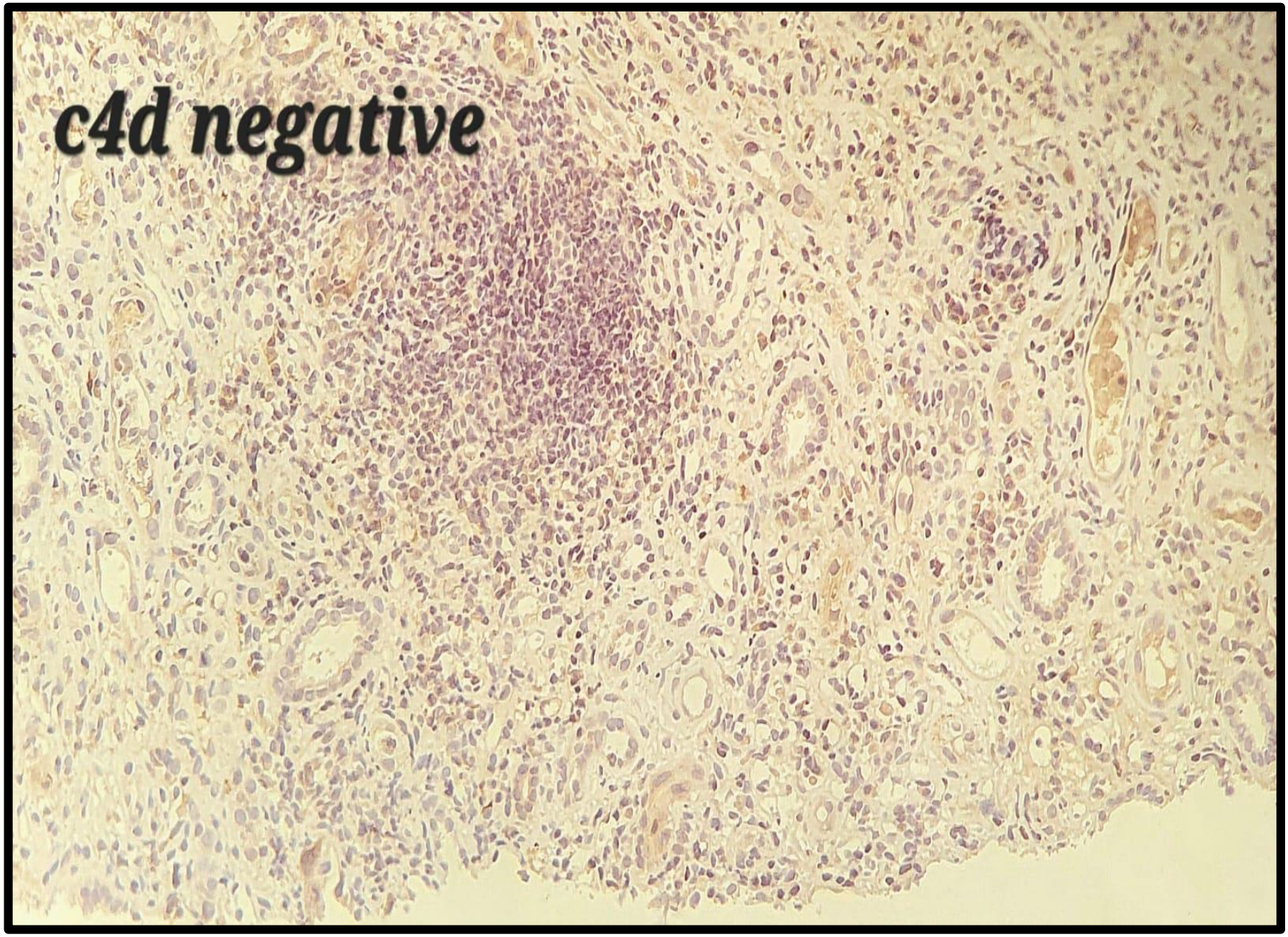
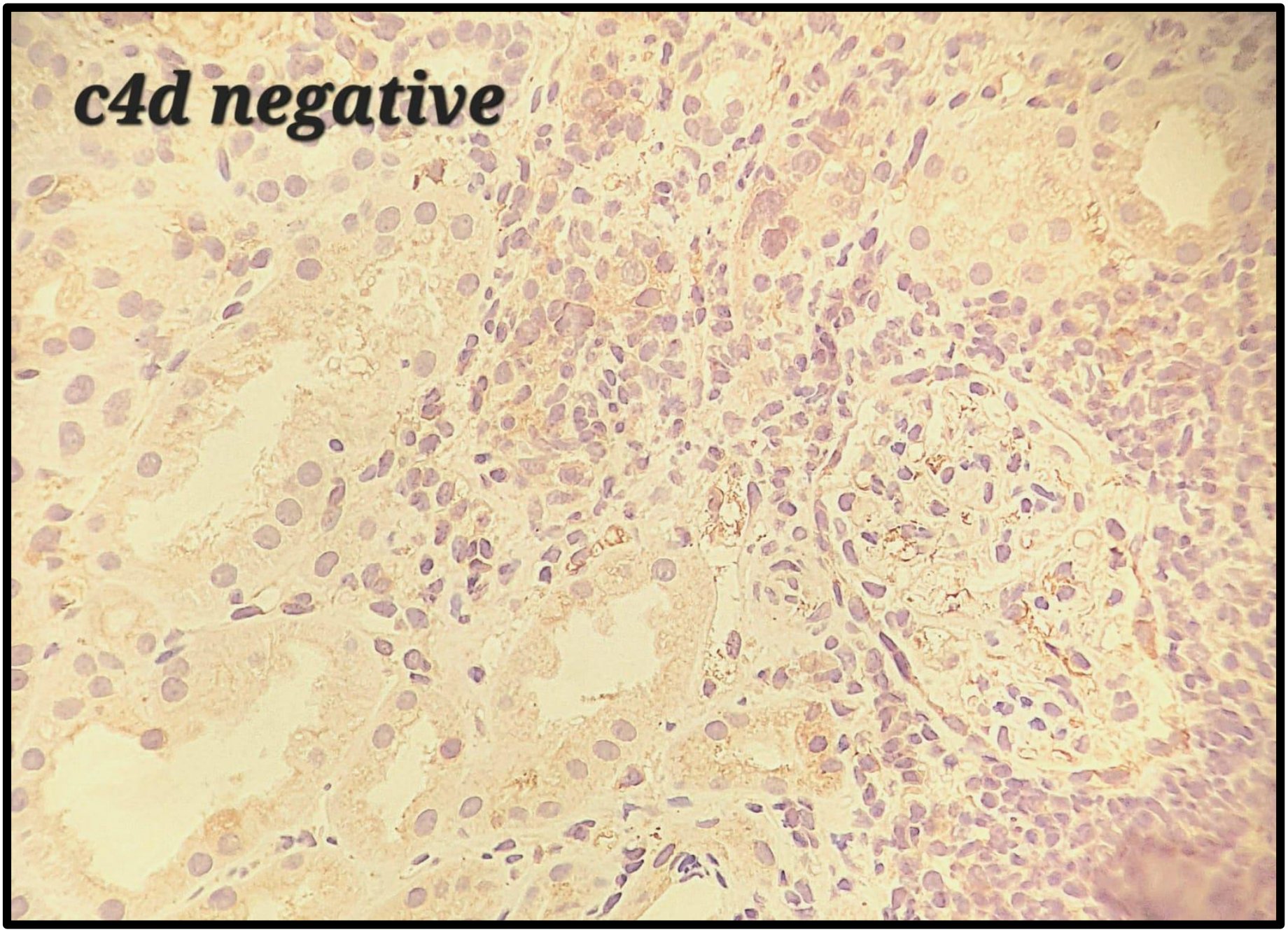
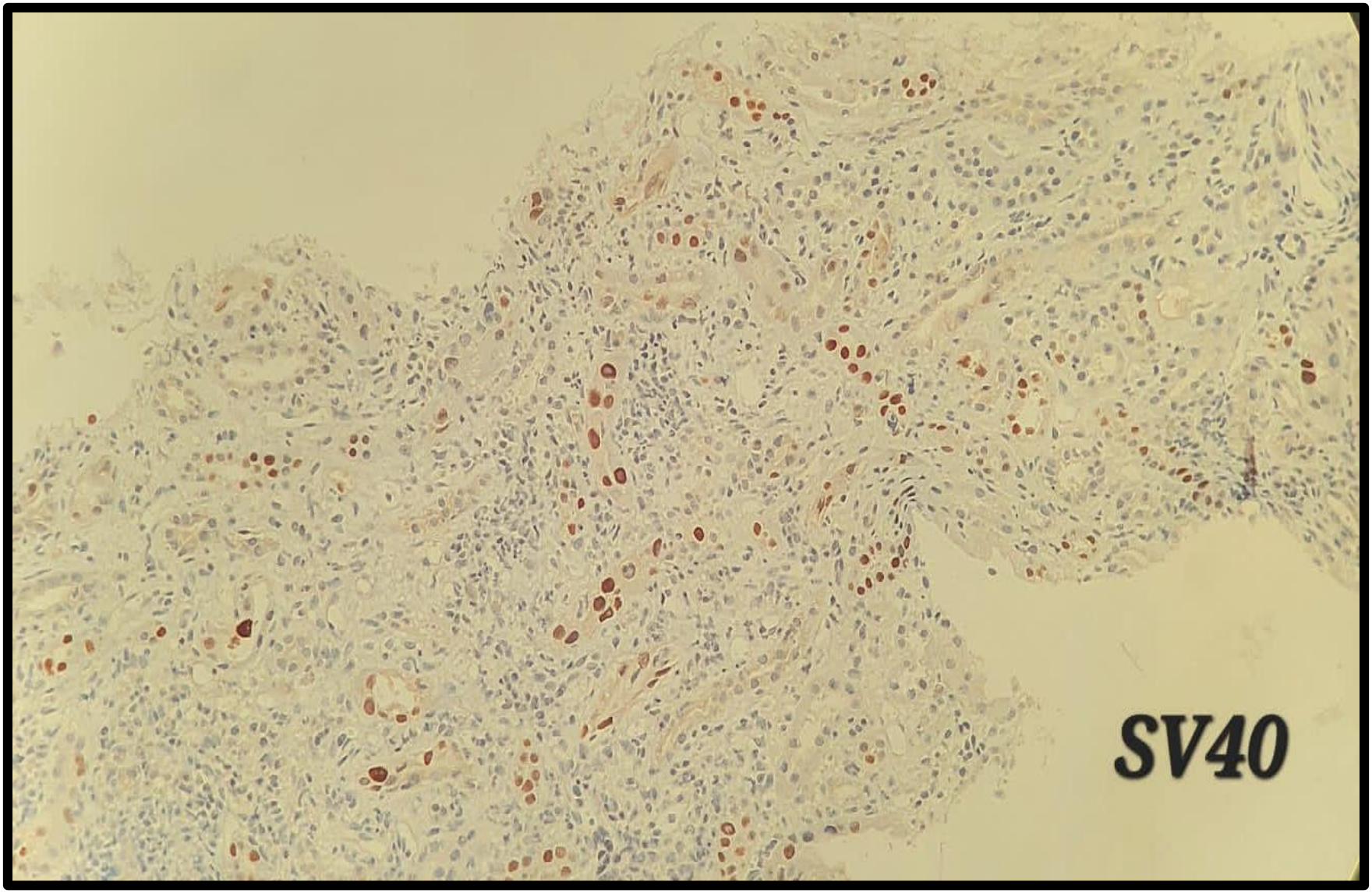

