Pathology of Renal Transplant

Part 1

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King Faisal Specialist Hospital & Research Centre
Gen. Org. مؤسسة عامة

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Objectives

- Renal allograft biopsy adequacy
- Renal allograft biopsy processing
- Pathological features of allograft rejection
- Banff Schema and update
- Thrombotic microangiopathy in renal allograft
- Polyoma virus nephropathy pathological features
- Teaching cases

Renal Allograft Biopsy

- What do I need to KNOW?
  - Clinically indicated vs. protocol
  - Patient age and sex
  - Primary disease (if known)
  - Date of transplantation and type of graft
  - Immunological status of the recipient
  - Biochemical / renal profile – protein and haematuria are important
  - Immunosuppressive therapy / regimen (& any possible Rx prior to Bx); levels
  - Systemic diseases (e.g., DM, HTN, chronic hepatitis)
  - Other information (e.g., viral load)

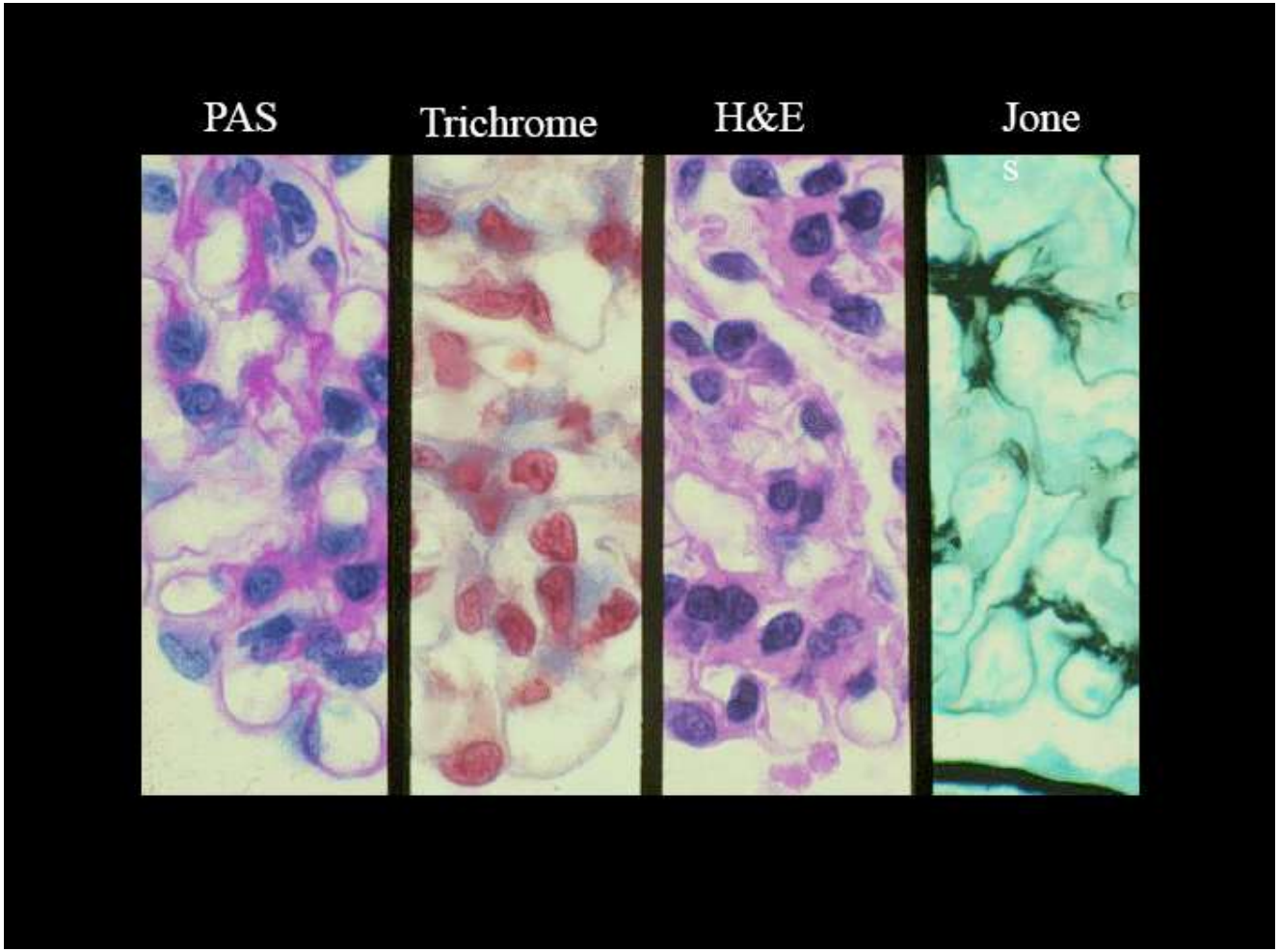
Renal Allograft Biopsy

- Adequacy of renal allograft biopsy:

  For an allograft biopsy specimen it is recommended that an adequate specimen shall contain ≥10 glomeruli and >2 arteries while minimal requirement is for seven glomeruli and 1 artery. It is also recommended that at least 2 separate cores containing cortex be obtained or there should be two separate areas of cortex in the same core.

The Banff 97 working classification of renal allograft pathology. Racusen et al. Kidney Int. 1999 Feb;55(2):713-23.

Renal Allograft Biopsy



Common Causes of Early and Late Allograft Dysfunction

Causes of Allograft Dysfunction	
Early graft dysfunction (<6 mo post transplant)	Late graft dysfunction (>6 mo post transplant)
Acute rejection Acute kidney injury Acute CNI toxicity Acute pyelonephritis Viral infections; CMV, adenovirus Urinary tract obstruction Arterial/venous thrombosis Donor related diseases	Late onset acute rejection Chronic active cellular & antibody mediated rejection Chronic CNI toxicity Hypertensive nephrosclerosis Renal artery stenois Recurrent/de novo glomerulonephritis

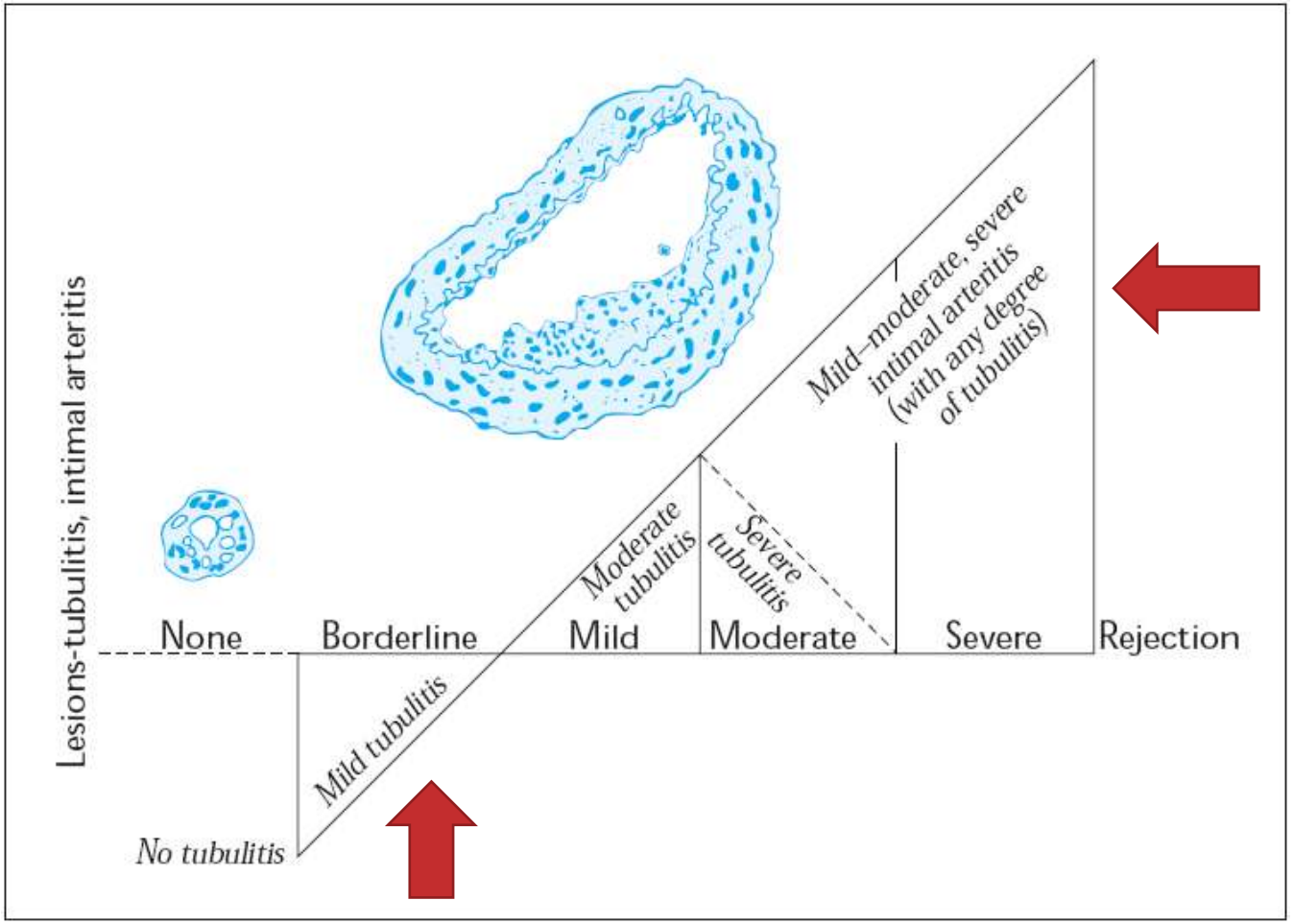
Diagnostic Categories of Renal Allograft – Banff '19 Update

- Classification of renal allograft rejection:
  1. Normal biopsy or nonspecific changes
  2. Antibody-mediated rejection (ABMR)
     - Active ABMR
     - Chronic active ABMR
     - Chronic inactive ABMR
  3. Borderline changes "Suspicious" for acute T-cell mediated rejection
  4. T-cell-mediated (cellular) rejection:
     - Acute: Grade I (A & B), Grade II (A & B) and Grade III
     - Chronic active: Grade IA, IB and II

Sis B, et al. Am J Transplant 2010;10:464-471

Hass M, et al. Am J Transplant 2018;18:293-307

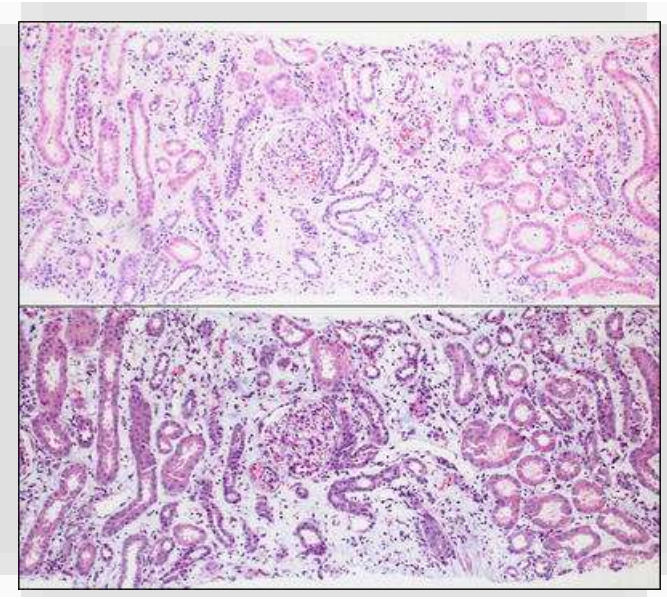
Acute T-Cell-Mediated (Cellular) Rejection

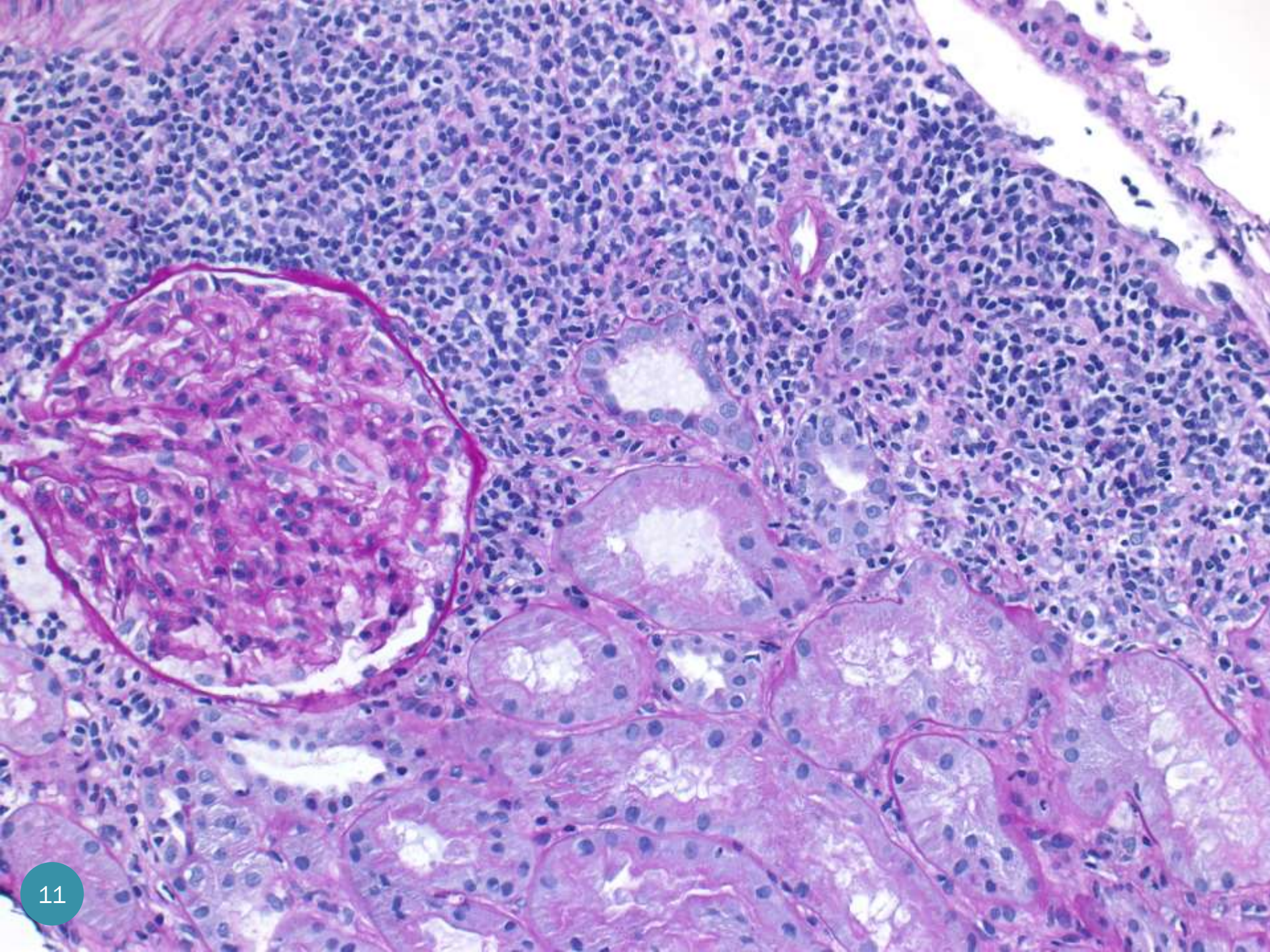


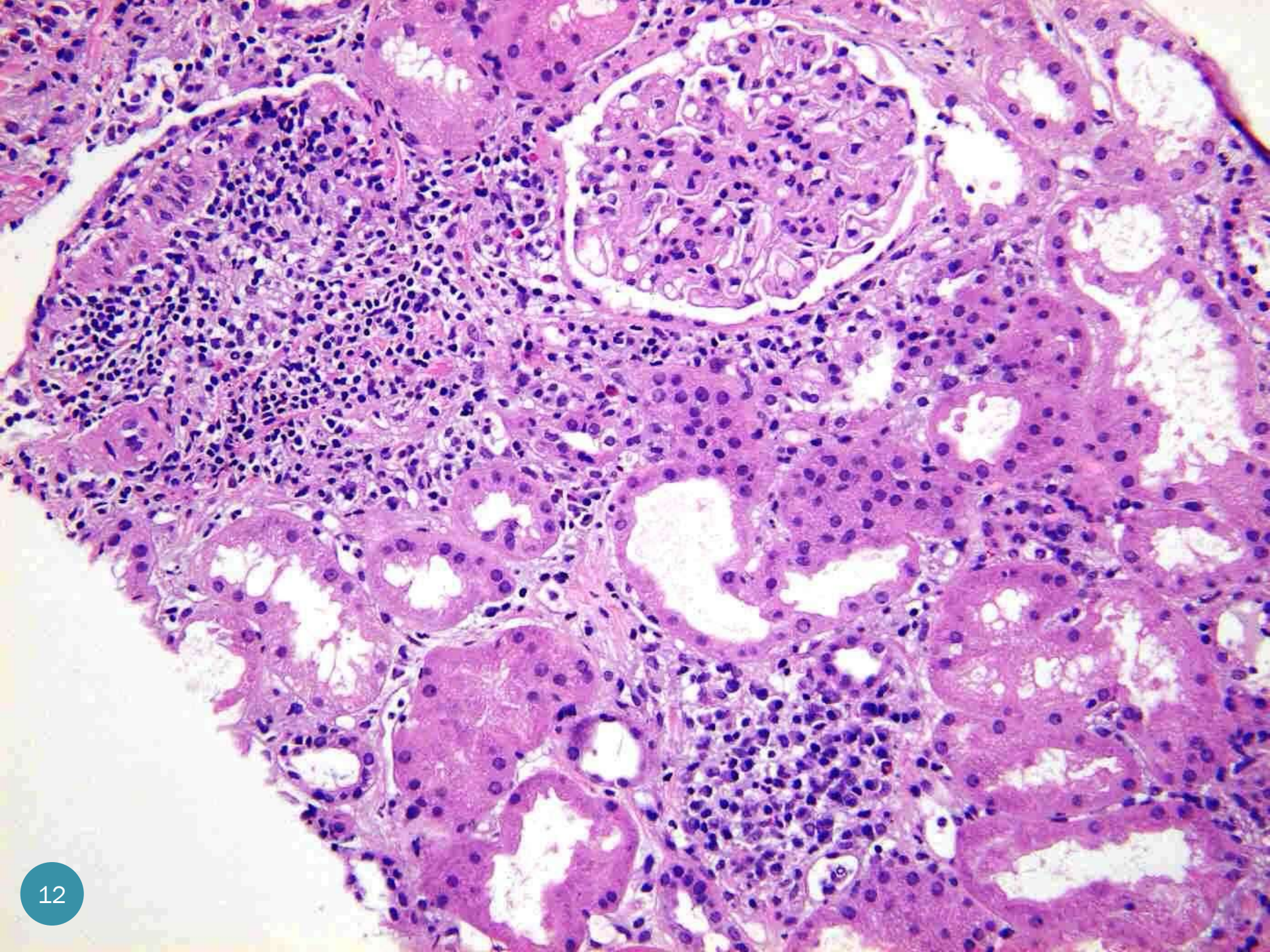
Acute T-Cell-Mediated (Cellular) Rejection

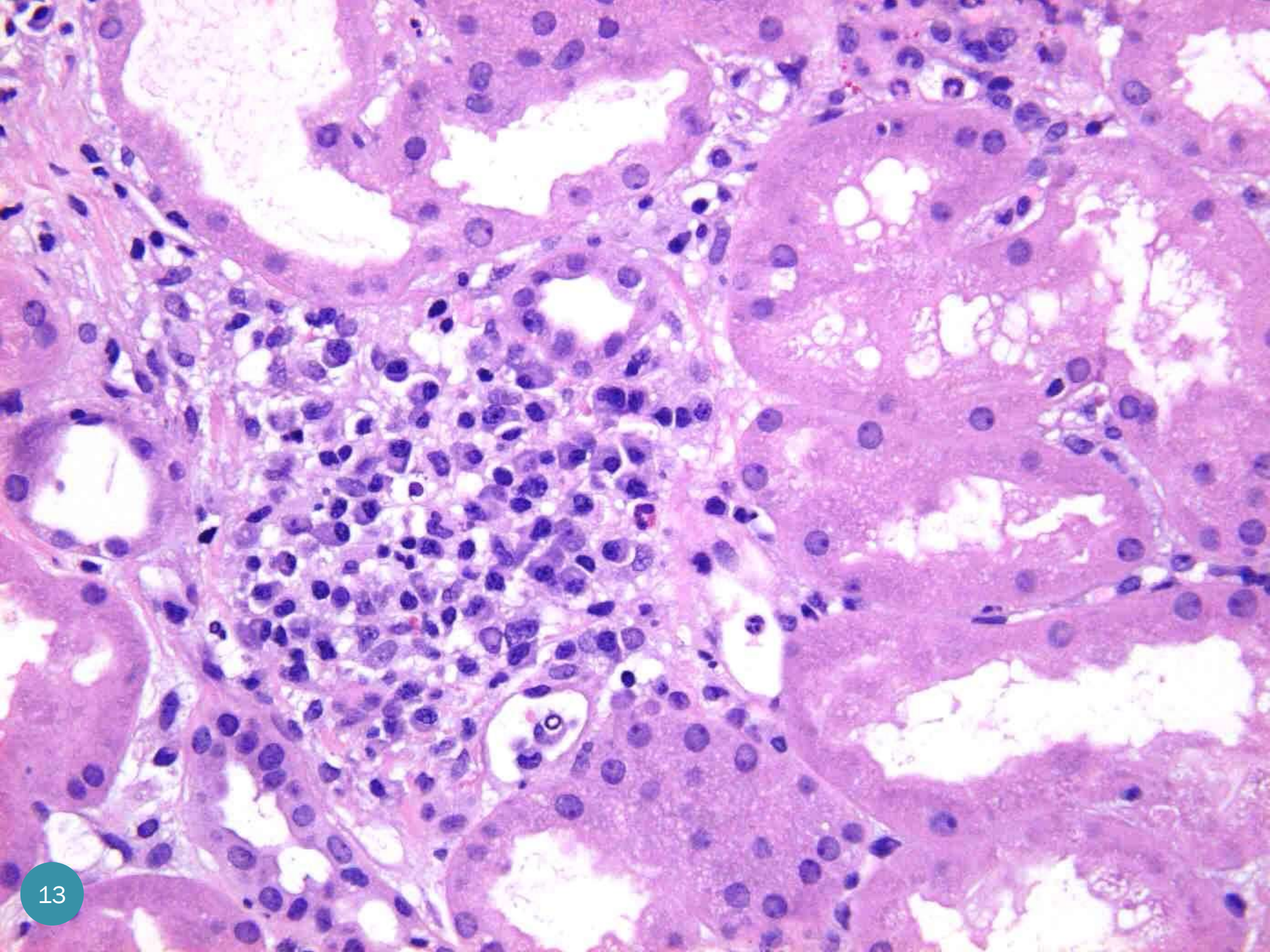
Interstitial Inflammation score

i0	No or trivial interstitial inflammation
i1	10 to 25% of parenchyma inflamed
i2	26 to 50% of parenchyma inflamed
i3	more than 50% of parenchyma inflamed





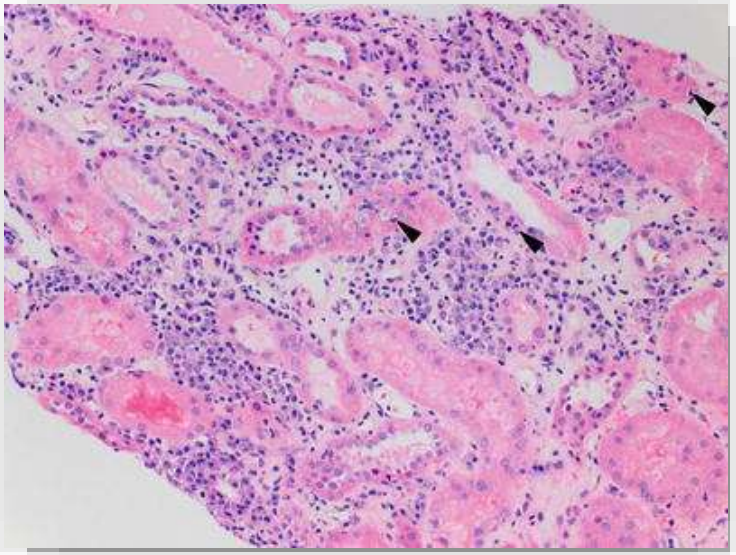




Acute T-Cell-Mediated (Cellular) Rejection

Tubulitis score

T0	No mononuclear cells in tubules
T1	Foci with 1 to 4 cells/tubular cross section (or 10 tubular cells)
T2	Foci with 5 to 10 cells/tubular cross section
T3	Foci with > 10 cells/tubular cross section, or the presence of at least two areas of tubular basement membrane destruction accompanied by i2/i3 inflammation and t2 tubulitis elsewhere in the biopsy

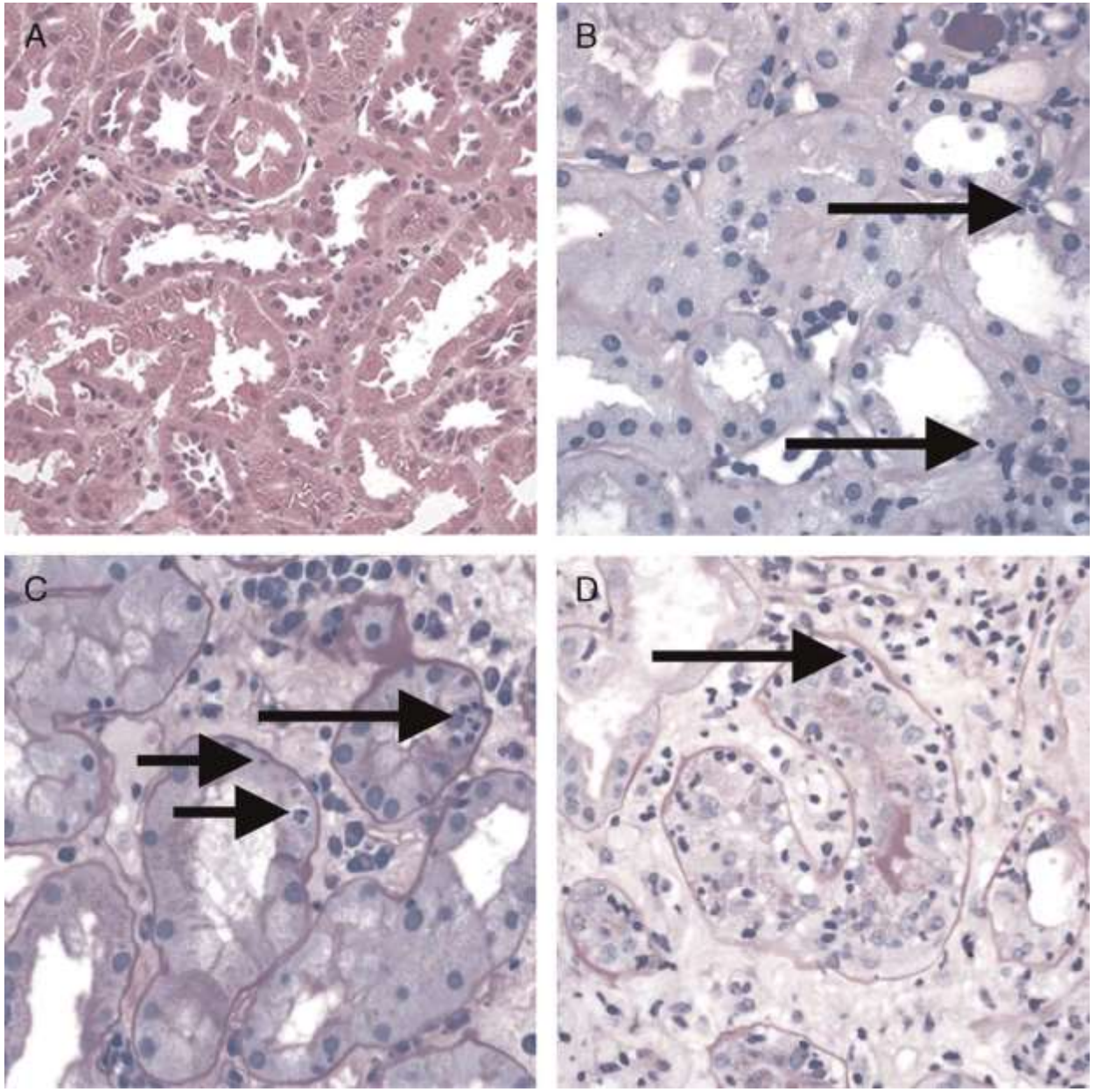


t0—No mononuclear cells in tubules or single focus of tubulitis only.

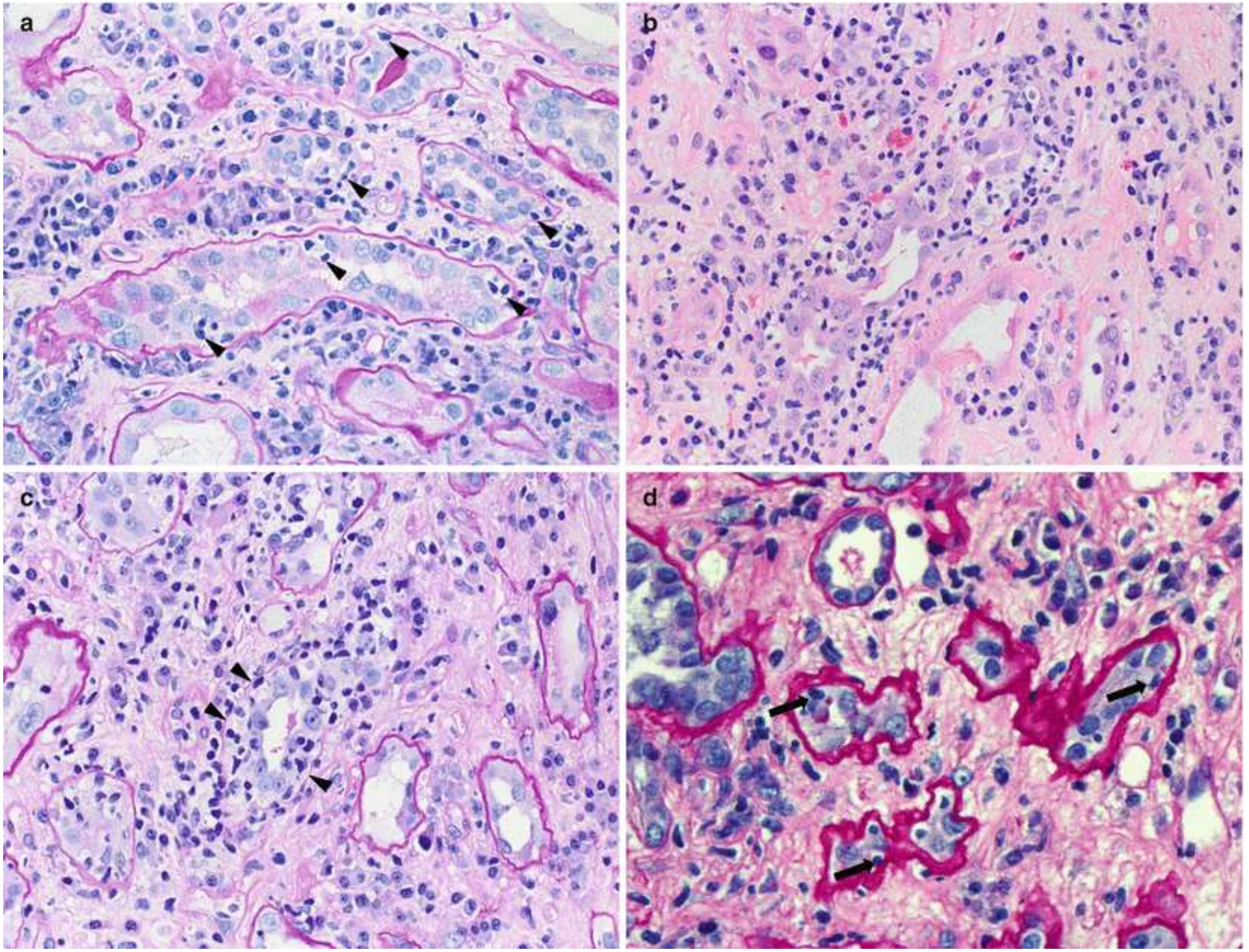
t1—Foci with 1 to 4 mononuclear cells/tubular cross section (or 10 tubular cells).

t2—Foci with 5 to 10 mononuclear cells/tubular cross section (or 10 tubular cells).

t3—Foci with >10 mononuclear cells/tubular cross section or the presence of ≥2 areas of tubular basement membrane destruction accompanied by i2/i3 inflammation and t2 elsewhere.



Roufosse et al. Transplantation 2018;102:1795-1814



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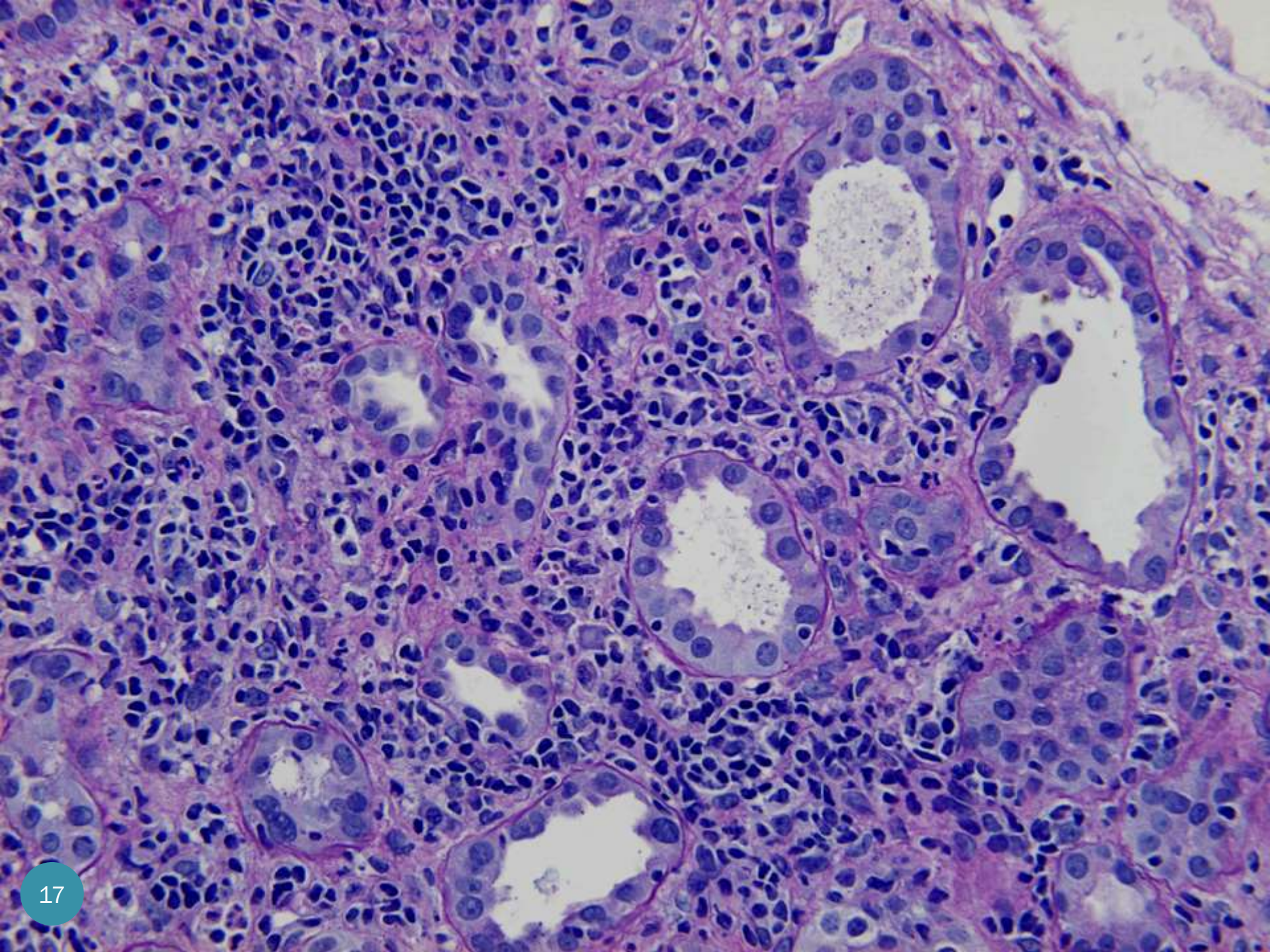
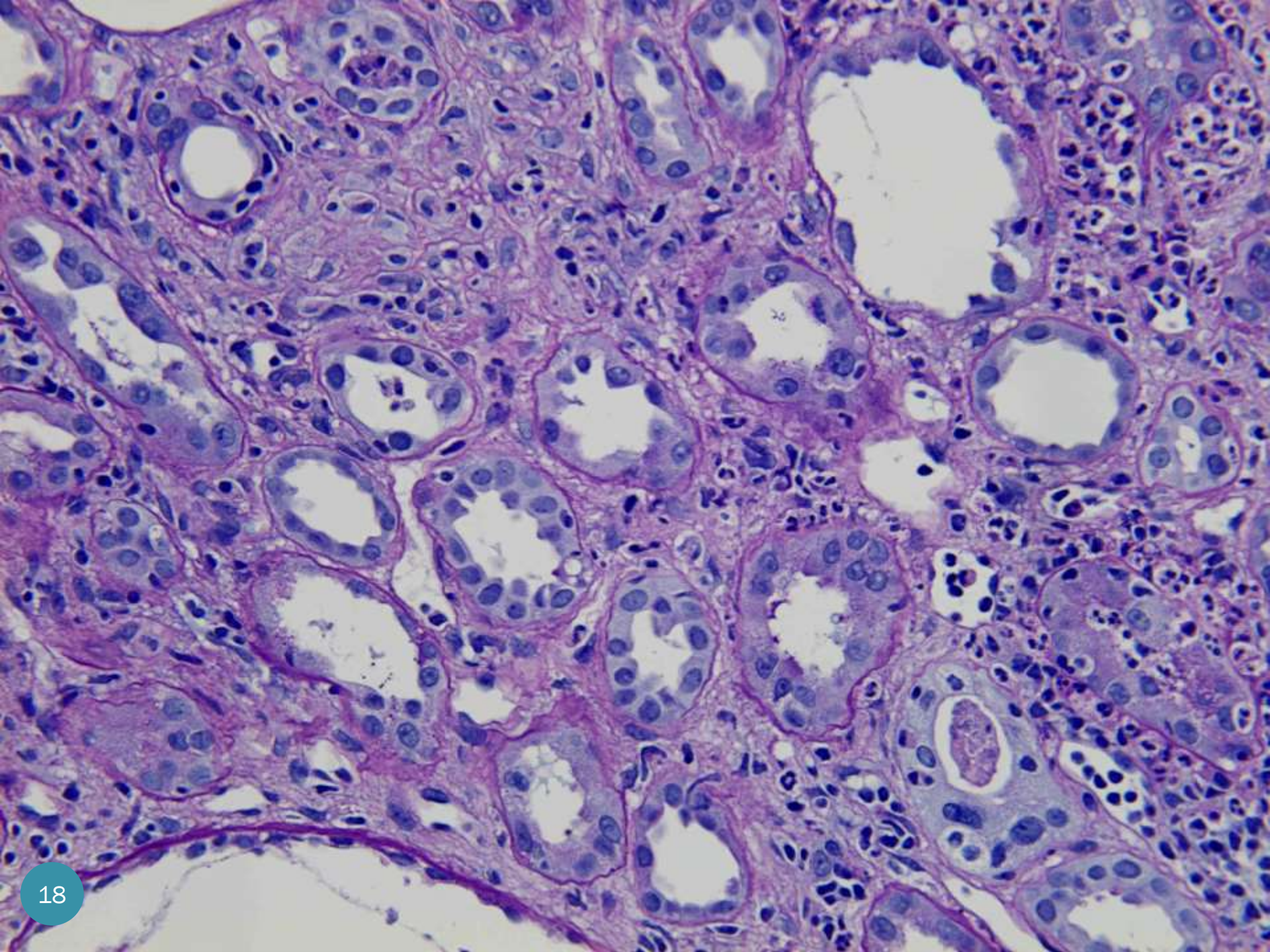
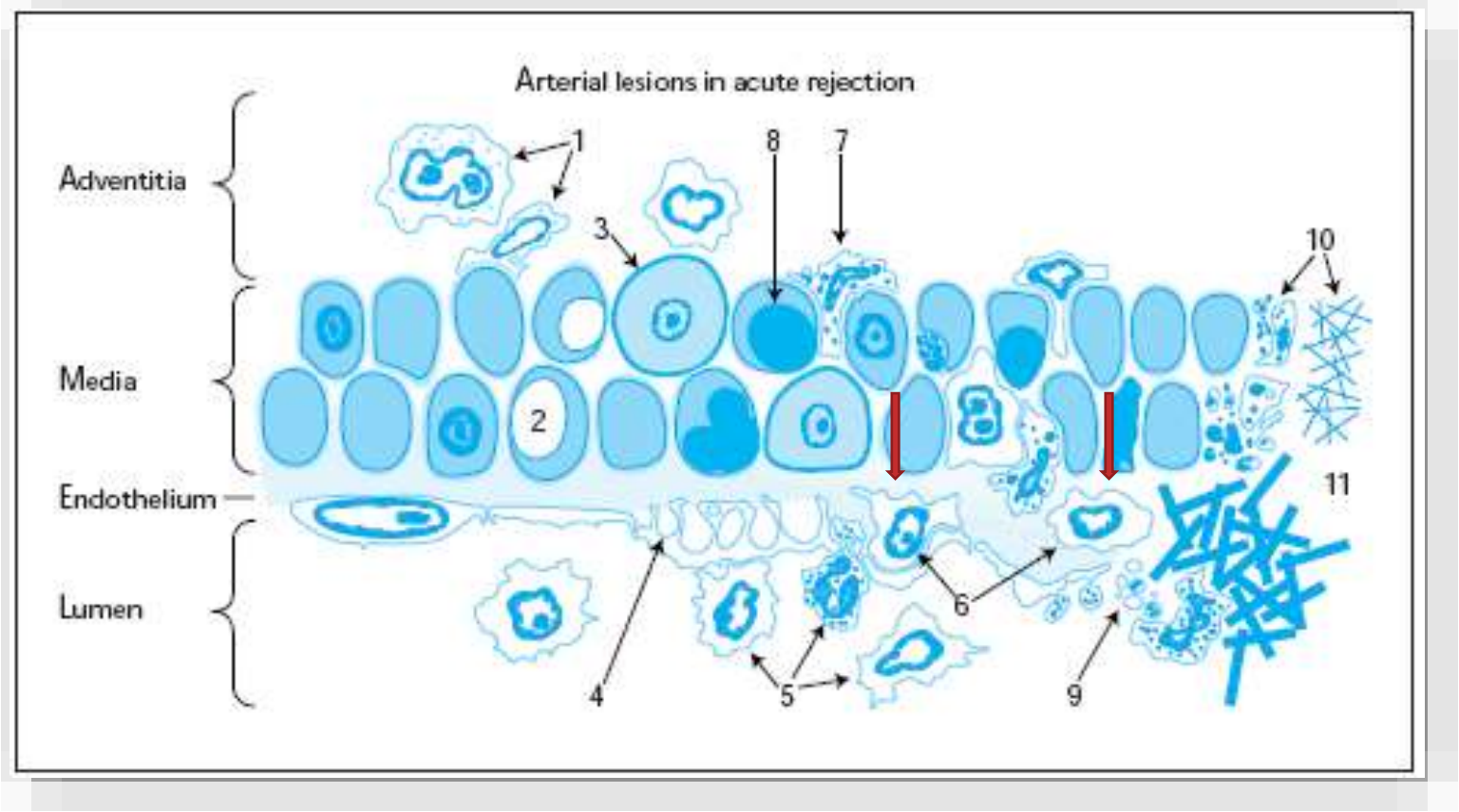


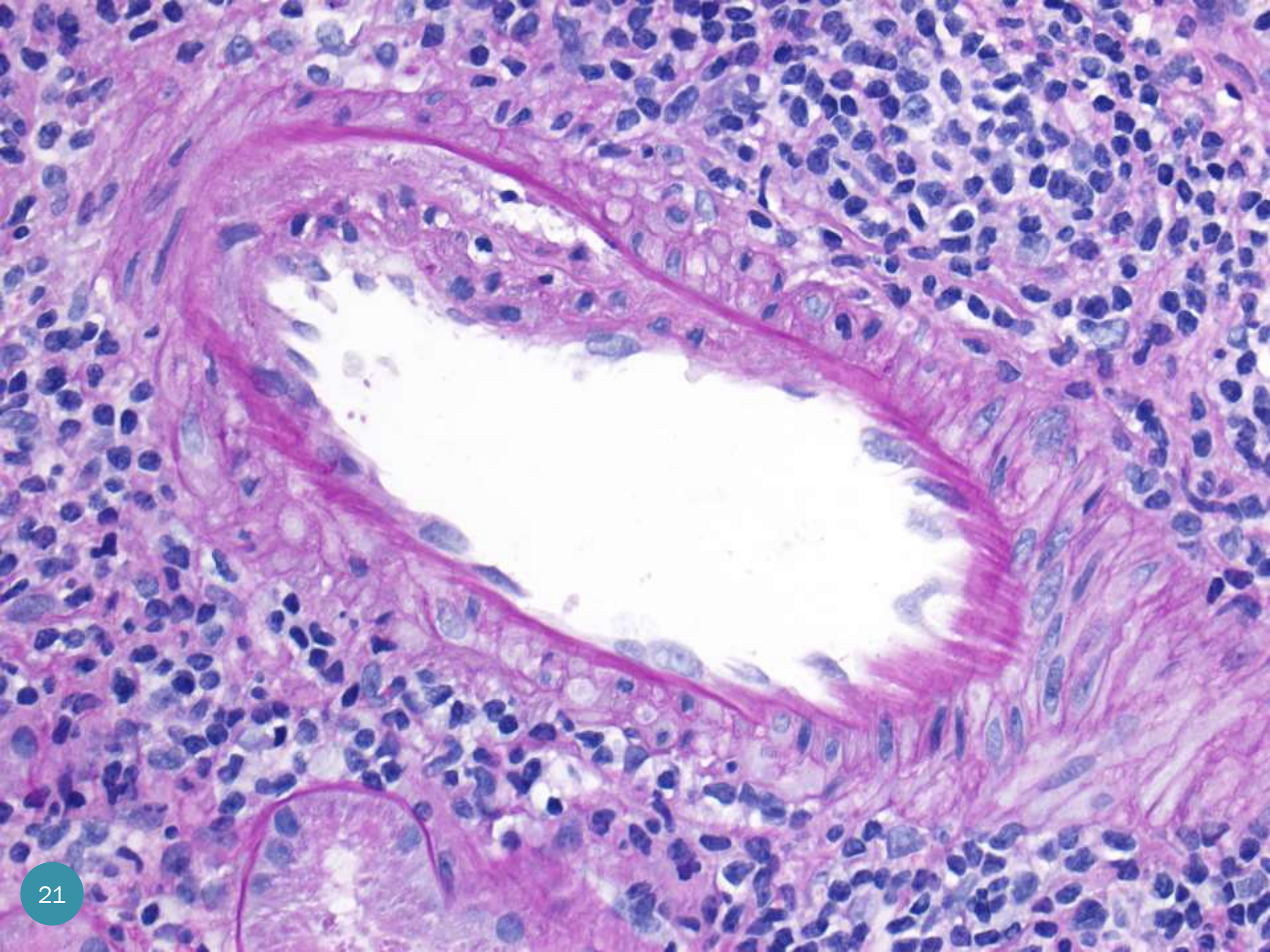


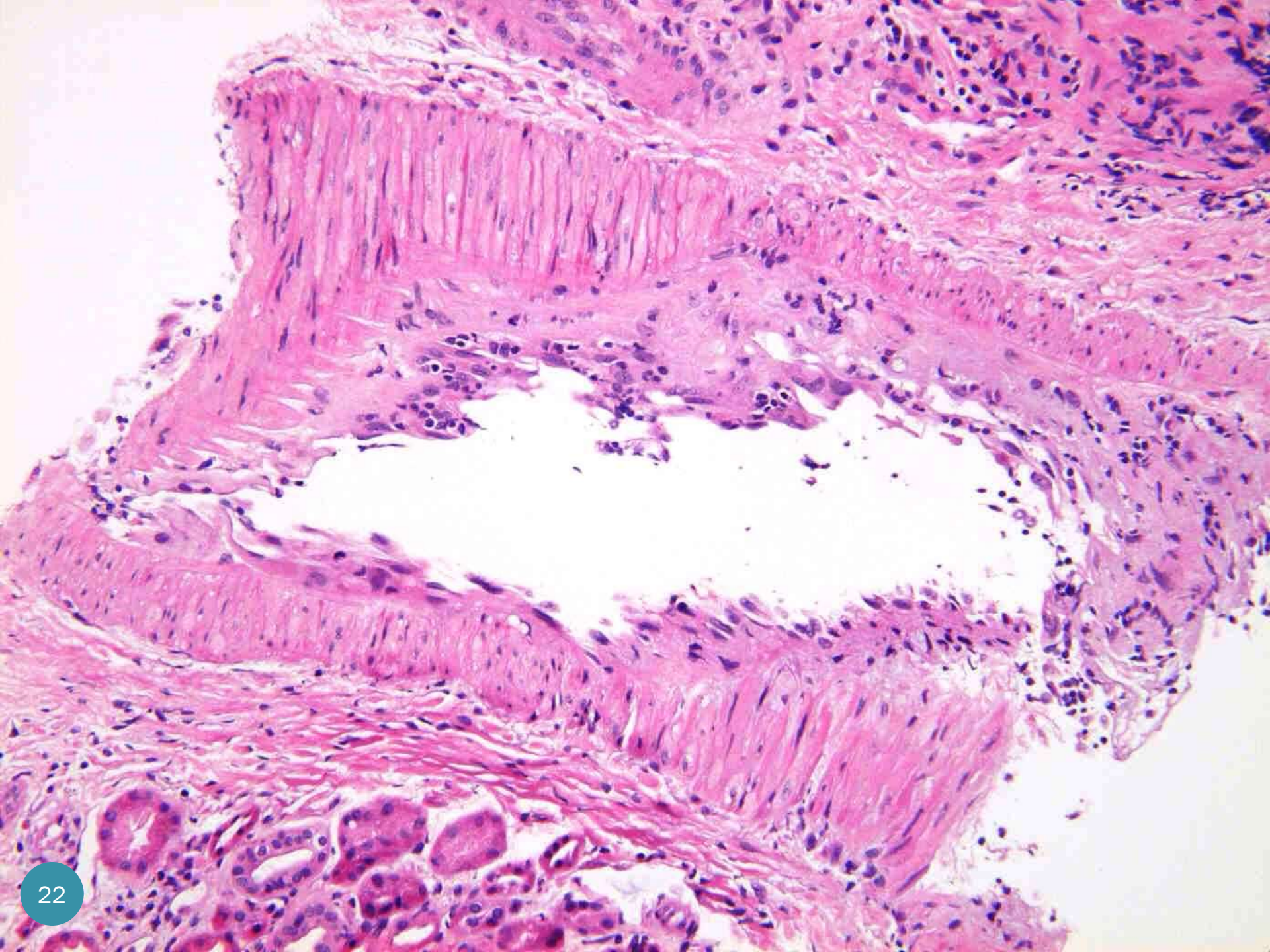
Acute T-Cell-Mediated (Cellular) Rejection

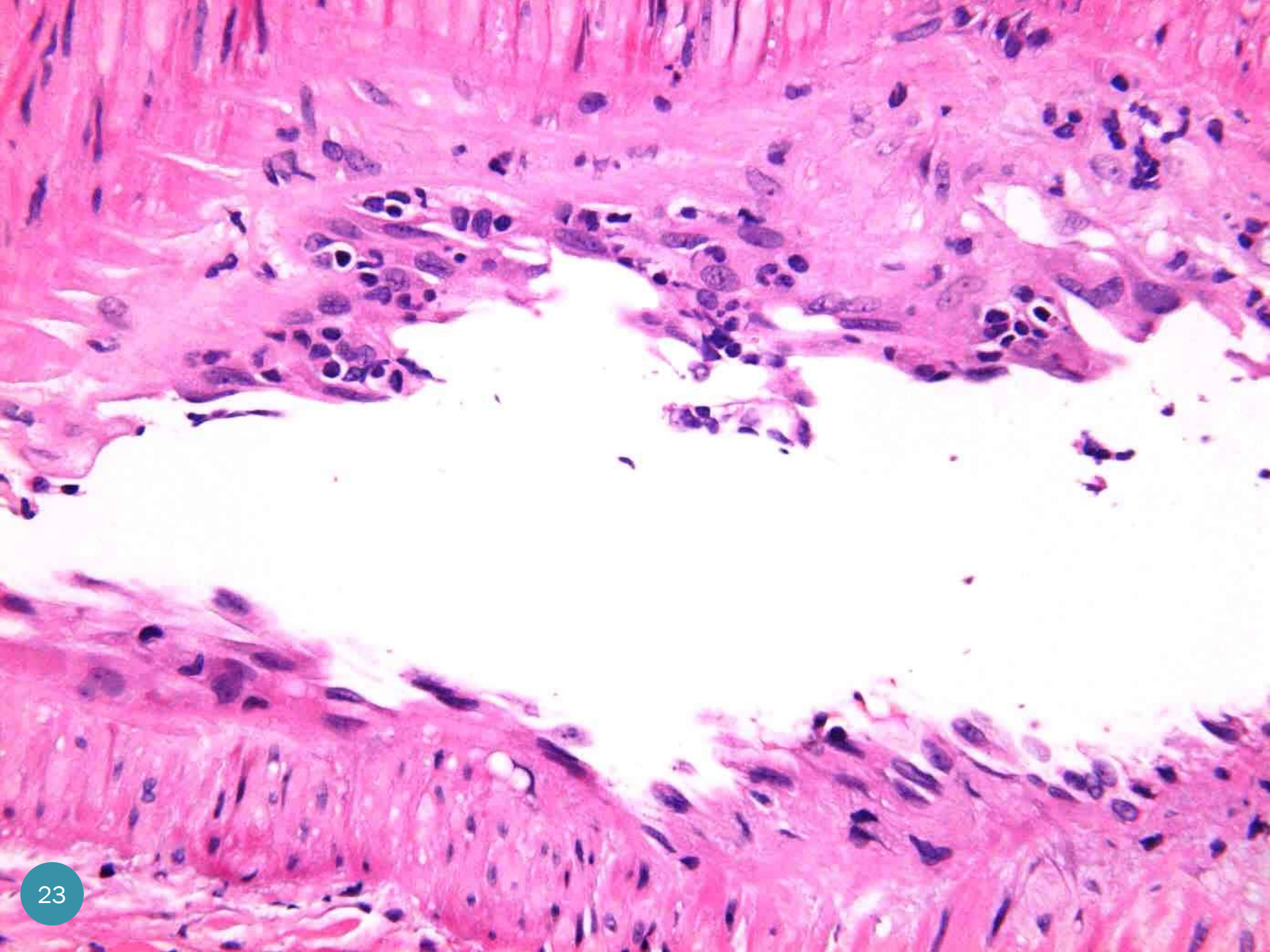
Intimal arteritis score

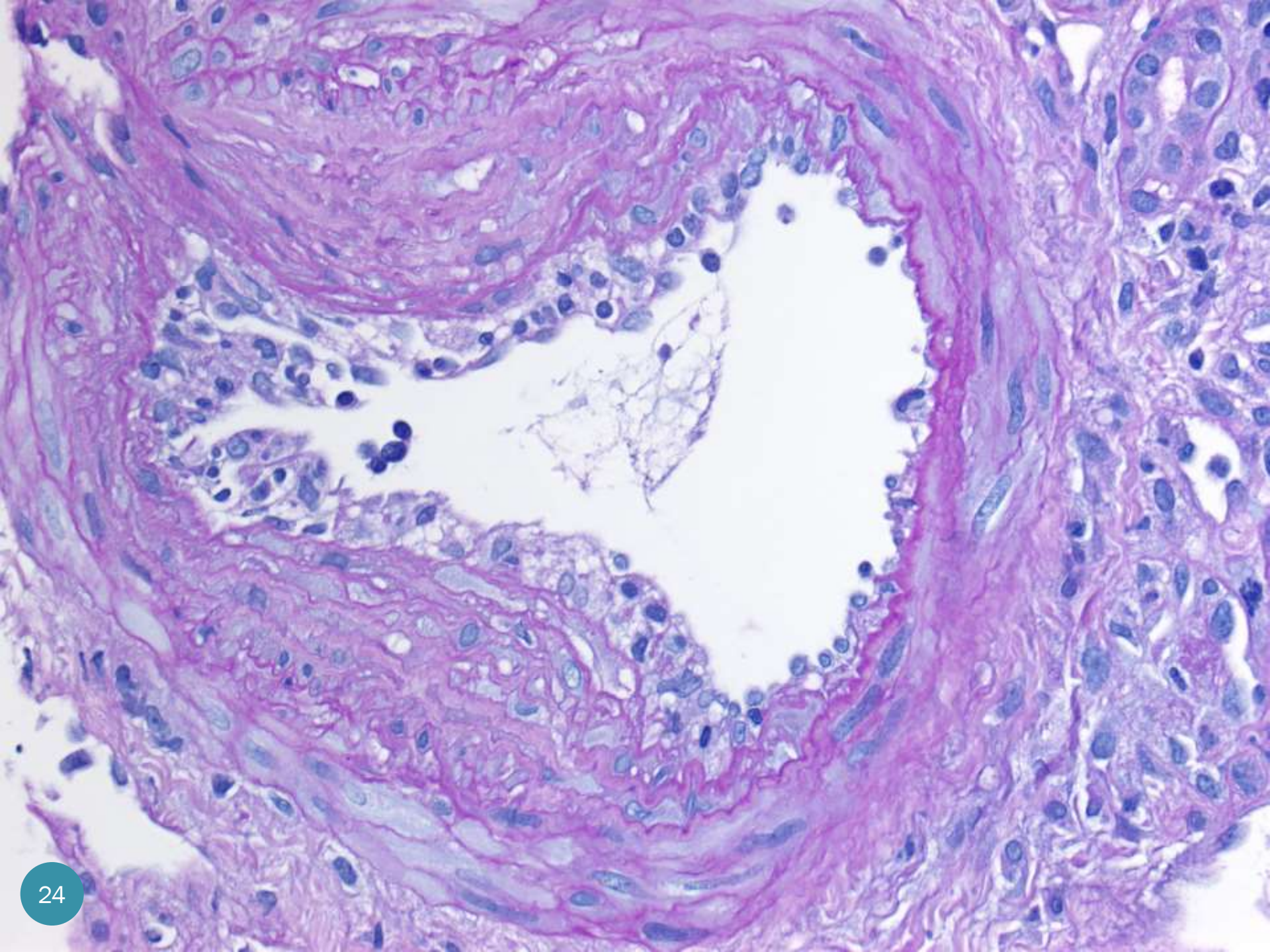
V0	No arteritis
V1	Mild-to-moderate intimal arteritis in at least one arterial cross section
V2	Severe intimal arteritis with at least 25% luminal area lost in at least arterial cross section
V3	Transmural arteritis and/or arterial fibrinoid change and medial smooth muscle necrosis with lymphocytic infiltrate in vessel

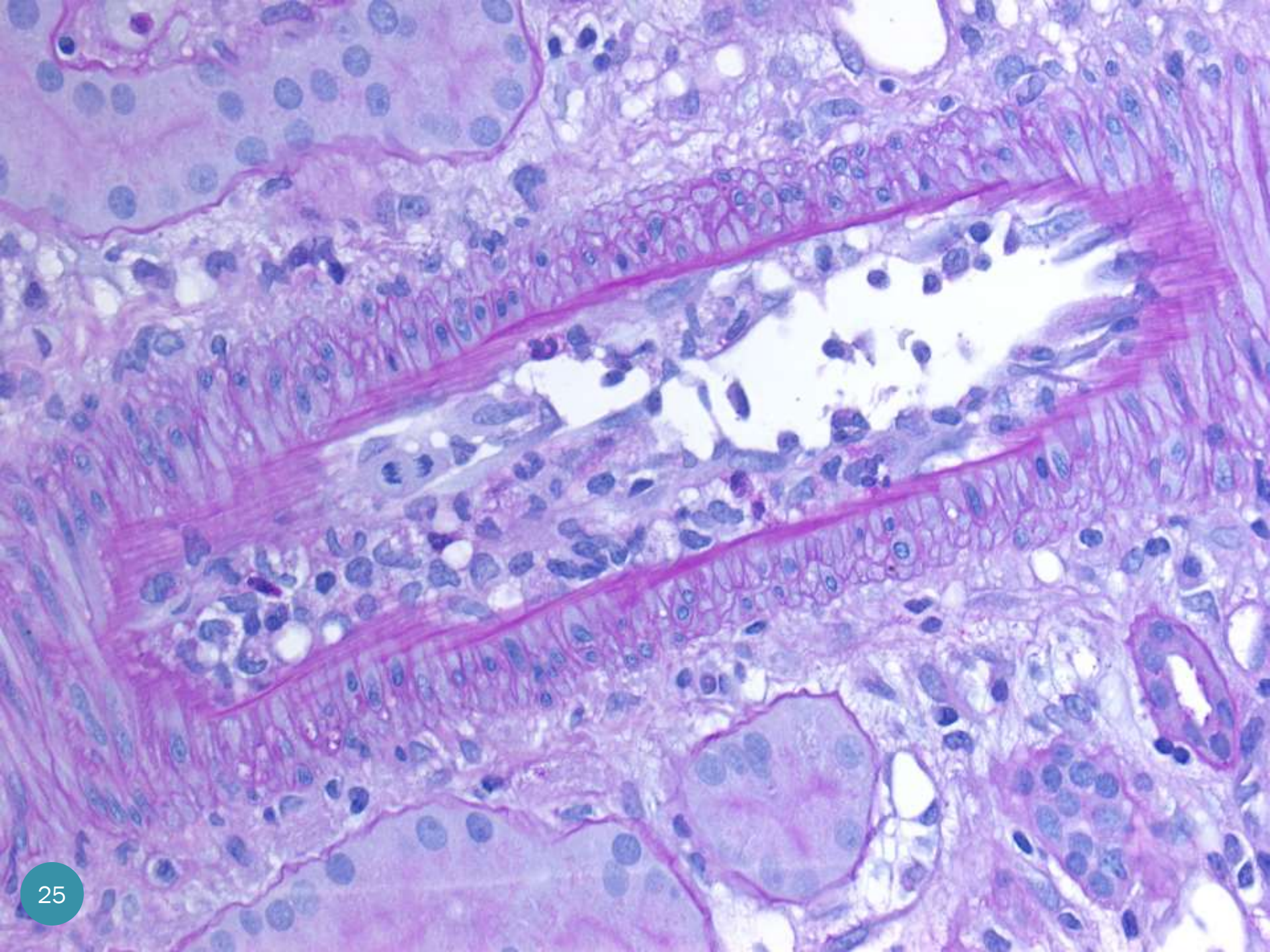

Arterial lesions in acute rejection
Adventitia
Media
Endothelium
Lumen
1
2
3
4
5
6
7
8
9
10
11

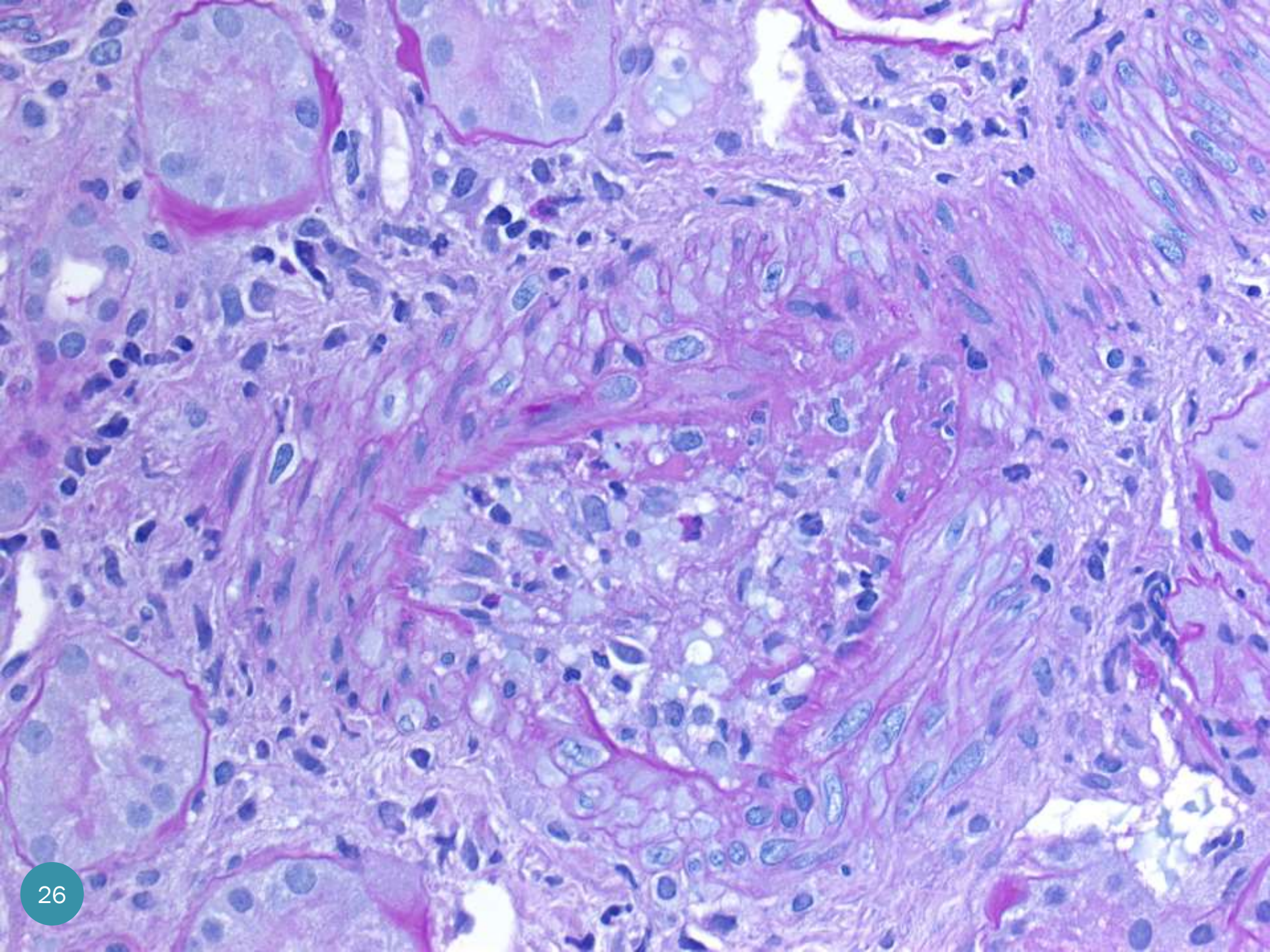


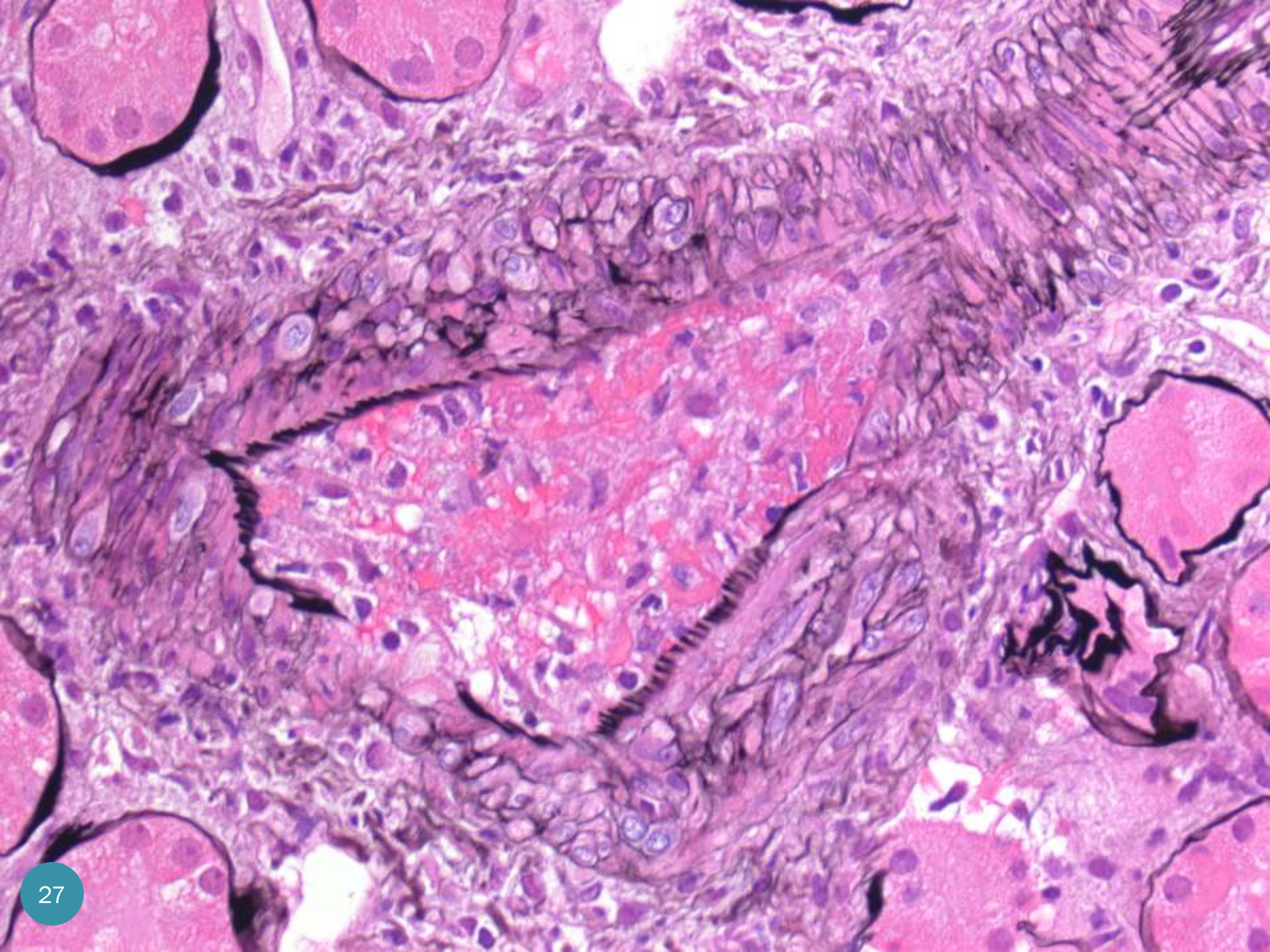


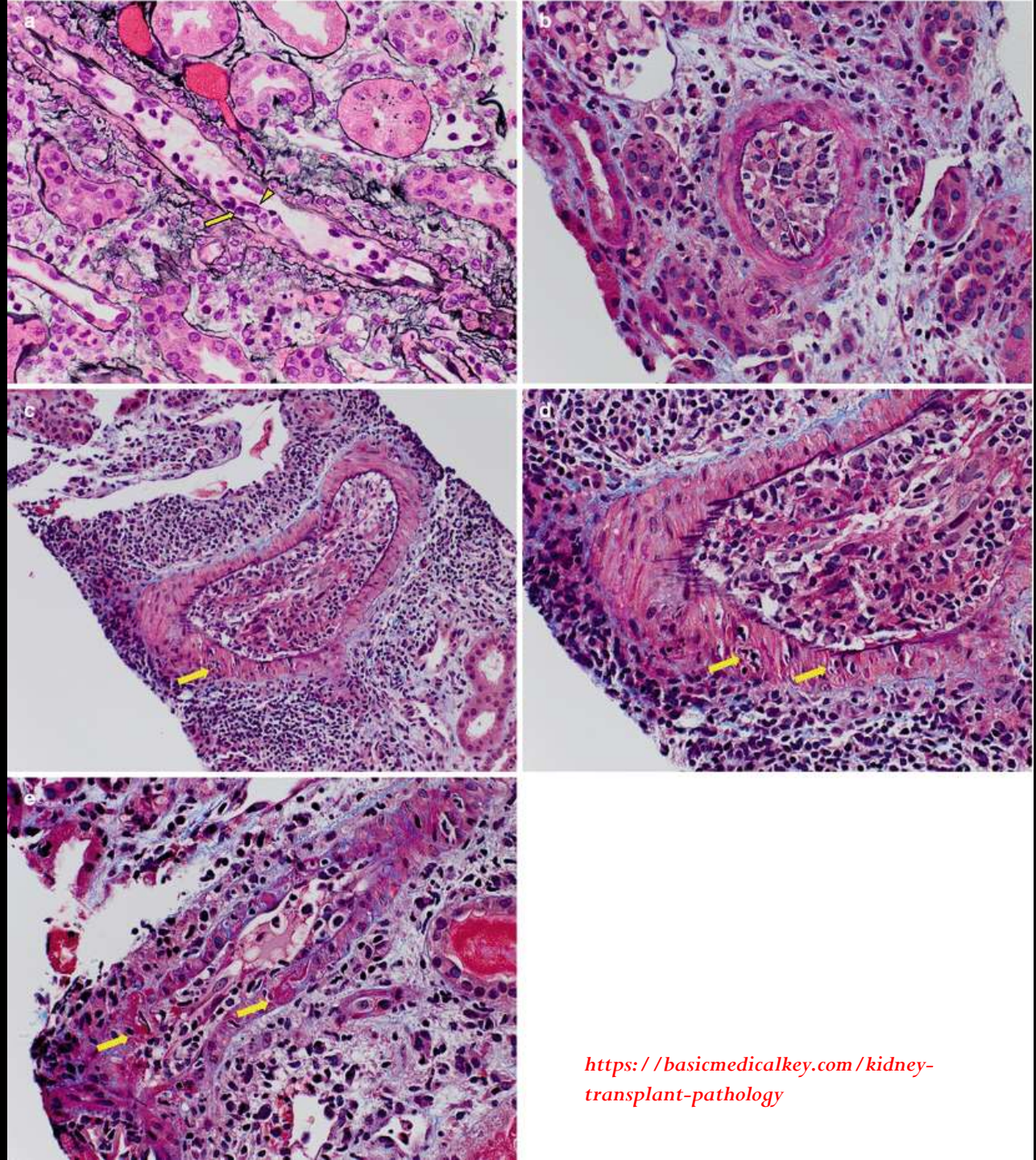












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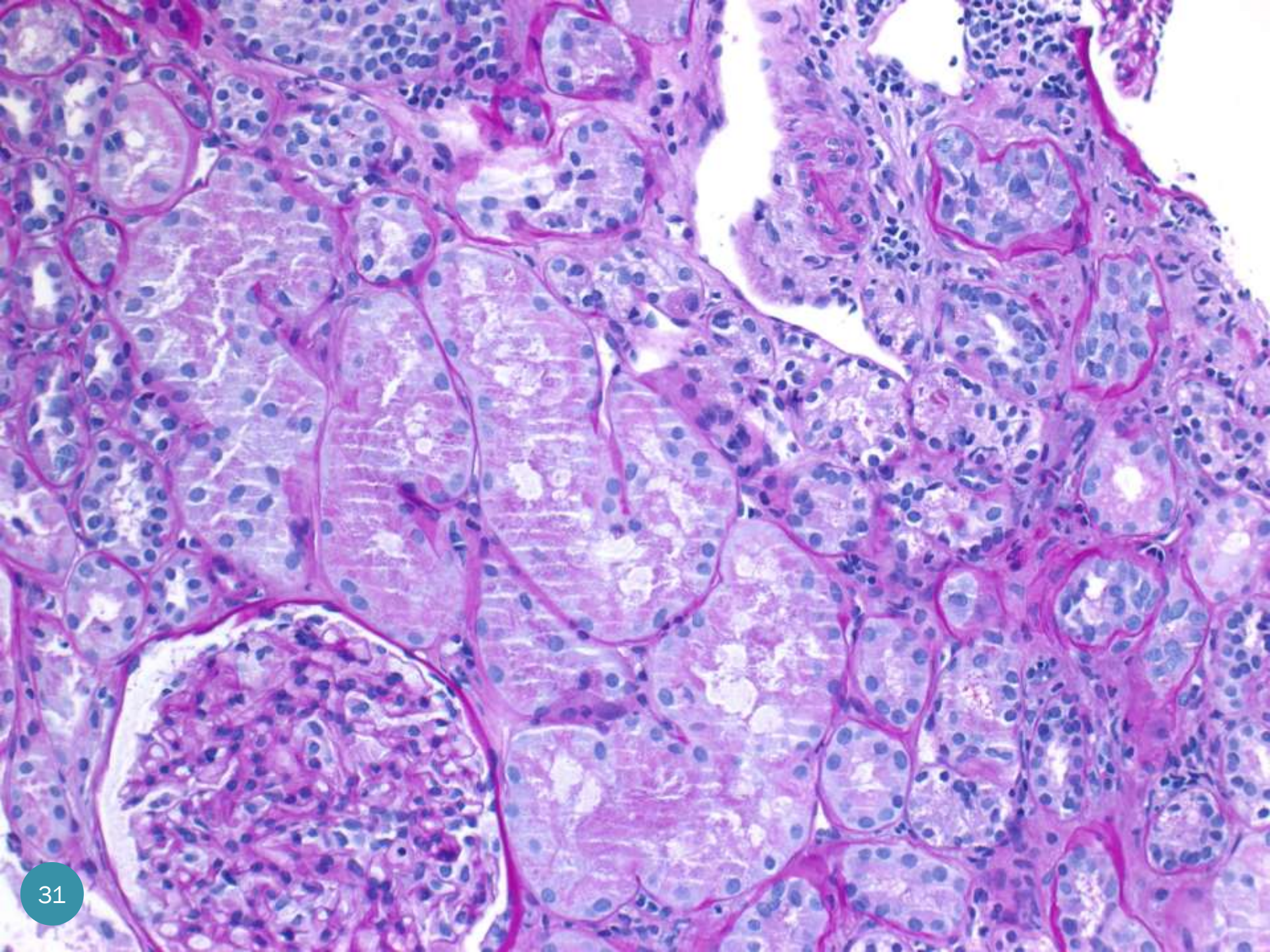
Acute T-Cell-Mediated (Cellular) Rejection

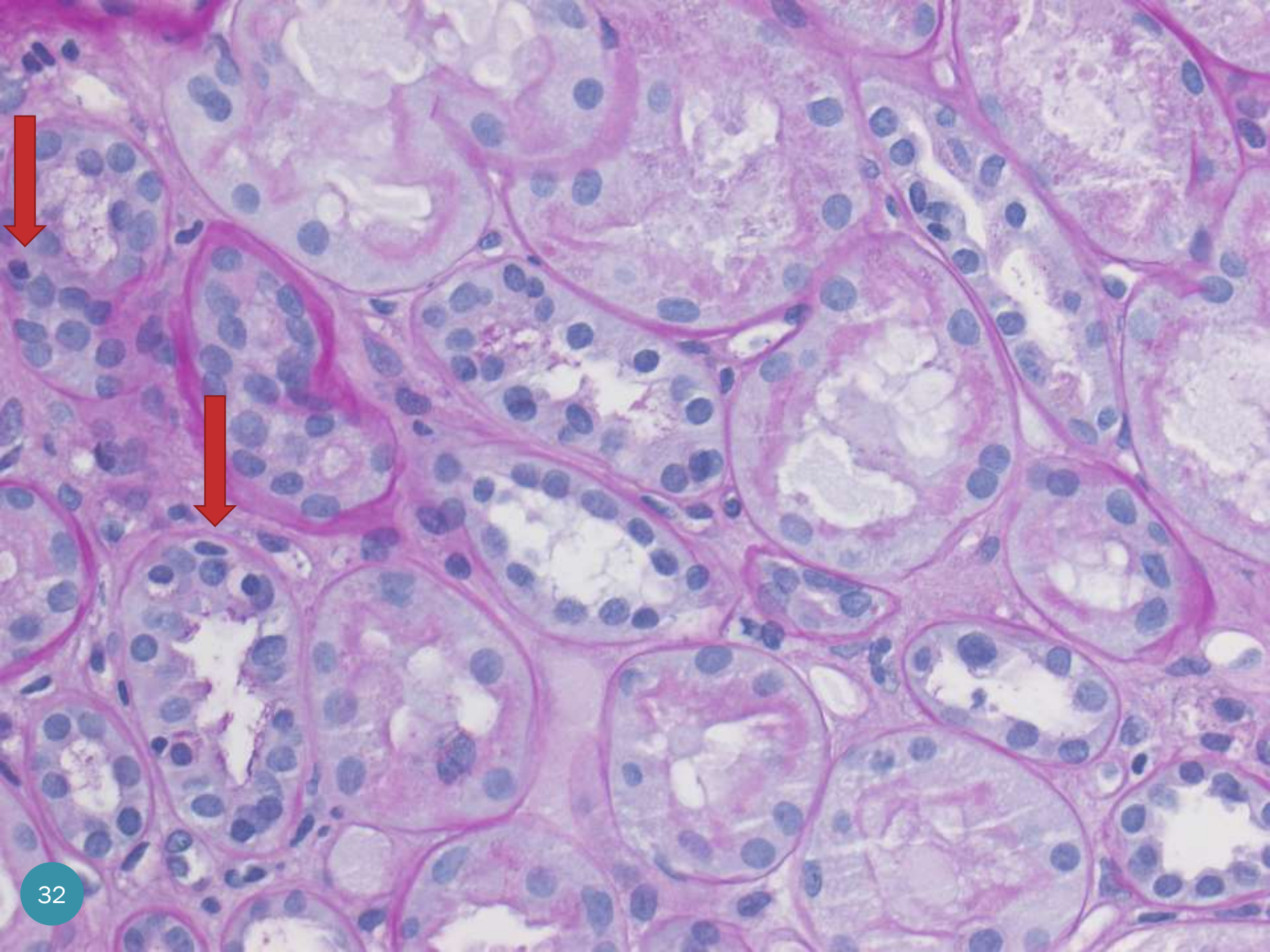
- Types / Grades of Acute TCMR:

Type	Histopathological Findings
IA	Cases with significant interstitial infiltration (>25% of parenchyma affected) and foci of moderate tubulitis (>4 mononuclear cells/tubular cross section or group of 10 tubular cells)
IB	Cases with significant interstitial infiltration (>25% of parenchyma affected) and foci of severe tubulitis (>10 mononuclear cells/tubular cross-section or group of 10 tubular cells)
IIA	Cases with mild-to-moderate intimal arteritis (v1)
IIB	Cases with severe intimal arteritis comprising >25% of the luminal area (v2)
III	Cases with 'transmural' arteritis and/or arterial fibrinoid change and necrosis of medial smooth muscle cells with accompanying lymphocytic inflammation (v3)

Borderline Changes “Suspicious” for Acute T-Cell-Mediated Rejection

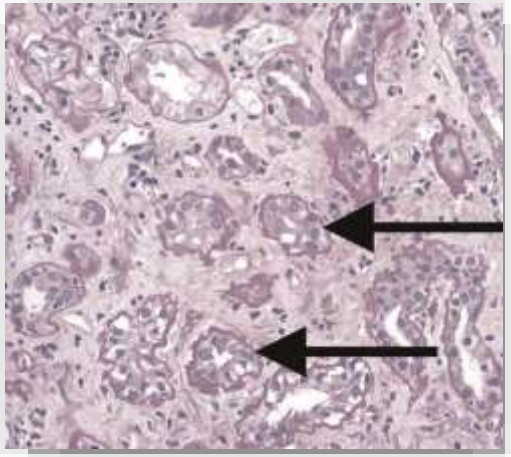
- This category is used when no intimal arteritis is present, but there are foci of tubulitis (t1, t2 or t3) with minor interstitial infiltration (i0 or i1) or interstitial infiltration (i2, i3) with mild (t1) tubulitis.