Masson Trichrome

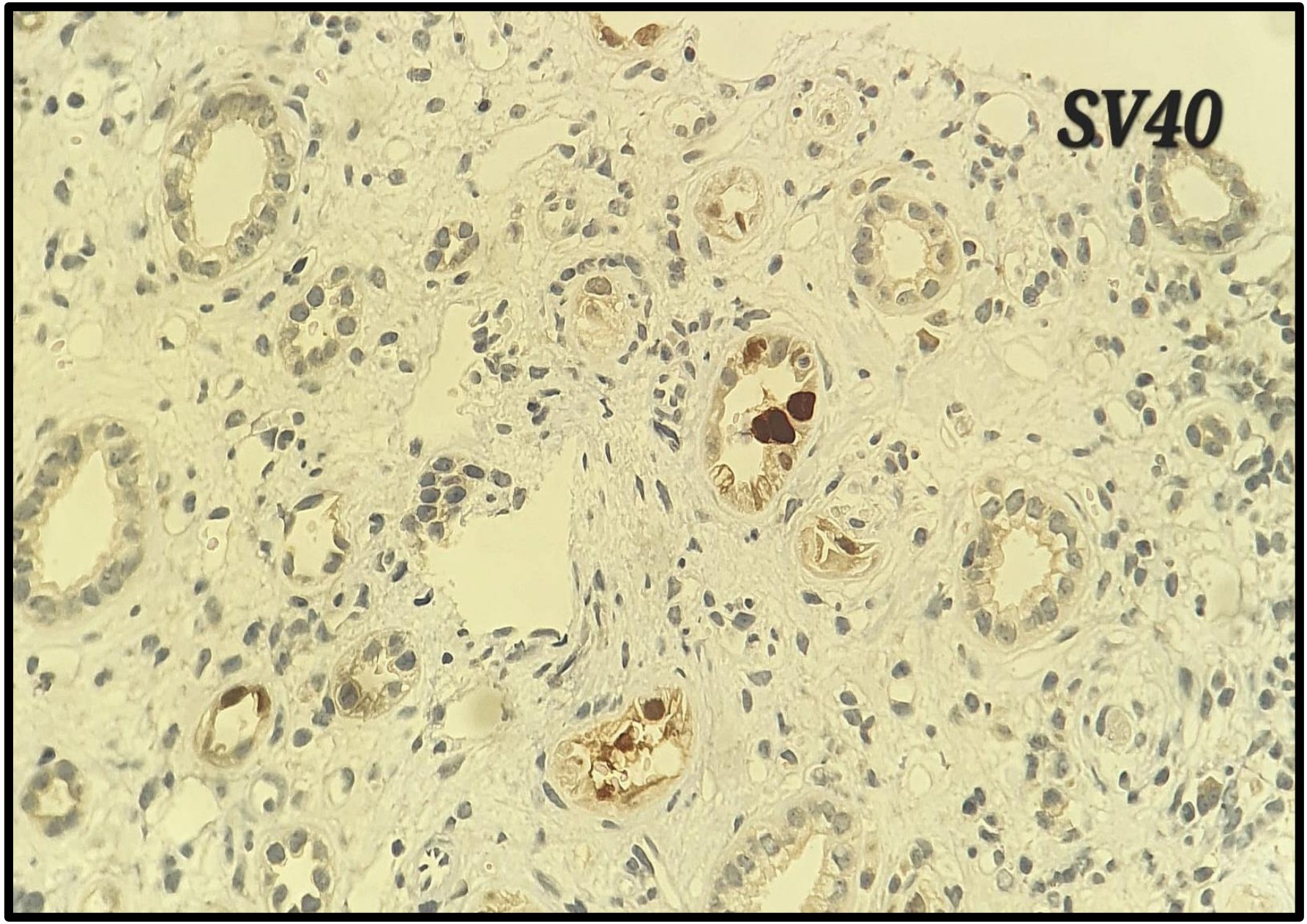

c4d +ve control


c4d negative


c4d negative

What else do you need now ?


SV40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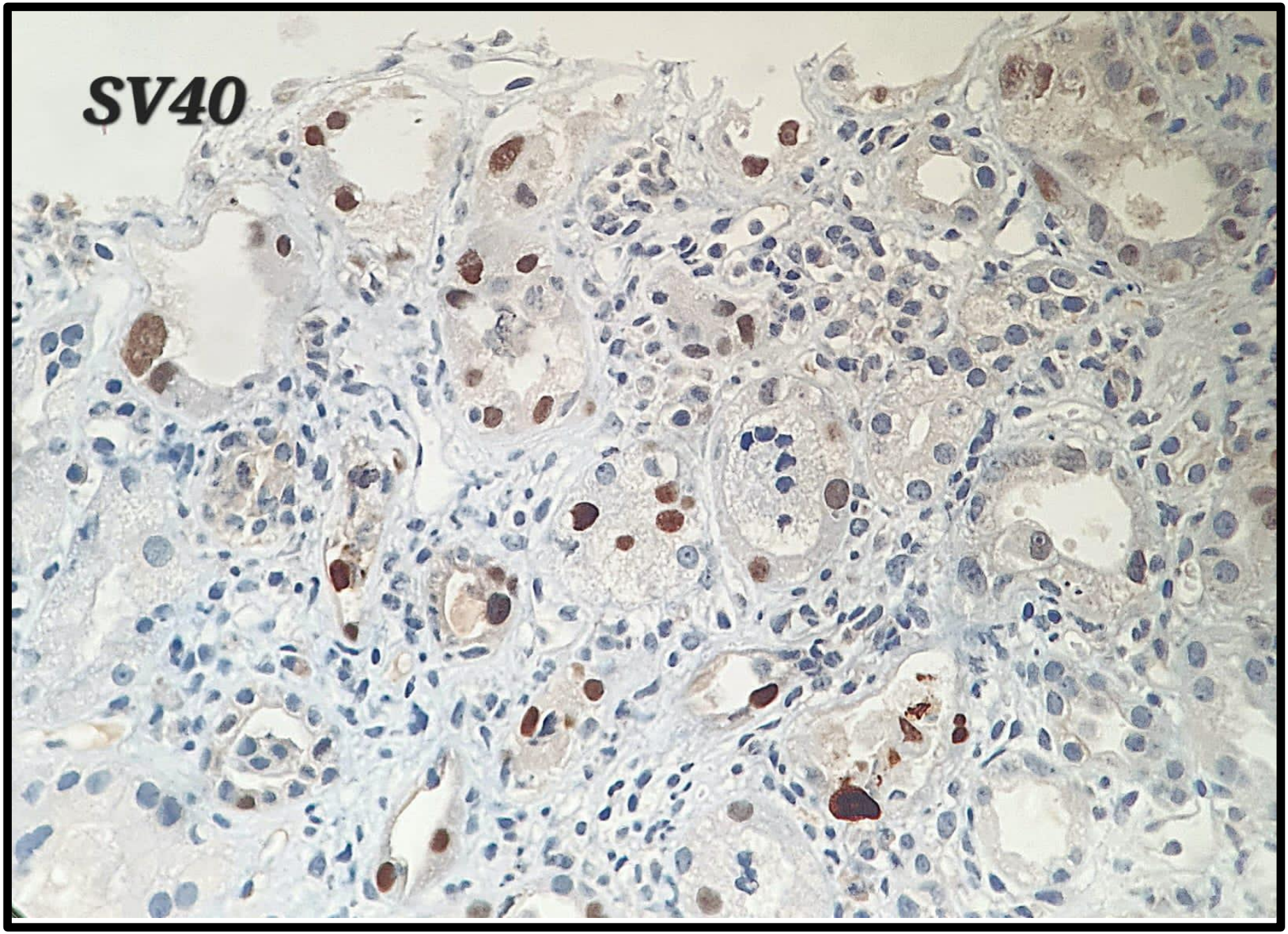
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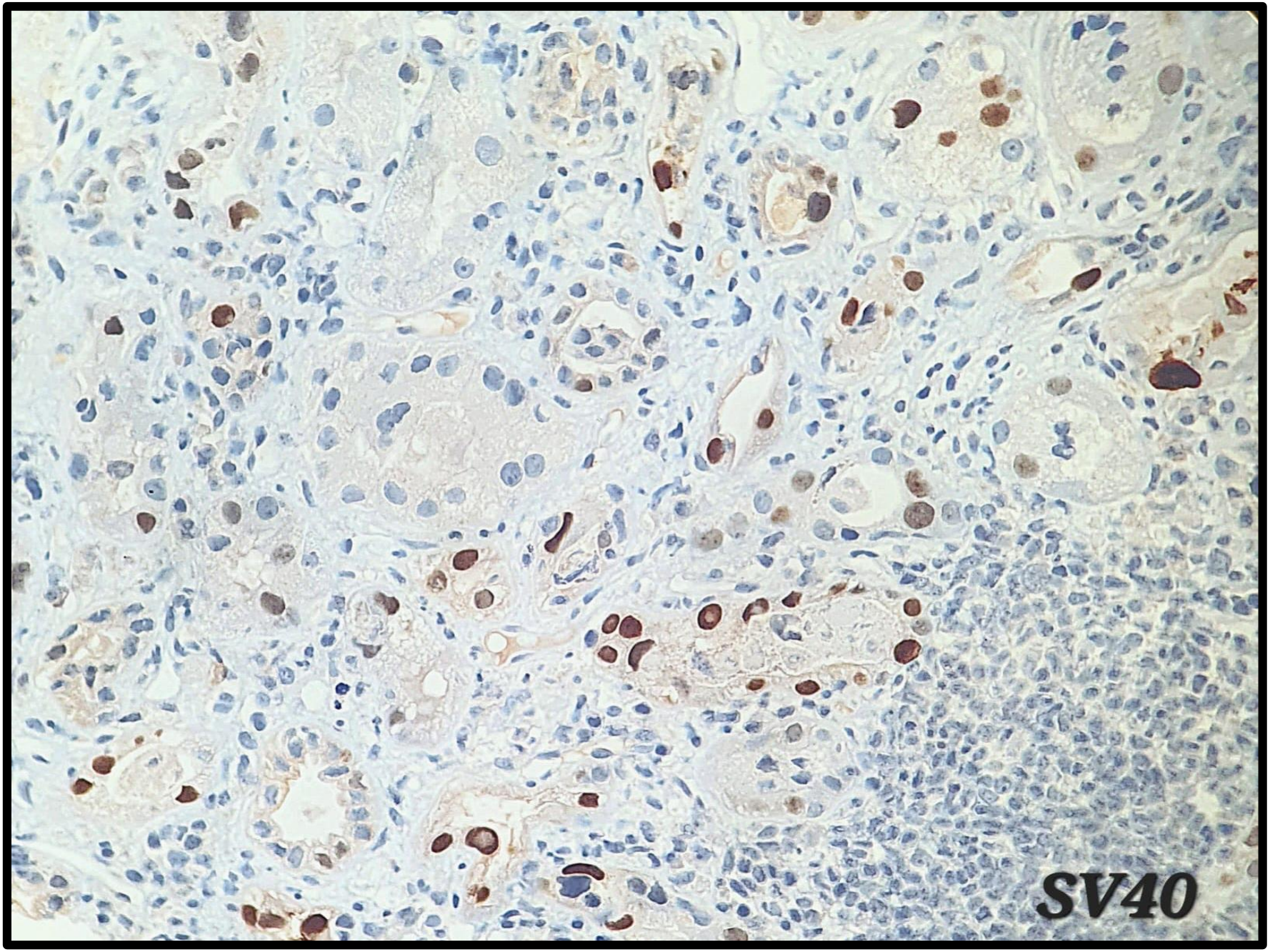
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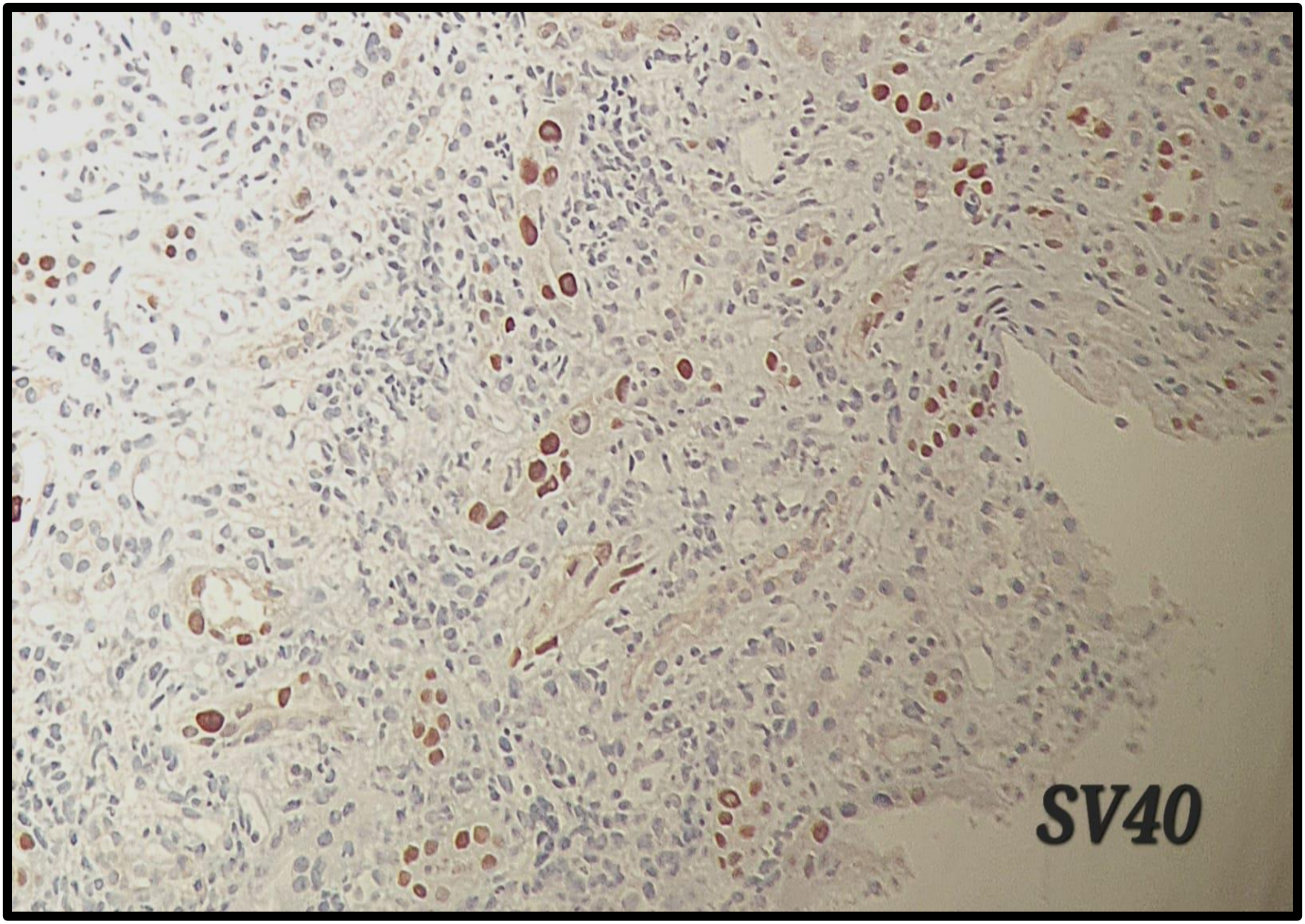
SV40