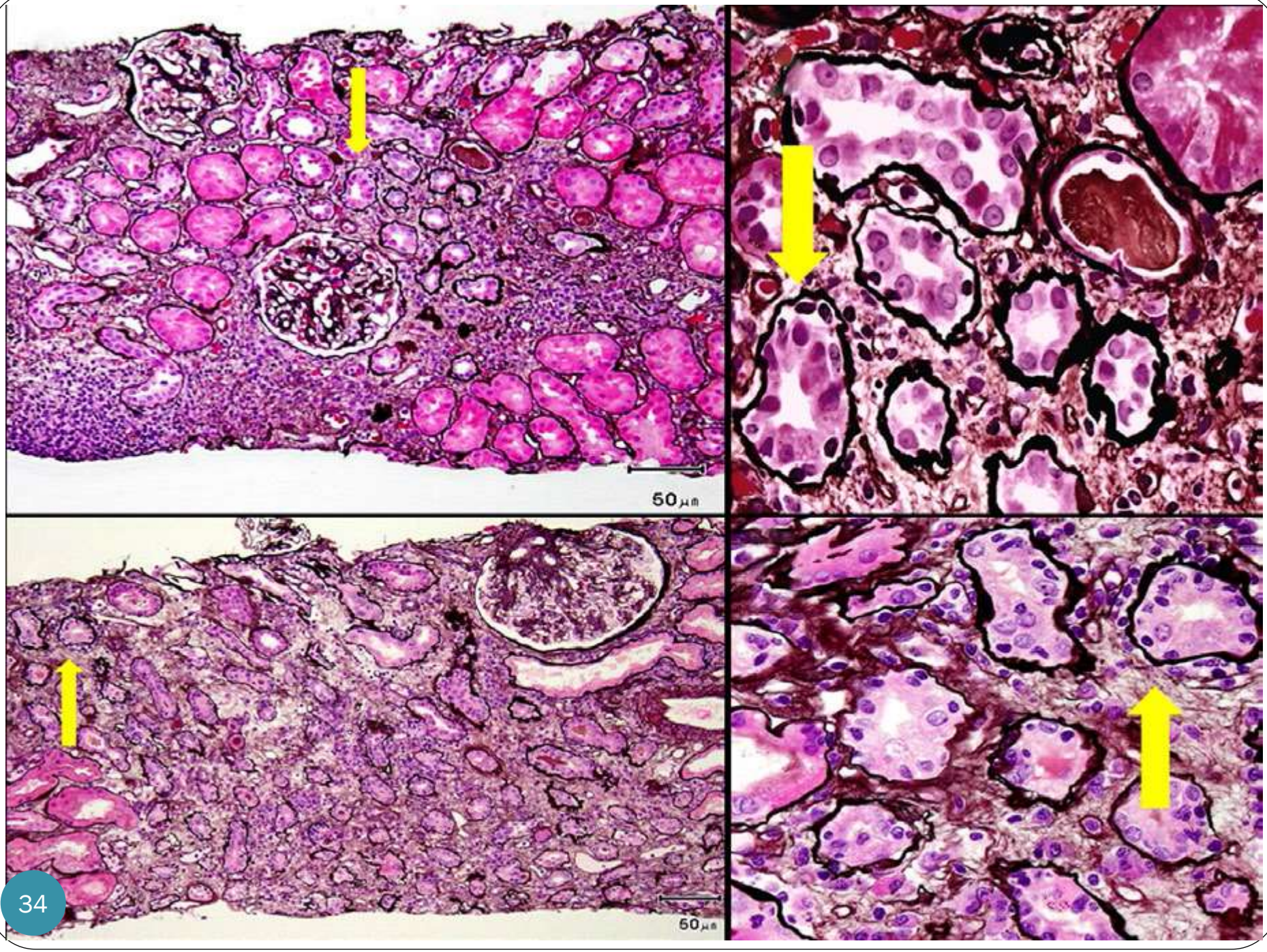




Chronic Active T-Cell Mediated Rejection

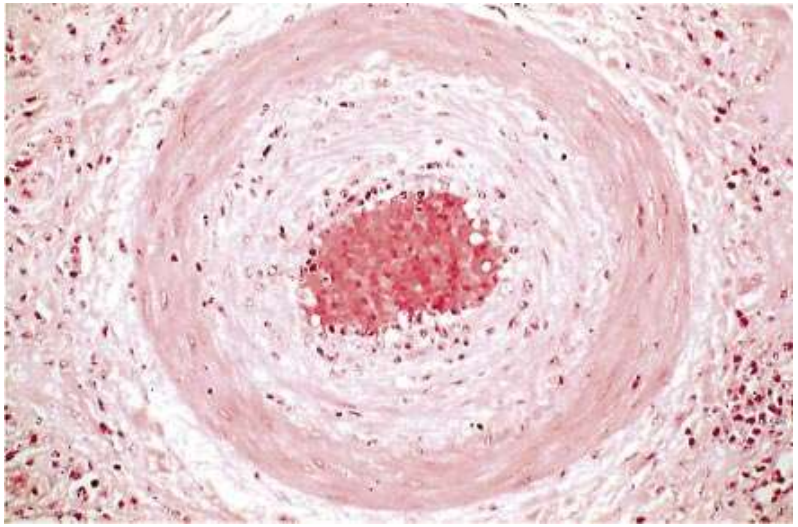
Chronic Active TCMR	
Grade IA	Interstitial inflammation involving >25% of the total cortex (ti score 2 or 3) and >25% of the sclerotic cortical parenchyma (i-IFTA score 2 or 3) with moderate tubulitis (t2) involving 1 or more tubules, not including severely atrophic tubules[5]; other known causes of i-IFTA should be ruled out
Grade IB	Interstitial inflammation involving >25% of the total cortex (ti score 2 or 3) and >25% of the sclerotic cortical parenchyma (i-IFTA score 2 or 3) with severe tubulitis (t3) involving 1 or more tubules, not including severely atrophic tubules[5]; other known causes of i-IFTA should be ruled out
Grade II[1]	Chronic allograft arteriopathy (arterial intimal fibrosis with mononuclear cell inflammation in fibrosis and formation of neointima)

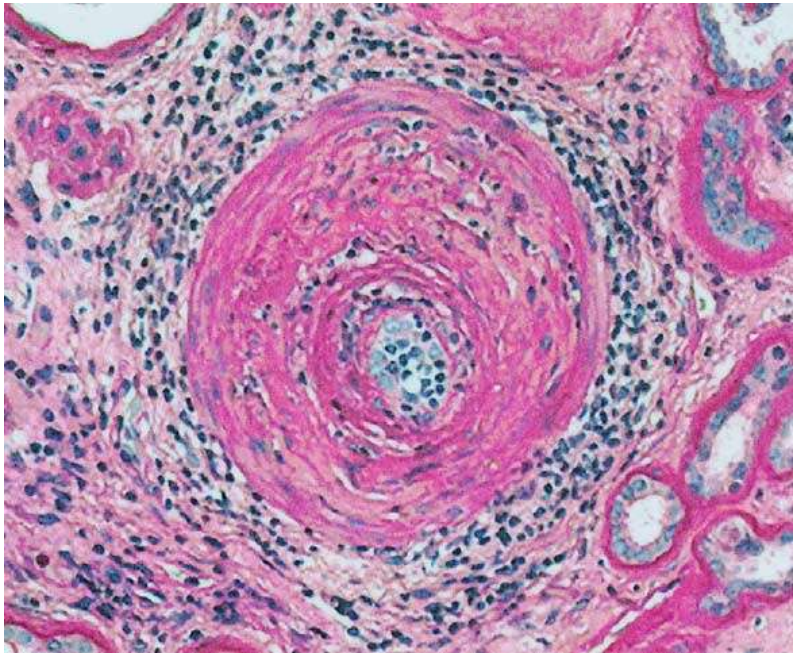



50µm
50µm

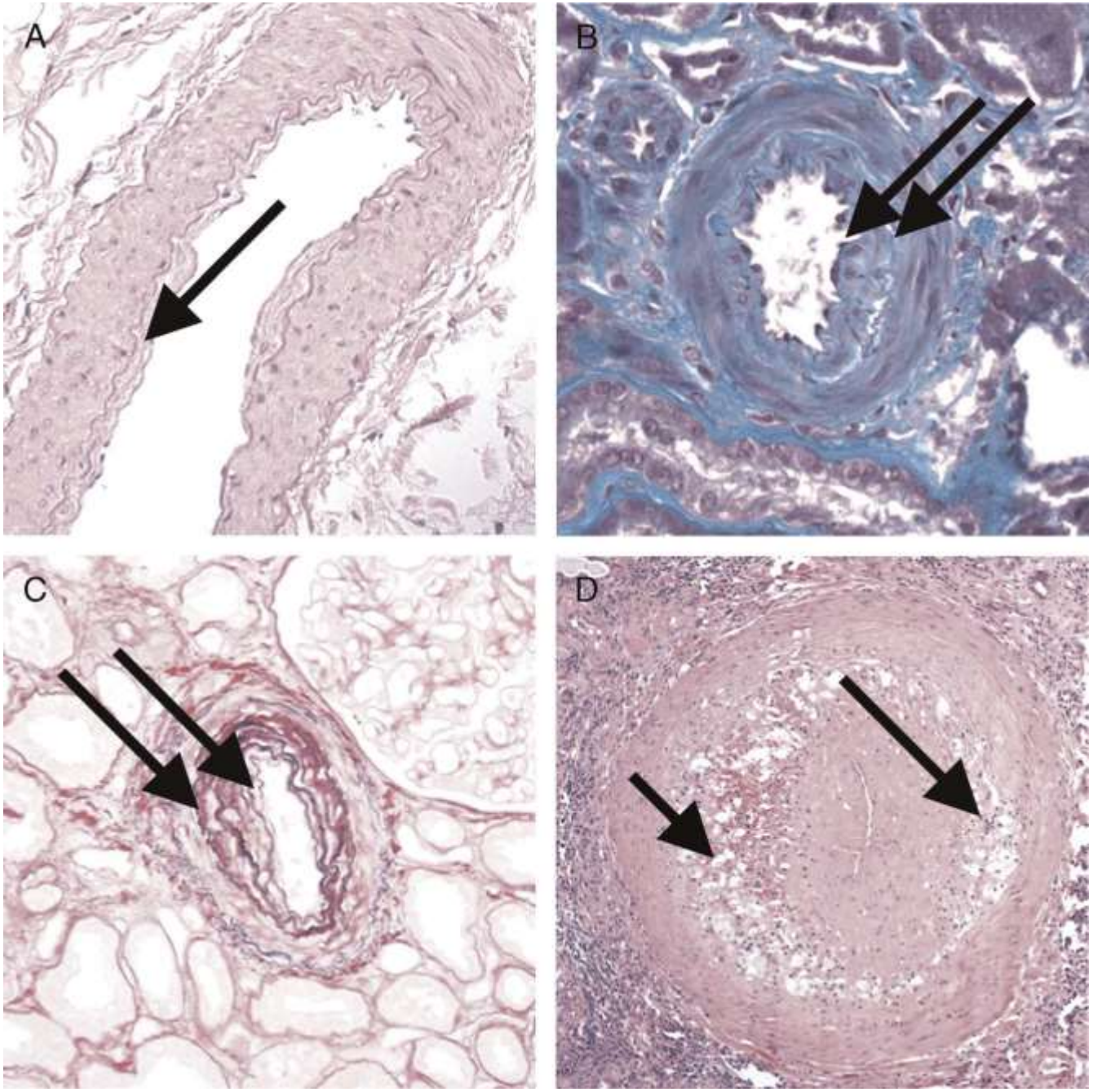
Chronic Active T-Cell Mediated Rejection

- Chronic TCMR, Grade II
  - Arterial intimal fibrosis with mononuclear cell infiltration in fibrosis and formation of neo-intima.





Chronic Active T-Cell Mediated Rejection Grade II



Roufosse et al. Transplantation 2018;102:1795-1814

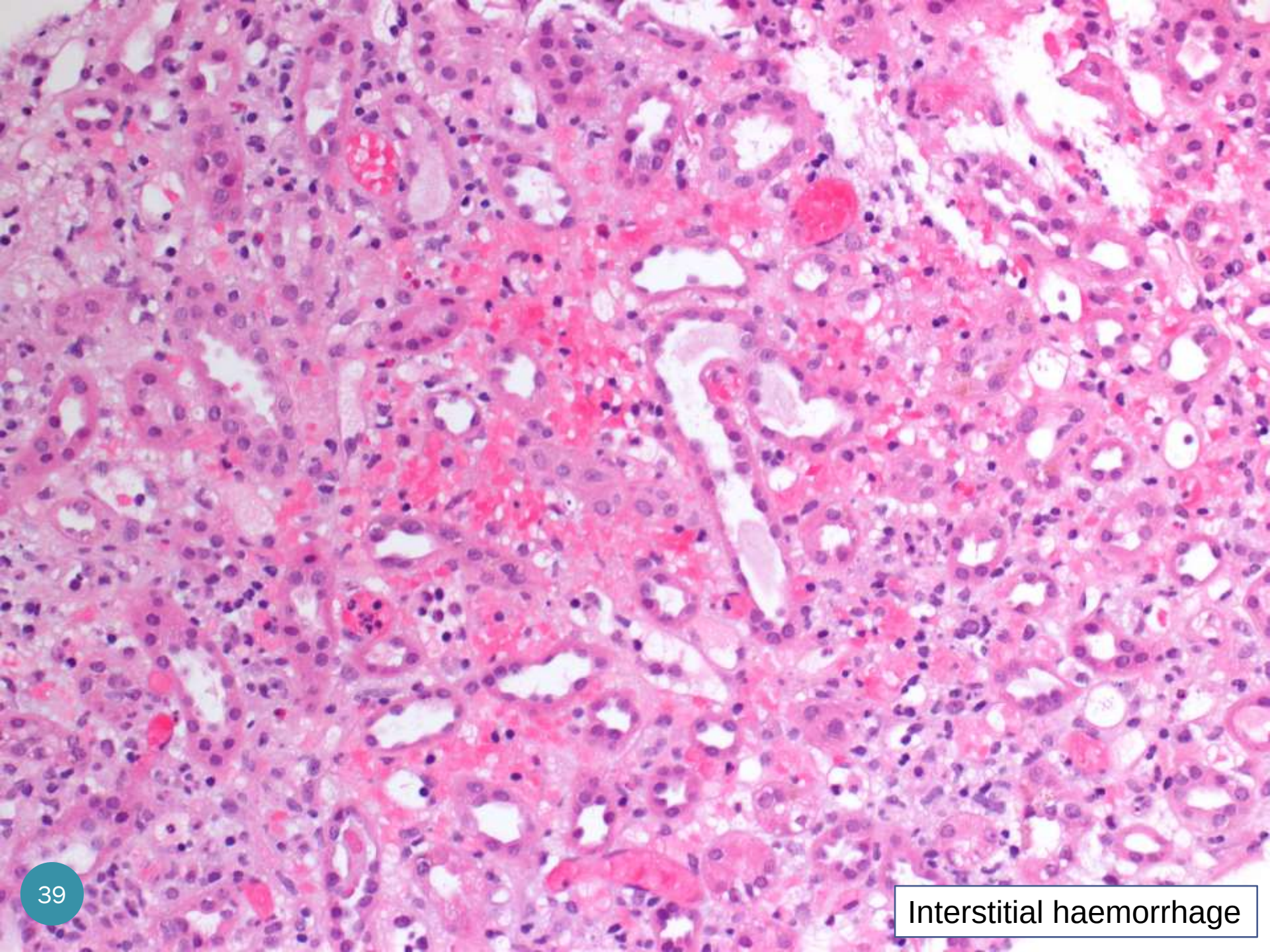
Active Antibody Mediated Rejection

- Antibody-mediated rejection histological features:
  1. ATN-like tubular injury / Acute kidney injury
  2. Glomerulitis
  3. Dilatation of the cortical peritubular capillaries
  4. Capillaritis (neutrophils and/or mononuclear leukocytes in peritubular capillaries)
  5. Arterial inflammation/fibrinoid change
  6. Interstitial oedema and haemorrhage
  7. C4d membranous circumferential positivity in the cortical peritubular capillaries (by IF or IHC).

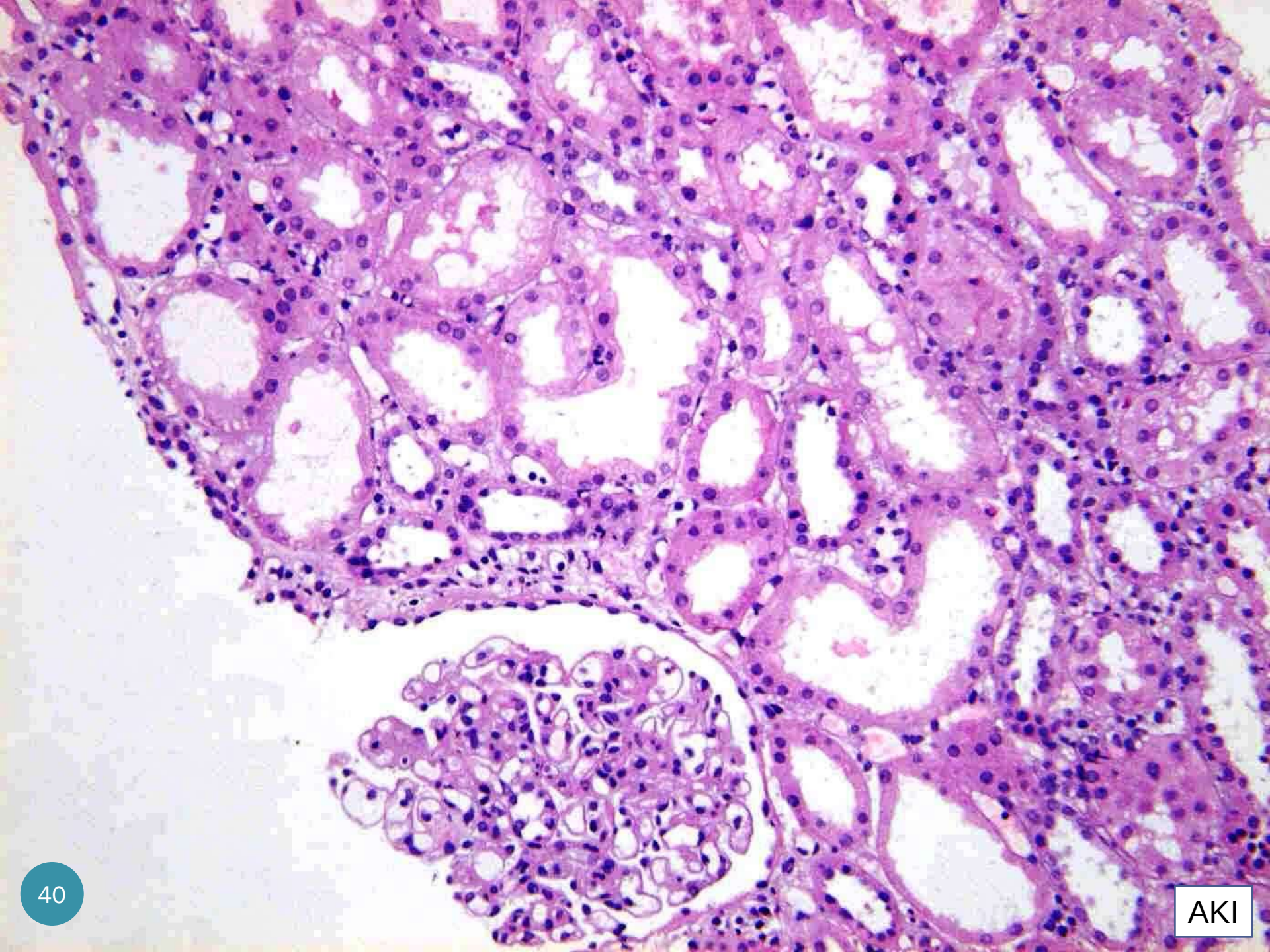
Active Antibody Mediated Rejection

Active ABMR; all 3 criteria must be met for diagnosis

1. Histologic evidence of acute tissue injury, including 1 or more of the following:
   Microvascular inflammation (g > 0 and/or ptc > 0), in the absence of recurrent or de novo glomerulonephritis, although in the presence of acute TCMR, borderline infiltrate, or infection, ptc ≥ 1 alone is not sufficient and g must be ≥ 1
   Intimal or transmural arteritis (v > 0)[1]
   Acute thrombotic microangiopathy, in the absence of any other cause
   Acute tubular injury, in the absence of any other apparent cause
2. Evidence of current/recent antibody interaction with vascular endothelium, *including 1 or more of the following*:
   Linear C4d staining in peritubular capillaries (C4d2 or C4d3 by IF on frozen sections, or C4d > 0 by IHC on paraffin sections)
   At least moderate microvascular inflammation ([g + ptc] ≥2) in the absence of recurrent or de novo glomerulonephritis, although in the presence of acute TCMR, borderline infiltrate, or infection, ptc ≥ 2 alone is not sufficient and g must be ≥1
   Increased expression of gene transcripts/classifiers in the biopsy tissue strongly associated with ABMR, *if thoroughly validated*
3. Serologic evidence of donor-specific antibodies (DSA to HLA or other antigens). **C4d staining or expression of validated transcripts/classifiers as noted above in criterion 2 may substitute for DSA; however thorough DSA testing, including testing for non-HLA antibodies if HLA antibody testing is negative, is strongly advised whenever criteria 1 and 2 are met**



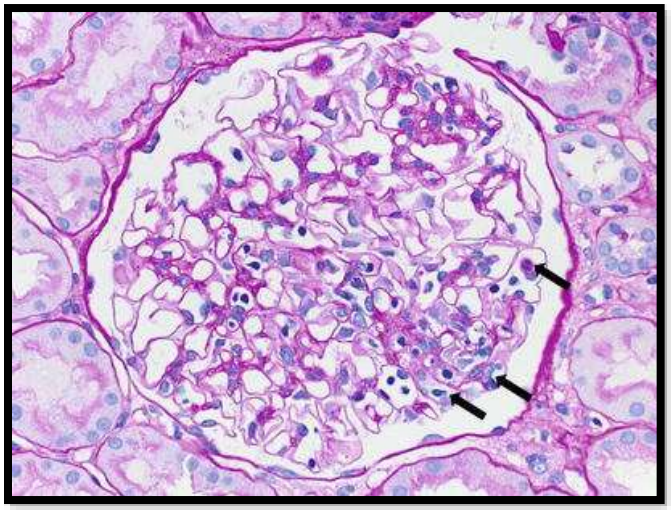
Interstitial haemorrhage

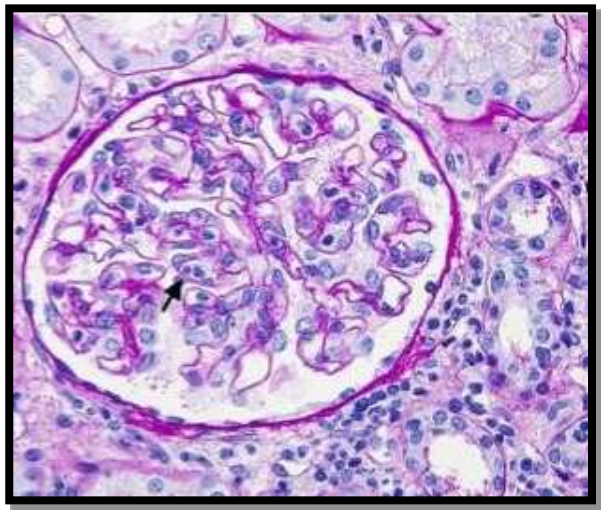

AKI

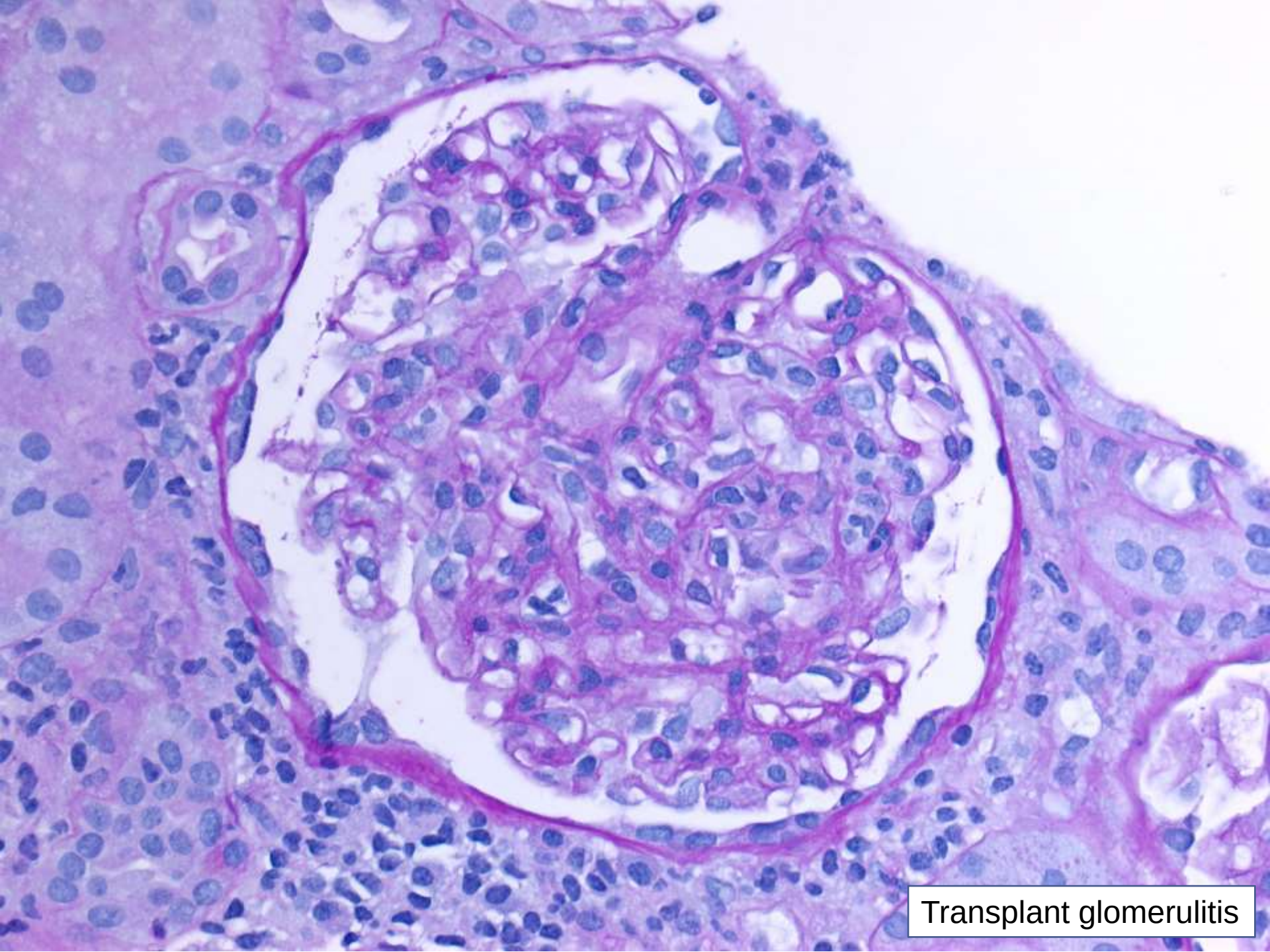
Active Antibody Mediated Rejection

Glomerulitis score

g0	No glomerulitis
g1	Glomerulitis in less than 25% of glomeruli
g2	Segmental or global glomerulitis in 25 to 75% of glomeruli
g3	Glomerulitis (mostly global) in more than 75% of glomerul



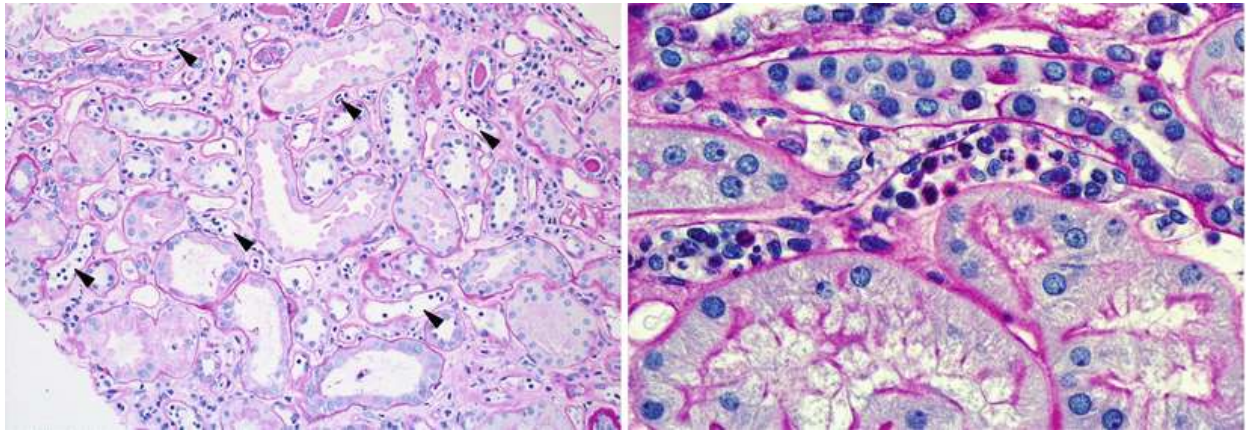



Transplant glomerulitis

Active Antibody Mediated Rejection

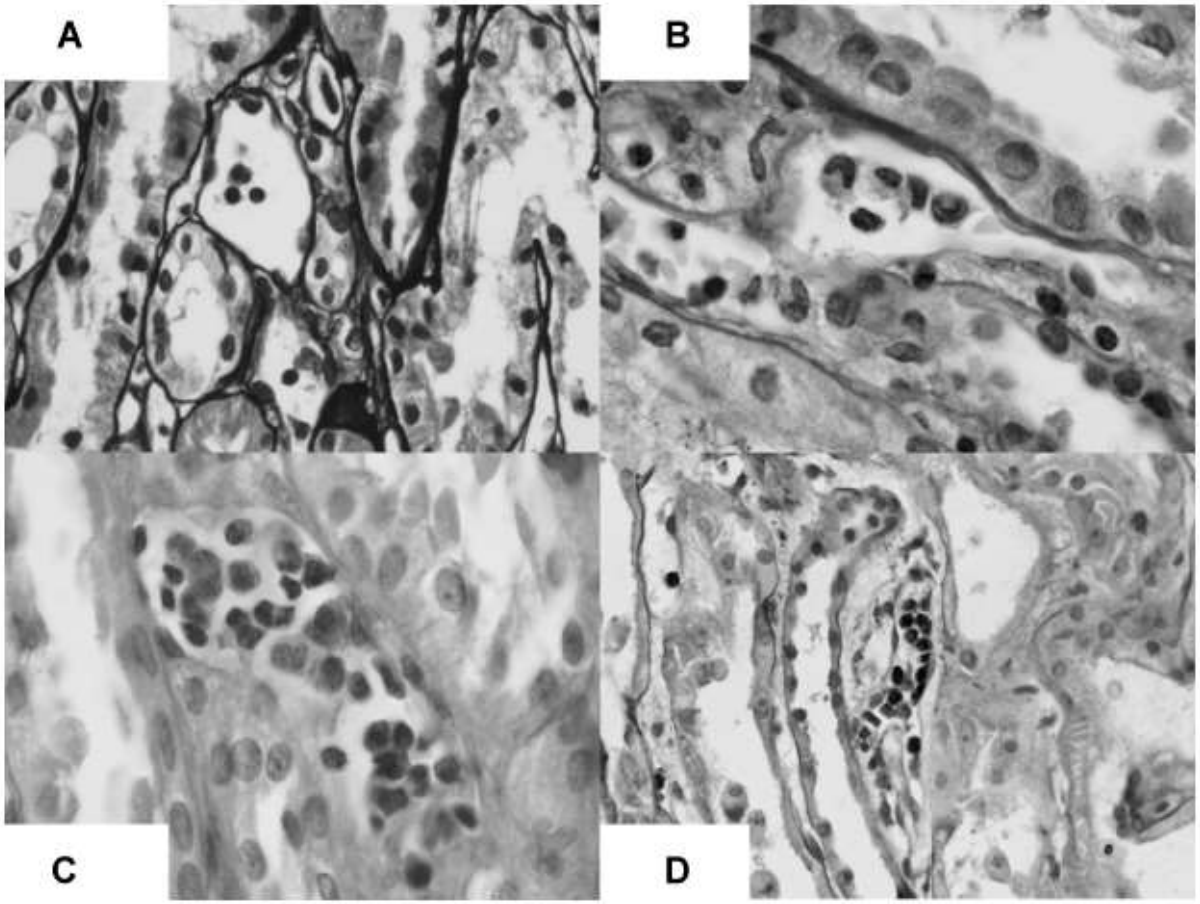
Classification of peritubular capillaritis (PTC)

ptc0	No significant cortical ptc, or<10% of PTCs with inflammation
ptc1	≥ 10% of cortical peritubular capillaries with capillaritis, with max 3 to 4 luminal inflammatory cells
ptc2	≥ 10% of cortical peritubular capillaries with capillaritis, with max 5 to 10 luminal inflammatory cells
ptc3	≥ 10% of cortical peritubular capillaries with capillaritis, with > 10 luminal inflammatory cells



Active Antibody Mediated Rejection

PTC1

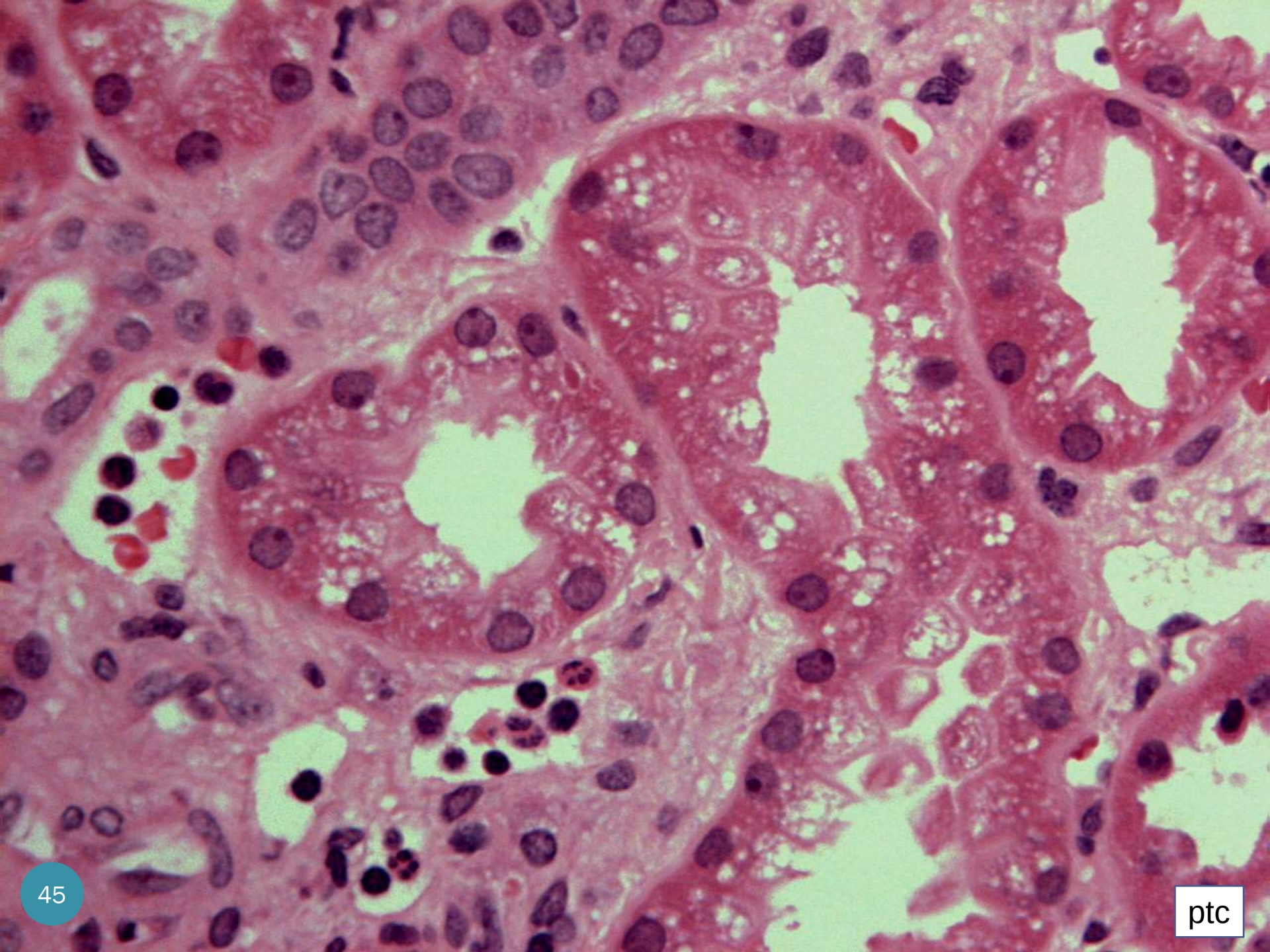


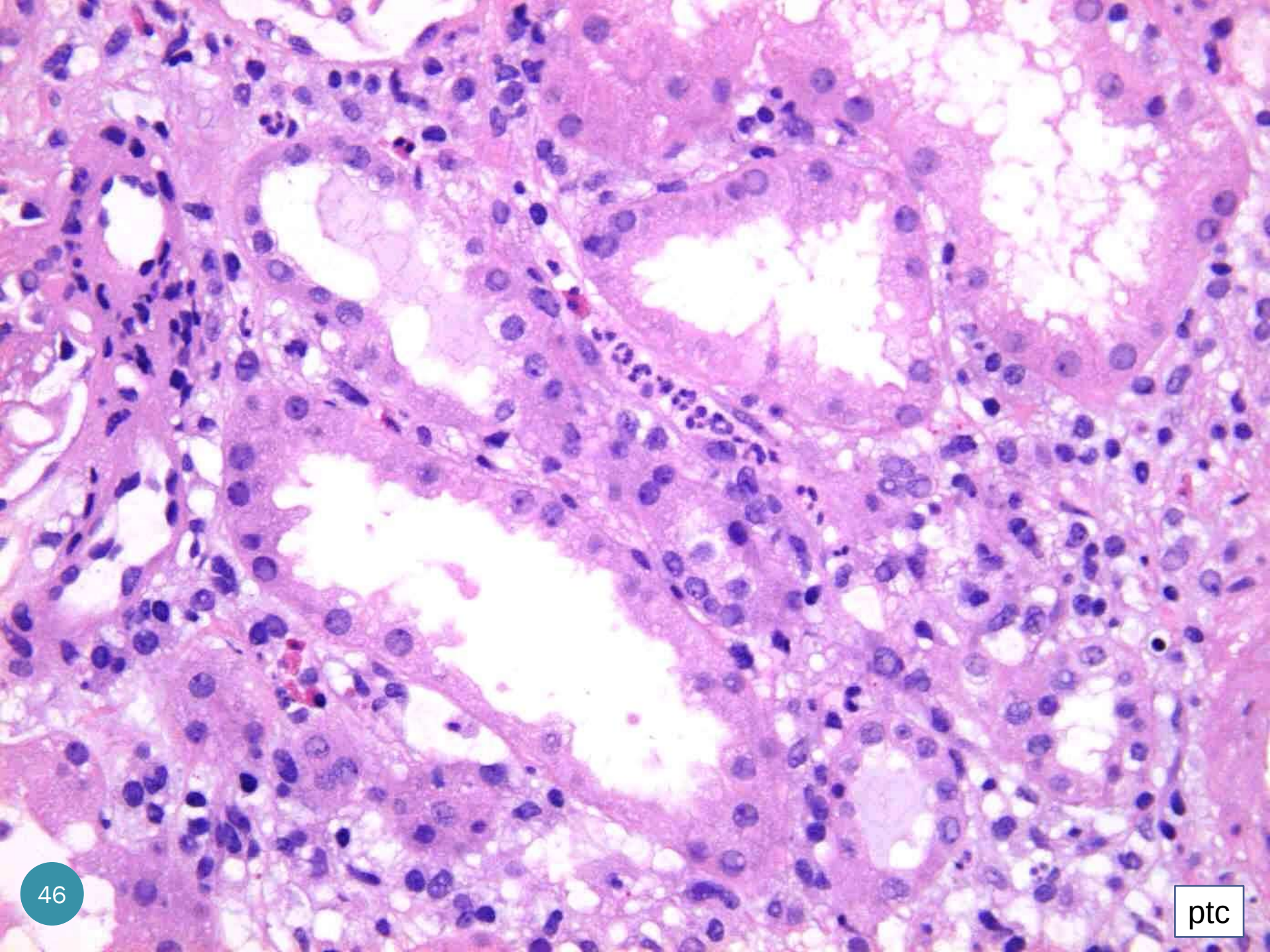
PTC2

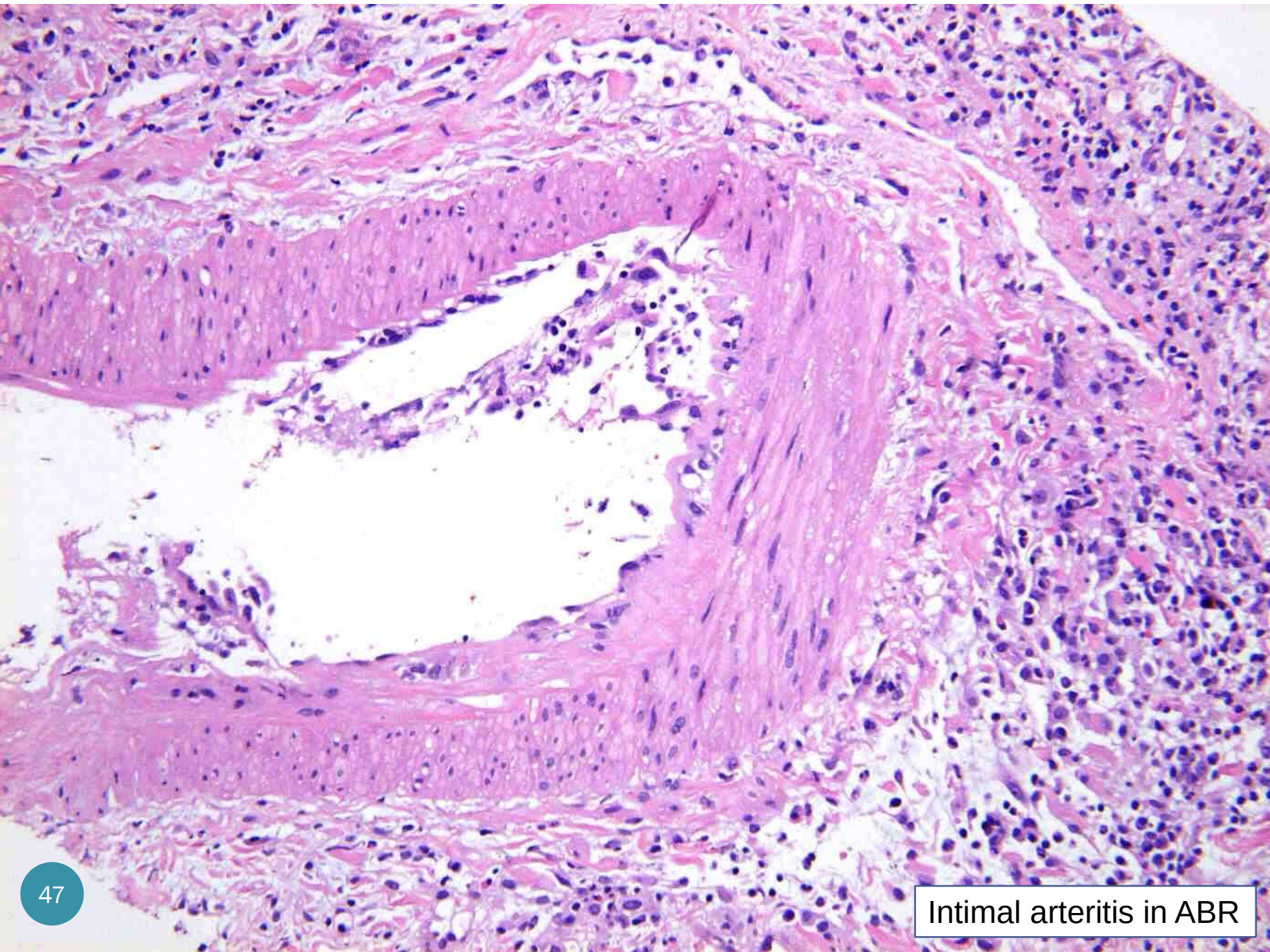
PTC3

PTC3

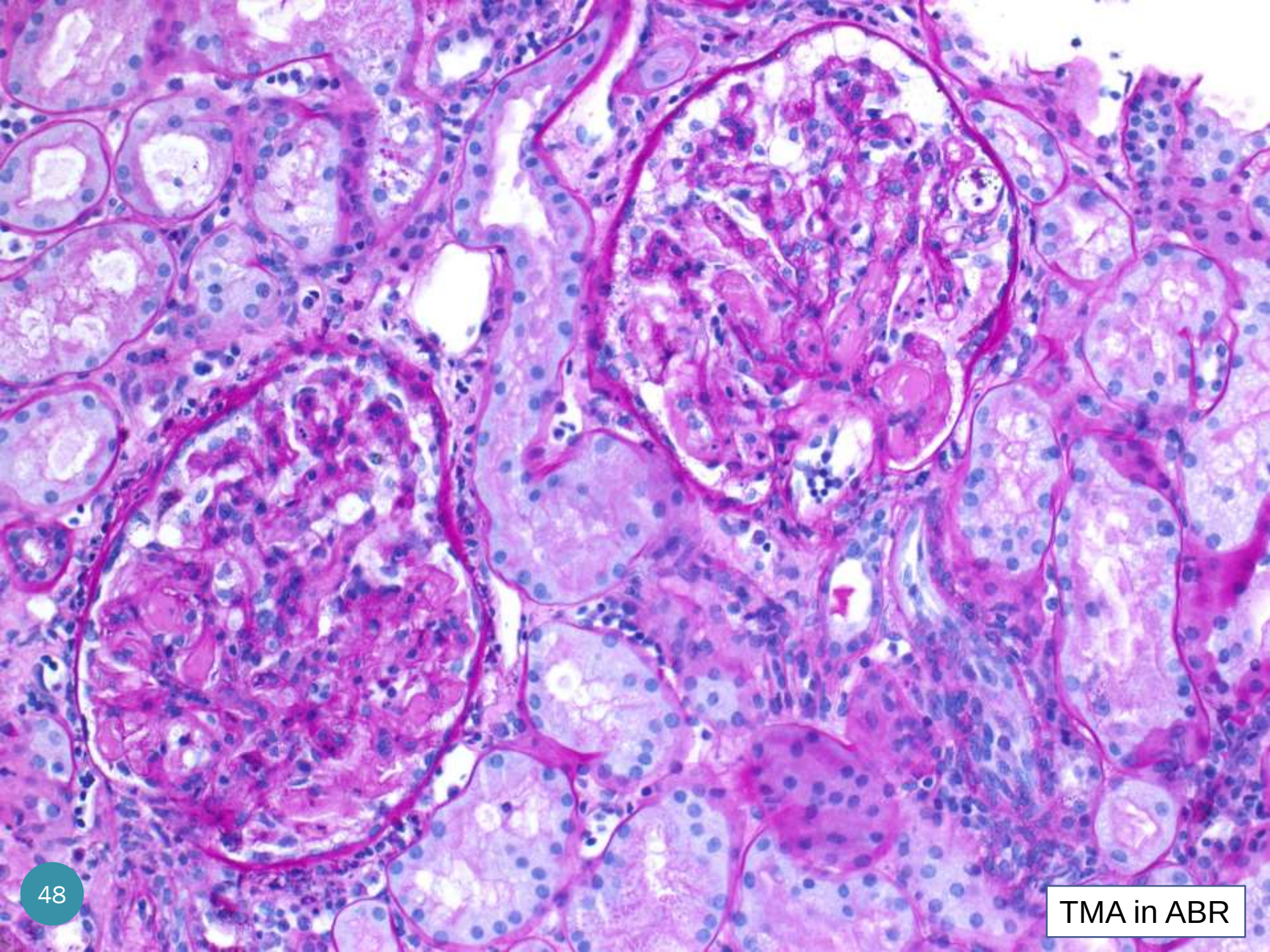
Gibson IW, et al. Am J Transplant 2008;8:819


45
ptc

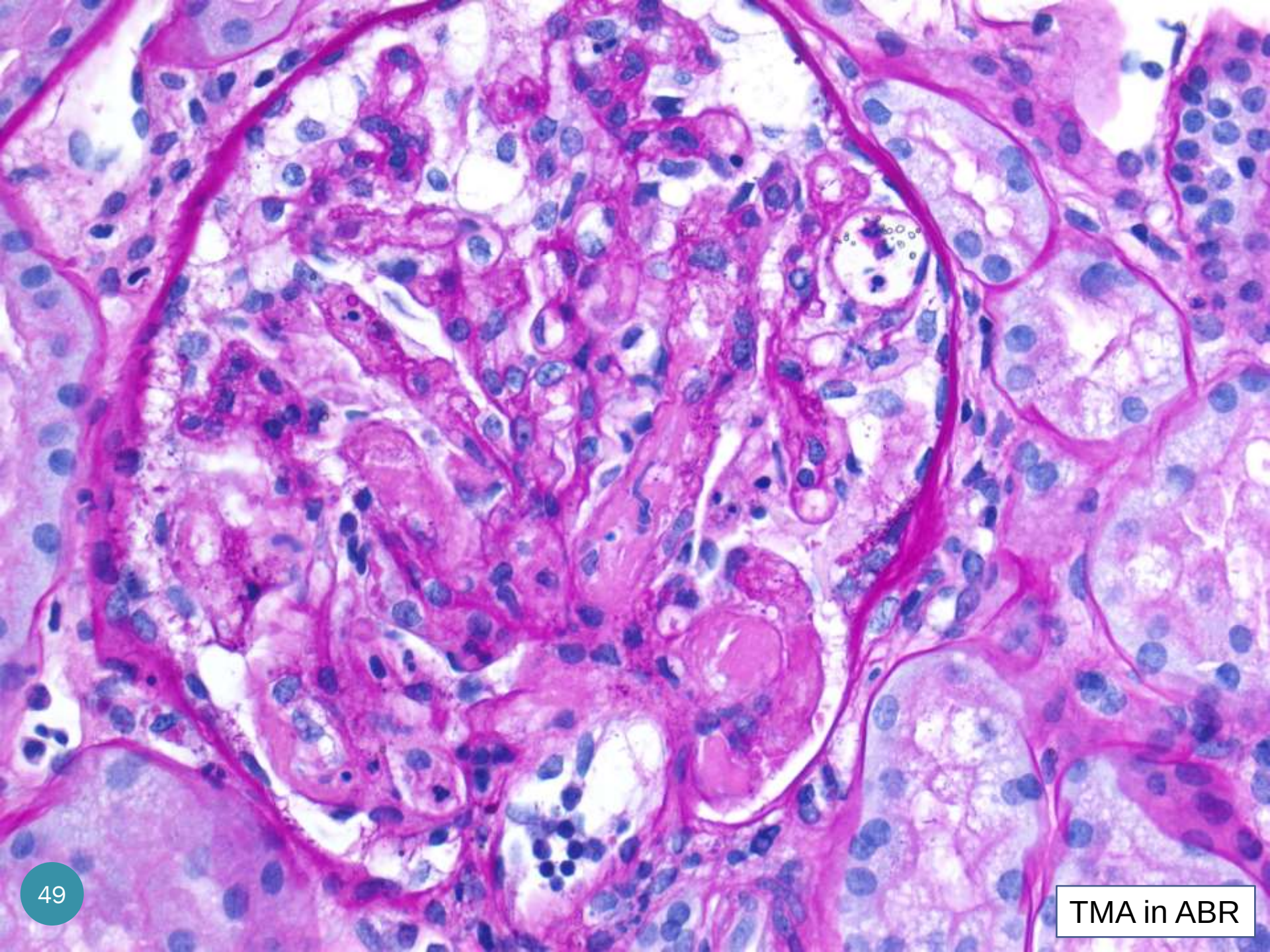

ptc



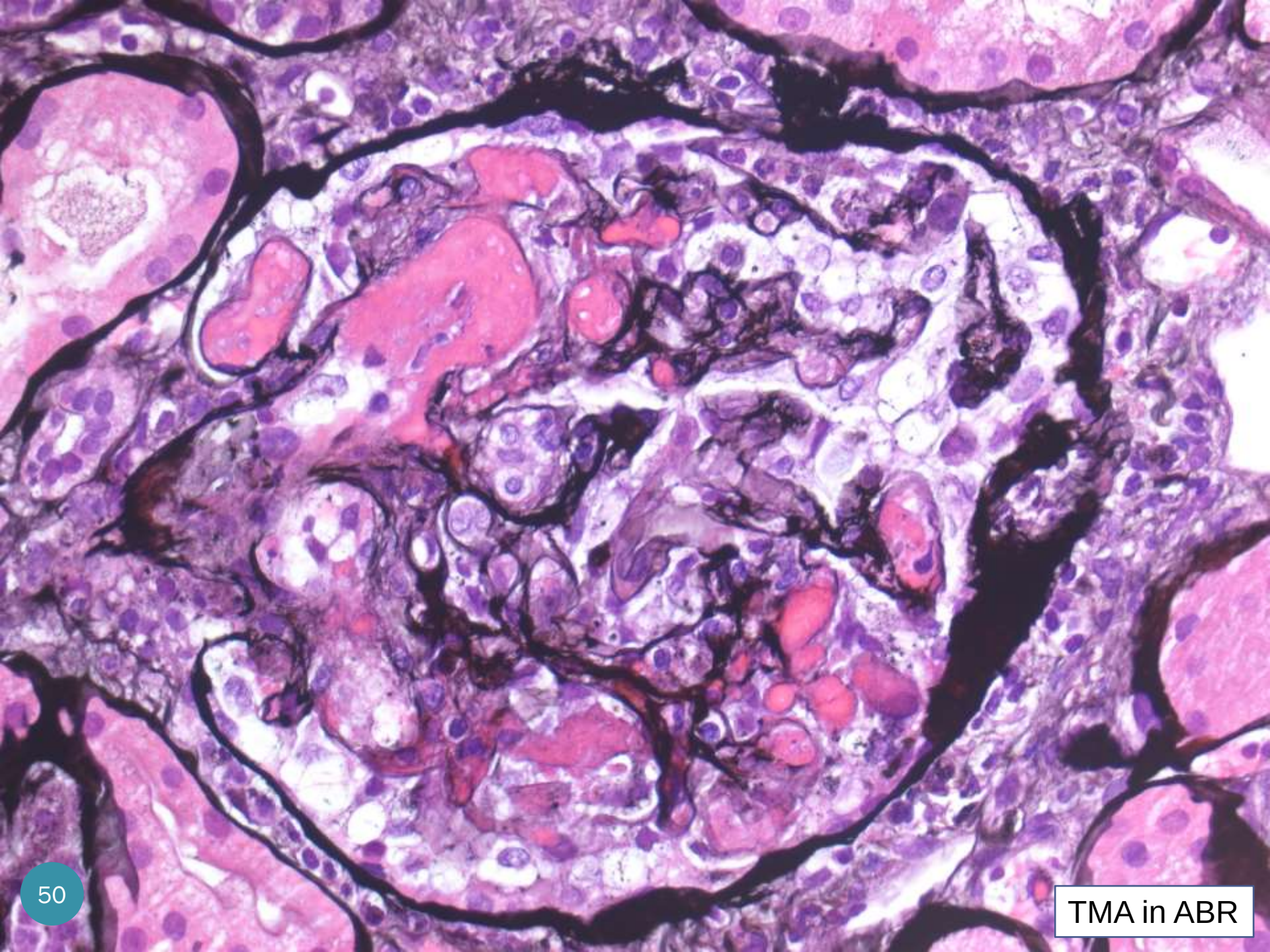
Intimal arteritis in ABR



TMA in ABR



TMA in ABR



TMA in ABR

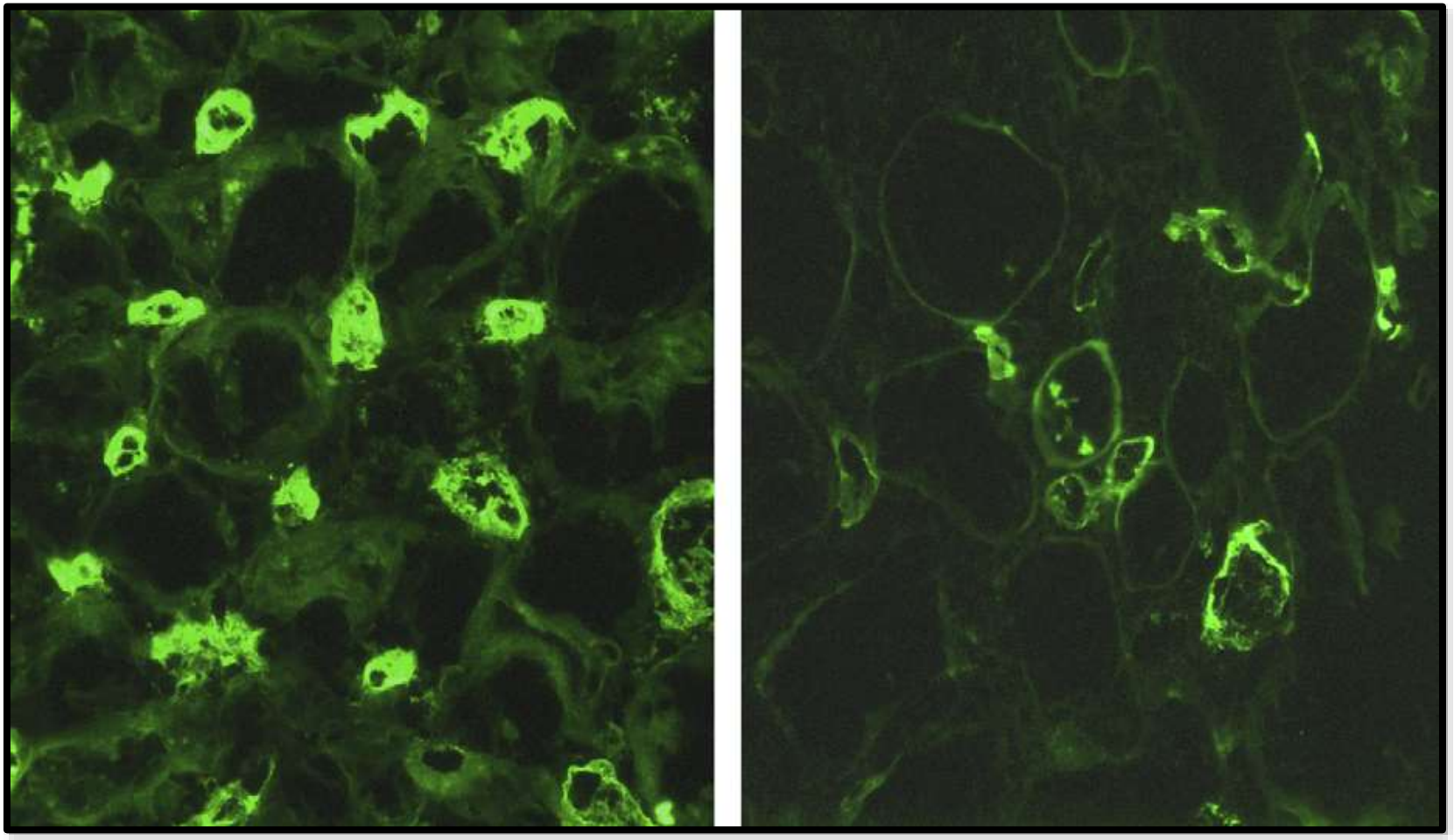
Active Antibody Mediated Rejection C4d

- Scoring of C4d staining is based on the percentage of stained tissue on IF/IHC that has a linear, circumferential staining pattern in PTC.
- The minimal sample for evaluation is 5 HPF of cortex without scarring or infarction.

C4d0:	Negative:	0%
C4d1:	Minimal C4d stain/detection:	1<10%
C4d2:	Focal C4d stain/positive:	10–50%
C4d3:	Diffuse C4d stain/positive:	>50%

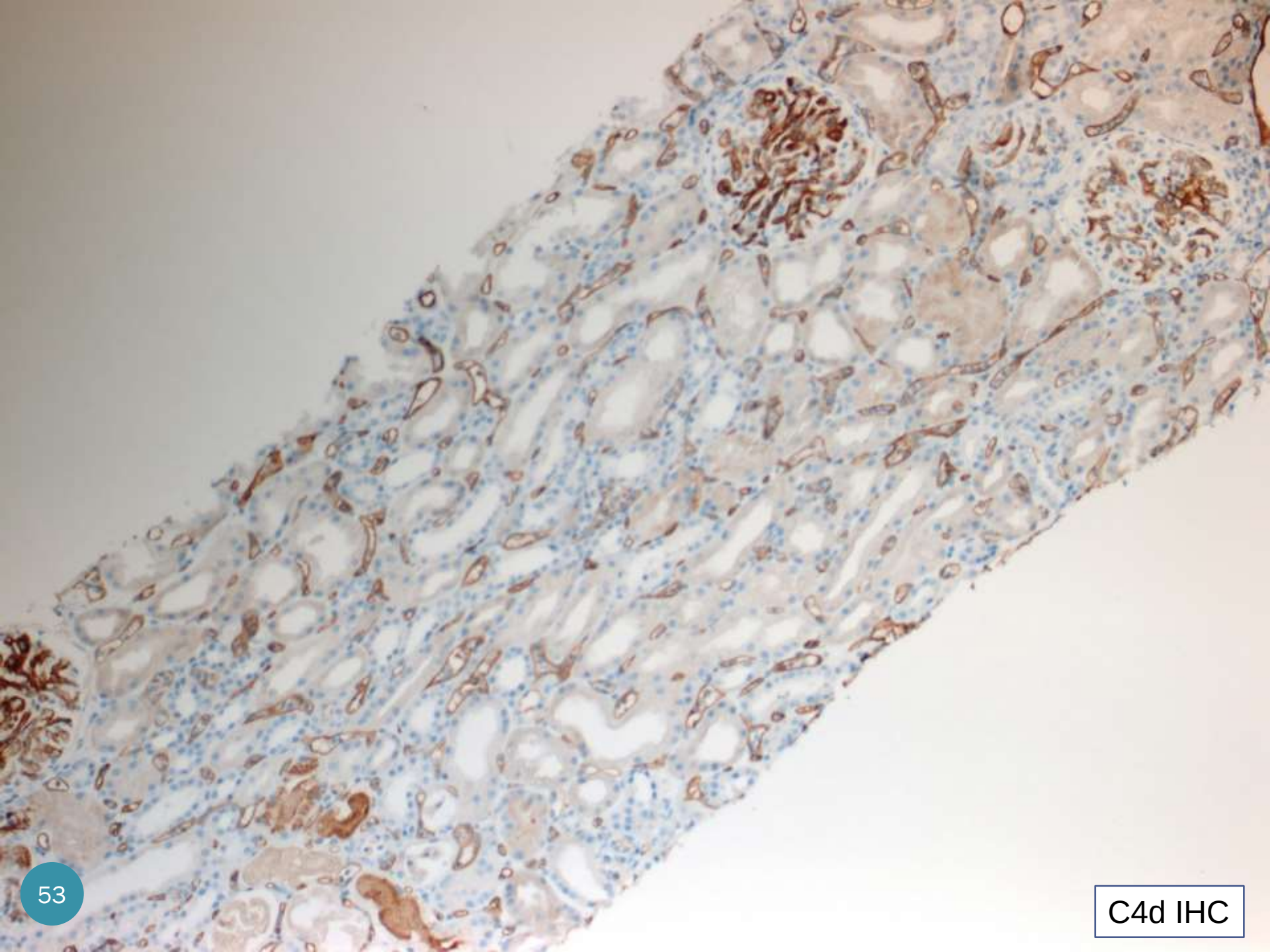
Solez K, et al. Am J Transplant 2008;8:753

Active Antibody Mediated Rejection C4d

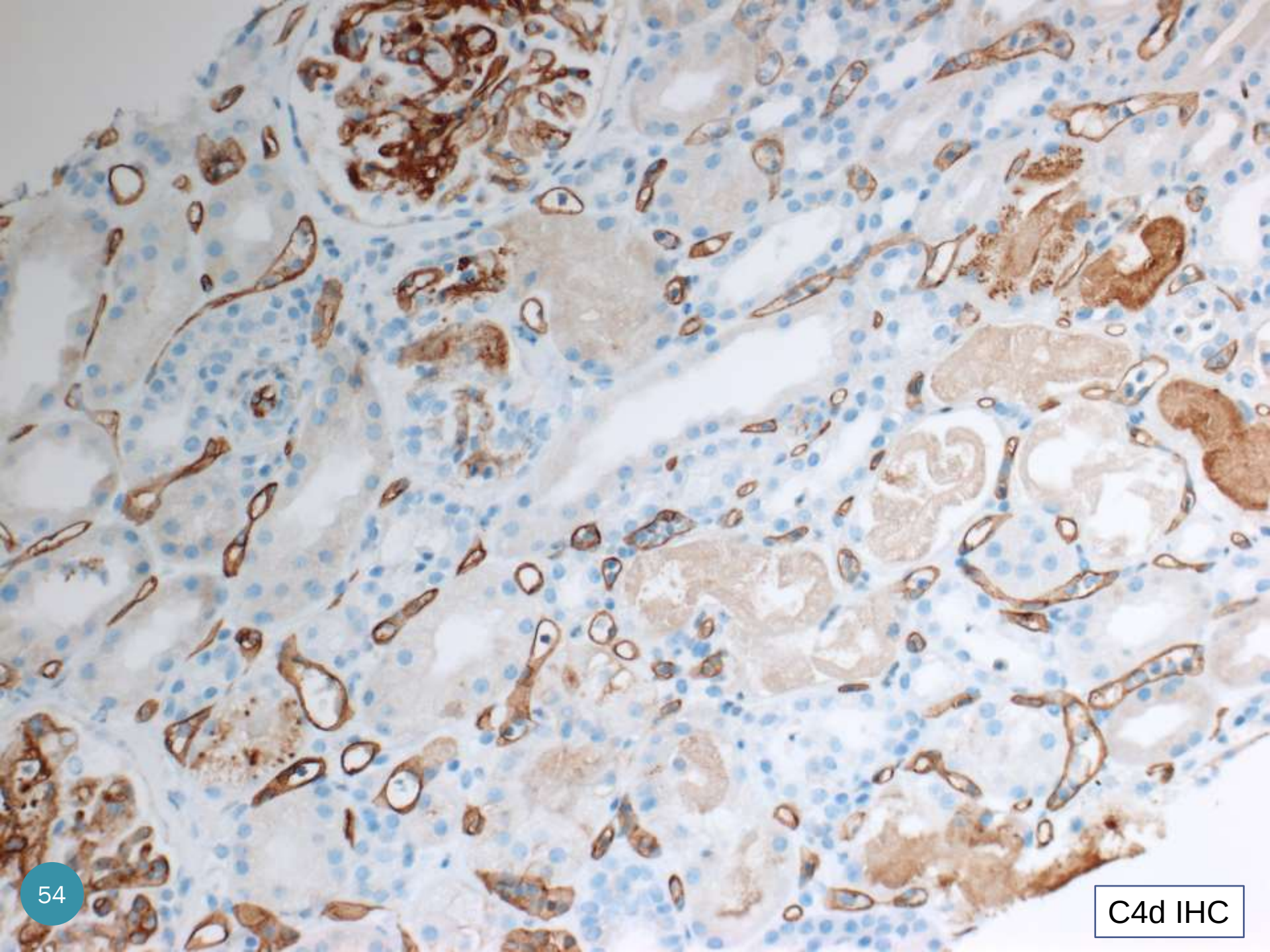


Diffuse C4d staining

Focal C4d staining



C4d IHC



C4d IHC

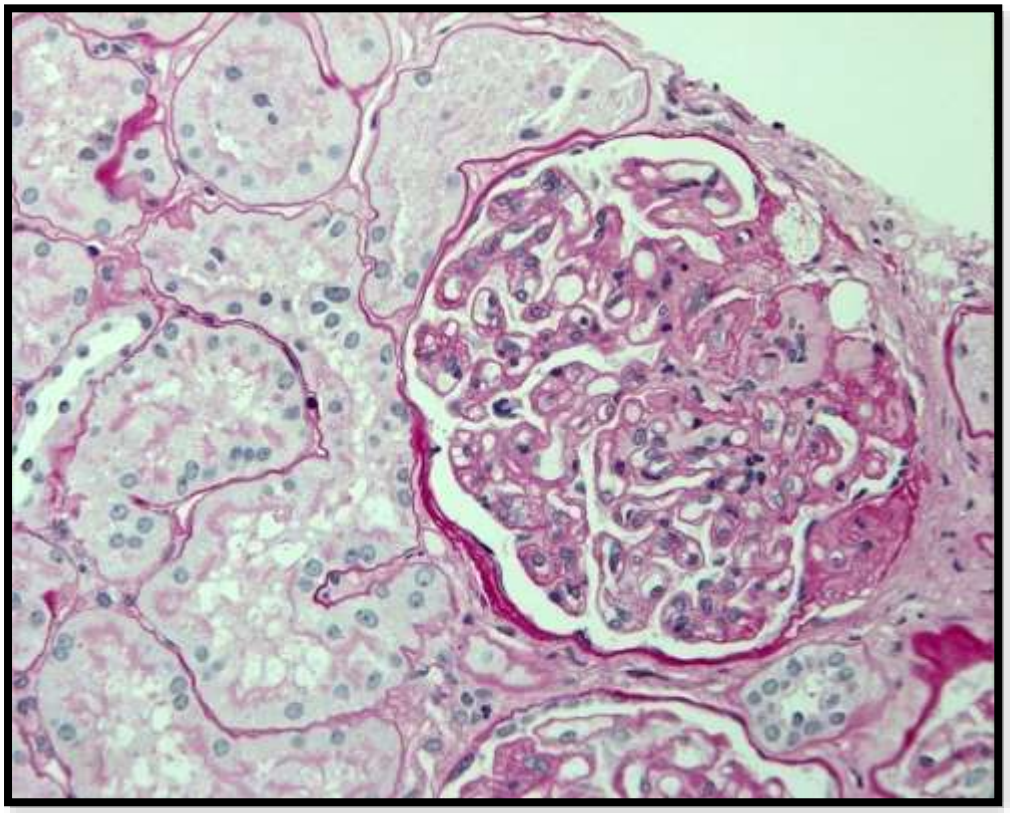
Chronic Active AMR

- In Banff schema, the criteria are triad of the following features:
  - Morphological features (one or more of the following):
    - Transplant glomerulopathy (duplication or “double contours” in the GBM).
    - Severe multilamination of the PTC basement membranes (requires EM).
    - Chronic arteriopathy with fibrous intimal thickening.
  - C4d deposition in the PTCs.
  - Serological evidence of donor-specific antibodies.

Solez K, et al. Am J Transplant 2007;7:518
Hass M, et al. Am J Trasnplant 2018;18:293

Chronic Active AMR

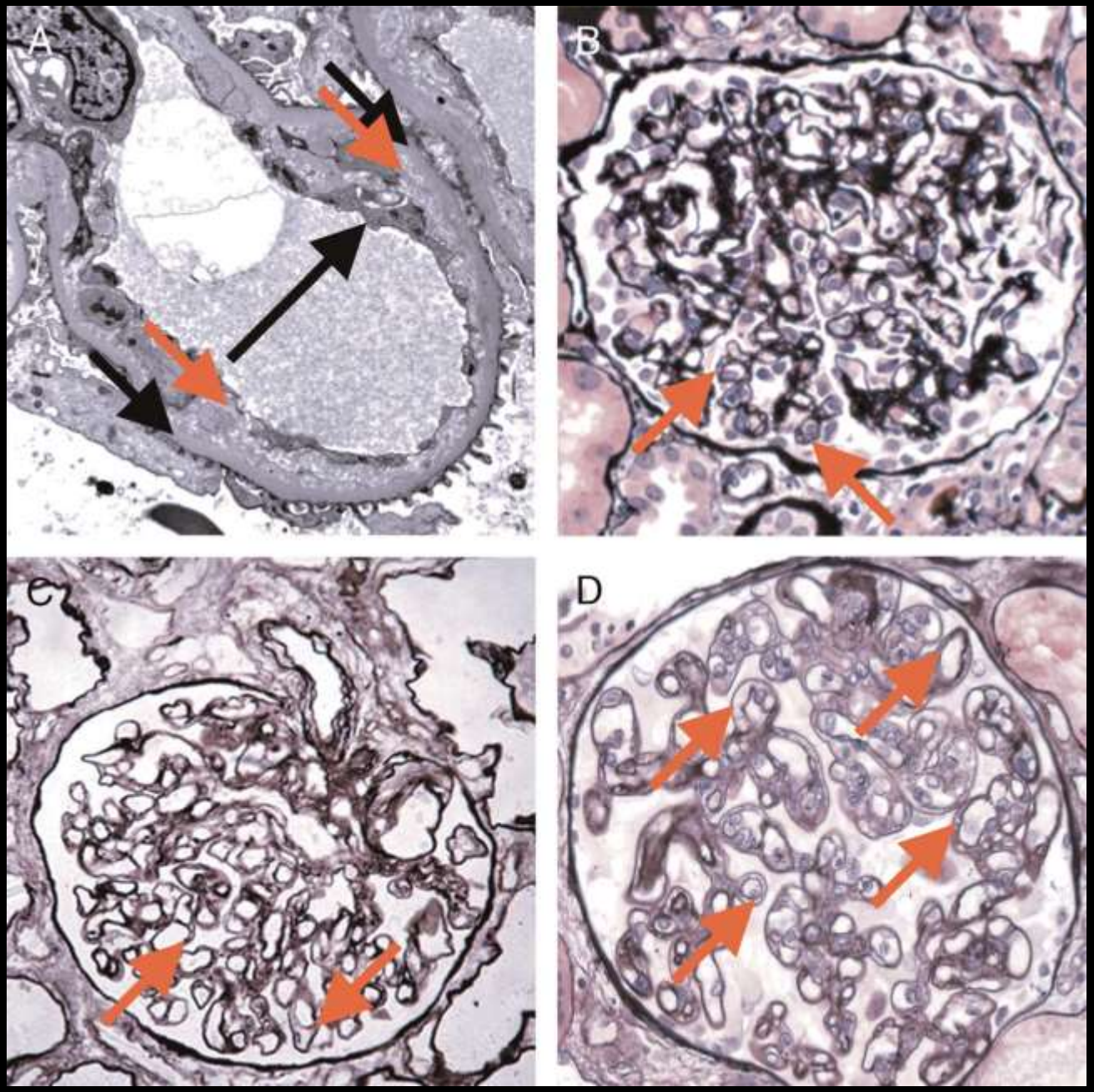
- Note:
  - If only two of the three principal elements are present, the diagnosis is considered to be 'suggestive'.
  - Even though this is a 'chronic' process, the presence of C4d indicates ongoing immunological activity.