Pathological Diagnosis

What is your DD ??

1. Rejection X
2. Prograf Toxicity X
3. Anti-GBM antibody disease X
4. BK Nephropathy

Final Diagnosis

Polyoma BK Nephropathy

Case history: Follow-up Treatment

- MMF was reduced by half; (500 mg daily)
- Advagraf was also reduced (4-5 mg daily) to maintain blood level ~~ 4-5 mg/dl
- No change in the prednisone dose (5 mg/day)
- Close follow up of kidney function once weekly
- Serum for BKPyV by PCR was obtained.

Smartlab
مختبرات سمارت لاب

JAS
Accreditation Unit
Med - 012

ilac-MRA

Patient:	راما نزار بشير	**Doctor:**	
Patient No.:	203857	**Transaction:**	203857003
D.B:	2000-01-01	**Age:**	23 Years
Gender:	Female	**Date/Time:**	2023-02-22 16:10:24

Biochemistry

Test	Value	Unit	Expected Value
Creatinine, Serum	1.34	mg/dL	0.50 – 0.90
Ferritin, Serum	108.6	ng/mL	13 – 150

Molecular Genetics Department

Method : Real Time PCR, Dual Labeled Probe

Sample : EDTA Blood

JC-BK Virus by PCR

Result : **Positive for BK virus , 3.5 X10^4 IU/ml**

Comment : Genetic materials extracted and amplified by RT-PCR , consists of oligonucleotide primers and dual-labeled hydrolysis probes and controls to be used in RT-PCR assays for the in vitro Quantitative detection and characterization of the JC/ BK Virus in specimens from patients. The analysis done by real time PCR and the internal control monitored to confirm the amplification.

Assay Analytical Sensitivity: 1 copy / ml
Assay Analytical Specificity: 99.9%

Laboratory data: follow Up

	30/10/21	18/4/22	21/5/22	20/6/22	4/9/22	17/11/22	15/12/22	20/1/23	25/2/23
Serum Creatinine (mg/dl)	0.8	1.55	1.35	1.4	1.35	1.4	1.5	1.45	1.4
Prograf level (mg/dl)	7.5	10.2	7	6.5	4.8	6.7	6.5	4.4	3.7
Advagraf (mg/day)	7	7	6	5	5	5	4	4	4 --- 5
Prednisone (Mg/day)	5	**5**	5	5	5	5	5	5	5
Cellcept	1 gm X2	0.5 gmX2	0.5 gmX1	0.5 gmX1	0.5 gmX1	0.5 gmX1	0.5 gmX1	0.5 gmX1	0.5 gmX1
		Biopsy							

Polyoma BK Nephropathy

- BK polyomavirus (BKPyV) is a small DNA virus that establishes life-long infection in the renal tubular and uroepithelial cells of most of the world's population.
- BK Polyoma virus (BKPyV) is a ubiquitous virus with a worldwide seroprevalence of approximately 80-90 %.
- For the majority, infection is quiescent and benign.
- However, in immunocompromised patients, BKPyV can reactivate, and in some, lead to BKPyV-associated nephropathy (BKPyVAN).

Chong S, Rev Med Virol. 2019;29(4

BKV Clinical presentation

- Non-specific symptoms: Gradual increase in creatinine
- 30-60% of kidney transplant recipients develop BK VIRURIA and 10-20% develop VIREMIA
- Only 5-10% of the above develop BK nephropathy with some kidney dysfunction, ureteral stenosis, Tubulointerstitial nephritis

Treatment

- Prospective study of 200 new renal transplant recipients
- 23 developed BK viremia
- Anti-metabolite was stopped
- If viremia failed to clear after 4 weeks CNI dose was reduced (CSA trough of 100-200 ng/ml; TAC trough of 3-5 ng/ml)

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TRANSPLANT CENTER

Brennan et al. AJT 5: 582-594, 2005.

Treatment

- 22/23 (95%) cleared viremia by 1 year post-transplant[1]
- Mean time to clearance was 54 days
- 1 patient developed acute rejection related to immunosuppression reduction
- No patients developed BK nephropathy
- 5 Years Data[2]:
  - Patient survival was 91%
  - Graft survival was 84%.
- **The Problem:**
  - Development of Class II Donor Specific Antibodies[3]

MASSACHUSETTS GENERAL HOSPITAL
TRANSPLANT CENTER

[1]Brennan et al. AJT 5: 582-594, 2005
[2]Hardinger. AJT 2010; 10: 407–415
[3]Sawinsky. J Am Soc Nephrol 26: 966–975

Quinolones?

- In Vitro inhibition of replication[1] (Helicase)
- Retrospective data[2,3]: May be?
- Prospective Randomized Controlled Trial[4]: No Joy

Outcome	Levofloxacin Group (n=20)	Placebo Group(n=19)	P Value
Reduction in BK viral load at 3 mo (%)	70.3±42.5	69.1±39.5	0.93
Patients with >50% reduction in BK viral load at 3 mo	15 (75)	13 (68)	0.73
Reduction in BK viral load at 6 mo (%)	82.1±34.7	90.5±22.2	0.38
Patients with >50% reduction in BK viral load at 6 mo	16 (84) (n=19)	17 (89) (n=19)	>0.99
Increase in BK viral load at 3 mo	5 (25)	3 (16)	0.69
Sustained BK viremia at 3 mo	13 (65)	14 (74)	0.73
Sustained BK viremia at 6 mo	11 (58)	13 (68)	0.74
Allograft loss	0 (0)	2 (11)	0.49

[1].Ali SH. Antivir Ther 2007; 12:1.
[2].Gabardi. CJASN 5: 1298–1304, 2010
[3].Wojciechowski 2012. Transplantation 15;94
[4].Lee BT. CJASN 9: 583-589; 2014

Other tools?

- **mTORi**:
  - In Vitro data suggest antiviral properties[1]
  - Rapamicin blocks replication compared to Tacro[2]
  - Clinical Trials ongoing
- **IVIg**
  - Has BK neutralizing antibodies[3]
  - Trials ongoing. (DSA data encourage this use)
- **Donor/Recipient Matching[4]**
  - Pre-transplant Viruria before tx is a risk factor (with donor = the
  - probable source, 24/28 pair plus in SRTR data)
  - D+/R- serostatus is a risk factor. D/R serotype? (I-IV)
  - ? CMV like approach in the future. ? Vaccines
- **BK specific T cells, Donor Derived CTL.**

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TRANSPLANT CENTER

1 Liacini. 2010. Transplantation Dec 27;90(12):1450-7
2 Hirsch. 2016. AJT Mar;16(3):821-32.
3 Sener. Transplantation 2006;81: 117–120
4 Schwartz. 100(4), April 2016, p 844–853

Cidofovir

- Cidofovir is a nucleotide analog of cytosine that is active against various DNA viruses and is approved for both HIV-associated cytomegalovirus (CMV) retinitis and the topical treatment of genital warts.

- Cidofovir has modest in vitro activity against polyomaviruses.
  - It should only be considered for treatment of BKPyVAN when other interventions have failed; it has been used anecdotally, in combination with antinucleoside therapy, for HIV-infected patients with progressive multifocal leukoencephalopathy (PML) resulting from polyomavirus infection.

Re-transplantation

- Retransplantation in patients with graft failure due to BK polyomavirus associated nephropathy (BKPyVAN) is a reasonable option and has been successfully performed.
- The absence of BKPyV replication should be confirmed prior to retransplantation.
- Because BKPyVAN appears to be donor derived and cytotoxicity mediated, this usually necessitates continued close screening following retransplantation.
- **NO NEED FOR Routine nephrectomy** of the failed allograft or of the native kidneys, which may serve as a reservoir and a source of reinfection .

Hirsch HH et al; Transplantation. 2005;79(10):1277.

Re-transplantation: Outcome

- In the largest study to examine this issue, outcomes were compared:
  - 341 patients who were retransplanted for first graft failure resulting from BKPyVAN
  - 13,260 patients who were retransplanted for first graft failure resulting from other causes.

- **At one year,** there was no significant difference in between the two groups:
  - The rates of acute rejection OR
  - Patient survival.

- **Five-year, death-censored graft survival rates were:**
  - 91 % for the BKPyVAN group
  - 84 % for the non-BKPyVAN group.

Leeaphorn N :Am J Transplant. 2020;20(5):1334

DEPARTMENT OF PATHOLOGY & LABORATORY MEDICINE

Order No : P1270 –22 Specimen Date: 18/4/2022
Patient No : 896760 Order No: 8397050 Room No: 506
Patient Name : راما نزار عبدالرحمن بشير
Age : 21 years Sex: Female
Doctor :رياض سعيد

Origin of Tissue: Transplanted Kidney biopsy.
Brief Clinical History: S/P LRK Tx 9/2021. Hearing impairment. ↑ Creatinine slowly from 0.8➔1.6 mg/dl. Negative proteinuria. (Spot urine 0.2 grams). Hematuria 24 RCC.
Pre-operative diagnosis: R/O Rejection Vs anti GBM.
Post-operative diagnosis:

Pathology Report

Gross Exam:

1) Specimen is received fixed in formalin, labeled with patient name and consists of 2 soft tissue needle biopsy fragments measuring 2 cm and 1.7 cm in length. Totally submitted in one cassette.
2) Specimen is received fresh in normal saline for immunoflourescence studies.