Chronic Active AMR

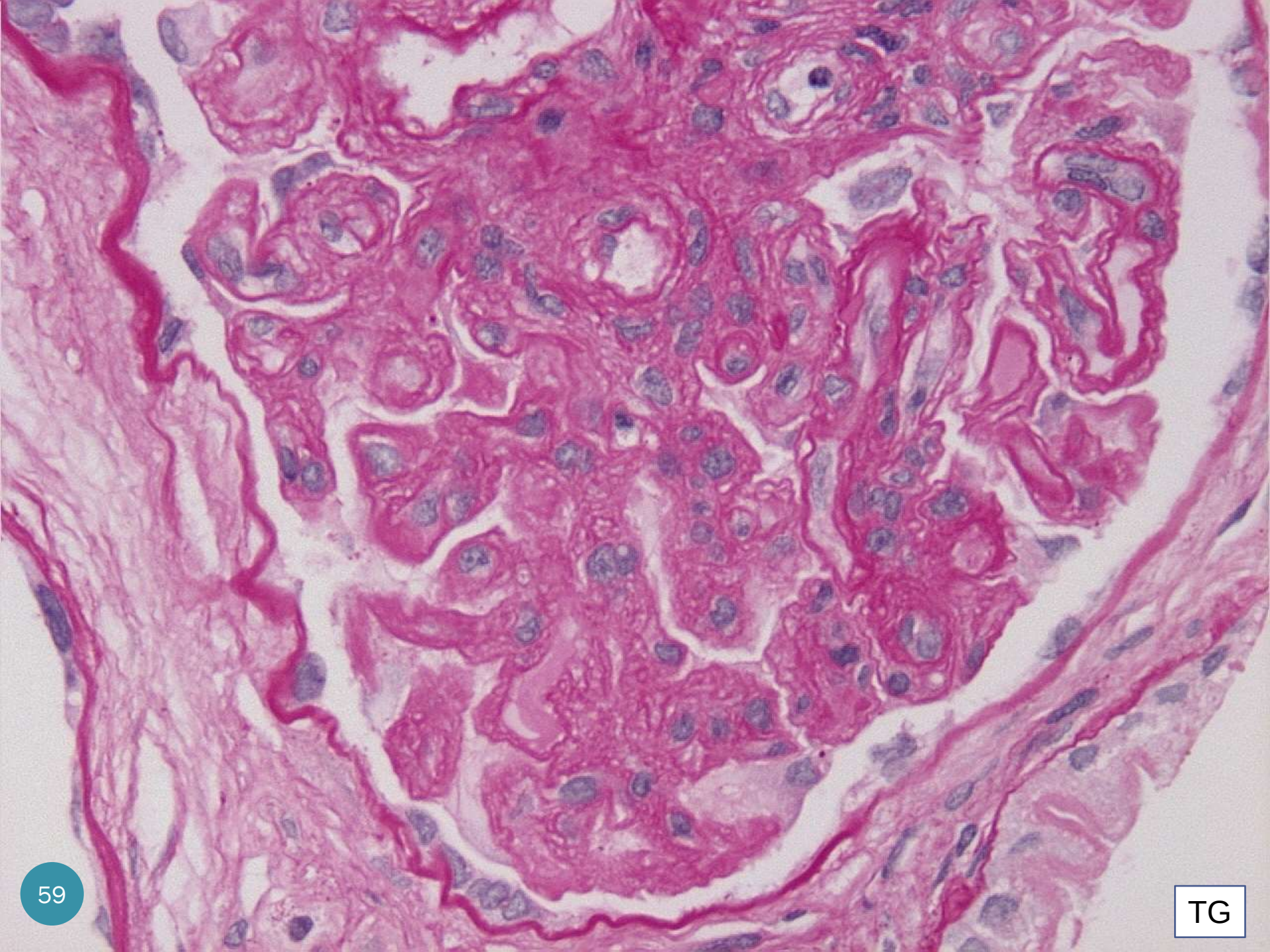
Criterion for allograft glomerulopathy

cg0	no GBM double contours by LM or EM
cg1	1a: no GBM double contours by LM but GBM double contours (incomplete or circumferential) in atleast 3 glomerular capillaries by EM with associated endothelial swelling and/or subendothelial electronlucent widening 1b: ≥ 1 glomerular capillaries with GBM double contours in 1 nonsclerotic glomerulus by LM. EM confirmation is recommended if available.
cg2	Double contours affecting 26 to 50% of peripheral capillary loops in the most affected of nonsclerotic glomeruli
cg3	Double contours affecting more than 50% of peripheral capillary loops in the most affected of nonsclerotic glomeruli



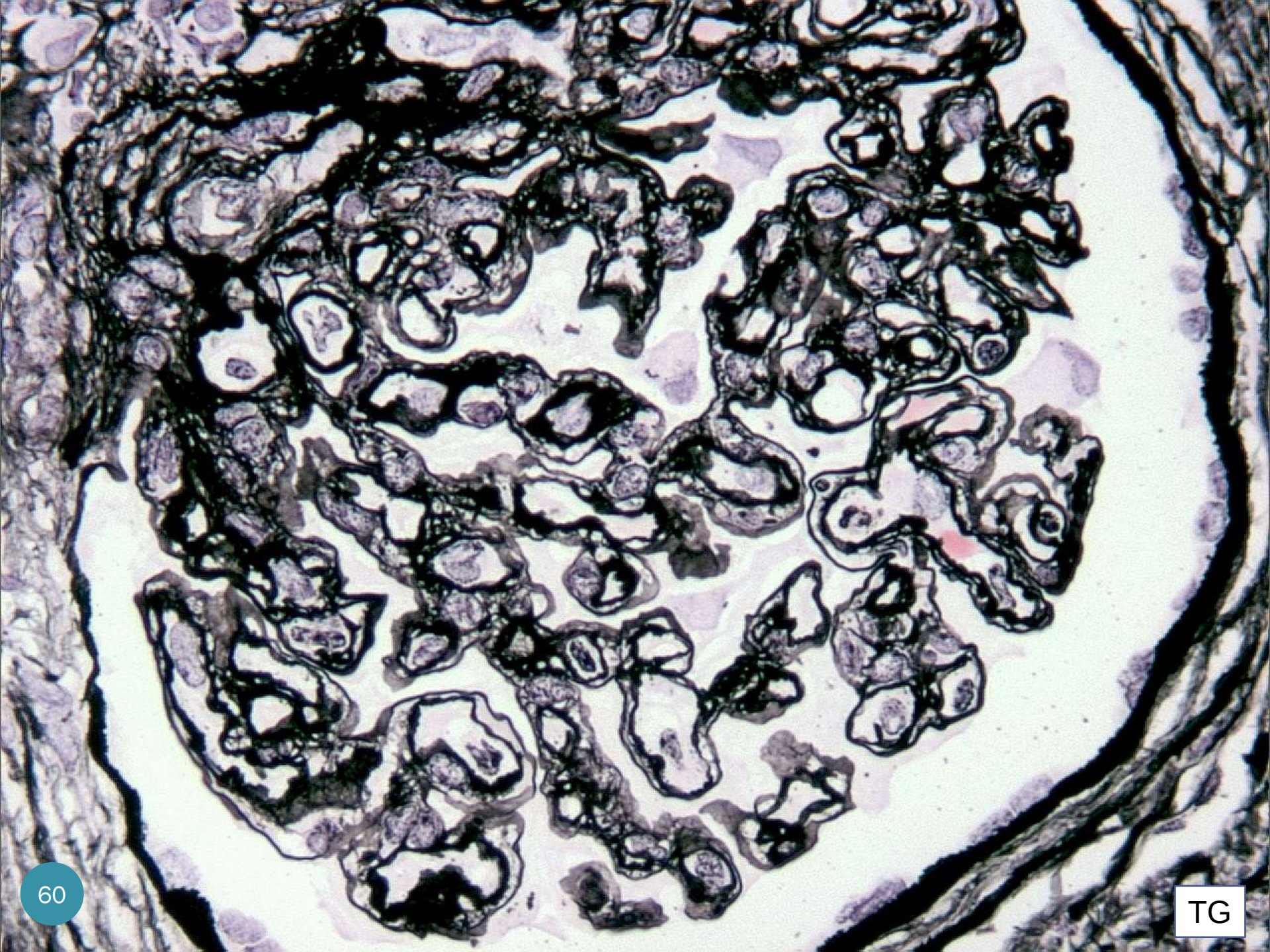
Roufosse et al. Transplantation 2018;102:1795-1814

TG



59

TG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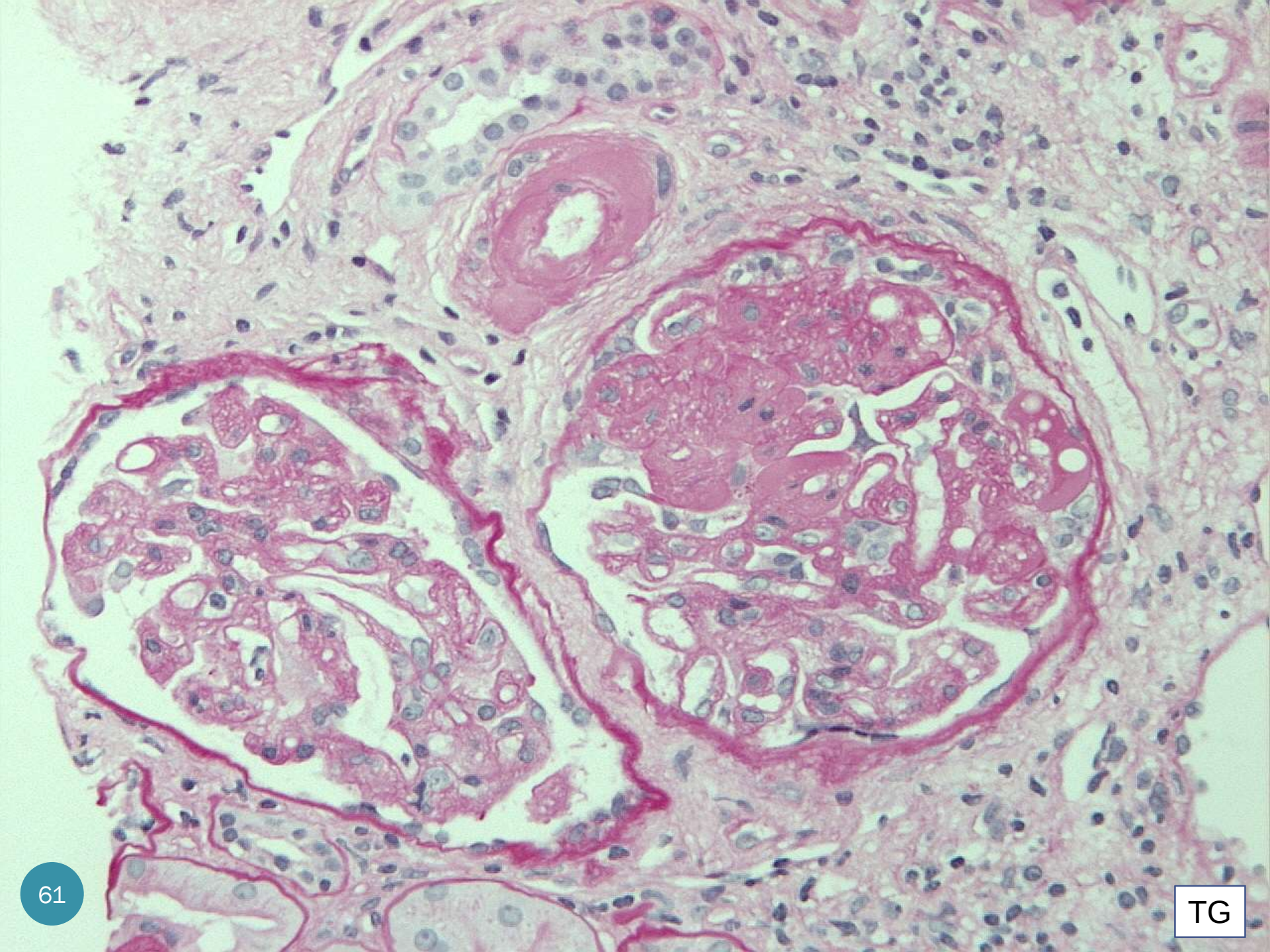
TG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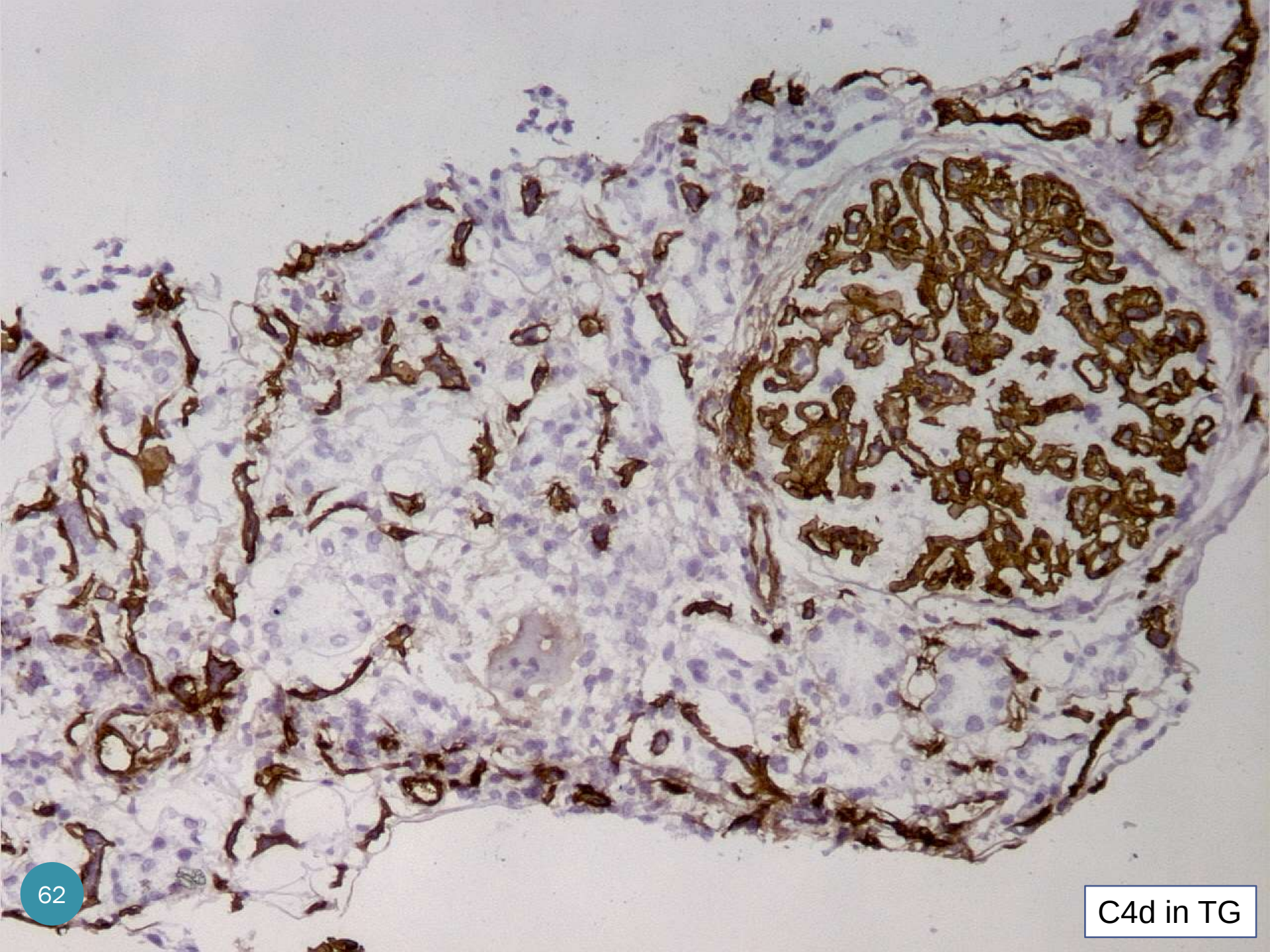
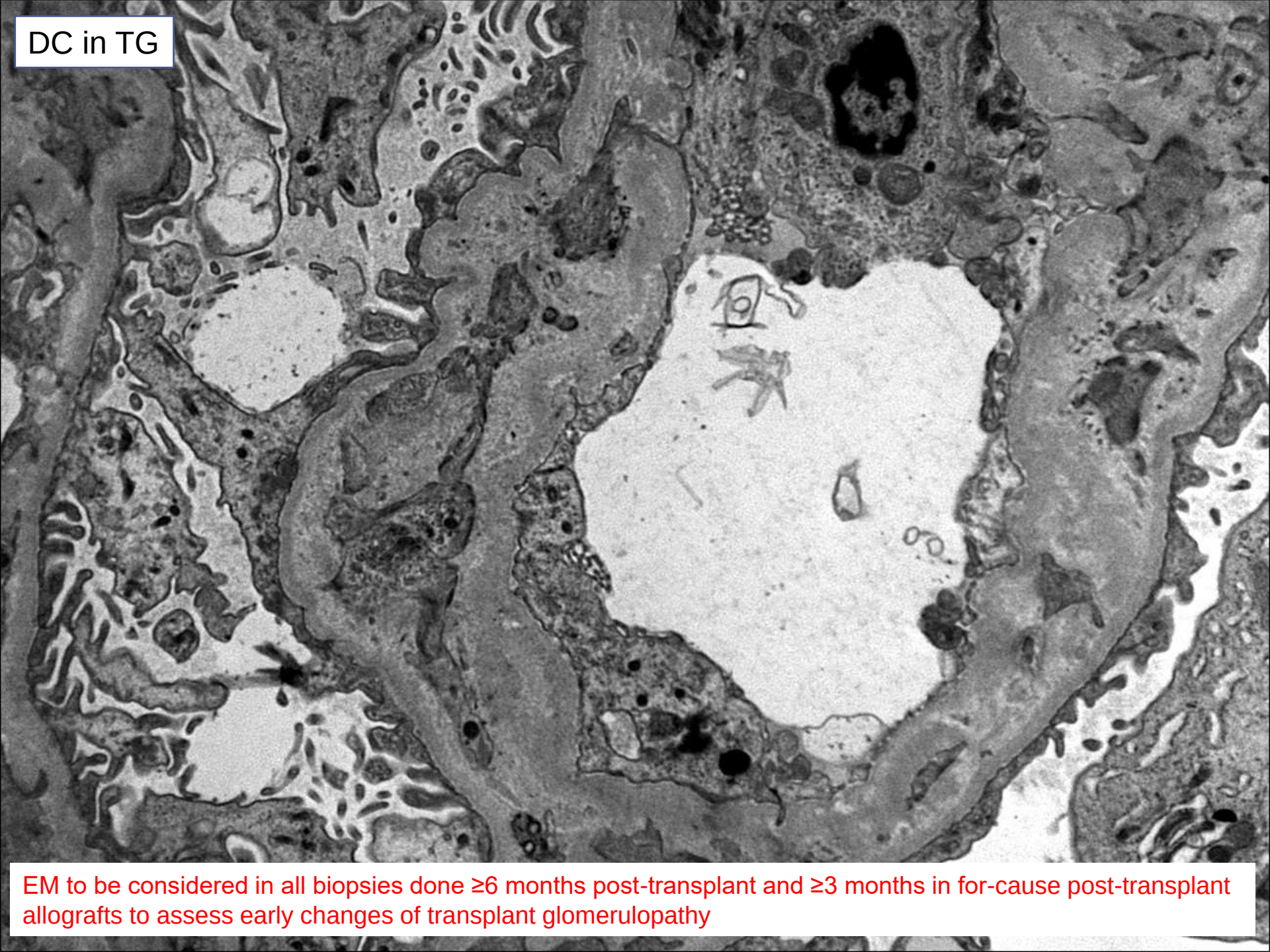
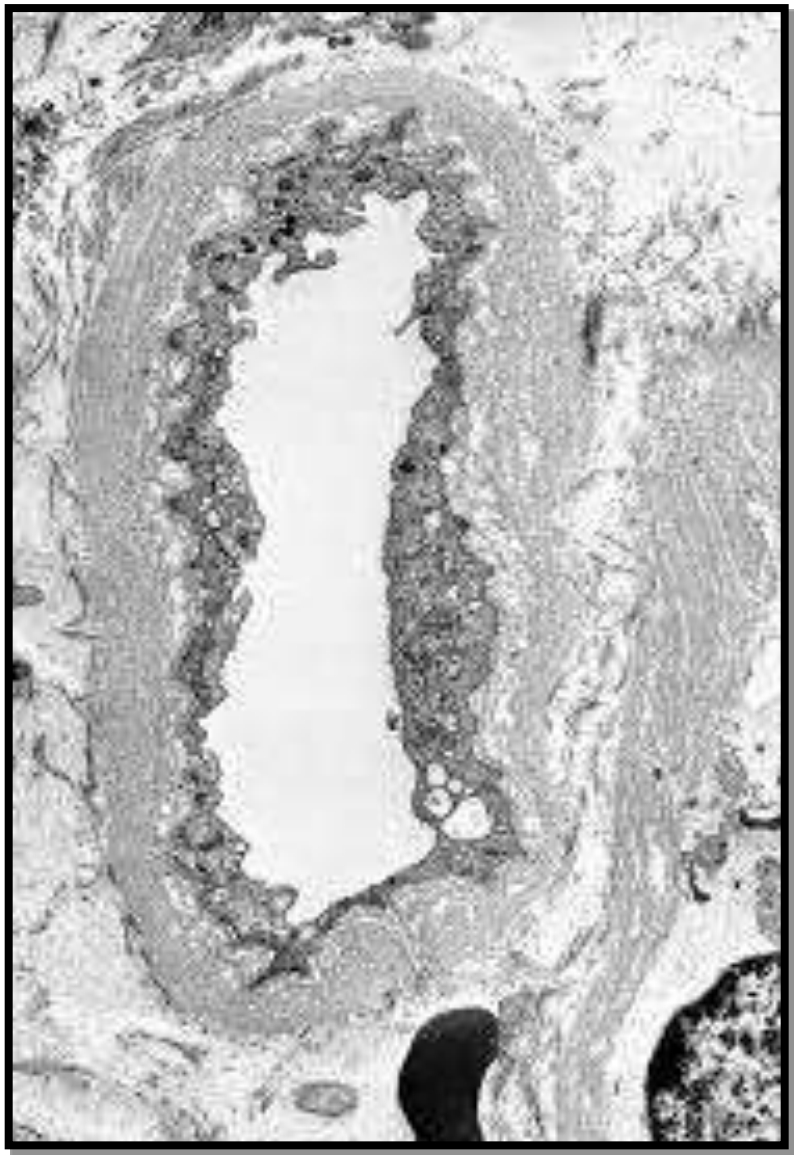
TG



C4d in TG

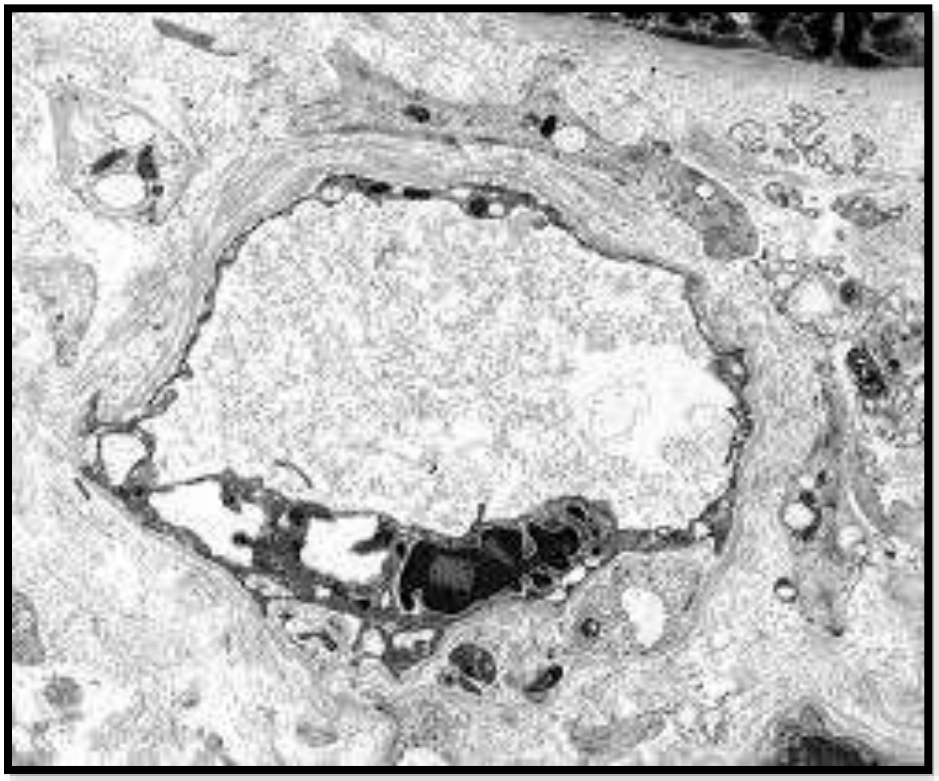


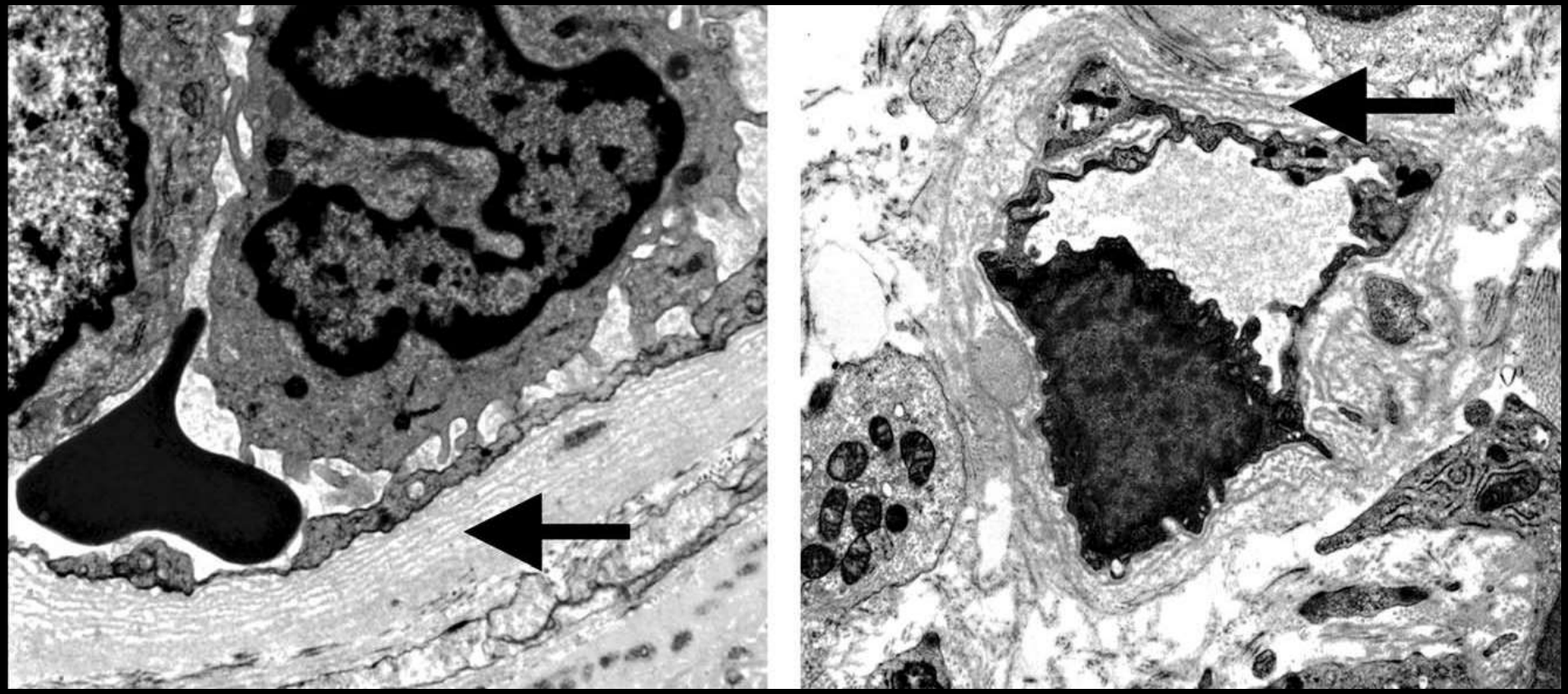
EM to be considered in all biopsies done ≥6 months post-transplant and ≥3 months in for-cause post-transplant allografts to assess early changes of transplant glomerulopathy



Ivanyi B et al and Solez K: Peritubular capillaries in chronic renal allograft rejection: a quantitative ultrastructural study. Hum Pathol 2000;31:129-38.

Gough J at al: Peritubular capillary basement membrane reduplication in allograft and native kidney disease: a clinicopathologic study of 278 consecutive renal specimens. Transplantation 2001;71:1390-3.





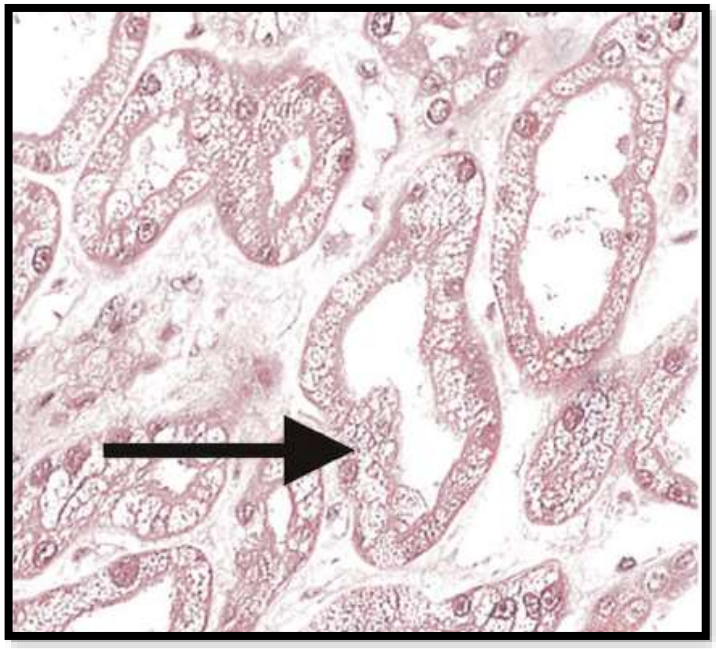
Specific Causes of Chronic Allograft Injury

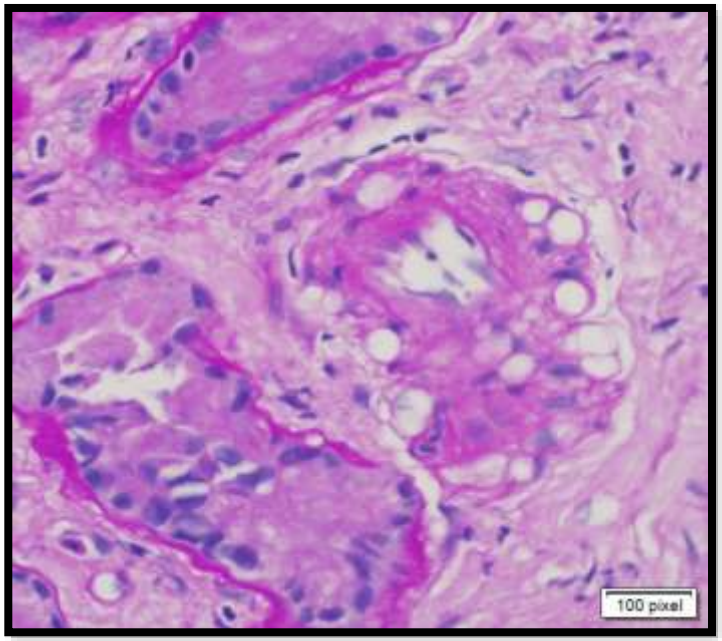
Causes of IF/TA (non-rejection)	
Etiology	Morphology
Chronic hypertension	Arterial/fibrointimal thickening with reduplication of elastica, usually with small artery and arteriolar hyaline changes.
CNI[1] toxicity	Arteriolar hyalinosis with peripheral hyaline nodules and/or progressive increase in the absence of hypertension or diabetes. Tubular cell injury with isometric vacuolization.
Chronic obstruction	Marked tubular dilation. Large Tamm–Horsfall protein casts with extravasation into interstitium, and/or lymphatics.
Bacterial pyelonephritis	Intratubular and peritubular neutrophils, lymphoid follicle formation.
Viral infection	Viral inclusions on histology and immunohistology and/or electron microscopy.

[1]CNI, calcineurin inhibitor toxicity.

Solez K et al. Banff '05 meeting report. American Journal of Transplantation 2007;7:518-526