Microscopic Exam:

Sections reveal 9 glomeruli in the submitted cores, all of which appear normal or show mild increase of mesangial cells and matrix. No glomerulolitis seen. Many of the tubules show enlarged hyperchromatic nuclei with viral-like inclusions, consistent with polyoma virus inclusions. Some tubules show isovacuolation of tubular epithelial cells. A dense patchy interstitial lymphocytic infiltrate is present. PAS stain reveals some atrophic tubules with thickened basement membranes. No tubulitis or vasculitis seen. Other special stains are non-contributory.

Immunoflourescence studies:

Only two glomeruli are present. Negative for IgG, IgA, IgM, C3, C4, fibrinogen, kappa and lambda light chains.
C4d immunohistochemical stain is negative.
SV40 immunohistochemical stain is positive for polyoma virus.

Diagnosis:

Transplanted kidney biopsy:

Polyoma virus-induced interstitial nephritis.

Hassan Z. Annab, M.D.
American Board of Pathology (AP/CP)

Date: 20/4/2022

Case 3 : History

- Mr. AJ is a 59-year–old male patient was admitted to Jordan hospital for evaluation of recently diagnosed Acute Kidney Injury (serum creatinine 7.2 mg/dl) and Anemia.
- This patient history dates back to several months when he experienced low back pains and numbness in both lower limbs.
- Treated with a variety of medications with minimal improvement.

Case 3 : History

- Back surgery with Cement fixation 2 weeks prior to admission was performed in Riyadh SA.
- Progressive decrease in the urine output and lower limb swelling in the last few days. No sphencteric problems.
- Laboratory date showed increased serum creatinine and the patient was told that he needs hemodialysis. So he decided to come back home.

Case 3 : Physical Examination

- The patient was in pain (pain score 6-7) and lying in bed difficult to ambulate , obese and pale.
- BP 155/96 mmHg, Afebrile, pulse rate 76/min
- Both cardiac and chest examination were normal
- No Pericardial friction rub
- ++ lower limb swelling

Case 3: Laboratory data

- CBC: hemoglobin, 10.7 gm/dl; WBCs, 12.500; platelets, 312,000
- **ESR: 130**
- Serum values:
  - **Creatinine : 7.17 mg/dl**; Potassium, 4.8 meq/L
  - Calcium: 10.7 mg/dl; Phosphorous:6.5 mg/dl
  - Uric acid: 13 mg/dl ; HCO3: 15 meq/dl
  - **Total Protein: 9 gm/l; Albumin: 3.1 gm/L**
- Urine: Few WBCs, few RBCs & ++ protein
  Proteinuria : 5 gm/day
- Both HCV & HBsAg were negative
- PTH level: 16.7 (up to 65), Vitamin D, 14.5

Case 3: Investigations

- Abdominal Ultrasound
  - Normal size kidneys , increased echogenicity
  - No Hydronephrosis
  - Normal liver, spleen and Pancreases
  - No lymph-adenopathy
- Chest X-ray Normal
- X-ray LSS:
  - Destruction of 4^{th}, 5^{th} lumber spines

What other tests you order now to help with the diagnosis ?

What other tests you order now to help with the diagnosis ?

SPE

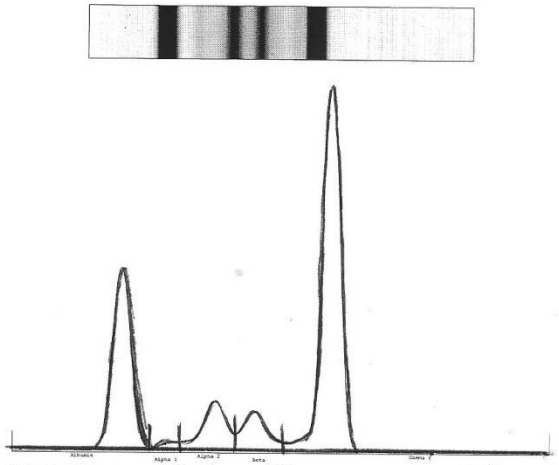
Bone marrow

JORDAN HOSPITAL

Patient :12/07/2011 No.: 1

Name
Age :
Sex : order No: 320734

Serum protein electrophoresis



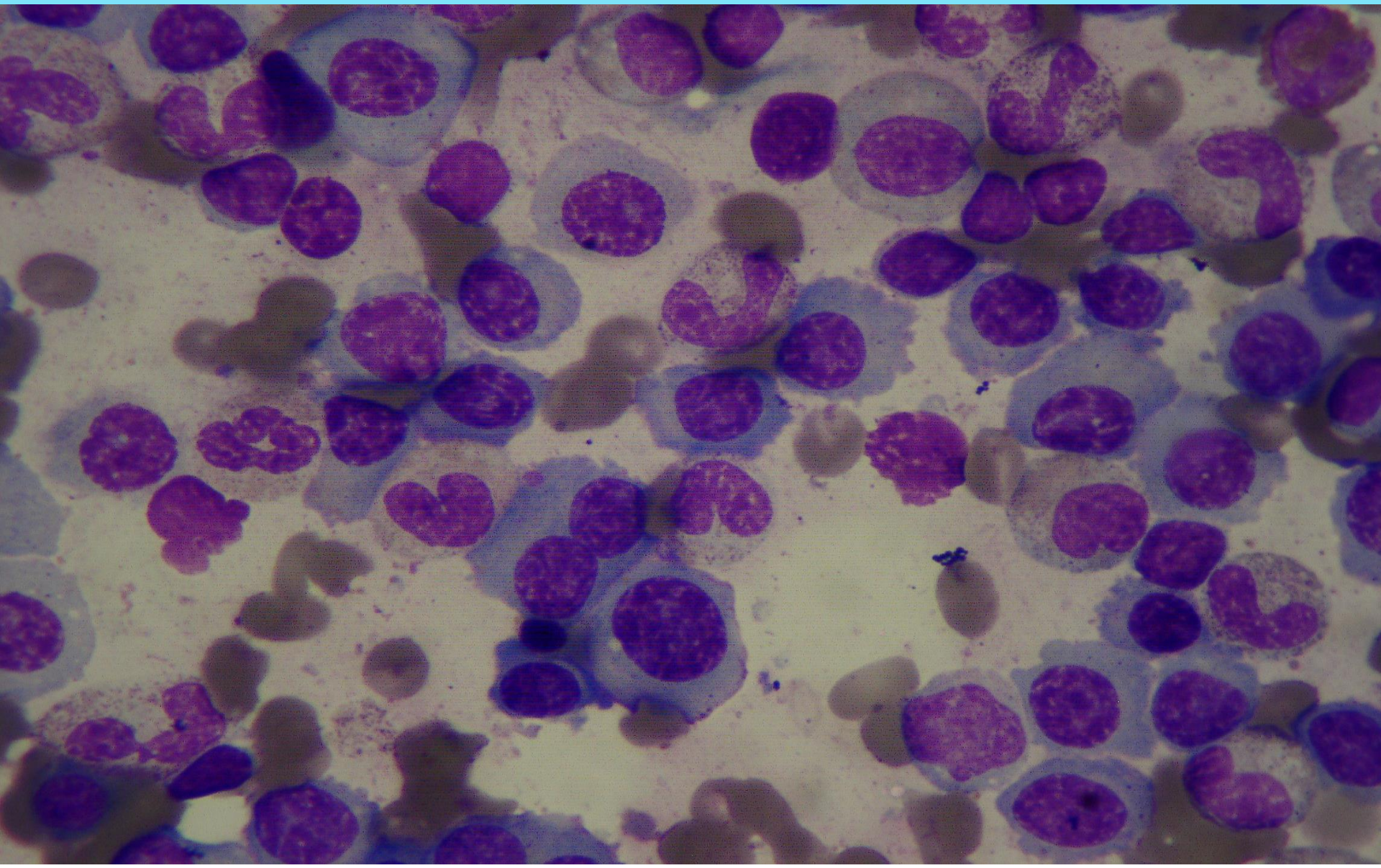
Total Protein = 10.7 g/dl A/G = 0.38

Fraction	%	g/dl	Normal: %	g/dl
Albumin	27.5	2.9	60-71	3.5-5.5
Alpha 1	2.0	0.2	1.4-2.9	0.1-0.4
Alpha 2	9.9	1.1	7-11	0.3-0.9
Beta	7.9	0.8	8-13	0.5-1.2
Gamma	52.7	5.7	9-16	0.6-1.7

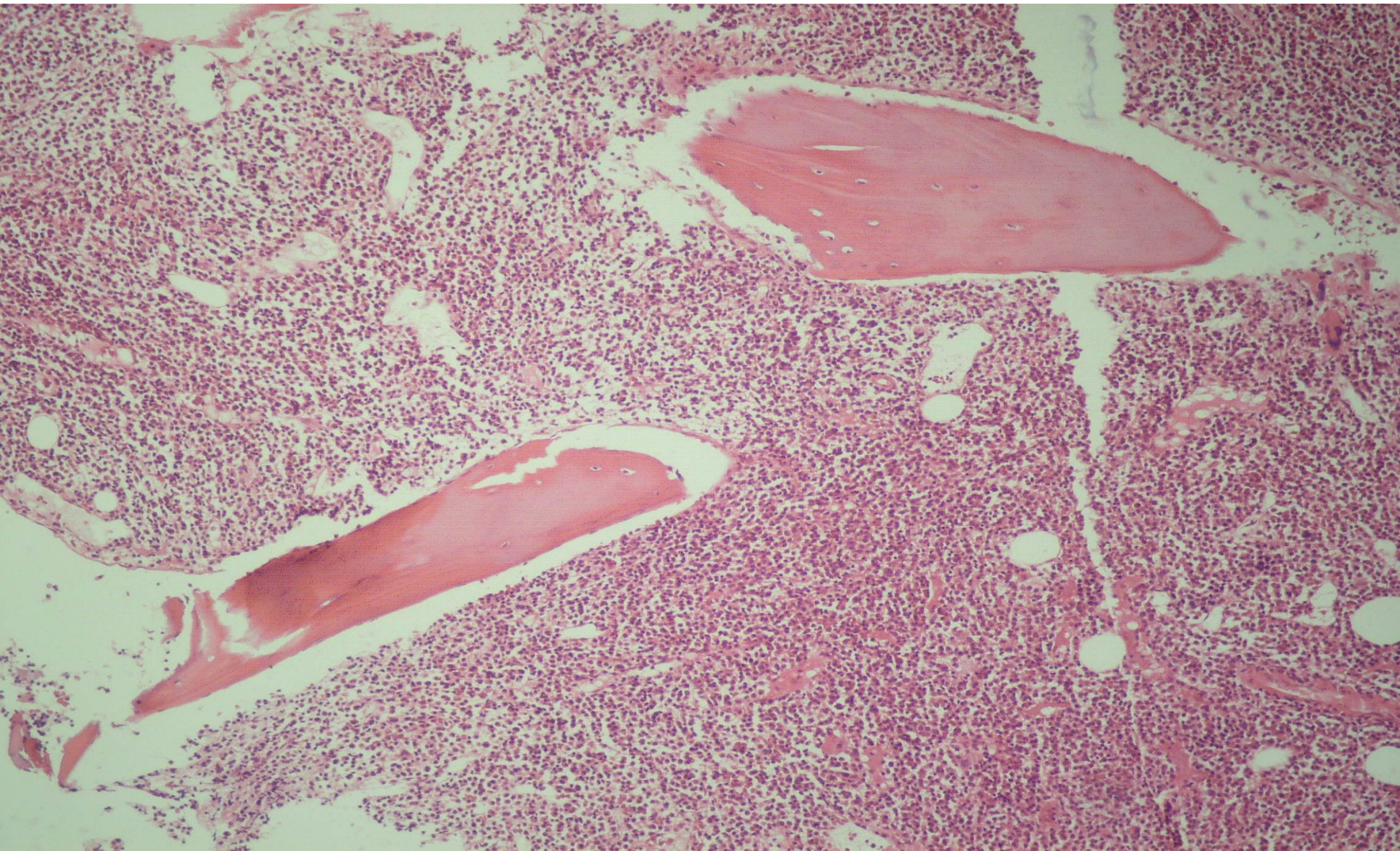
Comments :