Calcineurin Inhibitor Toxicity

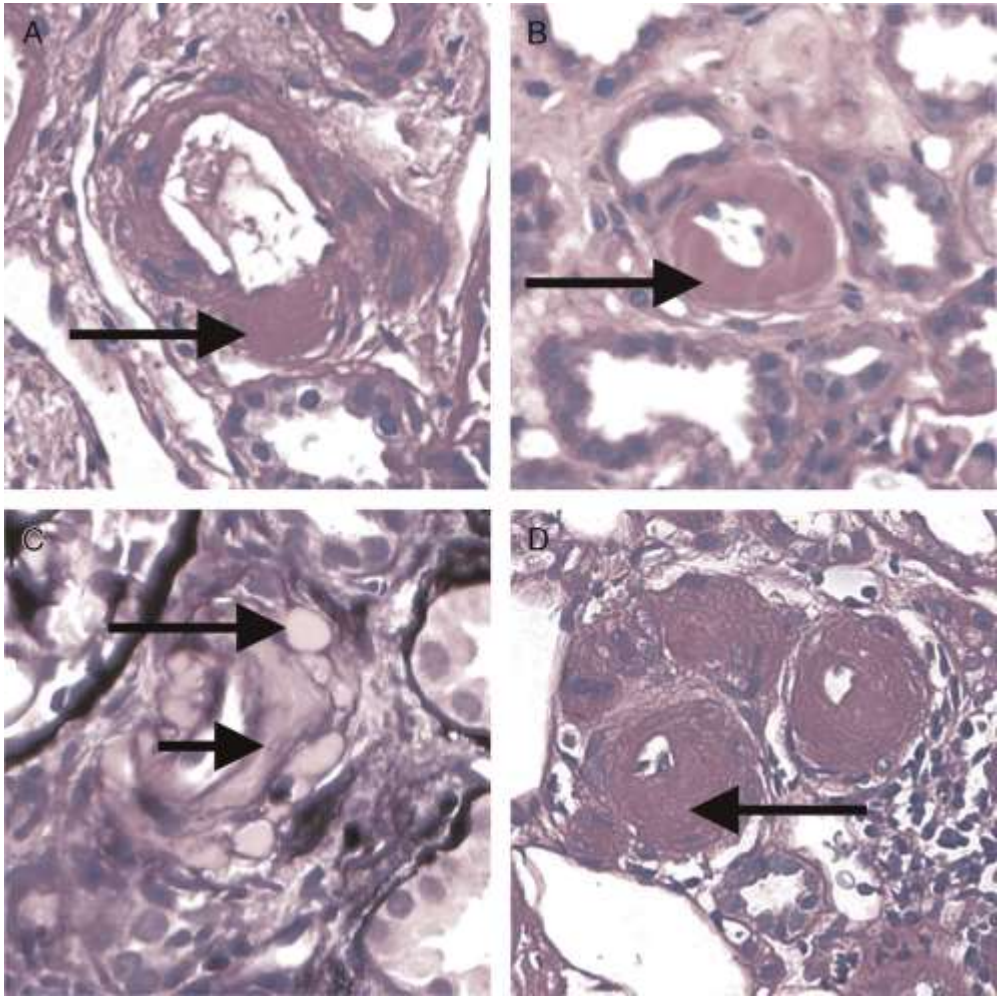




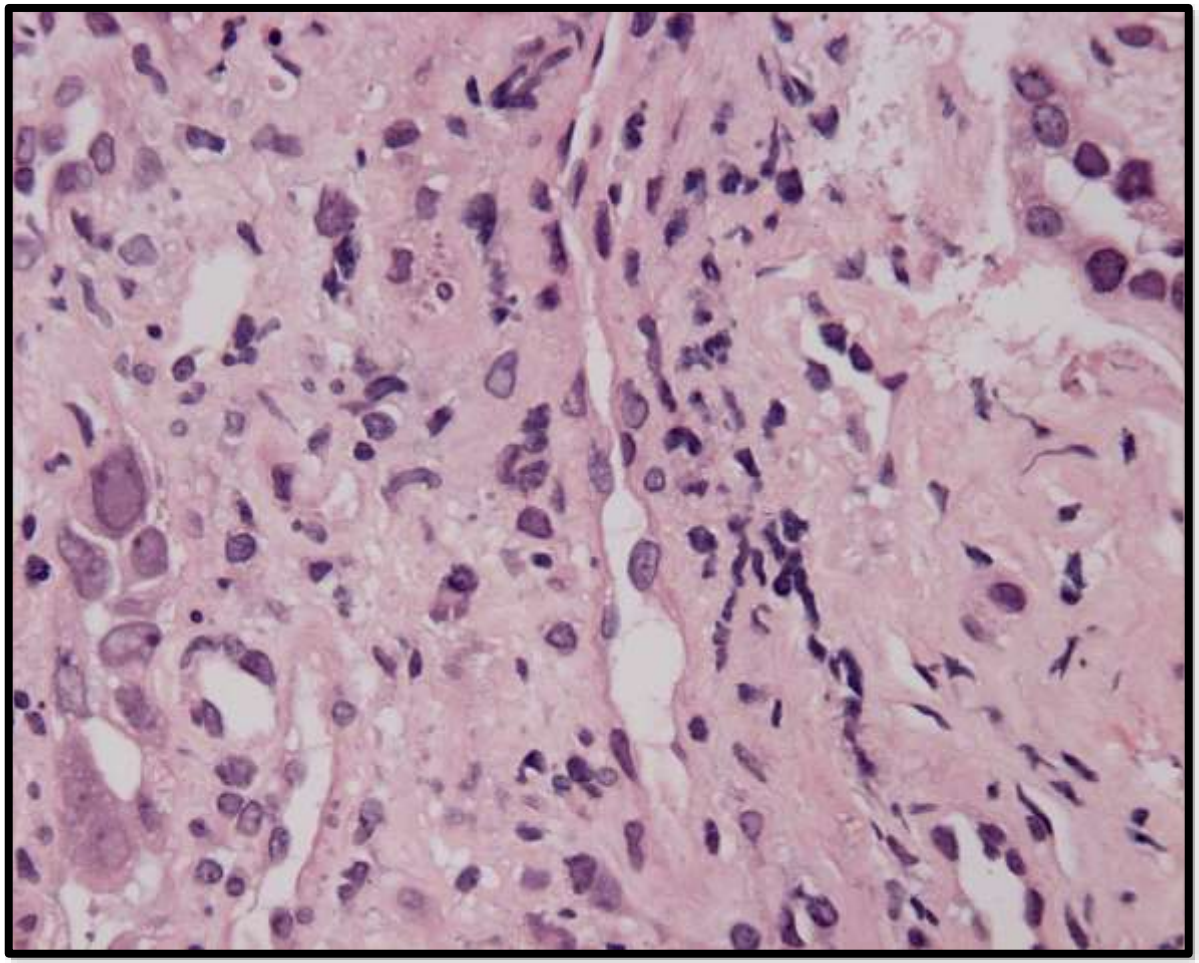
Acute CNI toxicity

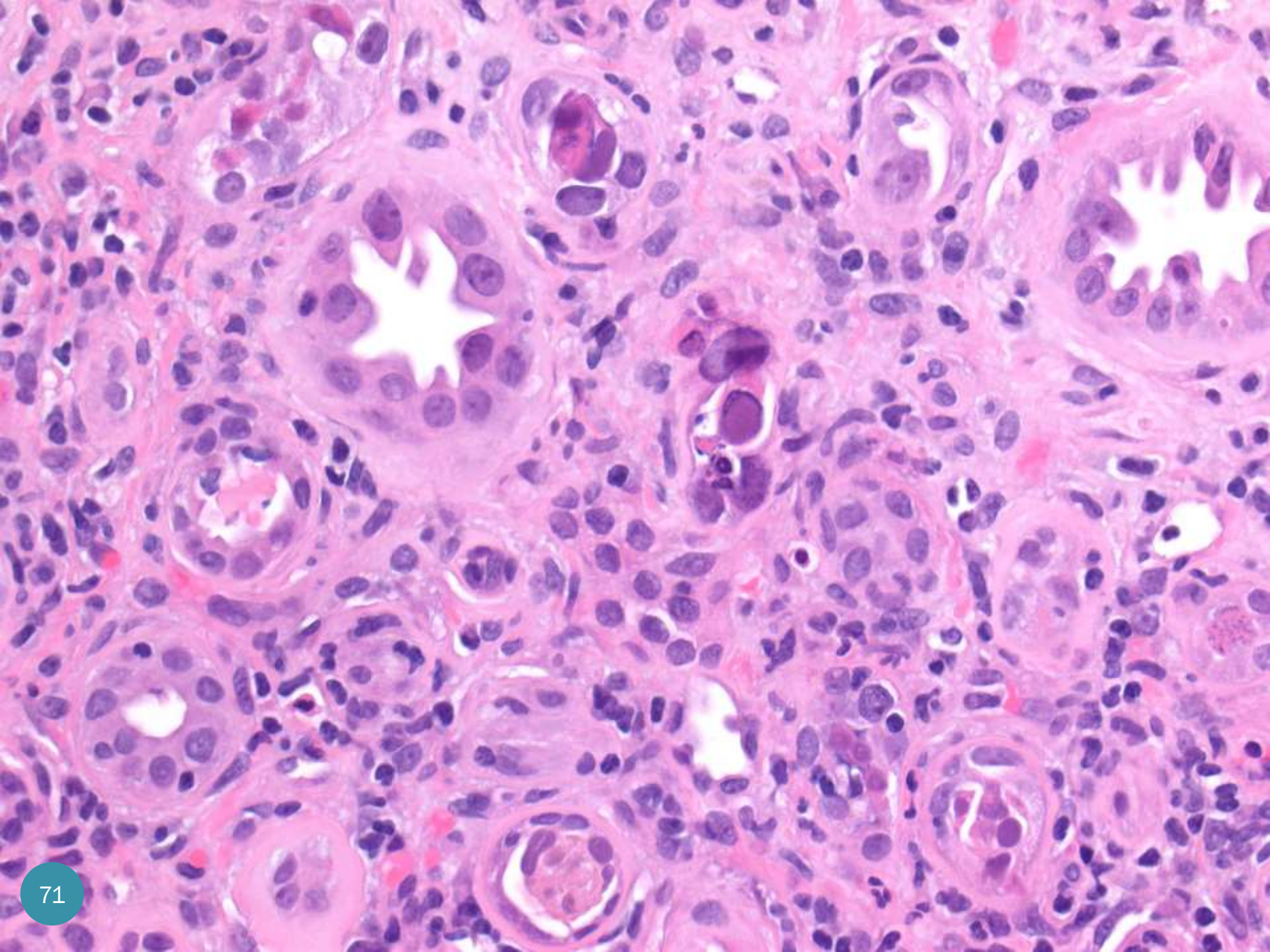
Calcineurin Inhibitor Toxicity

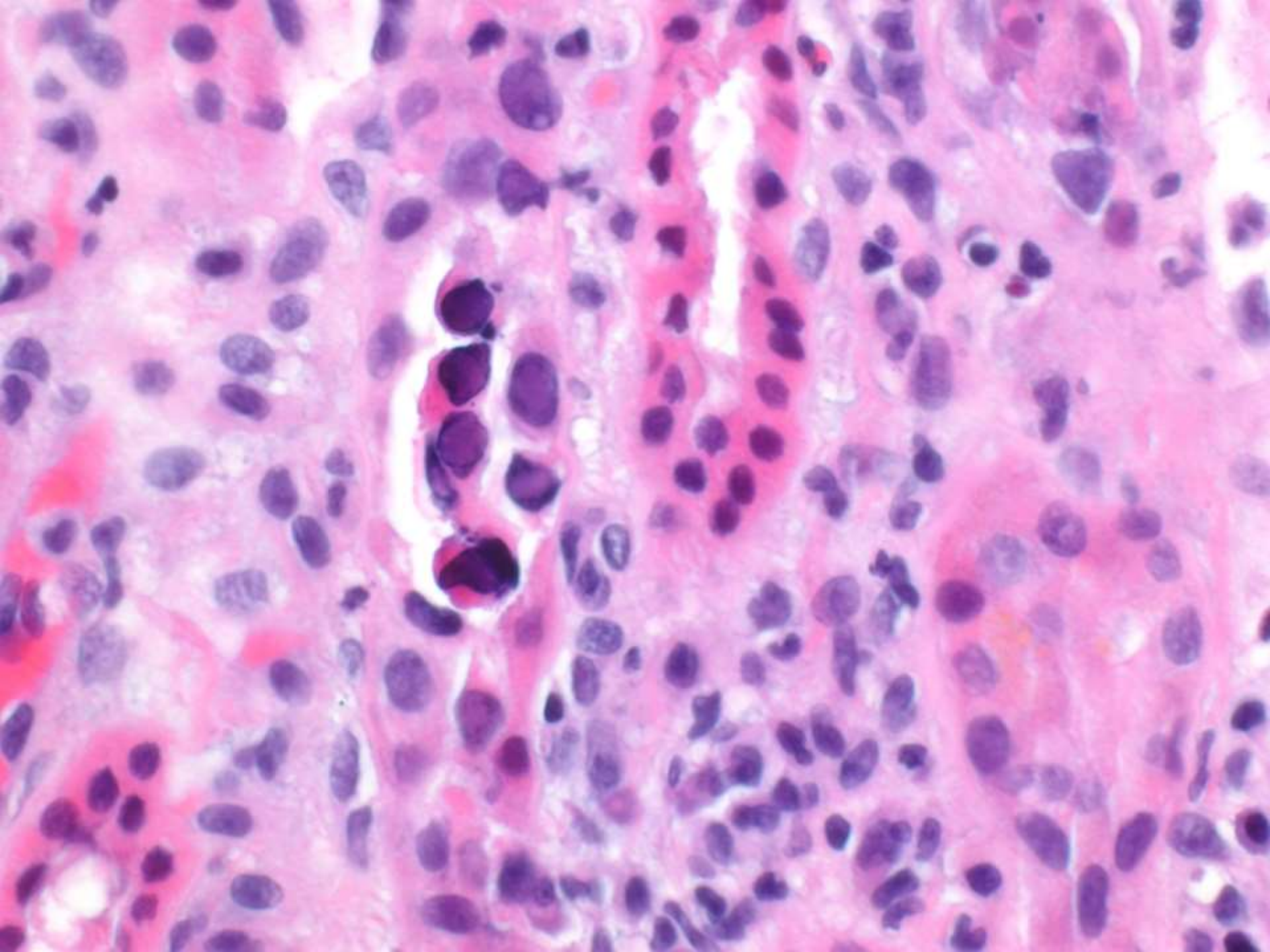
Chronic CNI toxicity

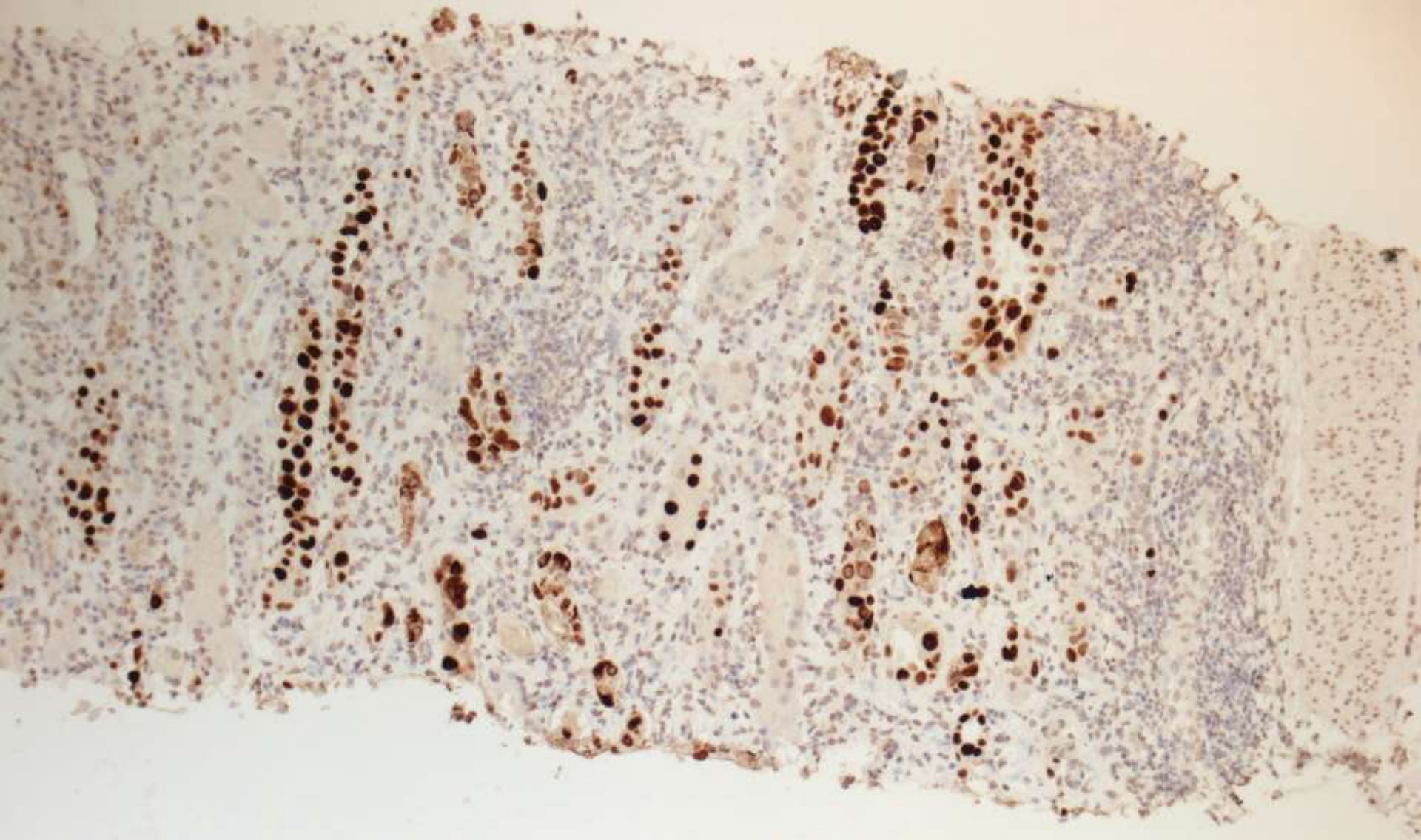


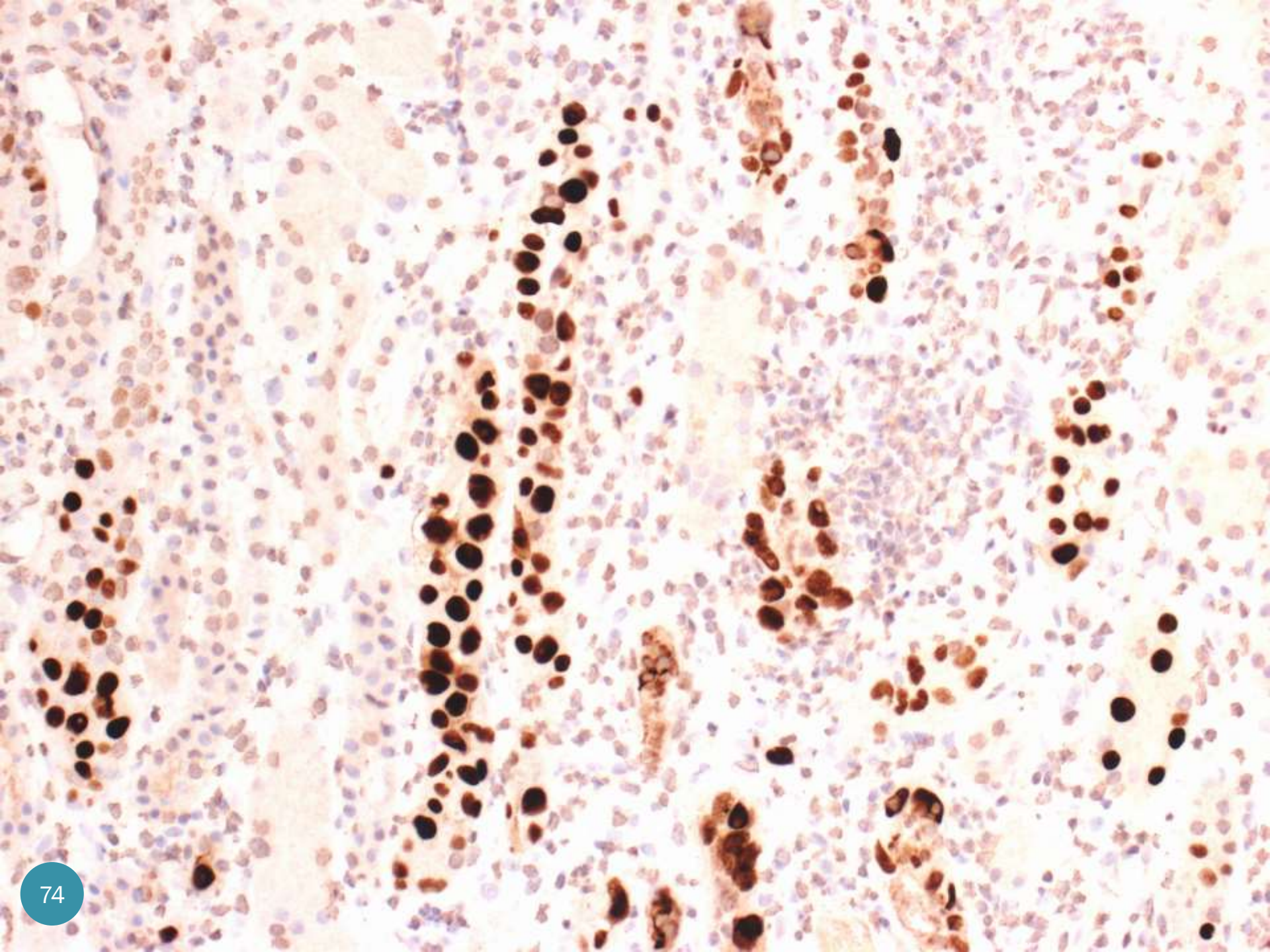
Polyomavirus Nephropathy









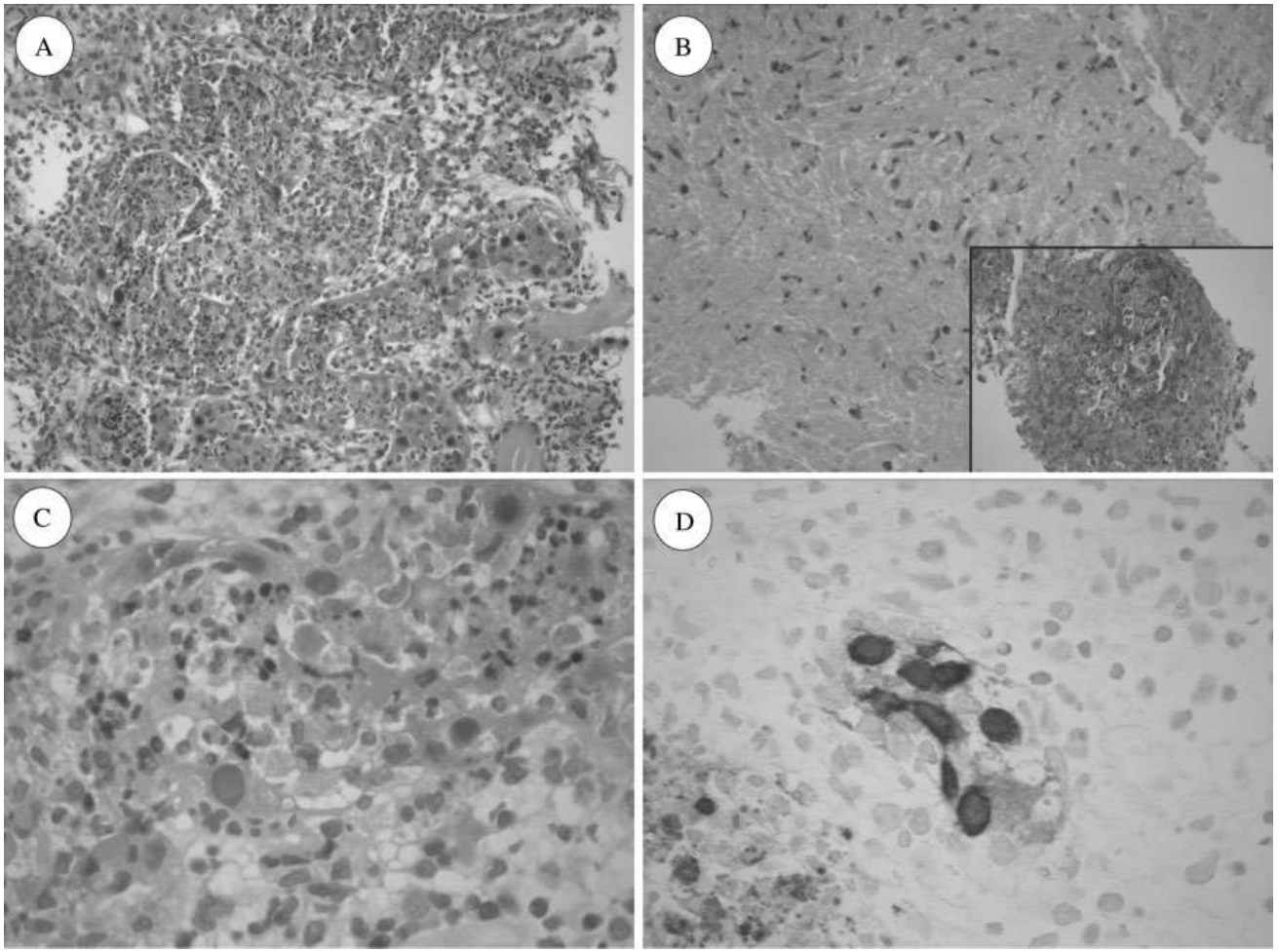


Polyomavirus Nephropathy

Banff Classes of Polyomavirus Nephritis	
Class	Viral Load and Fibrosis
1	pv1 + ci0-1
2	pv1 + ci-2-3 pv2 + ci0-3, or pv3 + ci0-1
3	pv3 + ci2-3
Tubules positive for virus: pv1 <1%, pv2 1-10%, pv3 >10% Interstitial fibrosis in cortex: ci0 0-5%, ci1 6-25%, ci2 26-50%, ci3 >50%	

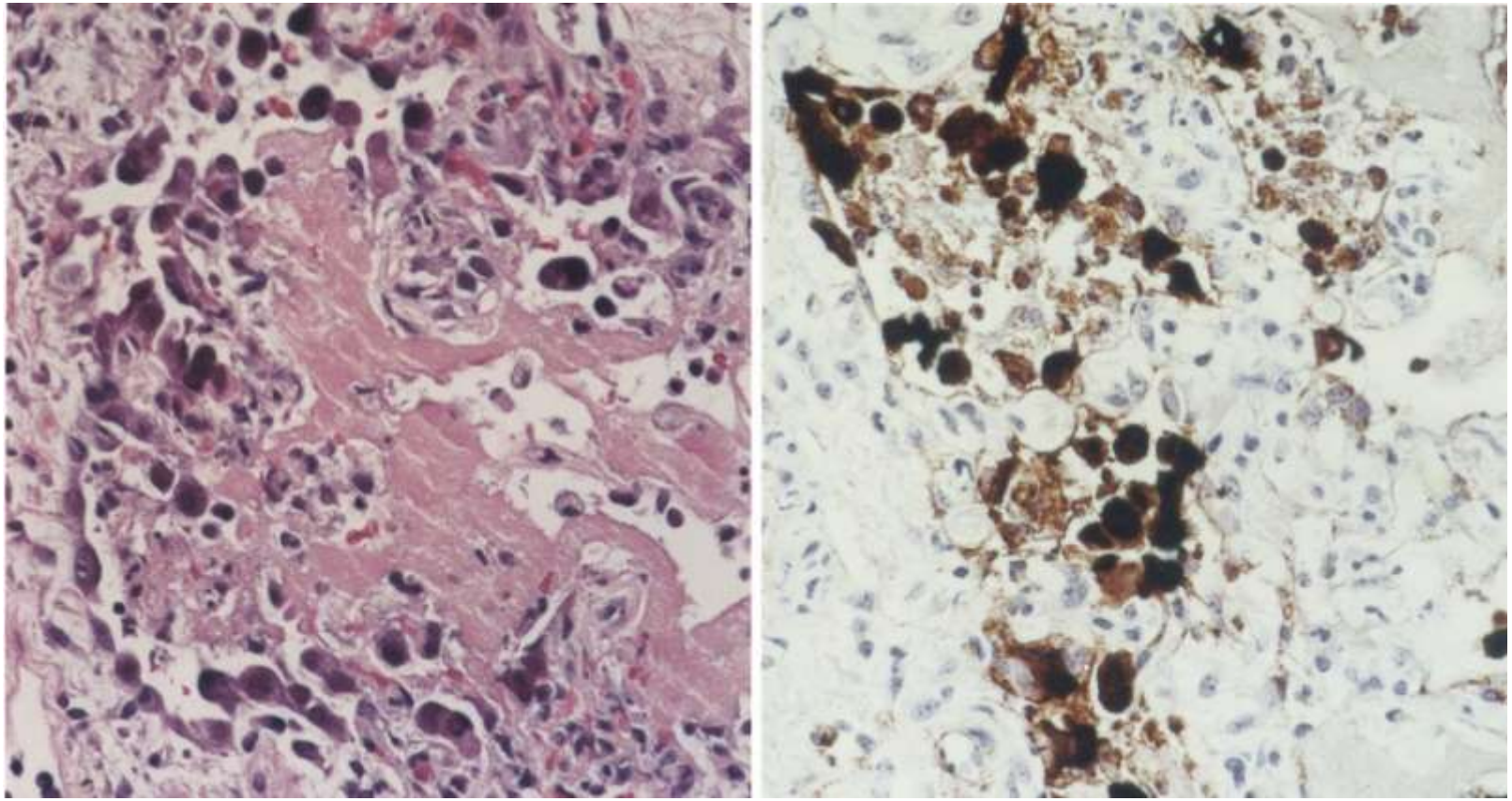
Nickeleit V, Singh HK, Randhawa P, et al. The Banff Working Group Classification of Definitive Polyomavirus Nephropathy: Morphologic Definitions and Clinical Correlations. J Am Soc Nephrol. 2018; 29: 680-693.

Adenovirus Nephropathy in Renal Allograft

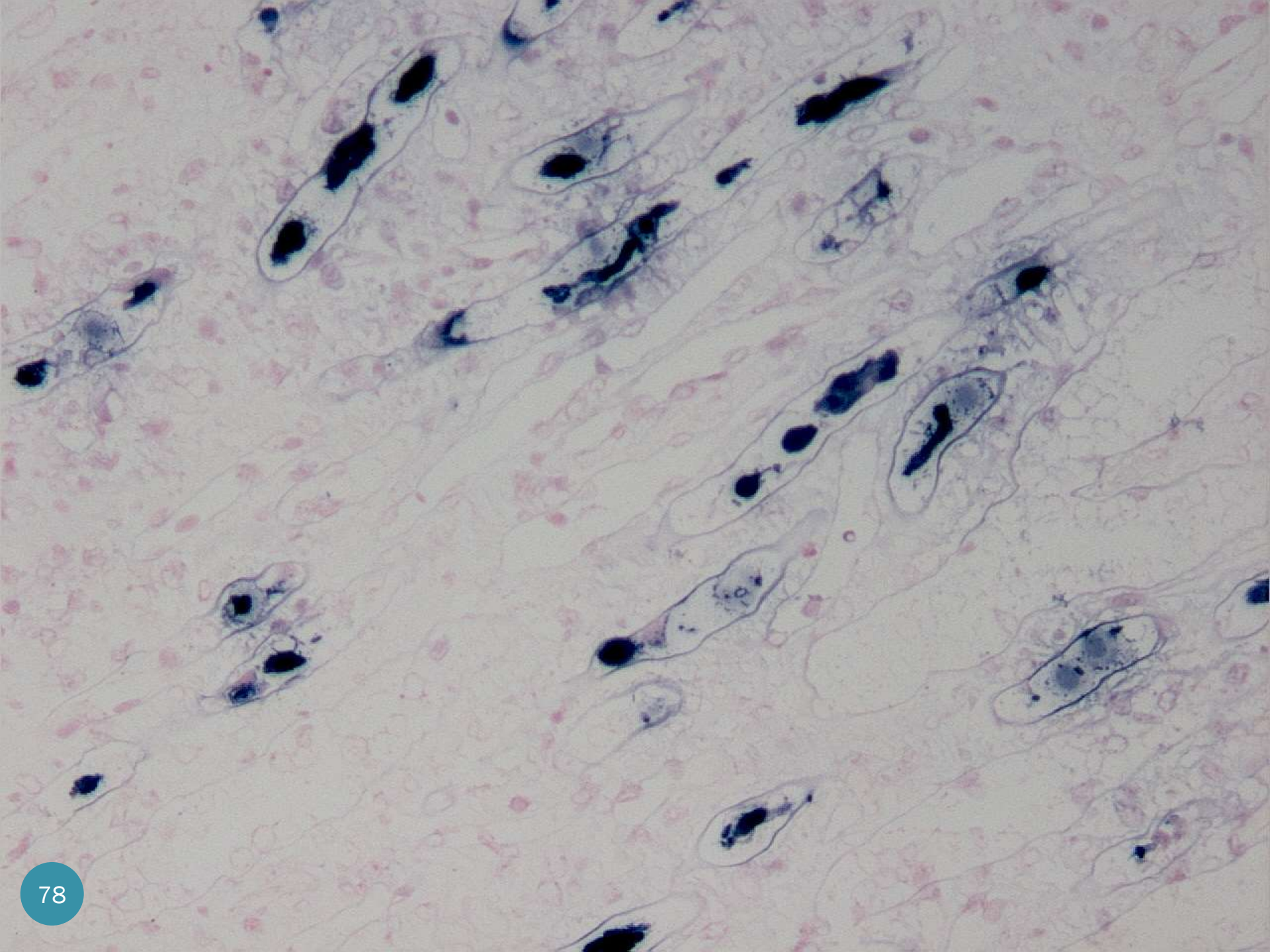


Alsaad KO et al. Nephrol Dial Transplant. 2007 Apr;22(4):1257-60

Adenovirus Nephropathy in Renal Allograft



Ardehali H et al. Transplantation. 2001 15;71:998-9



Thank you

Workshop #3:
RENAL PATHOLOGY WORKSHOP
Venue: Petale Royal Ballroom A

TIME	TOPIC	SPEAKER
	Moderator: Dr. Mohammed Akhtar	
1:00	Current Classification of vasculitis and associated glomerulopathies	Dr. Turki Al Hussain
1:45	Renal involvement in monoclonal gammopathies, including amyloidosis and fibrillar glomerulopathies	Dr. Hala Kassouf
2:30	Renal transplant pathology Part 1	Dr. Khaled Al Saad
3:15	15min Coffee Break	
	Moderator: Dr. Hala Kassouf	
3:30	Renal transplant pathology Part 2 (Interesting case review)	Dr. Khaled Al Saad
4:15	Interstitial Nephritis	Dr. Mohammed Akhtar
4:50	Conclusion	Dr. Mohammed Akhtar

Pathology of Renal Transplant

Part 2

Doha 2023

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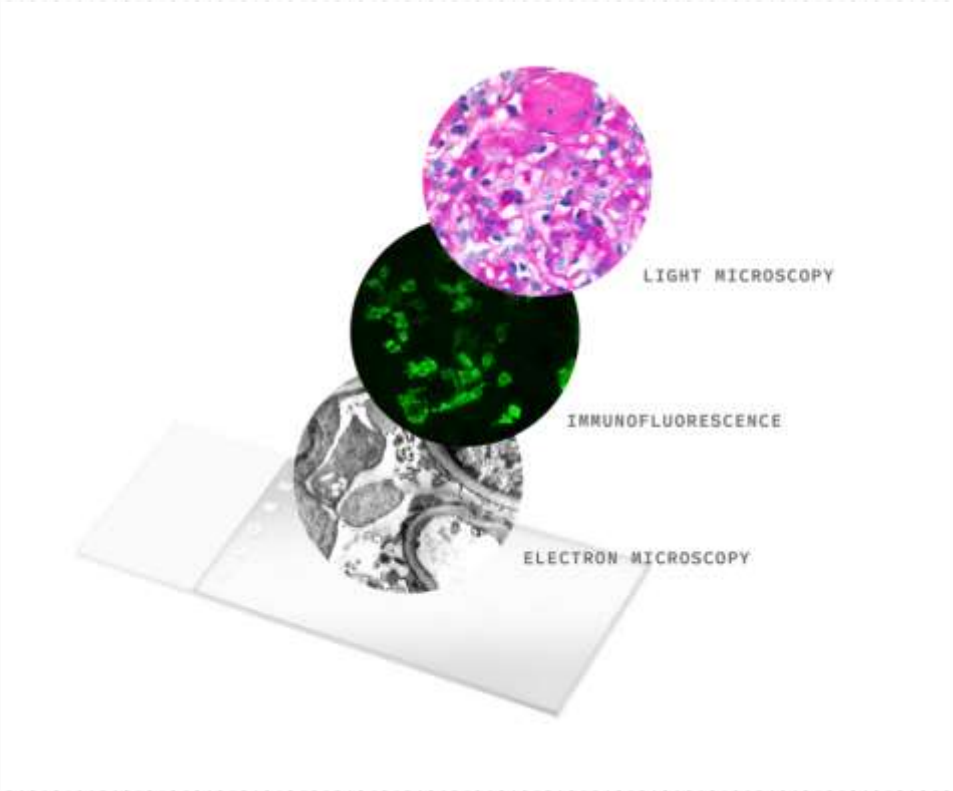
King Faisal Specialist Hospital & Research Centre
Gen. Org. مؤسسة عامة

Disclosure Statement

- I make the following declaration in relation to this CPD activity:
  - There is no conflict of interest.
  - There is no plagiarism or copying infringement.
  - The content is balanced and free of bias, either commercial or non-commercial.

Now let’s look at some cases



Case 1

- 42-year-old woman, known case of end stage kidney disease due to chronic hypertensive nephropathy, received living-related kidney transplant from her 21-year-old year old son.
- Within the following 24 hours, her urine output dropped to 915 ml.
- Graft Doppler Ultrasound revealed well-vascularized graft with no evidence of a vascular thromboembolic event. A renal scan demonstrated features suggestive of acute kidney injury.
- On the second day post surgery, the patient became anuric and developed volume overload and respiratory distress, which necessitated a session of hemodialysis.
- On the fourth day post surgery, the patient developed graft pain and became tachycardia and hypotensive. Abdominal ultrasound revealed a 20 cm peri-graft and retroperitoneal hematoma at the upper pole of the renal graft.

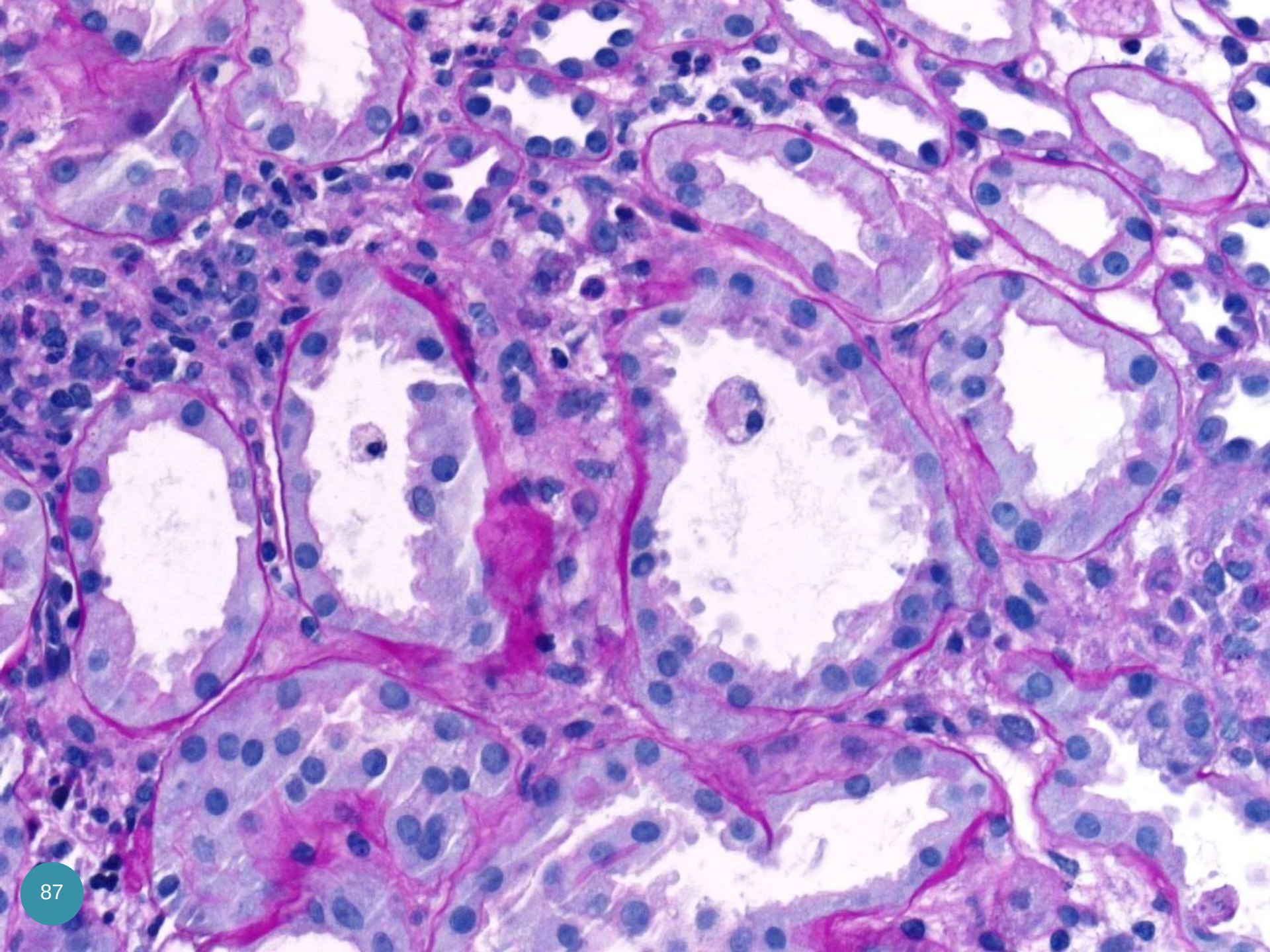
Case 1

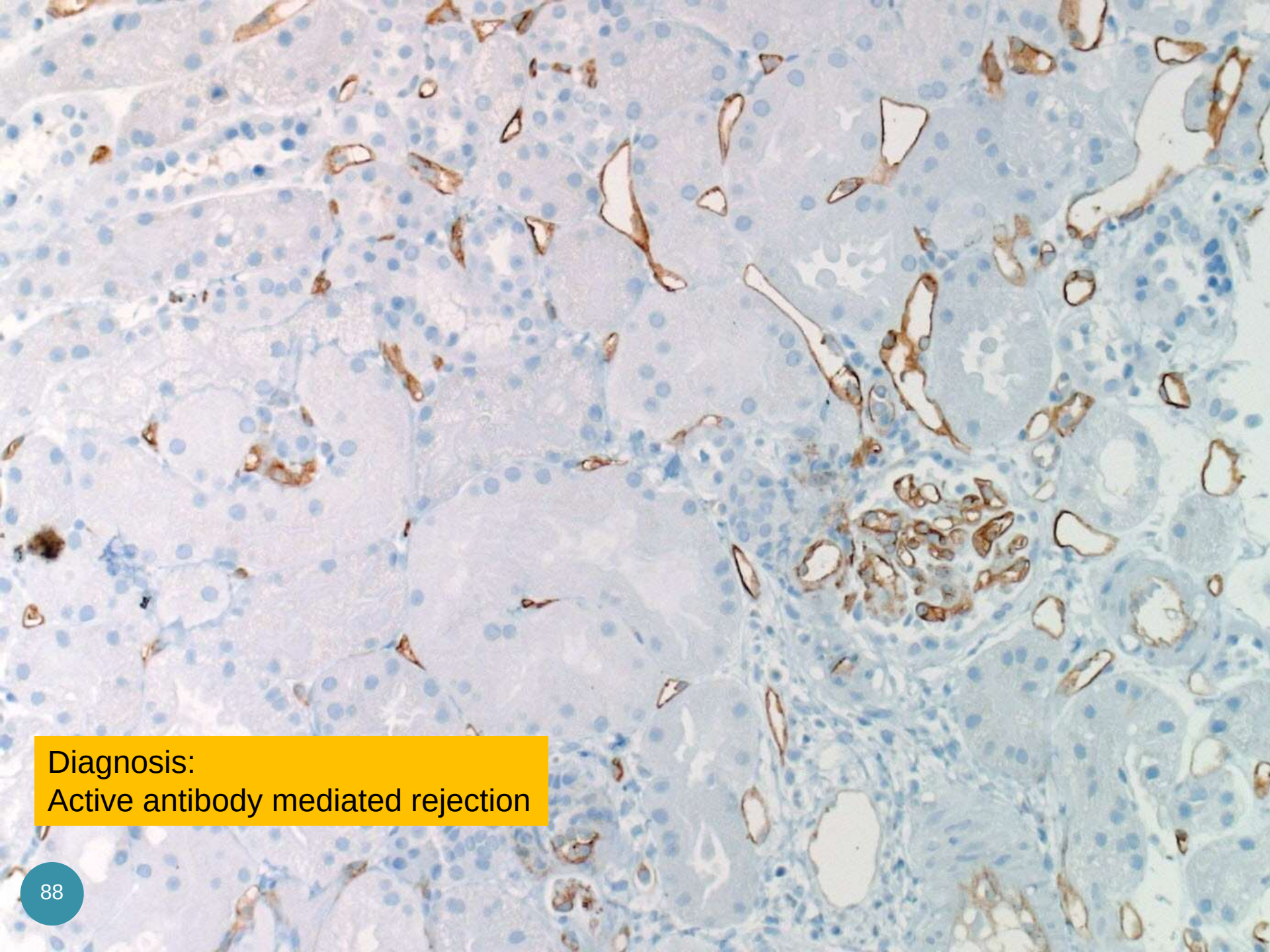
- The patient was immediately taken to the operating room → exploration of the renal graft.
- Findings:
  - Haematoma → evacuated
  - Laceration measuring 12 cm in length and extending along the convex border from the upper to lower pole of the kidney, causing evisceration of at least 1.5 cm in depth and exposing the kidney parenchyma, and was associated with active oozing → surgically salvaged
  - The graft vessels were patent and there was no bleeding from the vascular sites of anastomosis

Case 1

Laceration along the convexity of the renal allograft, extending from the upper to lower pole of the kidney

The urine output improved to 0.7 ml/kg/hr in the same day of re-exploration

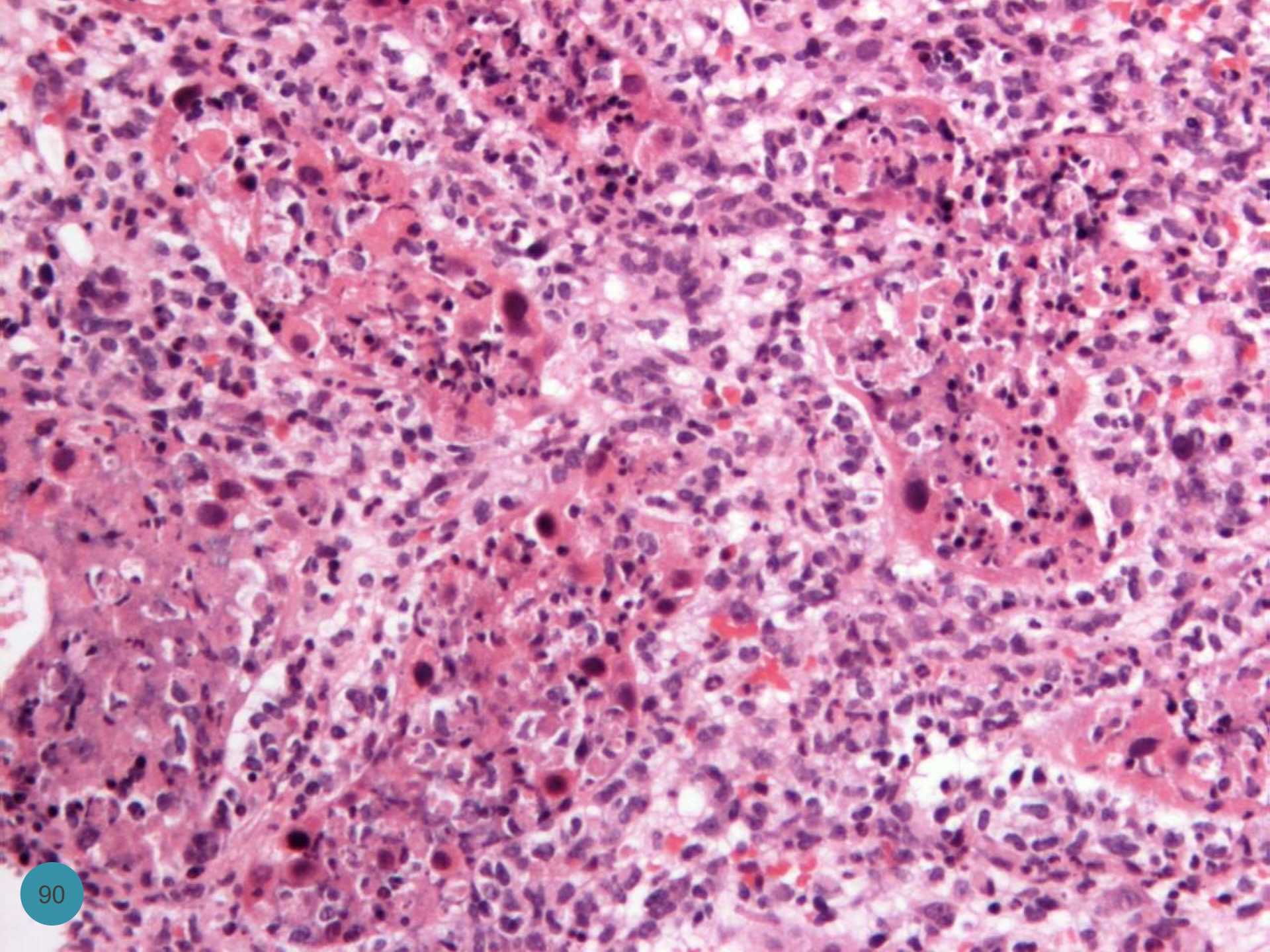


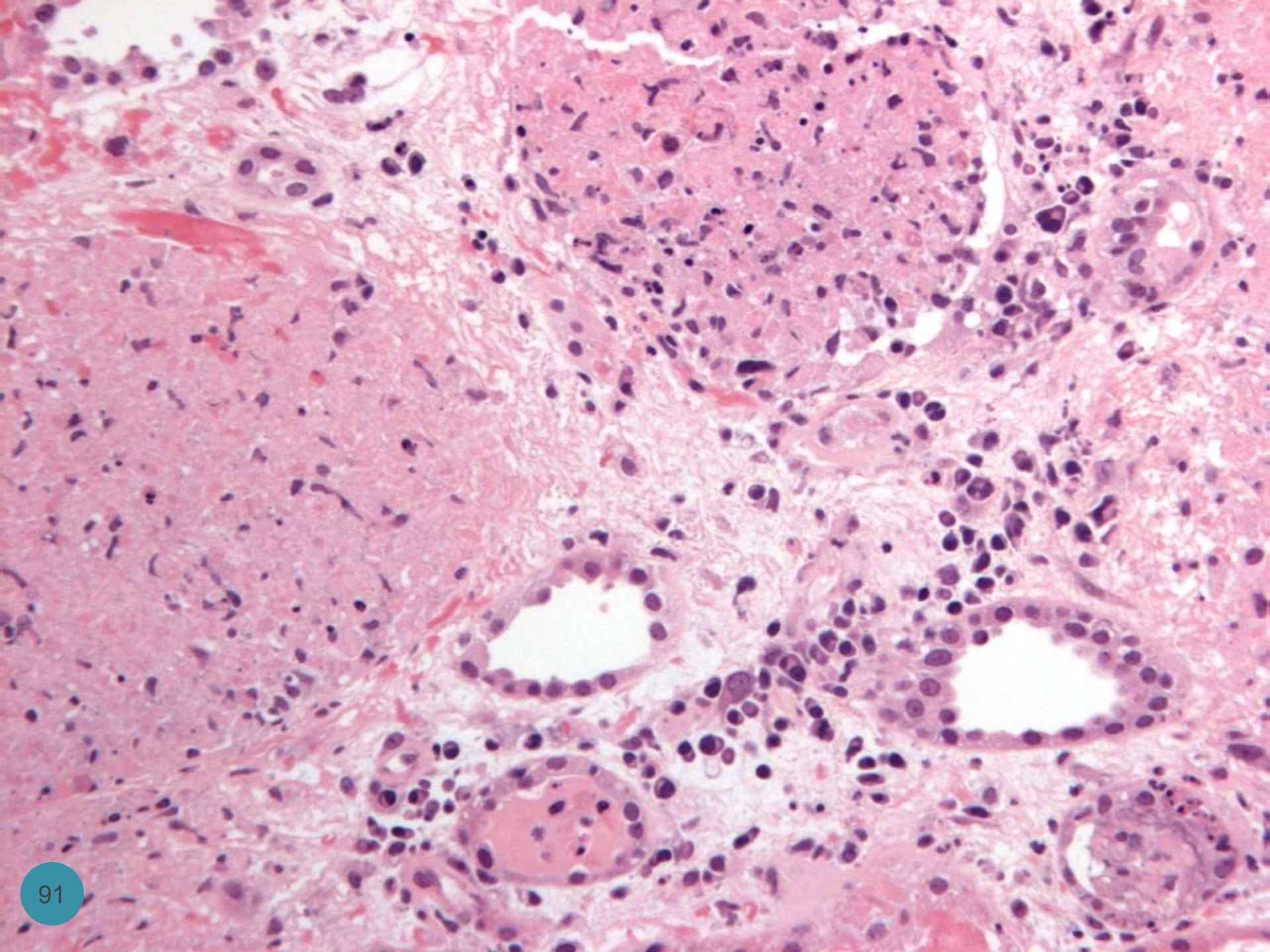


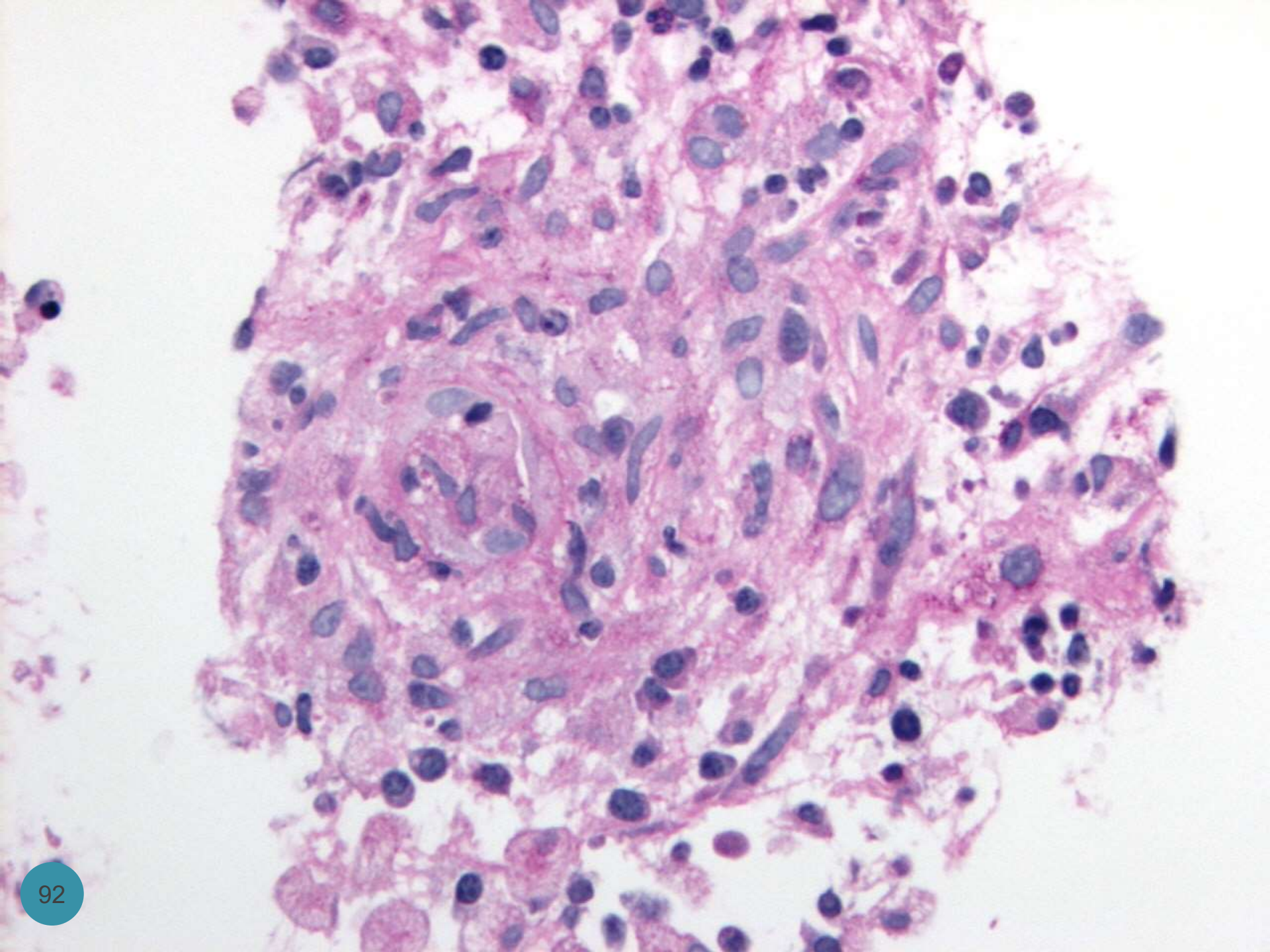
Diagnosis:
Active antibody mediated rejection

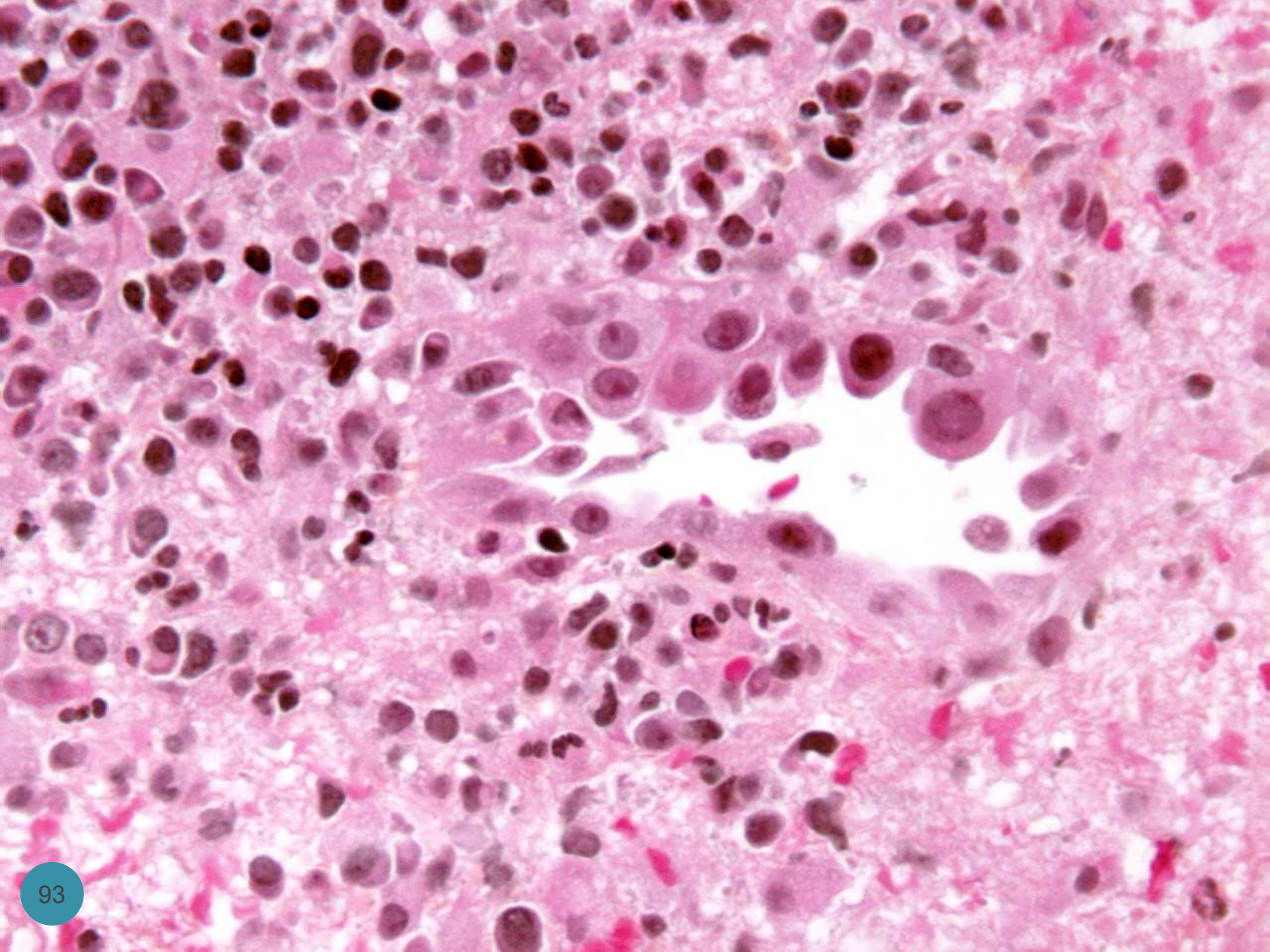
Case 2

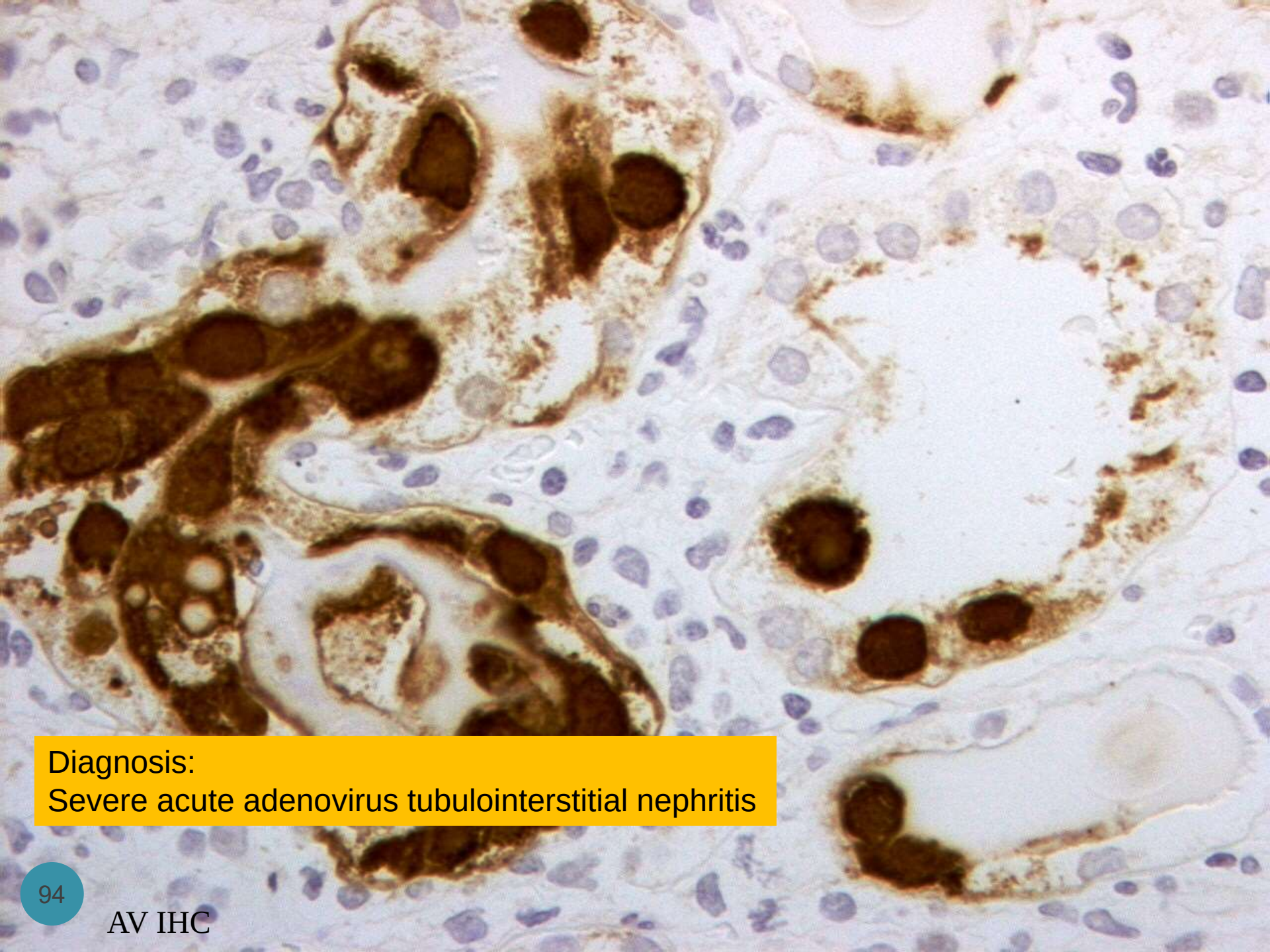
- 19-year-old male presented 12 years post renal transplant for ESRD secondary to idiopathic FSGS with:
  - Two weeks history of fever, chills, dysuria and pain over the site of the renal allograft.
  - Decreased urine output for 1 week.
  - Gross haematuria for 2 days.











Diagnosis:
Severe acute adenovirus tubulointerstitial nephritis

AV IHC

Case 3

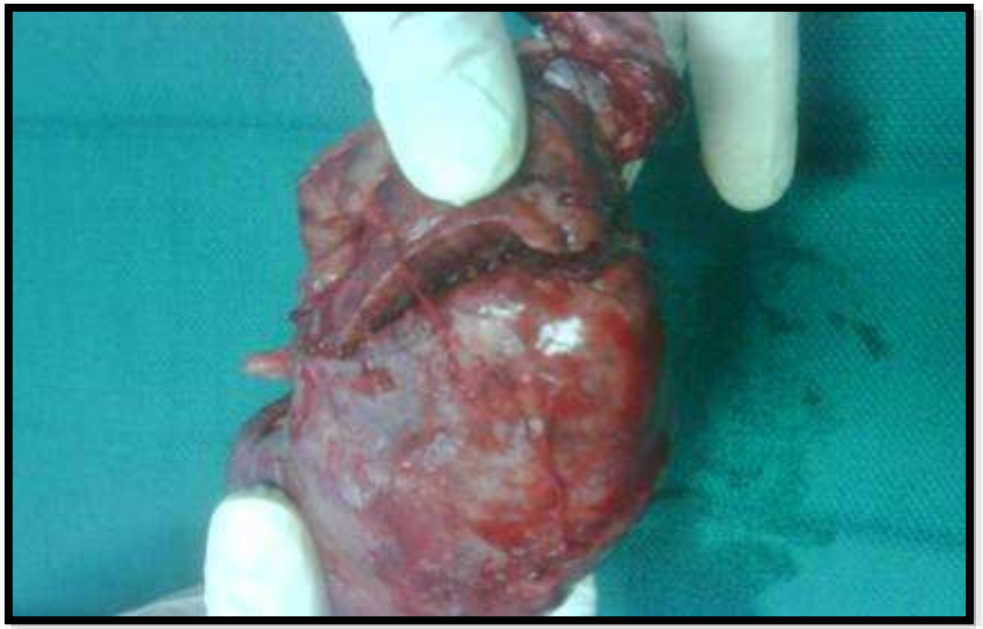
- 29-year-old man received living-unrelated kidney transplant abroad for ESKD secondary to neurogenic bladder.
- Forty-eight months after transplantation, the patient was diagnosed in another institution to have chronic allograft failure based on slow rising serum creatinine. No renal allograft biopsy was obtained.
- Sixty-three months after renal transplantation, the patient was first seen in our hospital, when he presented with hypoxic respiratory failure secondary to pneumonia, pulmonary oedema, and deteriorating kidney allograft function. Biopsy refused.
- Two months later (65 months post renal transplant), the patient was admitted because of abdominal pain, graft tenderness and gross haematuria.

Case 3

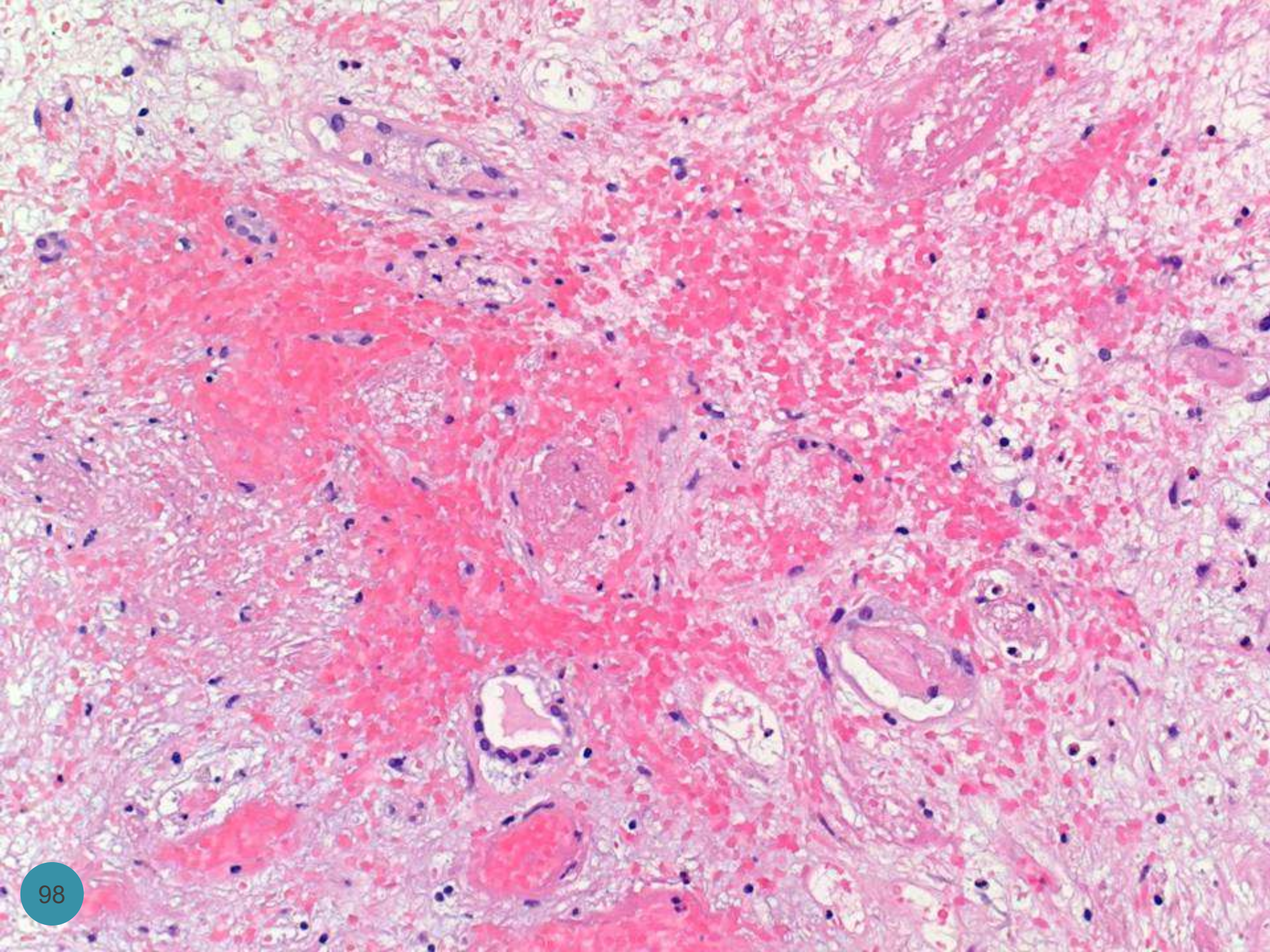
- An enhanced abdominal computed tomography (CT) scan revealed few scattered hyperdense foci in the renal allograft, in keeping with micro haemorrhage and micro perforations. The renal artery and vein were patent.

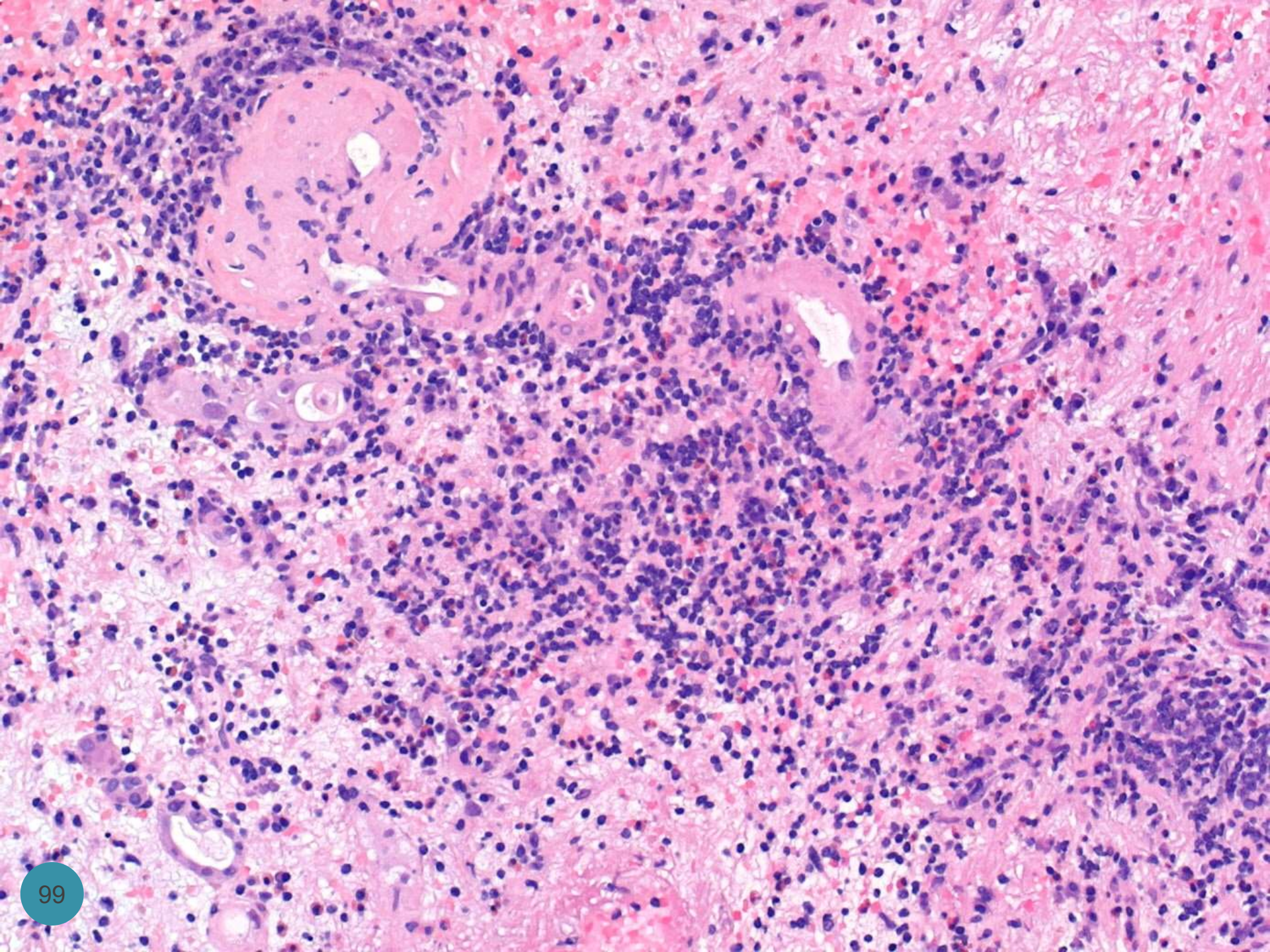
Case 3

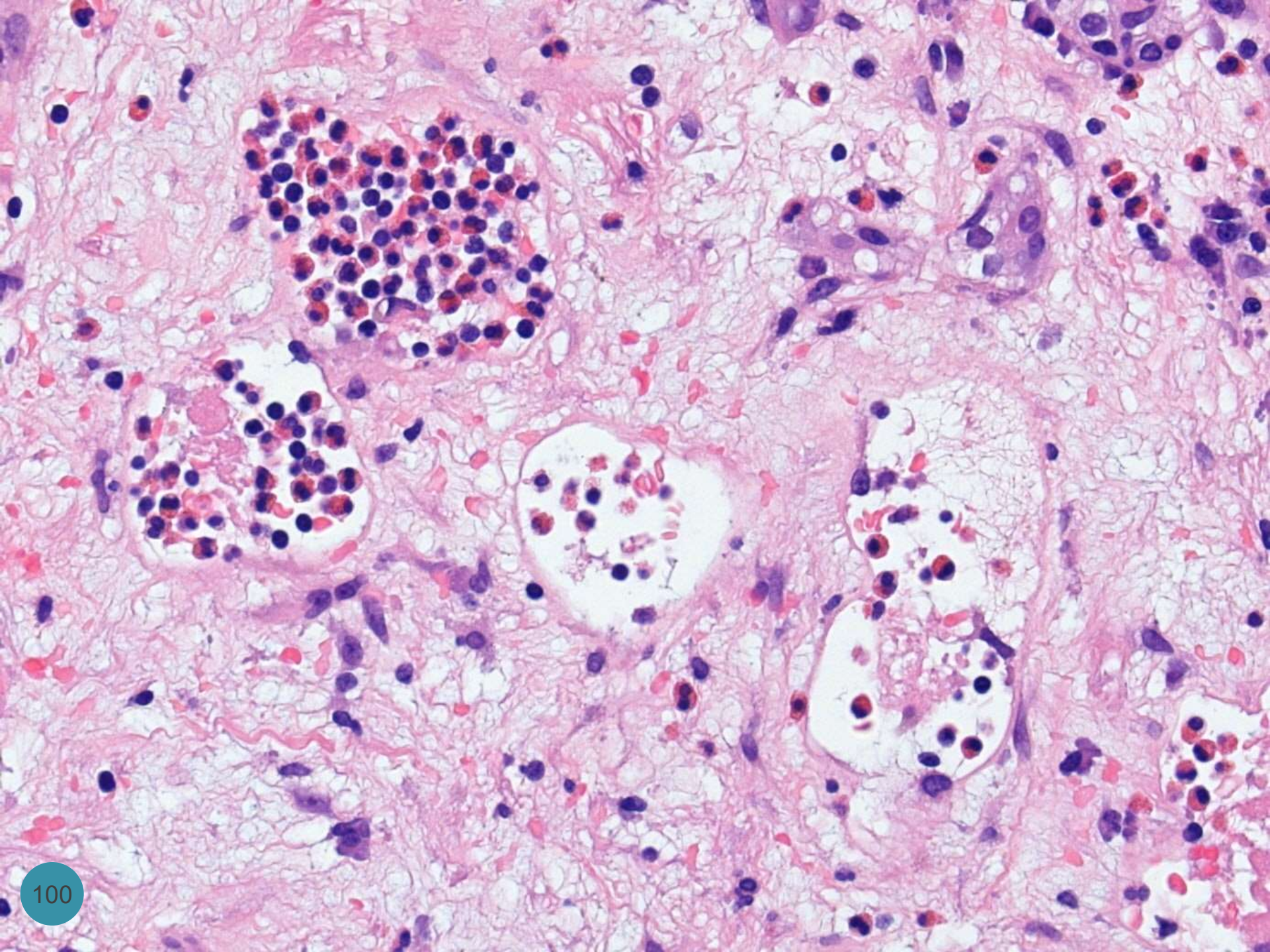
- The patient was taken to the operating room, where urinary bladder irrigation and washout revealed 3 litres of partially clotted blood.

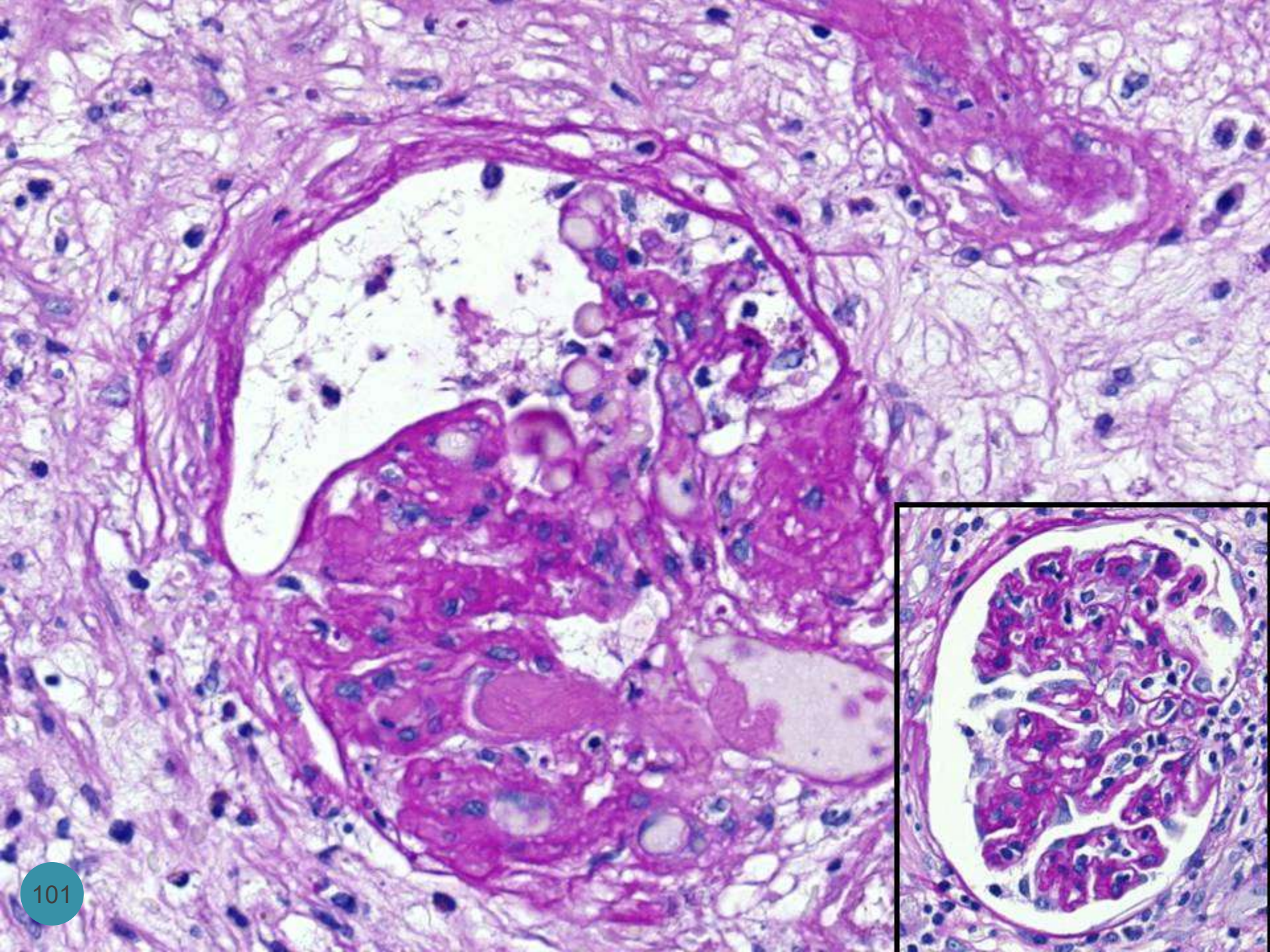


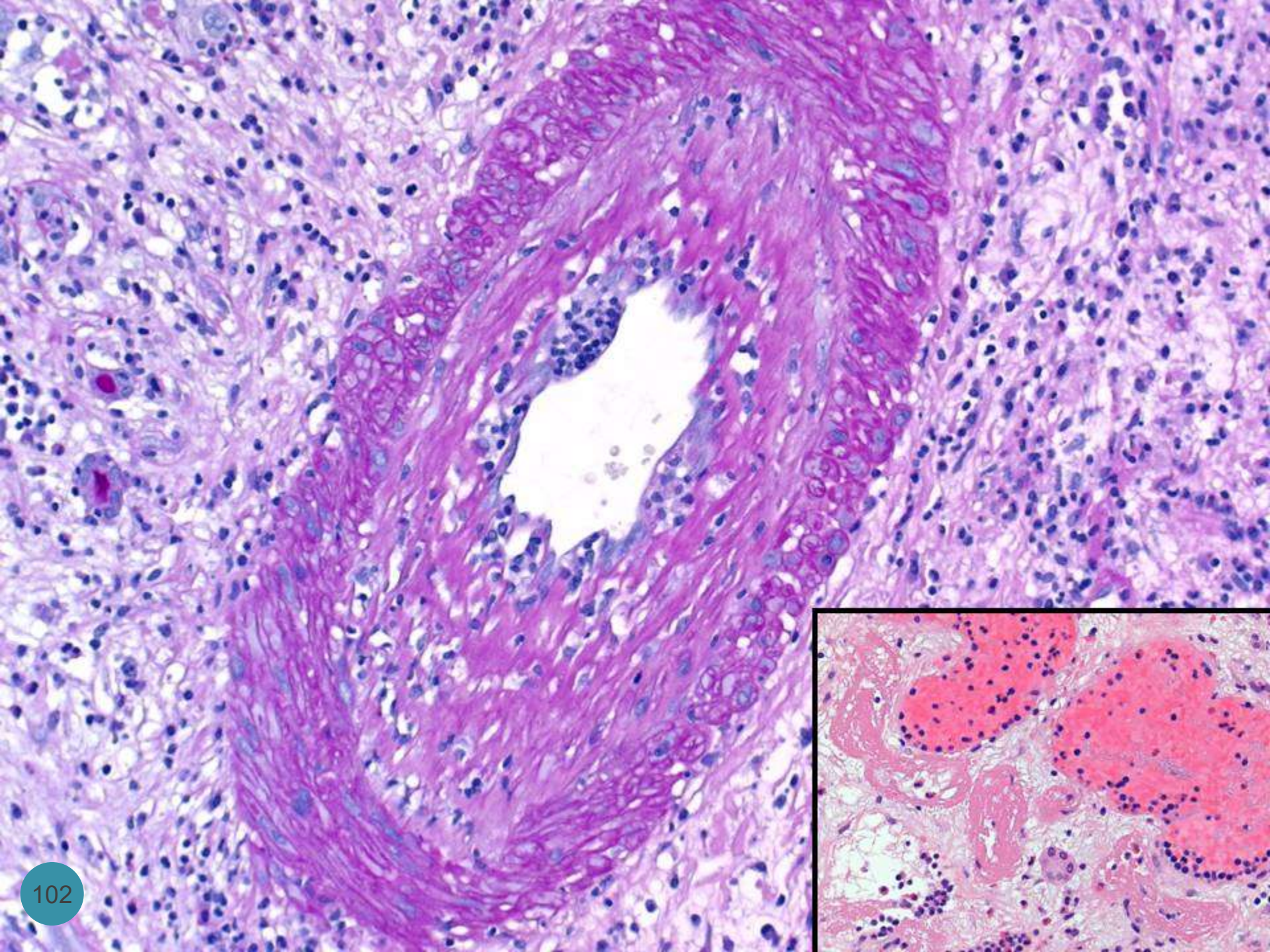
- Exploration of the renal graft showed ruptured graft.