Signature

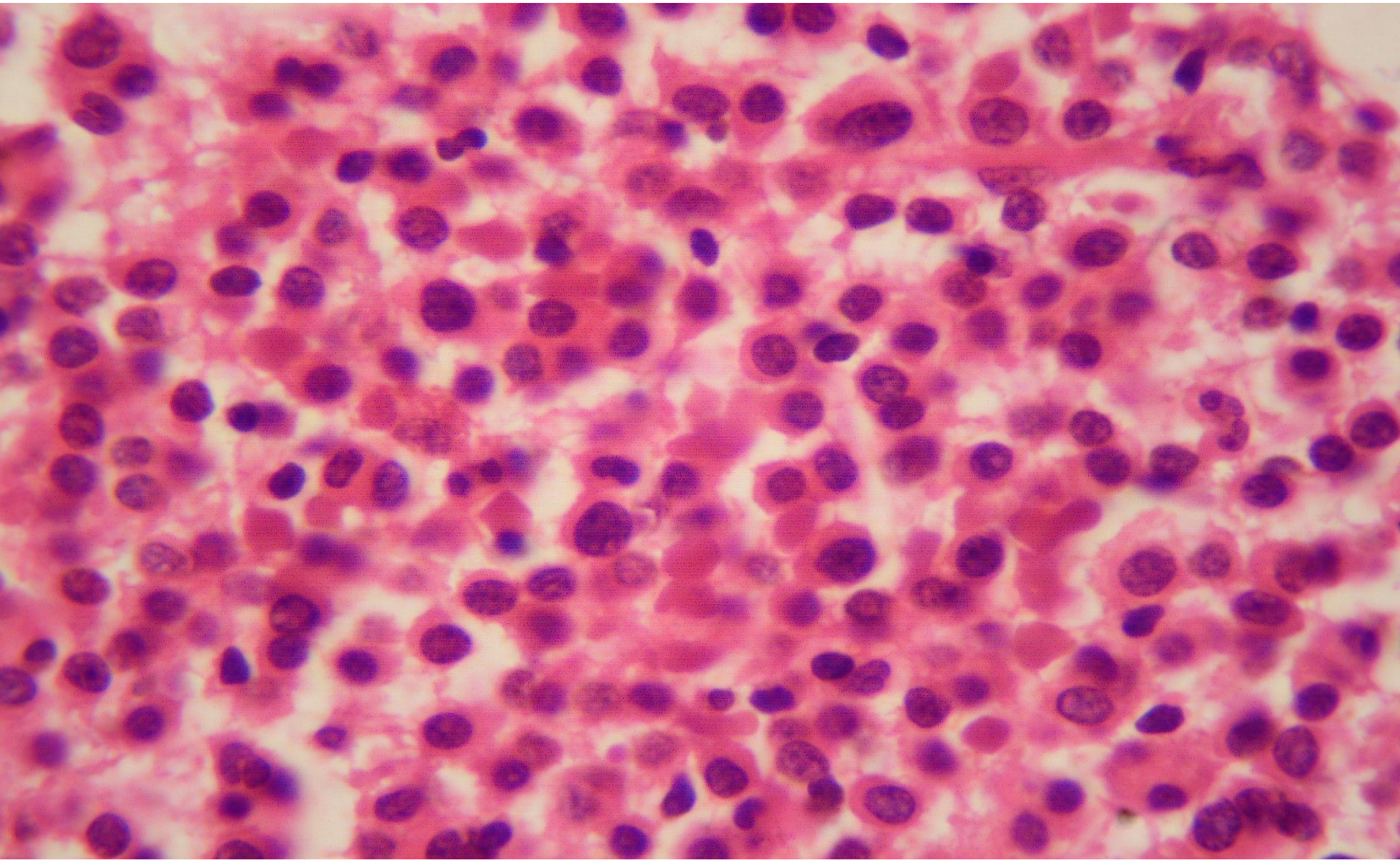
Case 3: Bone Marrow Aspirate



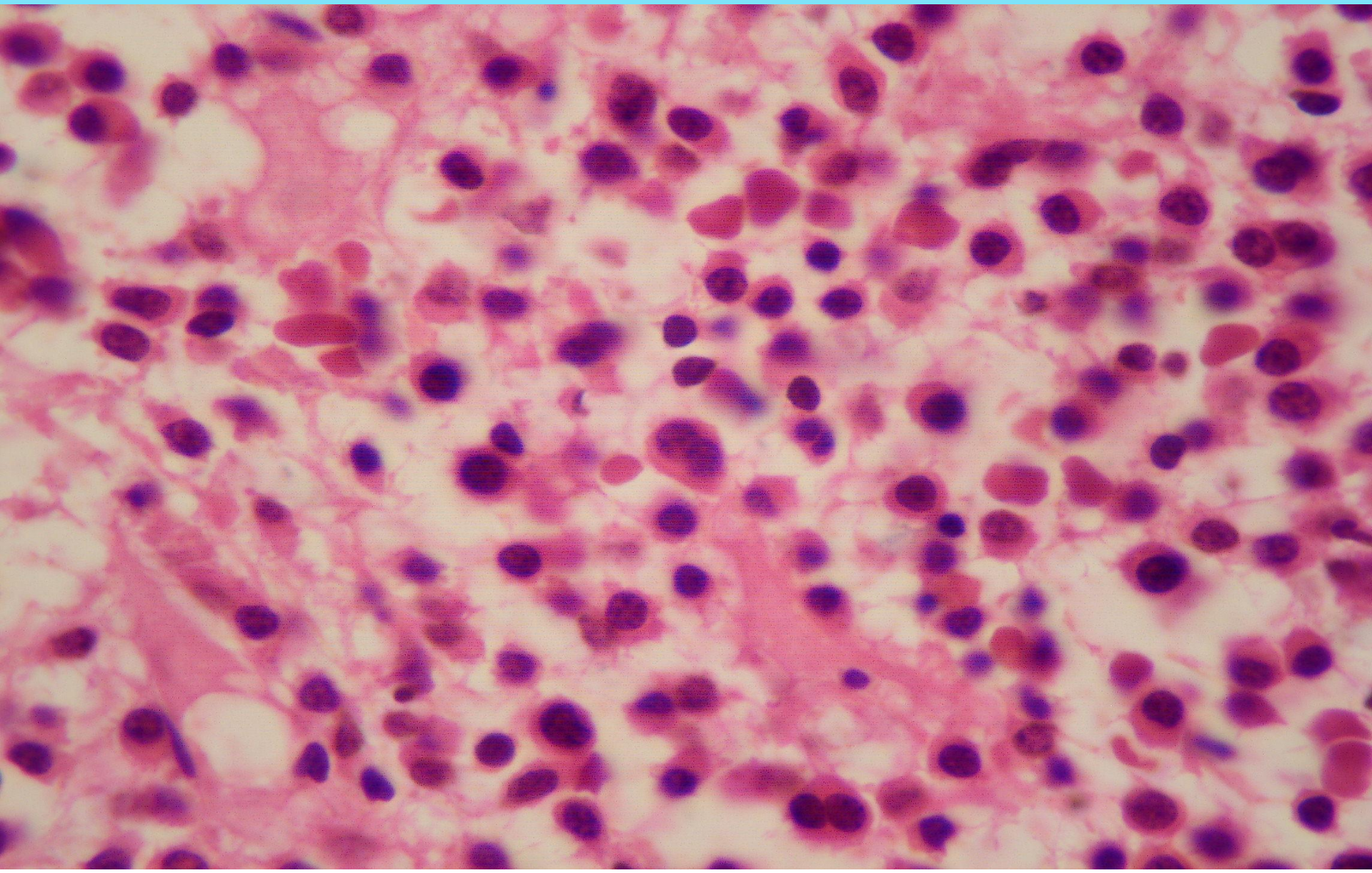
Case 3: Bone Marrow Biopsy



Case 3: Bone Marrow Biopsy



Case 3: Bone Marrow Biopsy



Acute Kidney Injury in Multiple Myeloma

So what is the most likely cause of this AKI in this patient ????

Acute Kidney Injury in Multiple Myeloma

Cohen DJ et al: Am J Med. 1984;76(2):247

DD

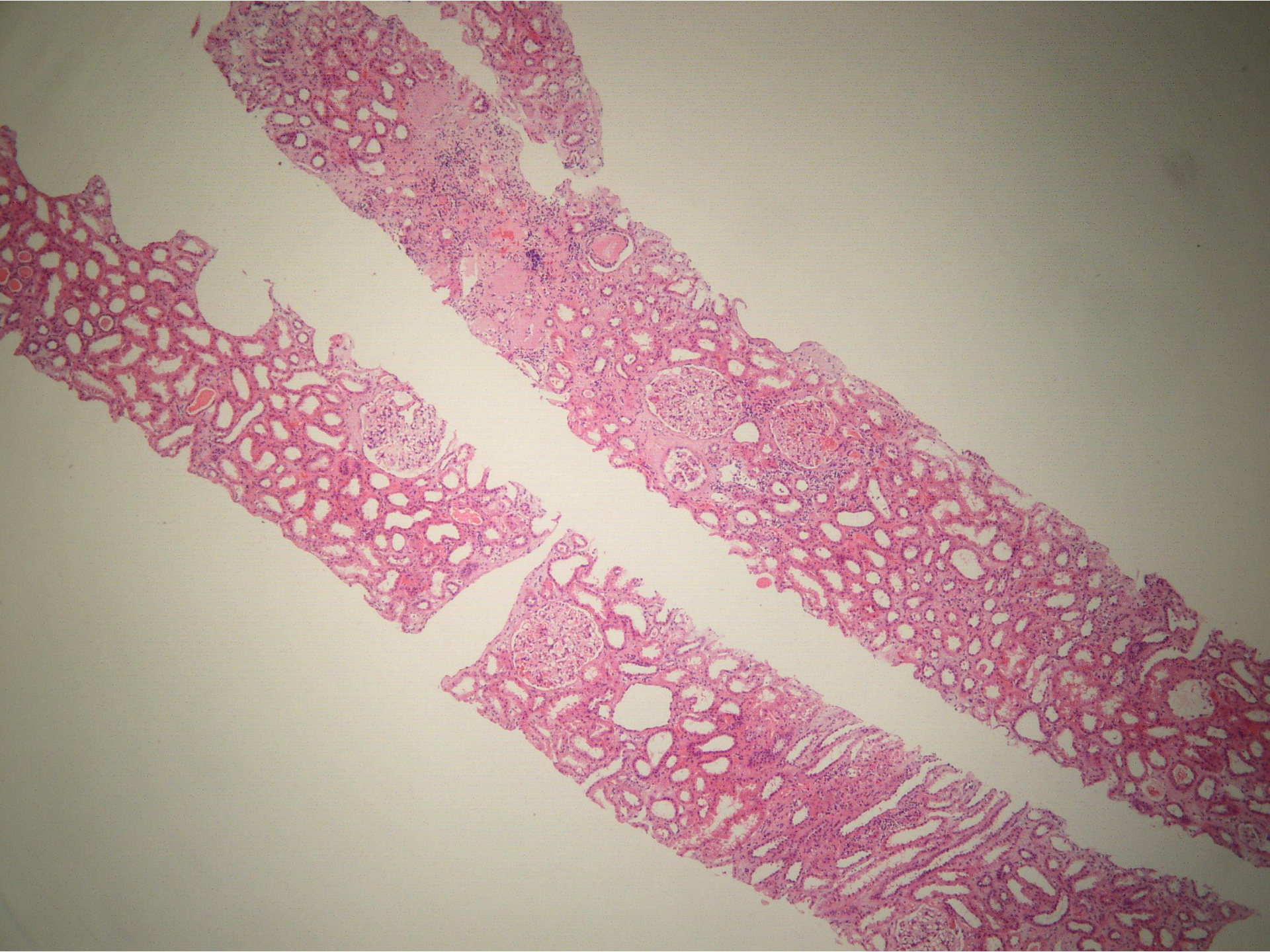
- Myeloma cast nephropathy.
- Hypercalcemia.
- Volume depletion.
- Hyperuricemia.
- Hyperviscosity (rare)
- Toxicity due to intravenous radio contrast media.
- Nonsteroidal anti-inflammatory agents.

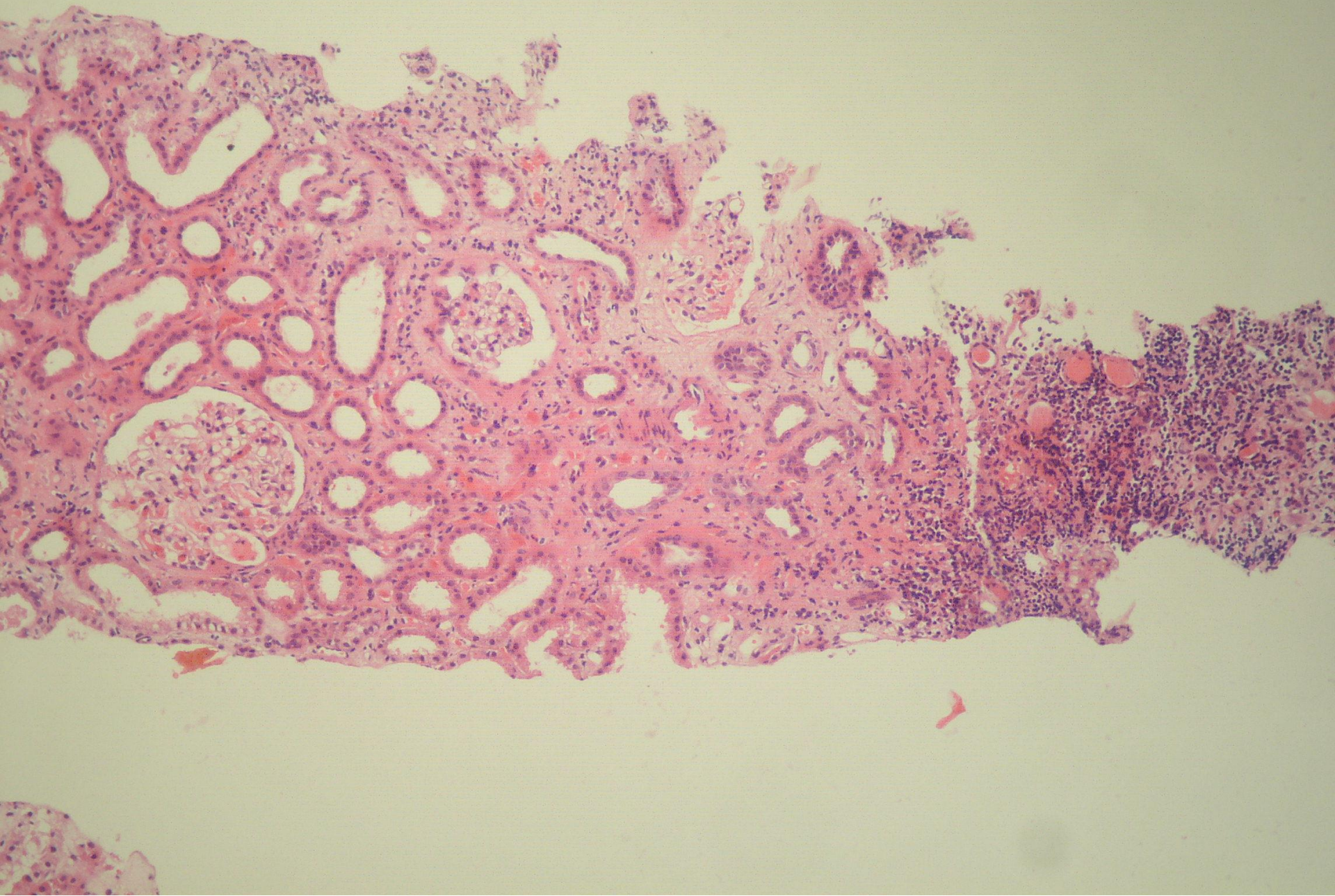
So what is the most likely diagnosis ????

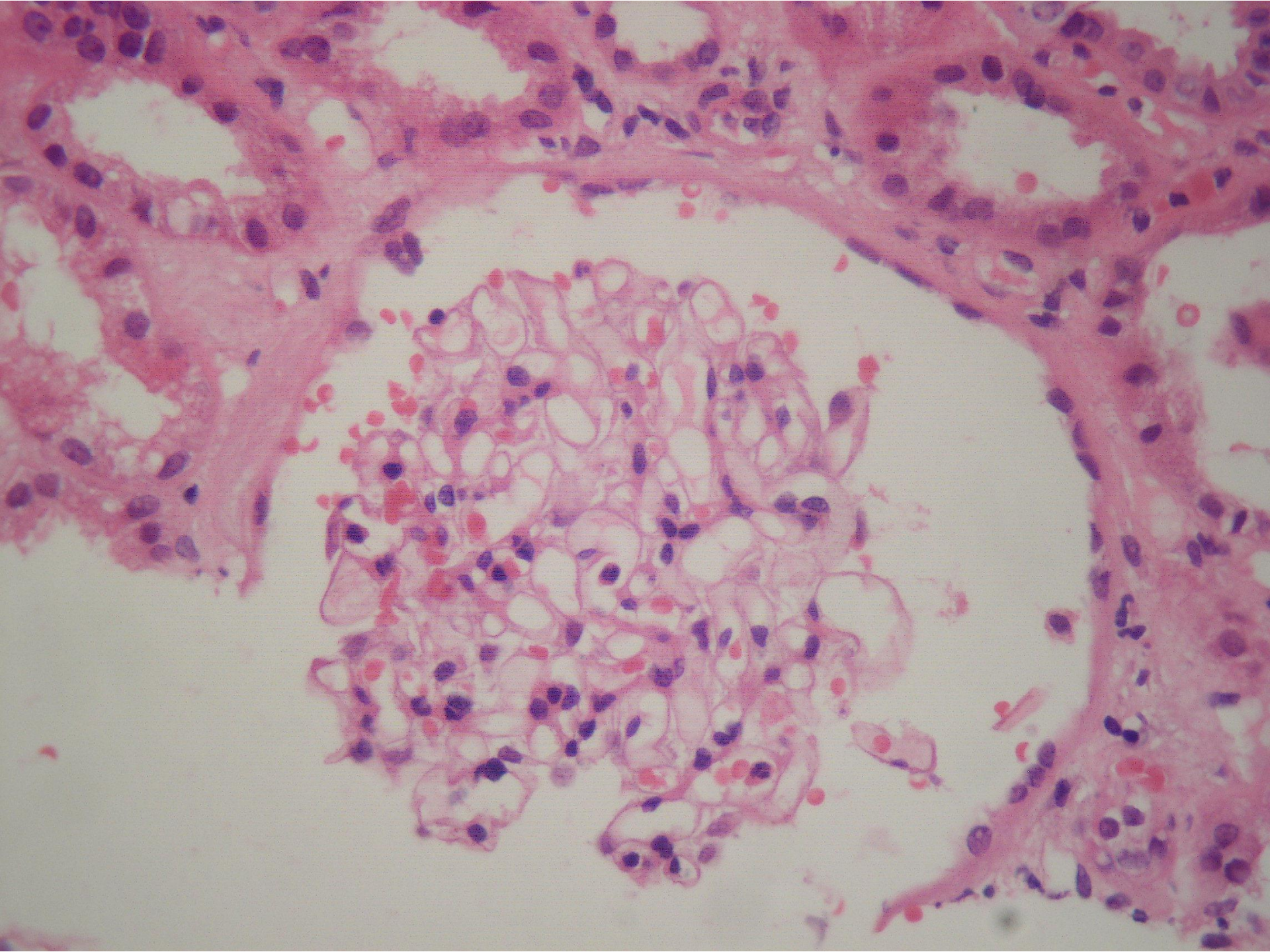
Kidney Biopsy

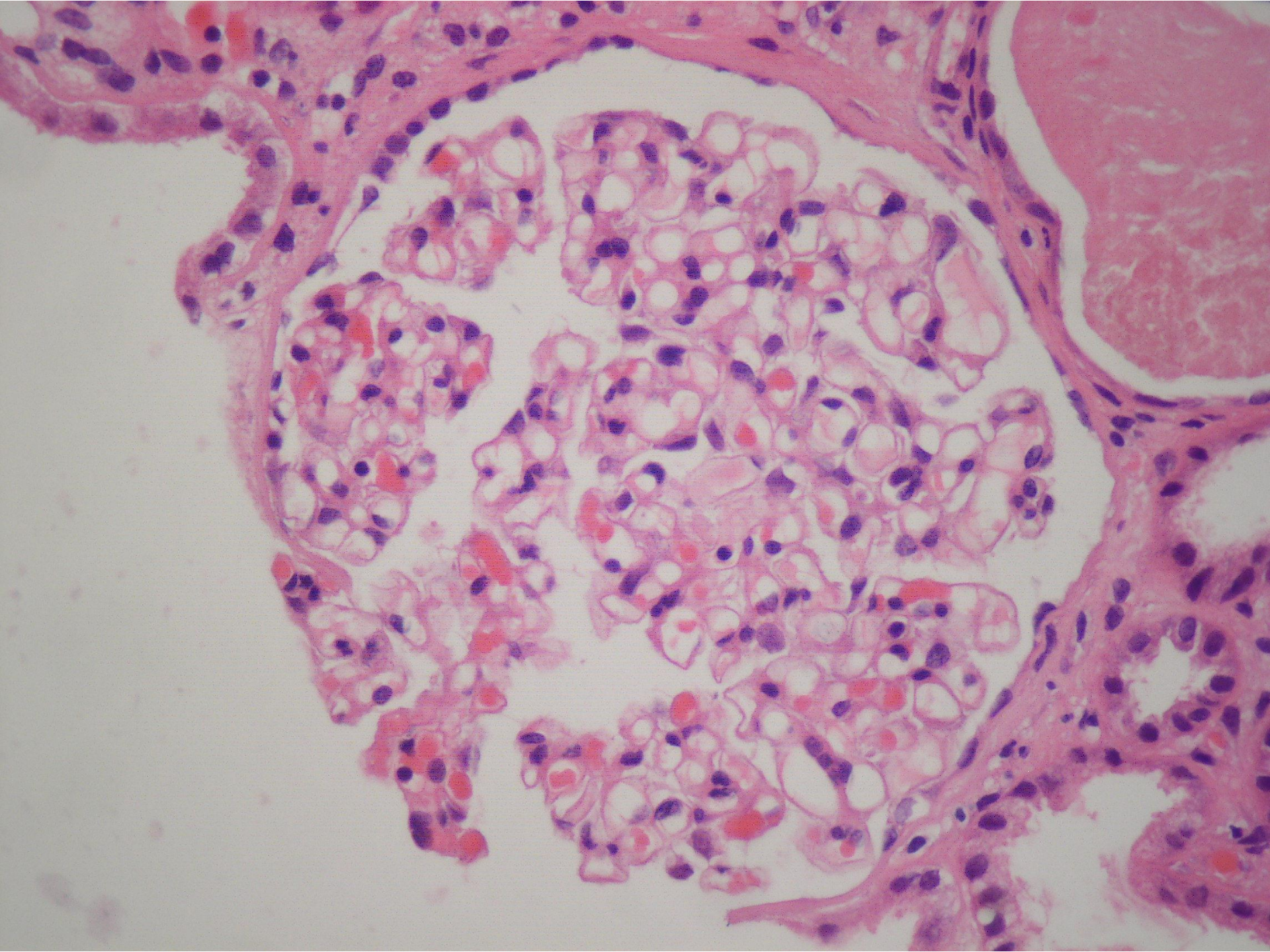
Case 3: Kidney Biopsy

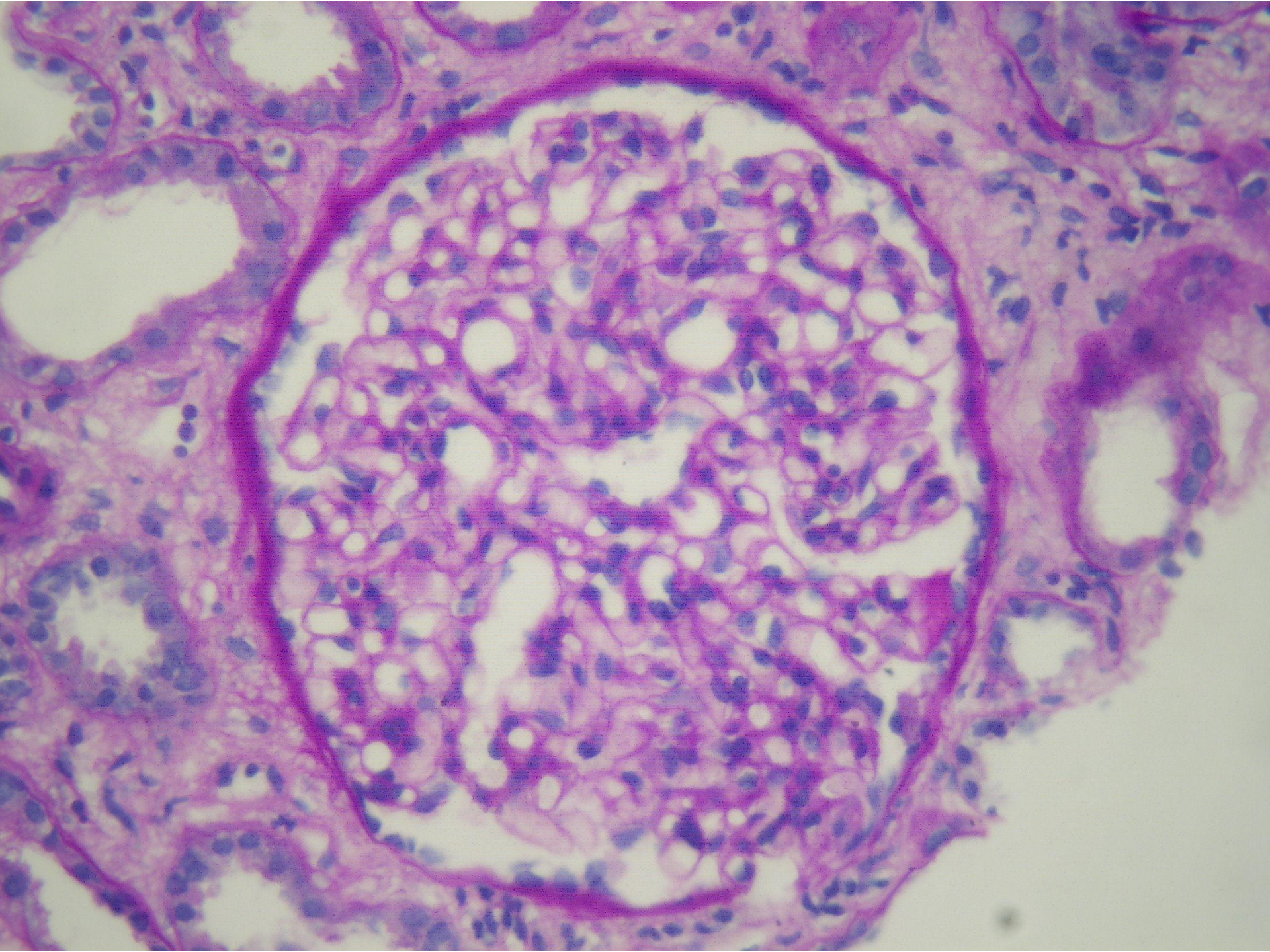
- **Light Microscopy:**
  - Sections reveal a total of 26 glomeruli .
- **Immunoflourescence studies:**
  - 6 glomeruli were seen.

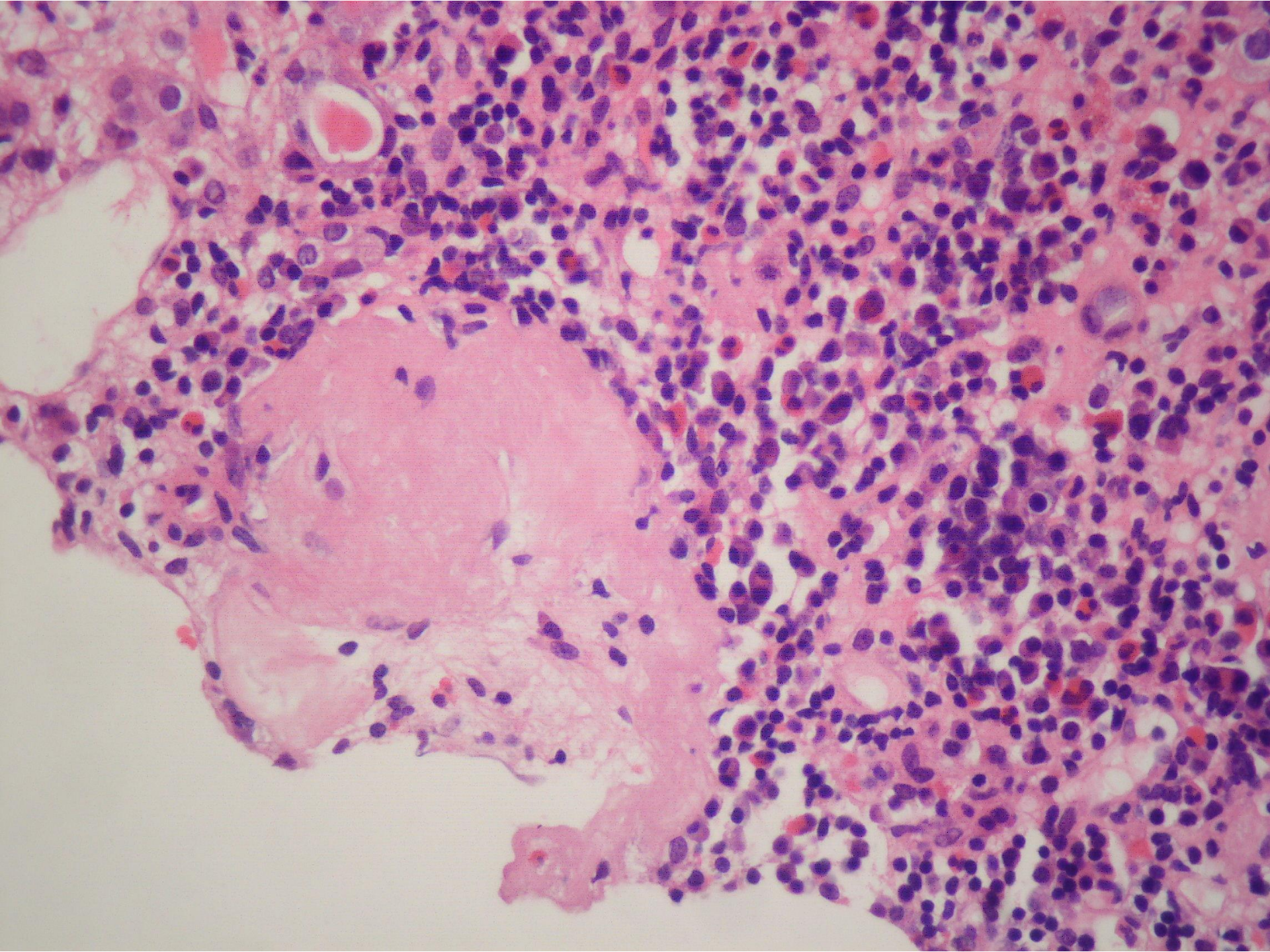


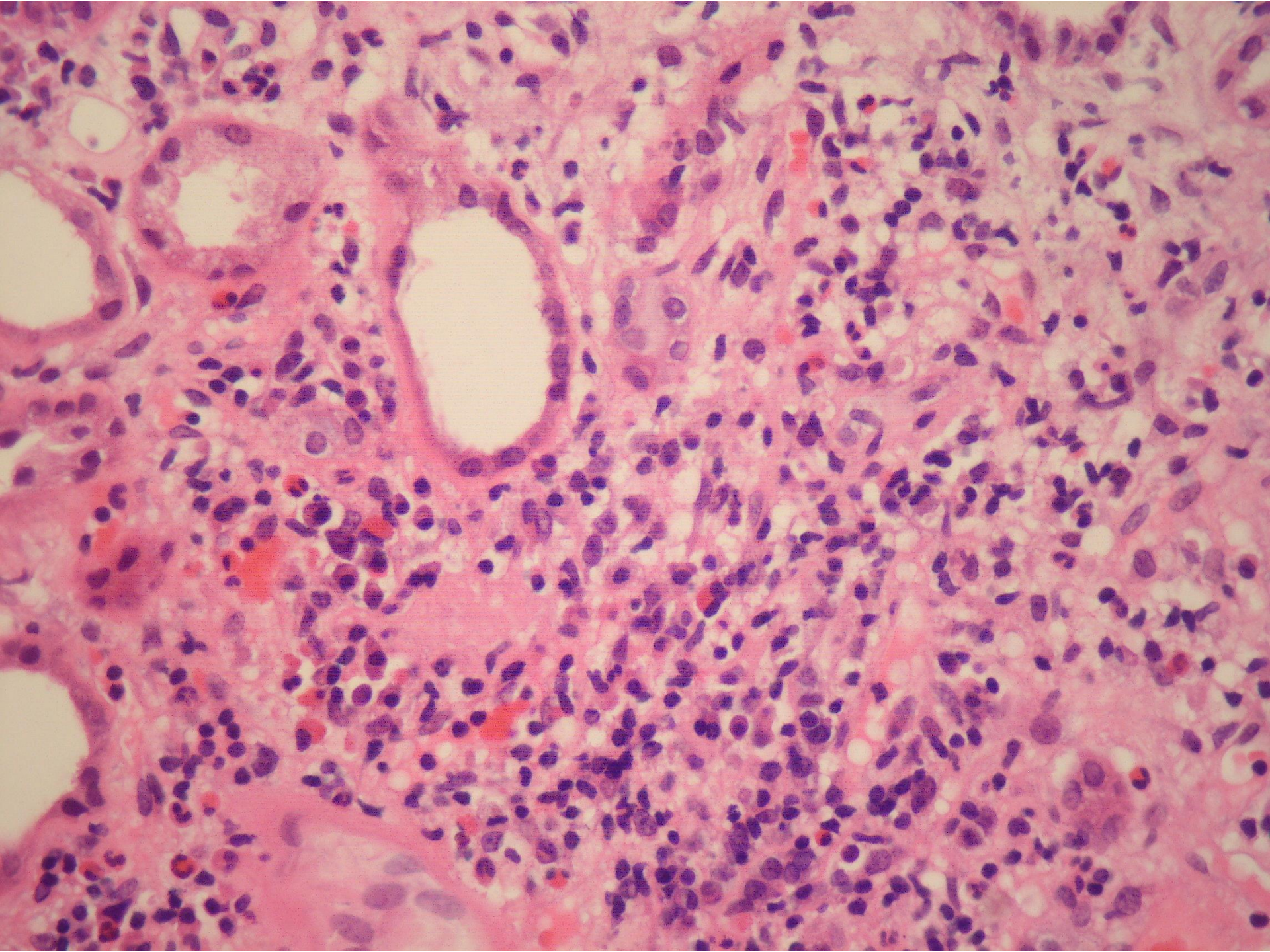


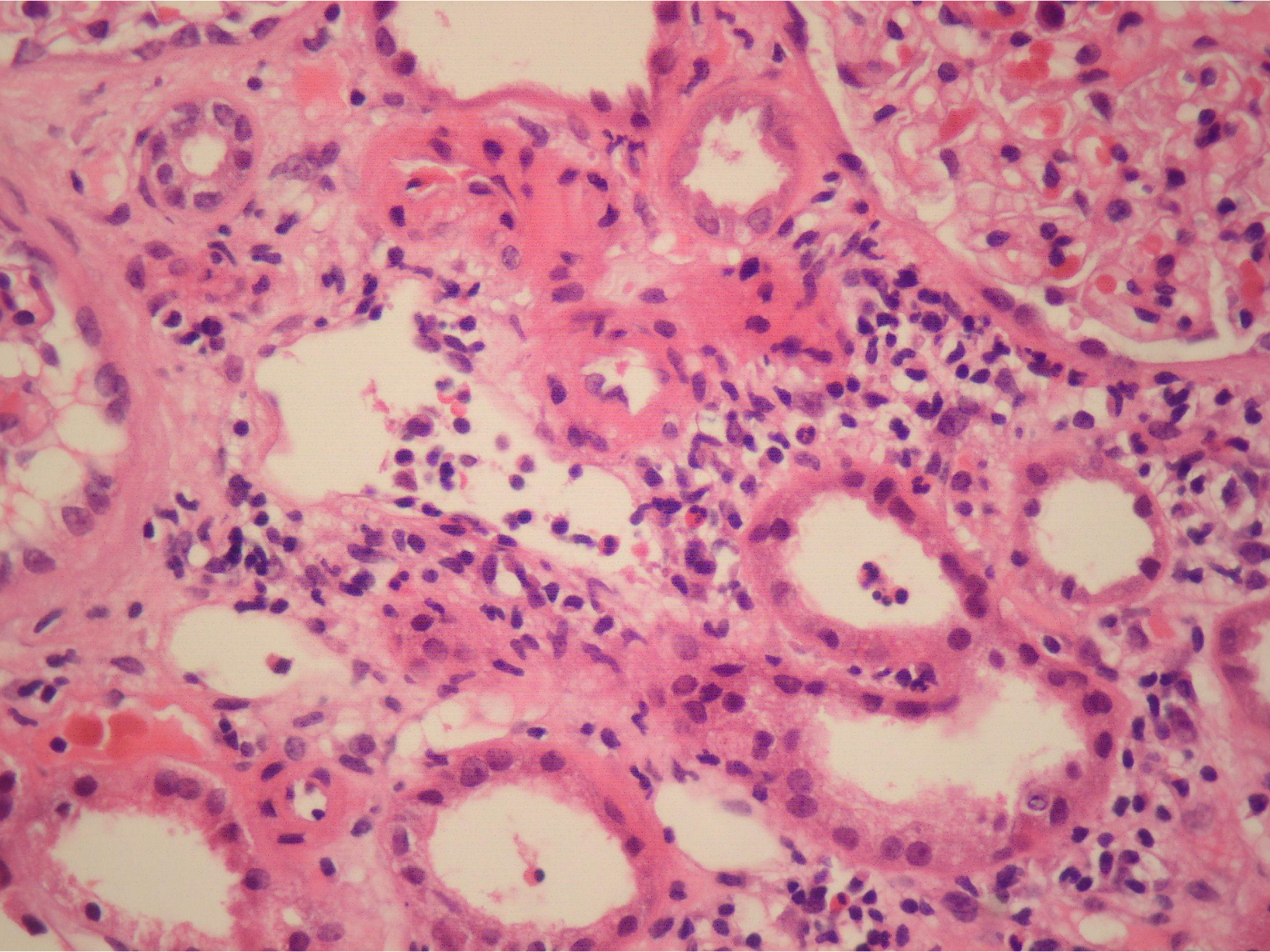


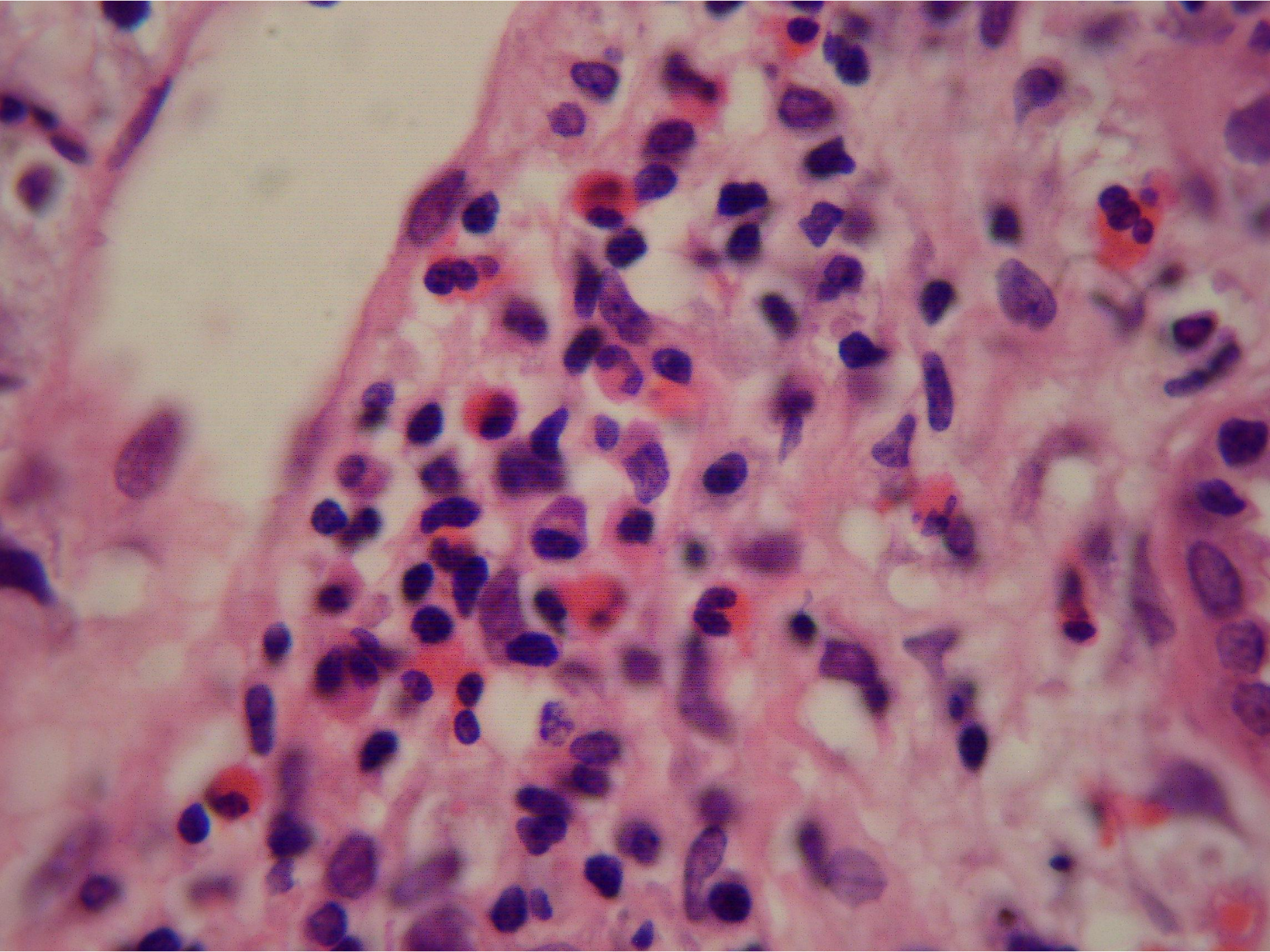


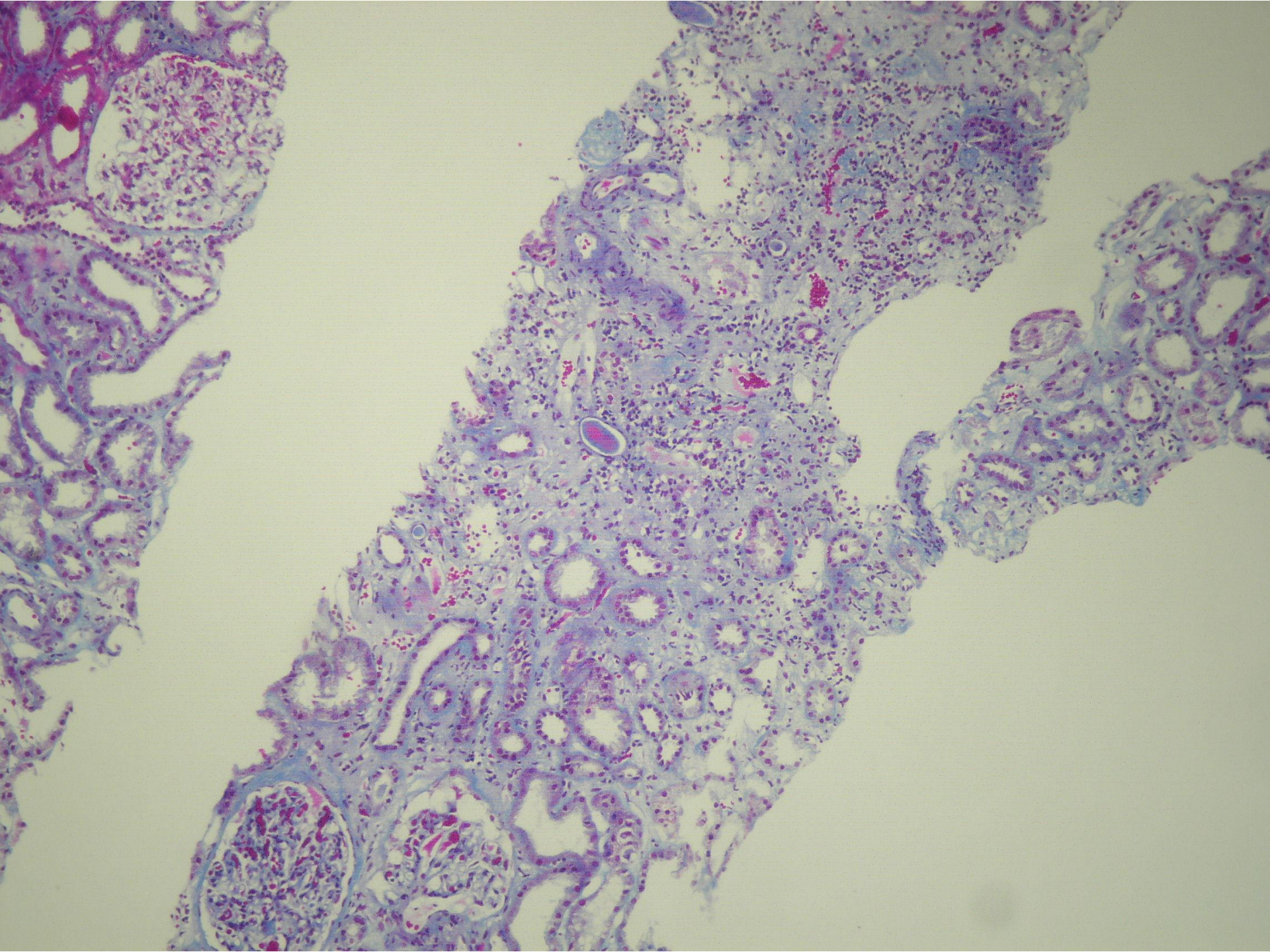












Case 3: Kidney Biopsy

- **Immunoflourescence studies:**
  - 6 glomeruli were seen.
  - Negative for IgG, IgA, IgM, C3, C4, and fibrinogen
  - Positive for both Kappa and Lambda light chain

Case 3: Kidney Biopsy

Pathological Diagnosis

- ***Acute Tubulointerstitial Nephritis (Mostly Drug Induced)***

Case 3: Management and follow up

- Hydration & Supportive treatment / Allopurinol
- Pulse Steroid therapy; 1 gm Solumedrol IV infusion Daily for 3 days.
- Dexamethasone orally after that
- Thaladomide 100 mg daily
- Excellent response to treatment with very good diuresis and progressive decline in serum creatinine and normalized within 7 days:
  - 7.1– 6.2—4.7—3.6—3—2.3—1.6 mg/dl

Case 3: Management and follow up

- The patient was transferred to KHCC later on for further treatment and possible bone marrow transplant.


Thank You