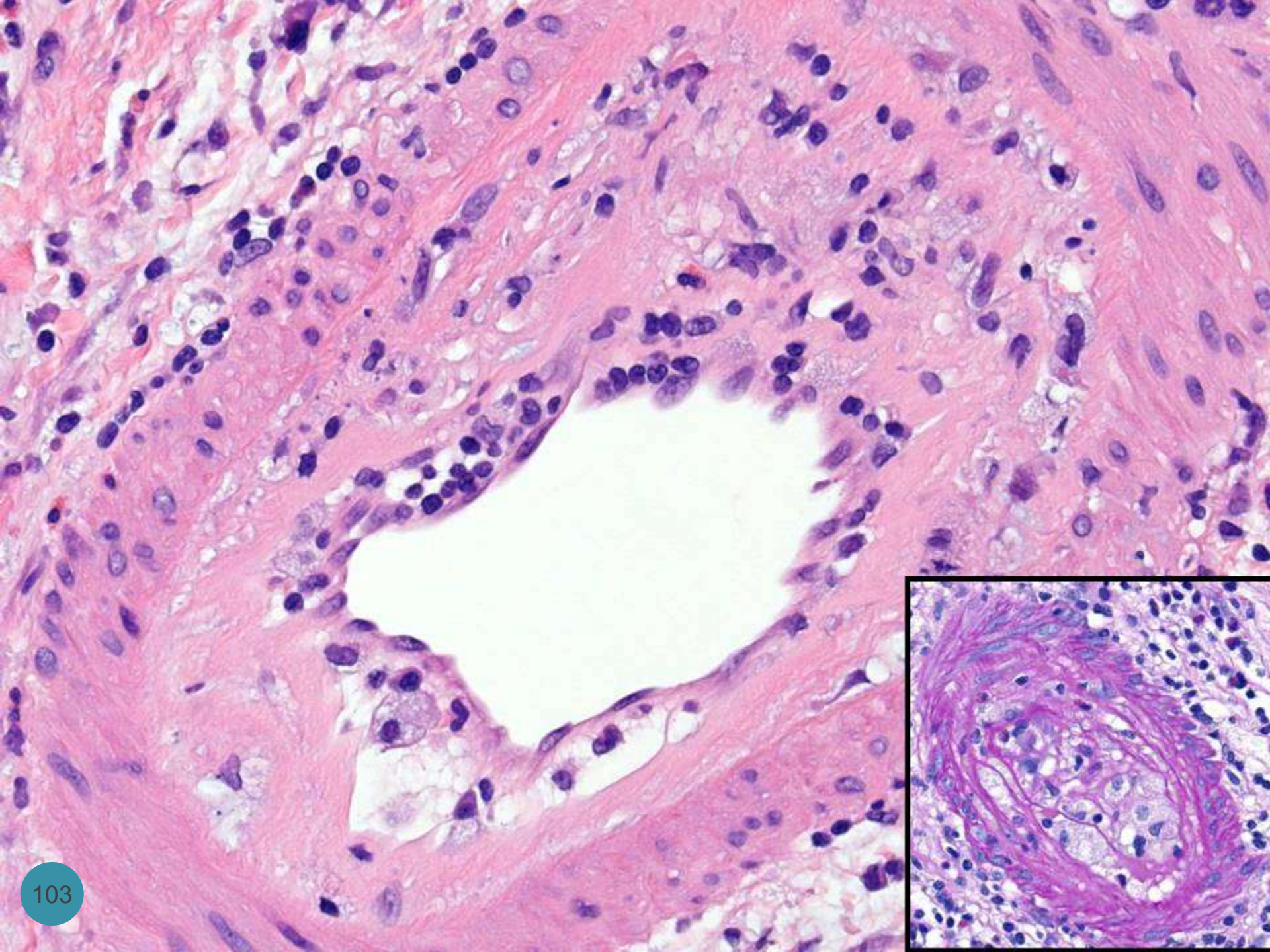


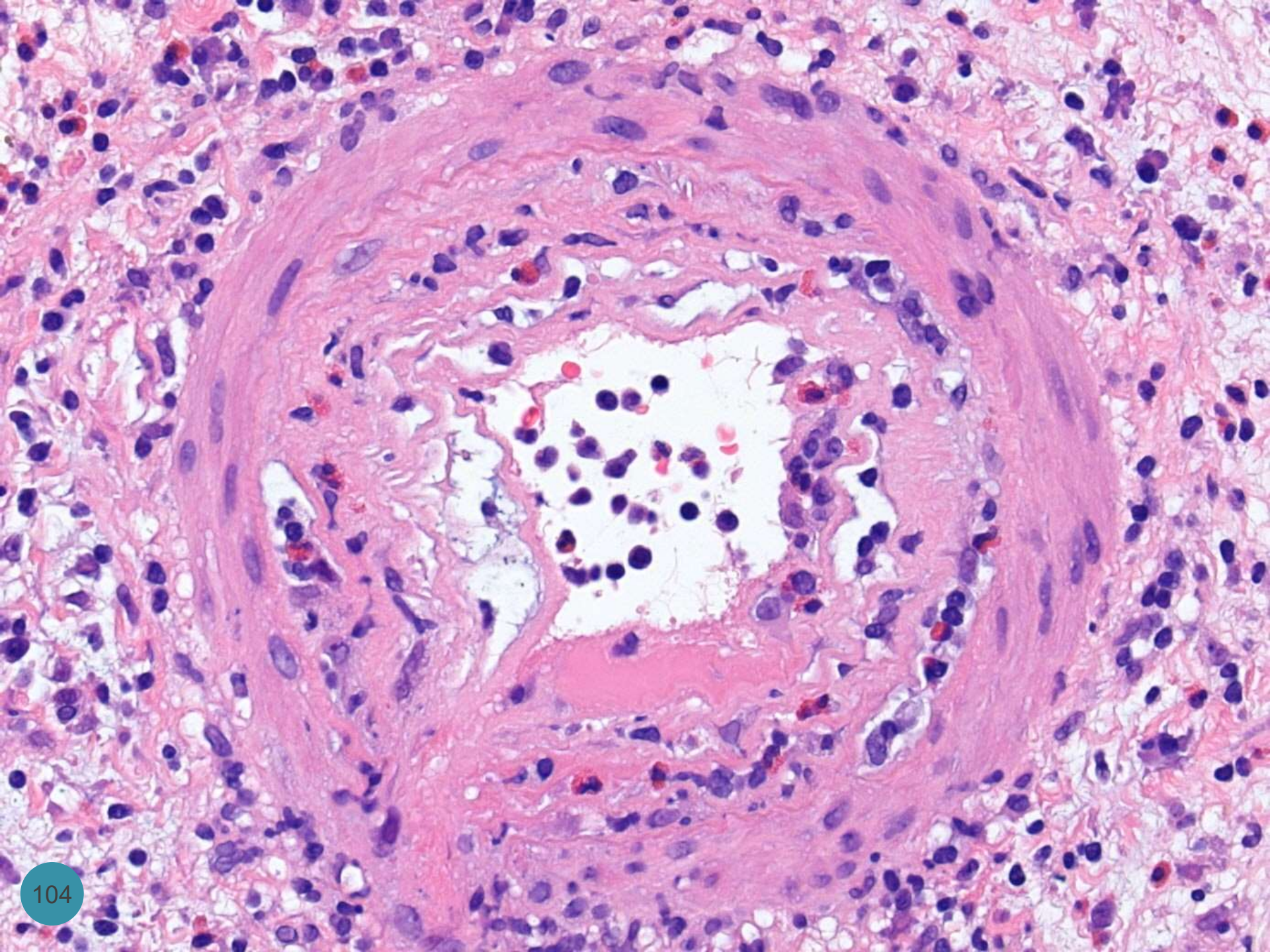


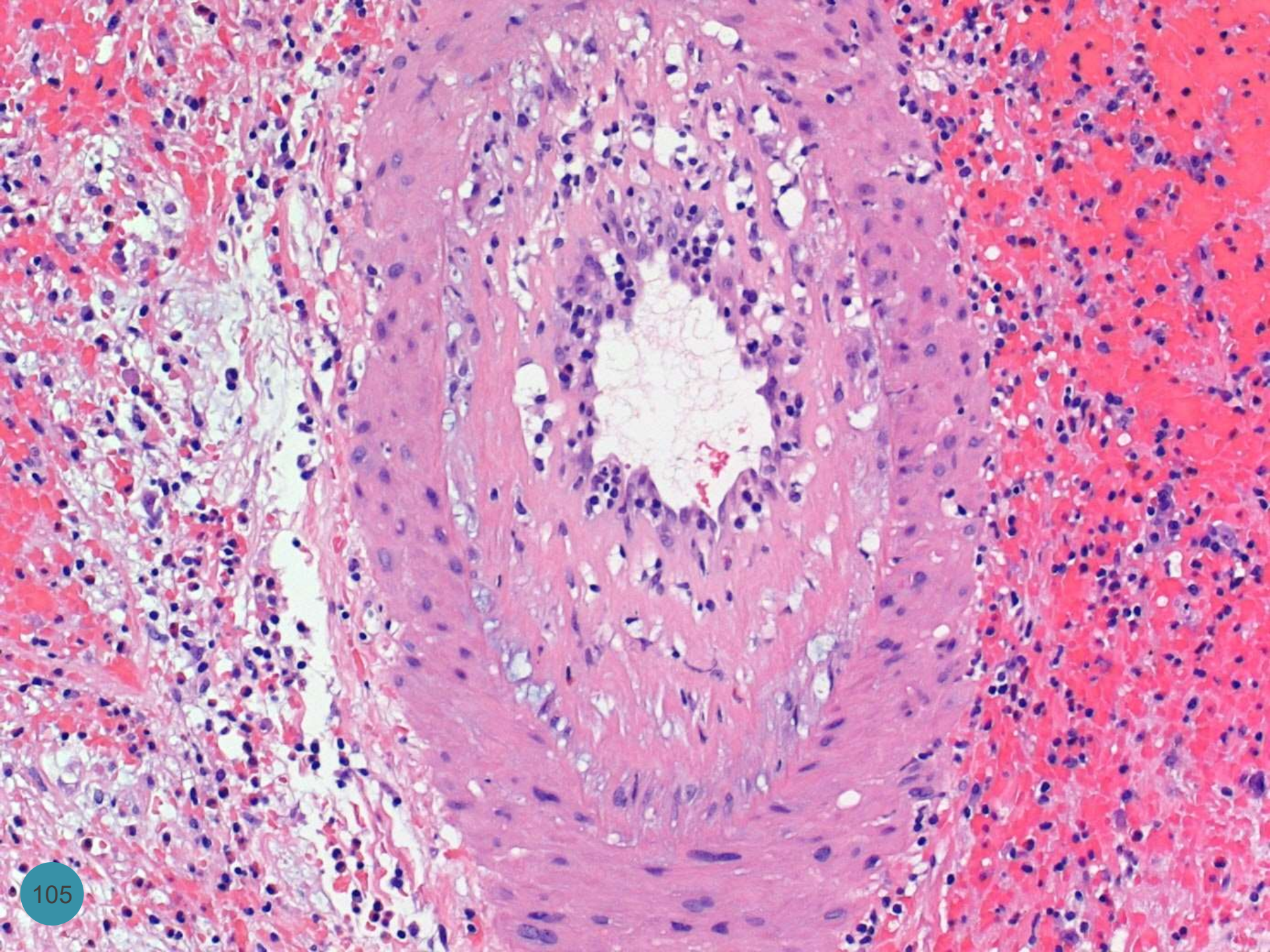


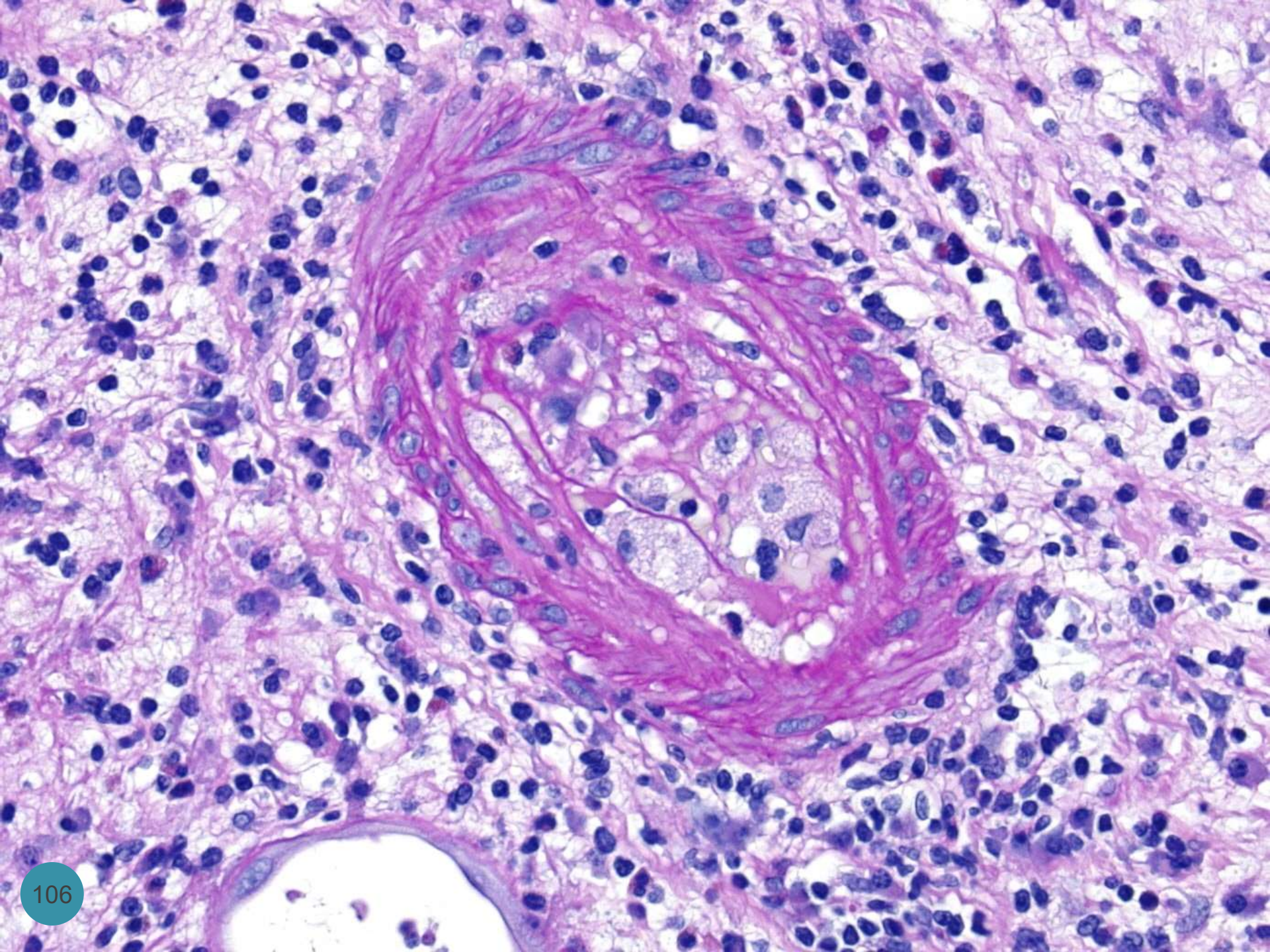


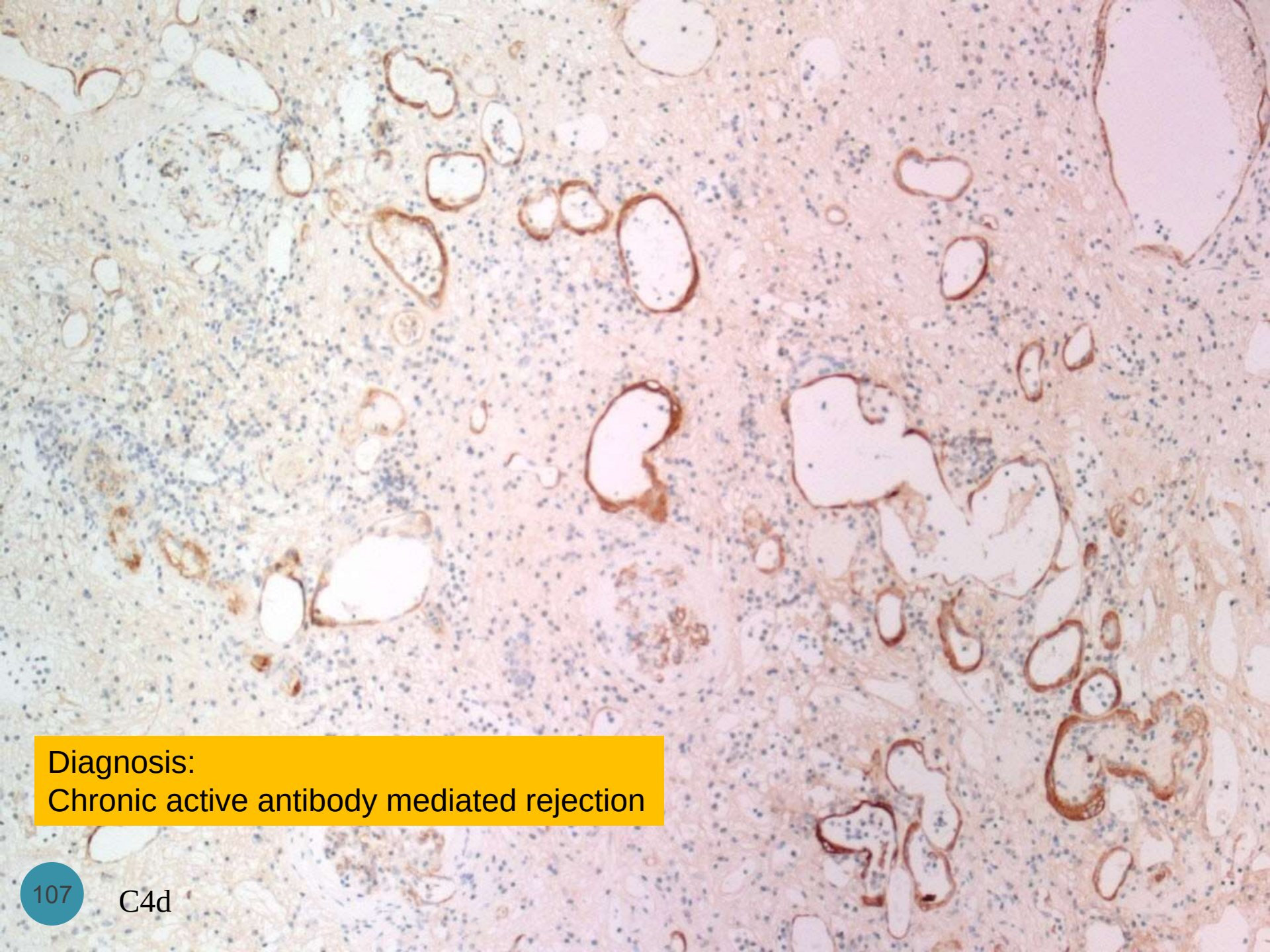










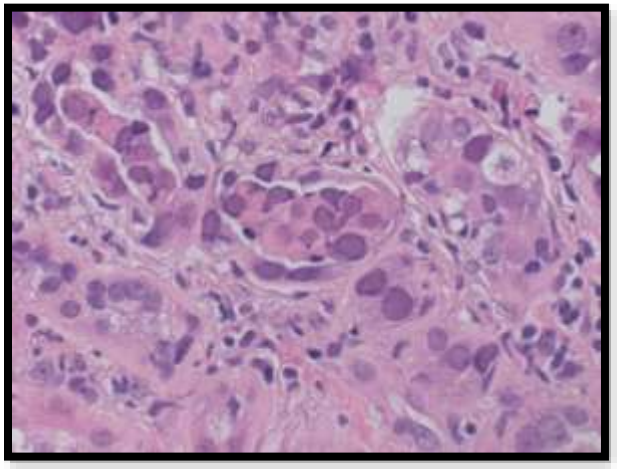


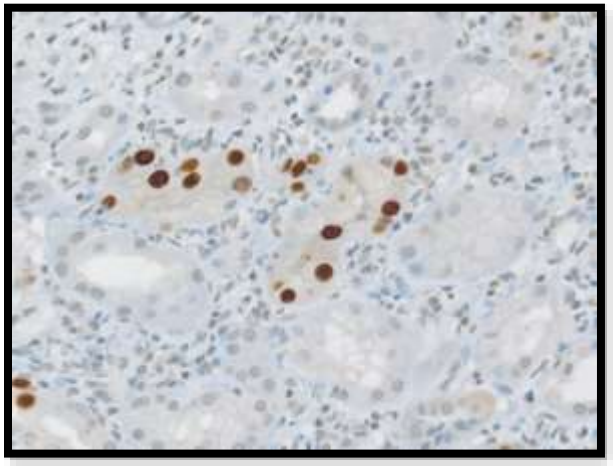
Diagnosis:
Chronic active antibody mediated rejection

C4d

Case 4

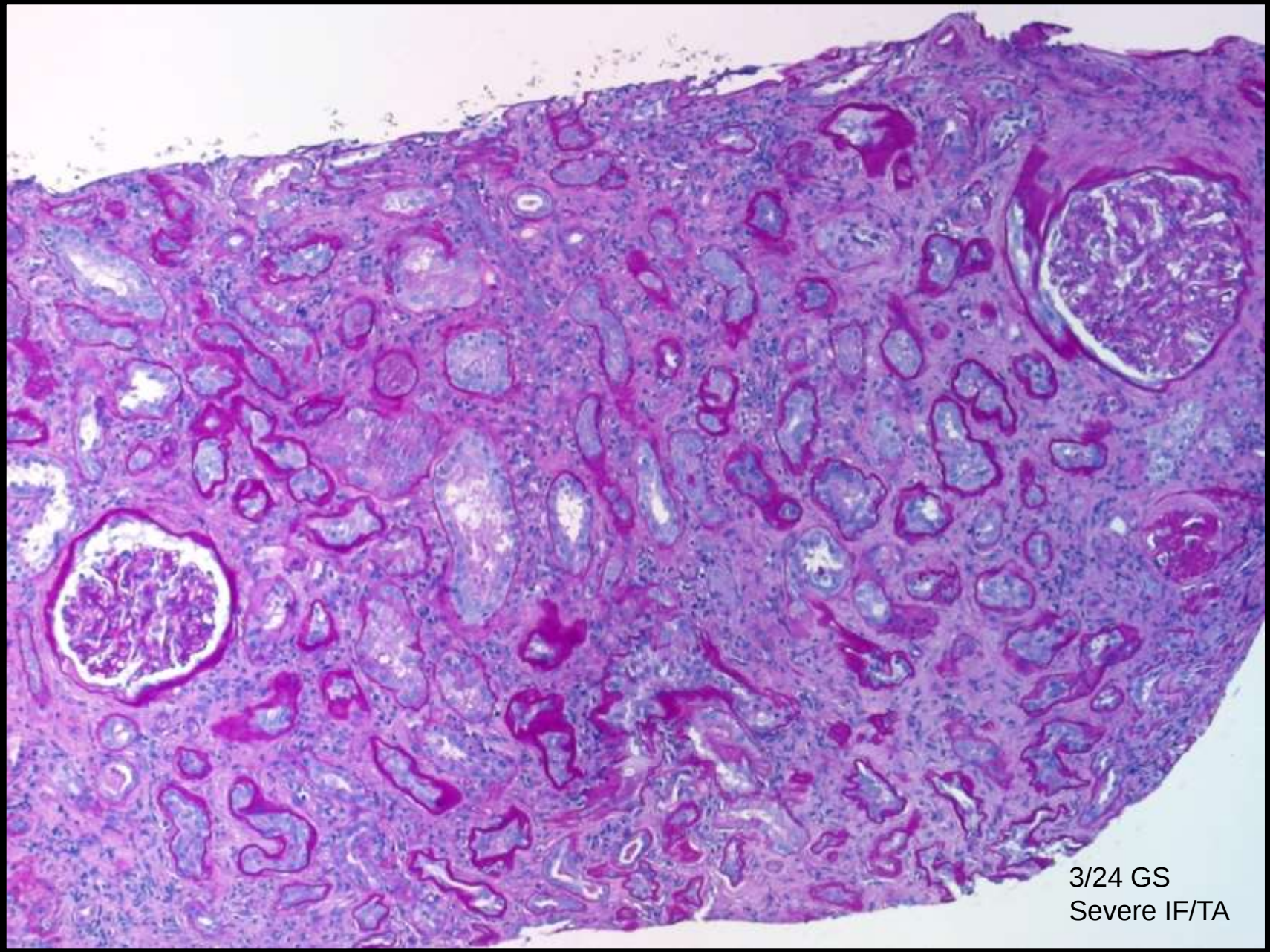
- 11-year-old male.
- Known case of renal osteodystrophy with progressive bone deformity and end stage kidney disease.
- Status post renal transplantation 30 months ago.
- Pots transplant clinical course:
  - Renal artery stenosis & hypertension
    - Angioplasty
  - Polyoma virus nephropathy, documented by two renal allograft biopsies.

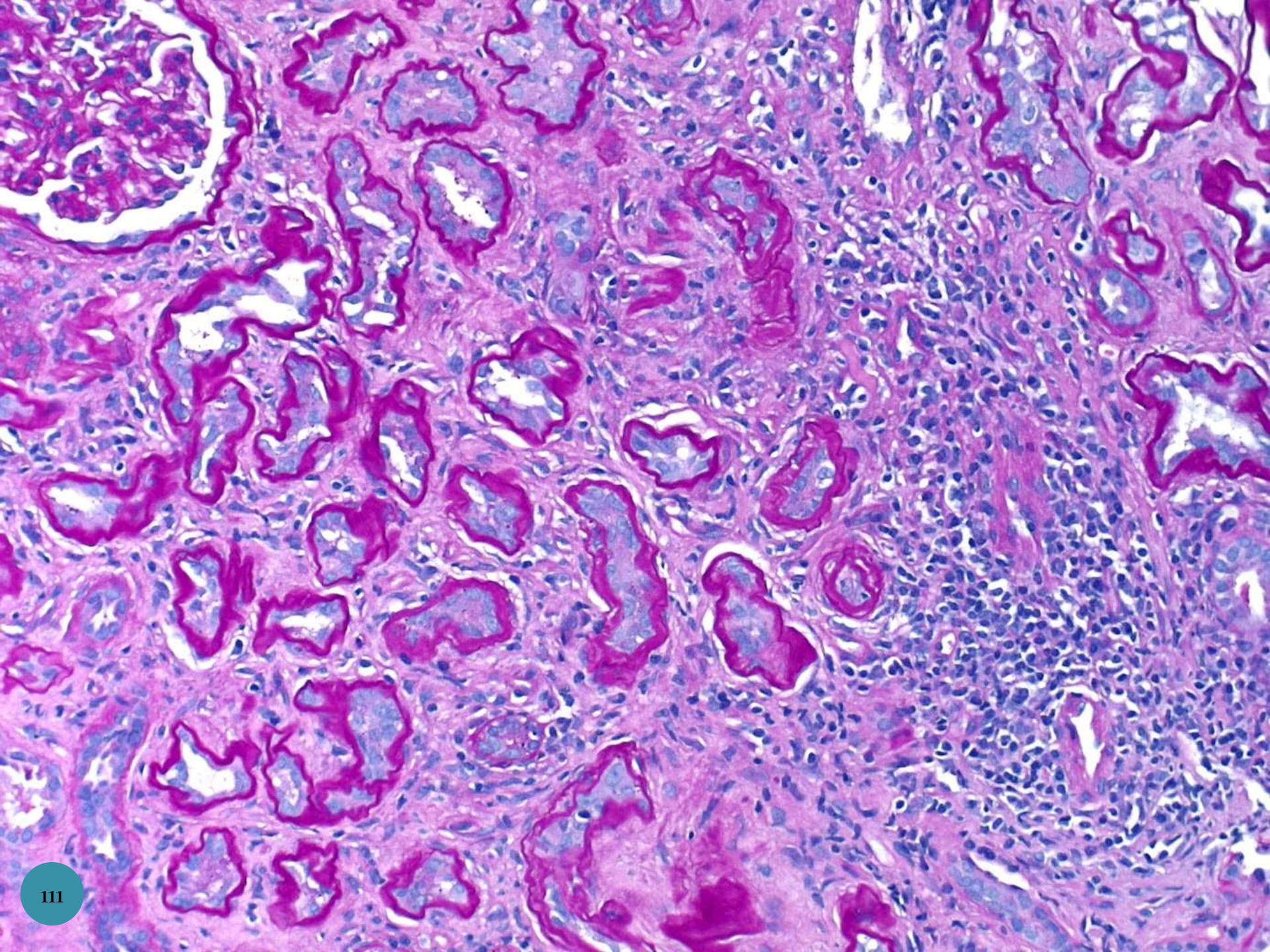


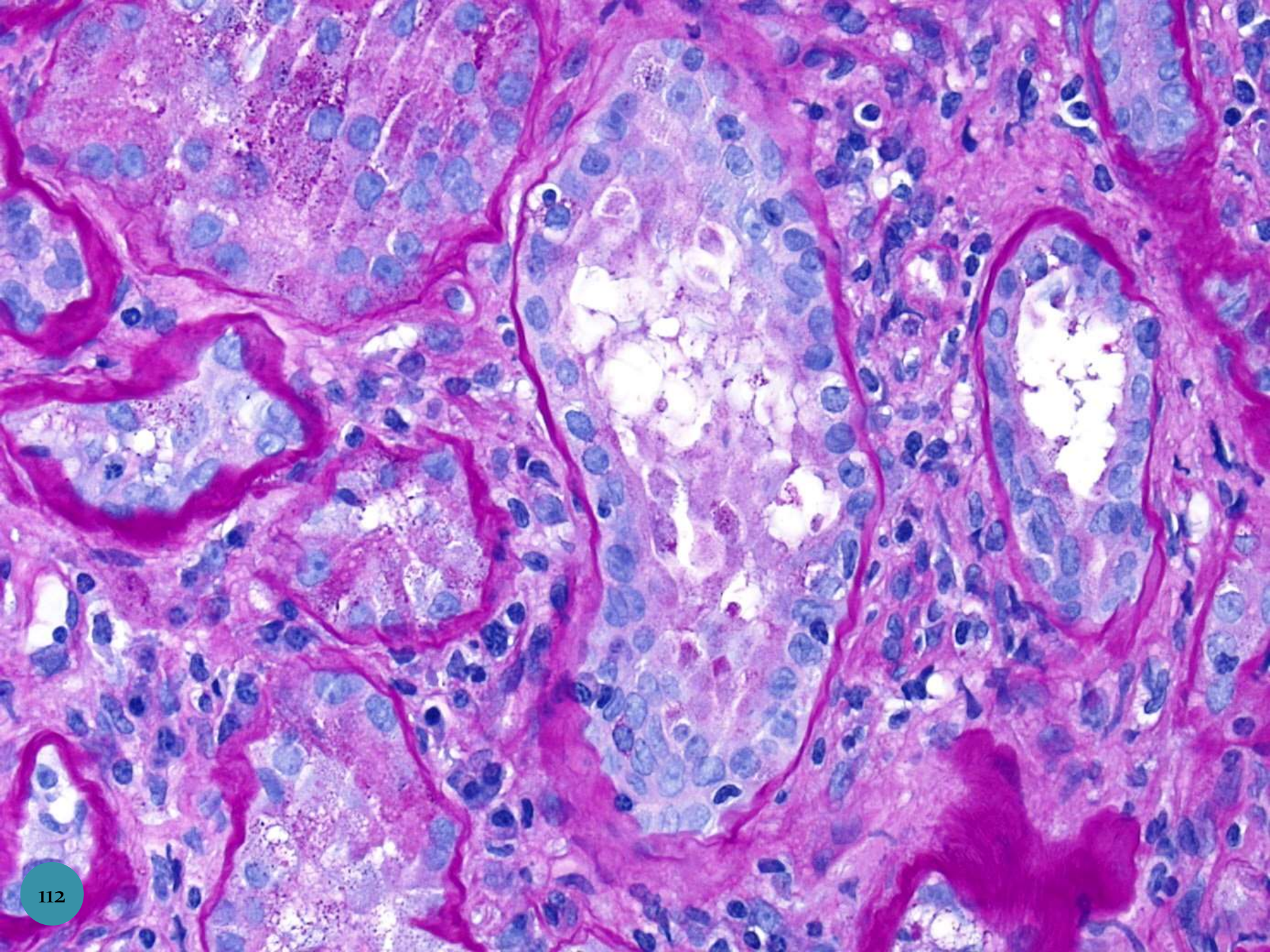


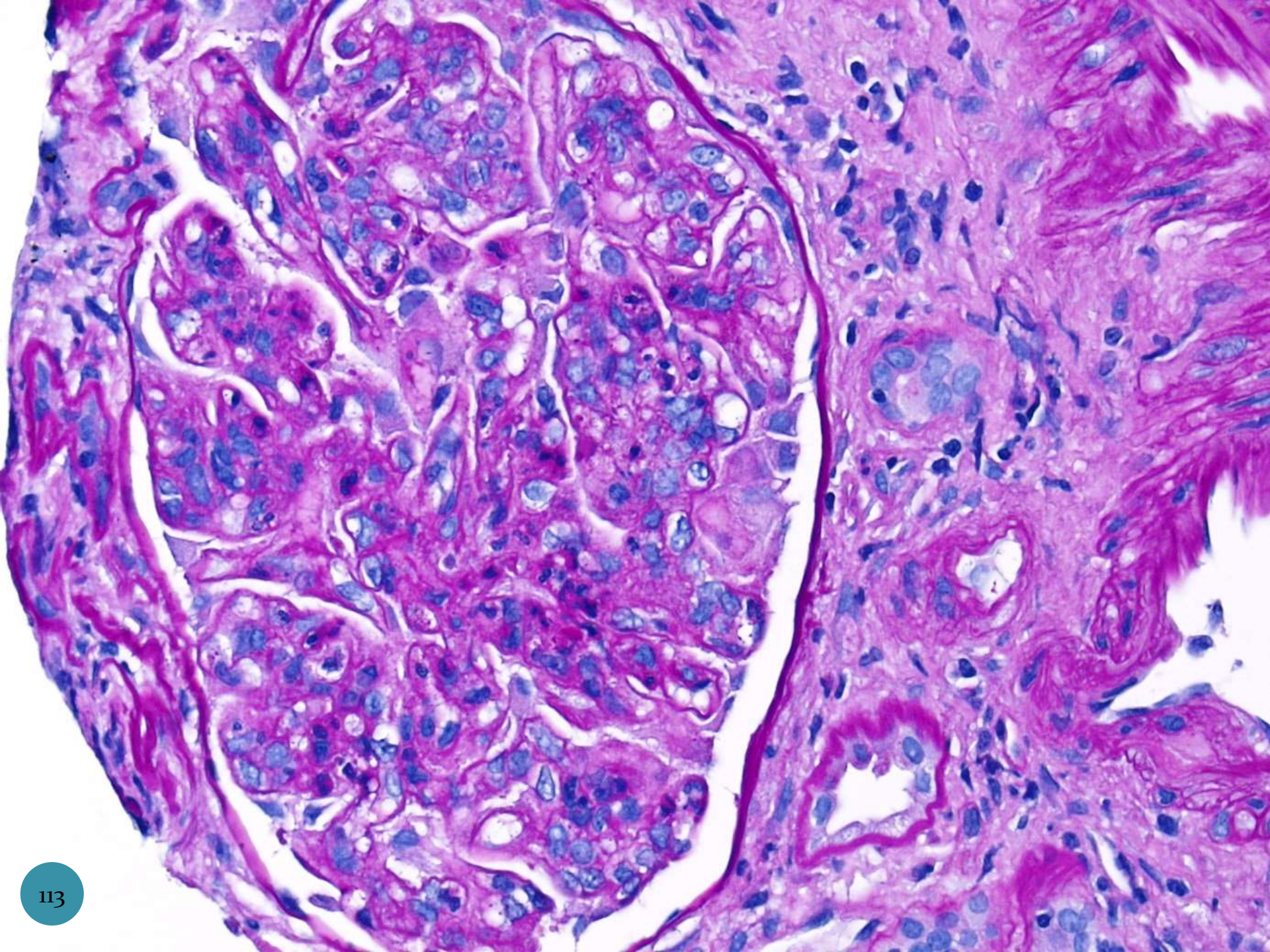
Case 4

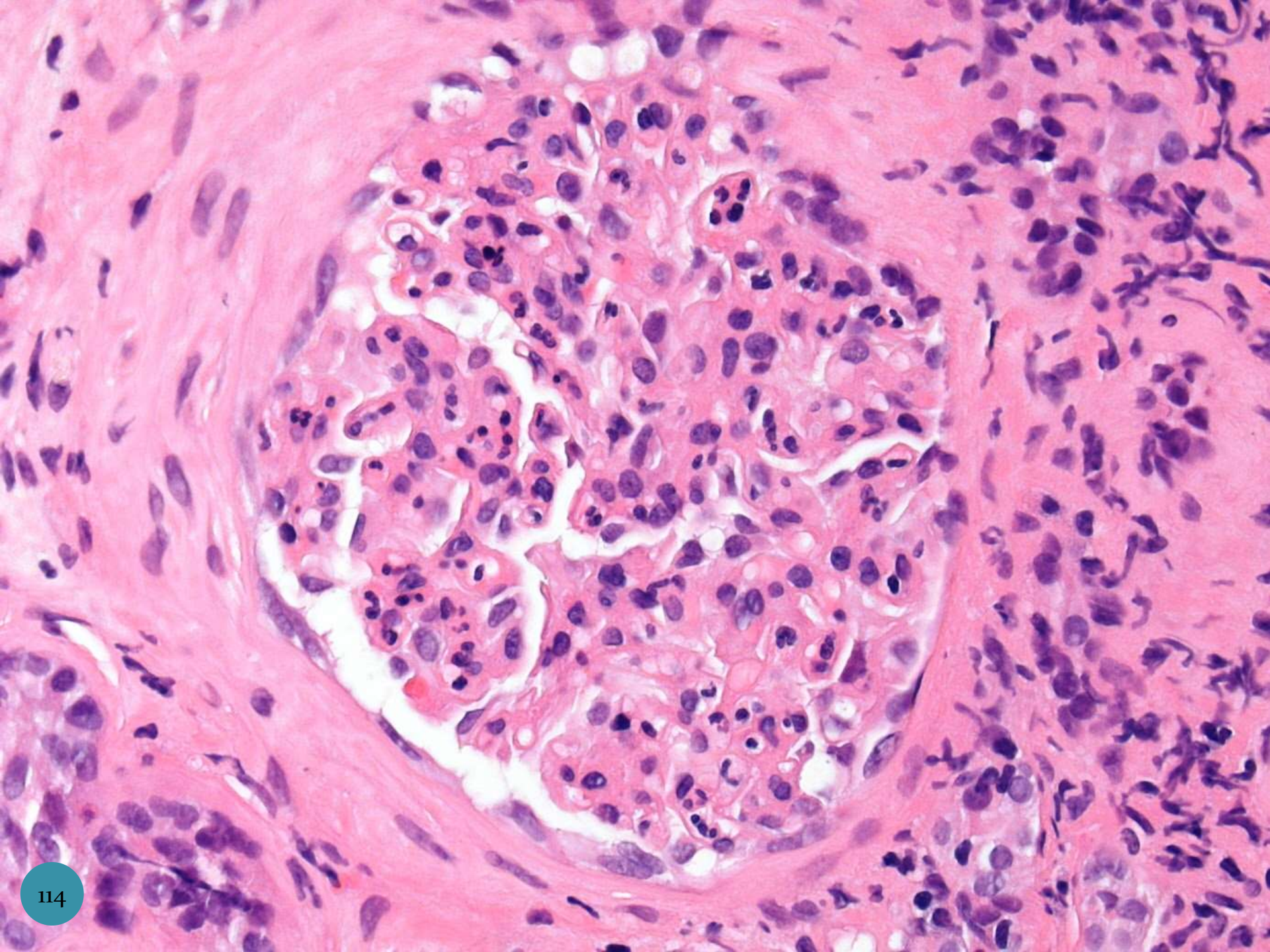
- Clinical presentation:
  - Lethargy, poor oral intake, sore throat and abdominal pain for 48 hours.
  - Serum creatinine 672 mmol/L.
  - Haematuria, mild proteinuria and low serum C3 level.
  - Last BK viral load (3 months before last Bx) 850 copies/ml

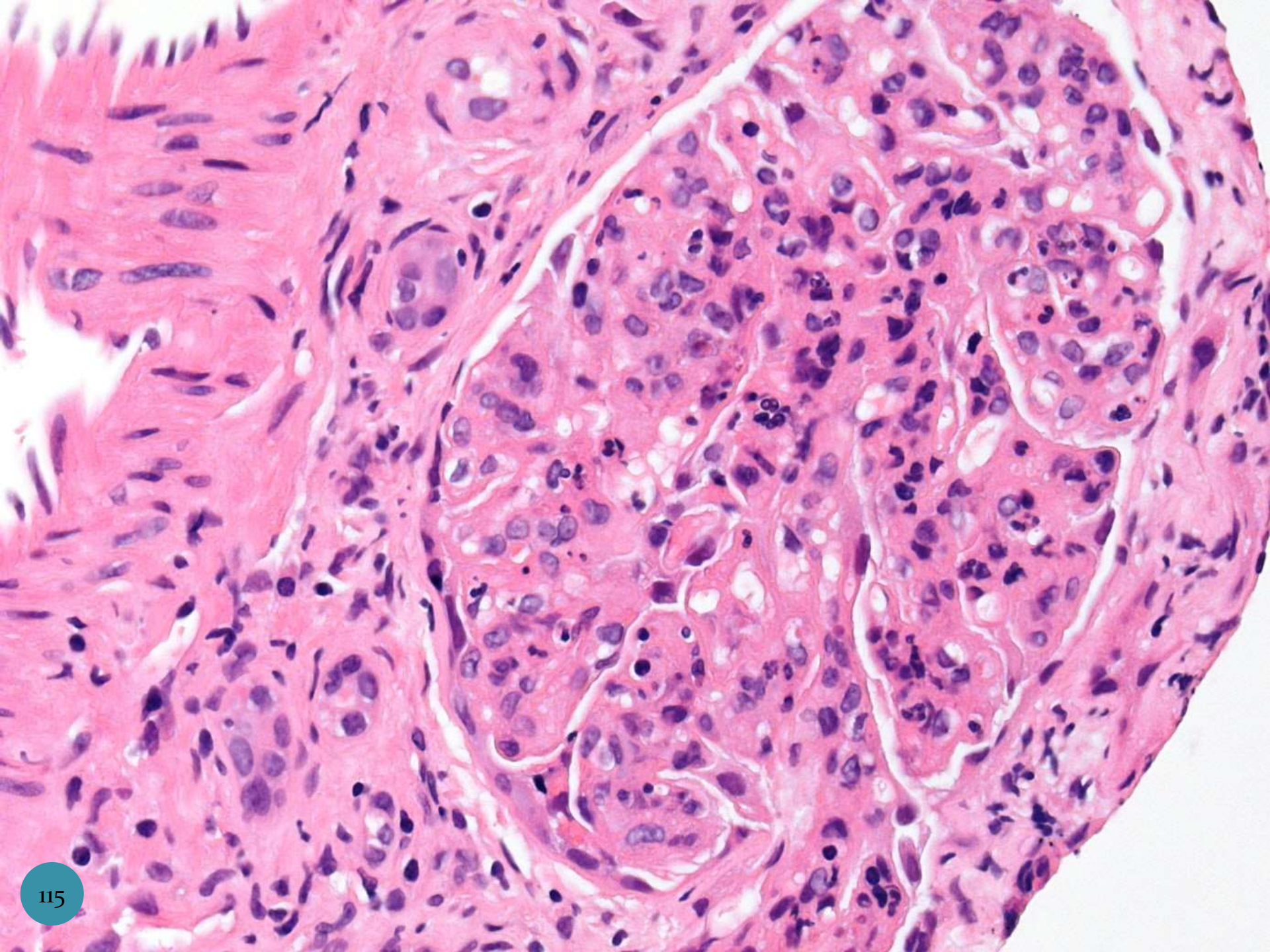

3/24 GS
Severe IF/TA

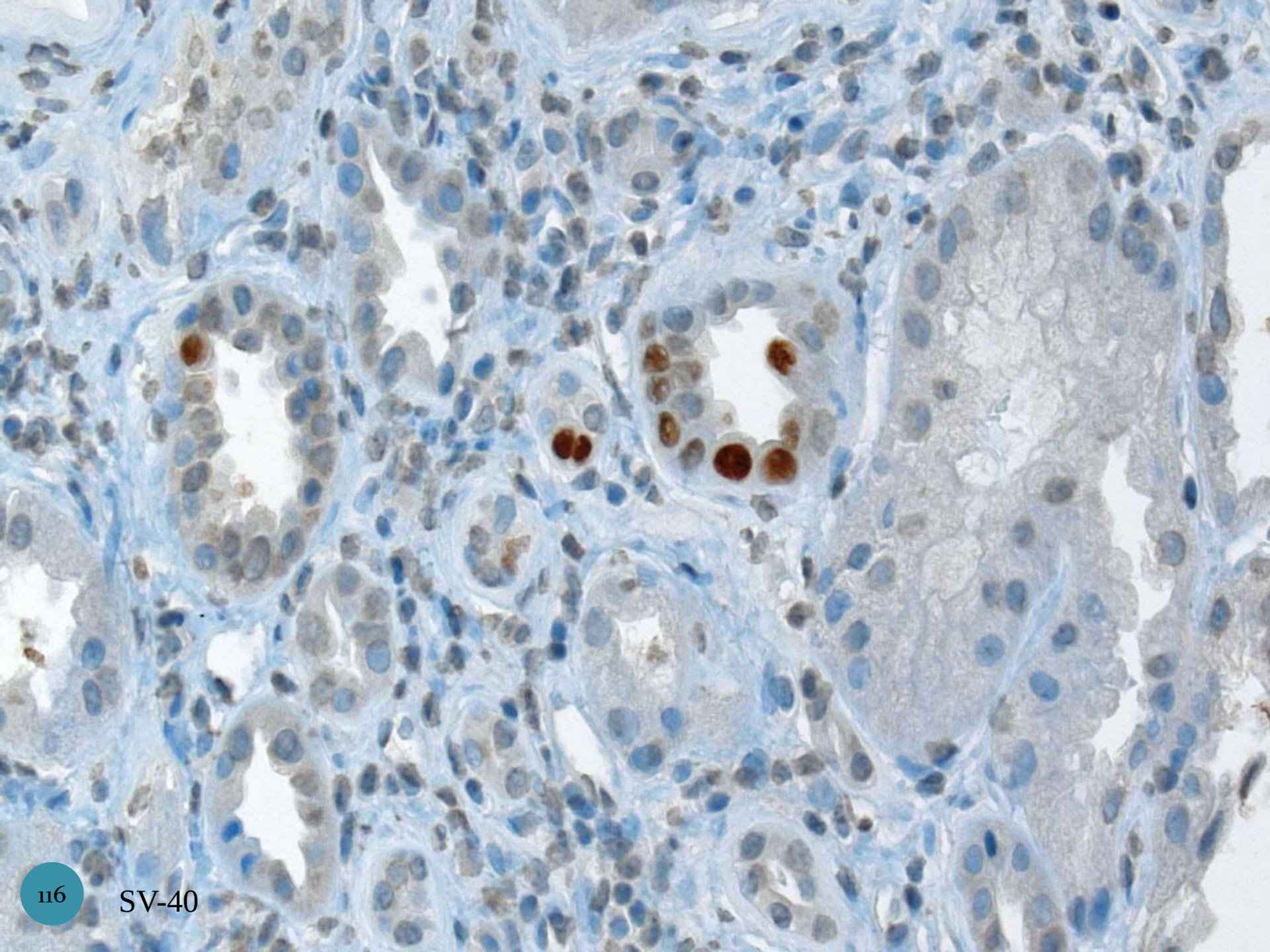








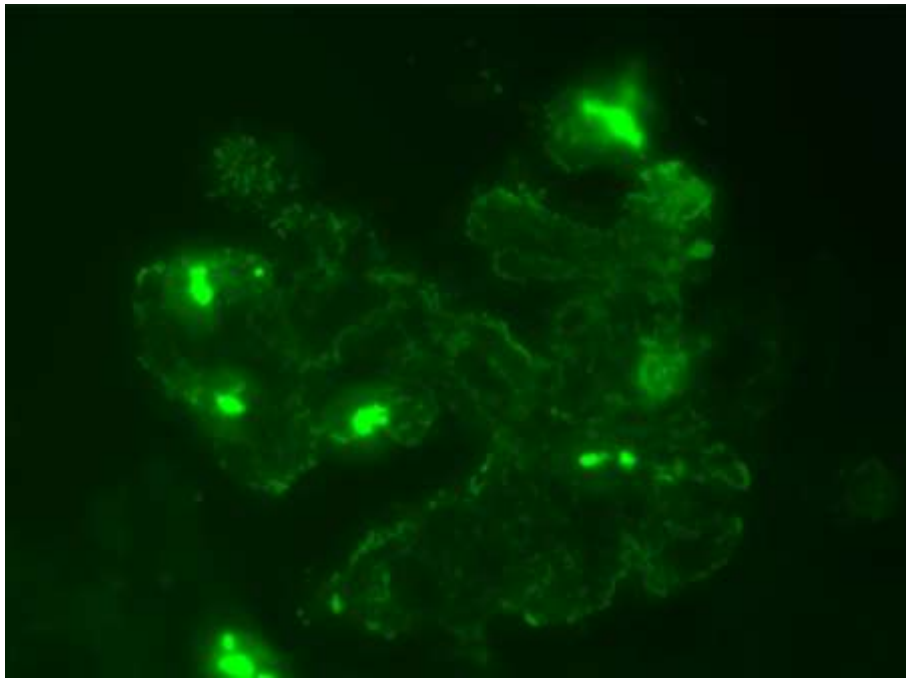


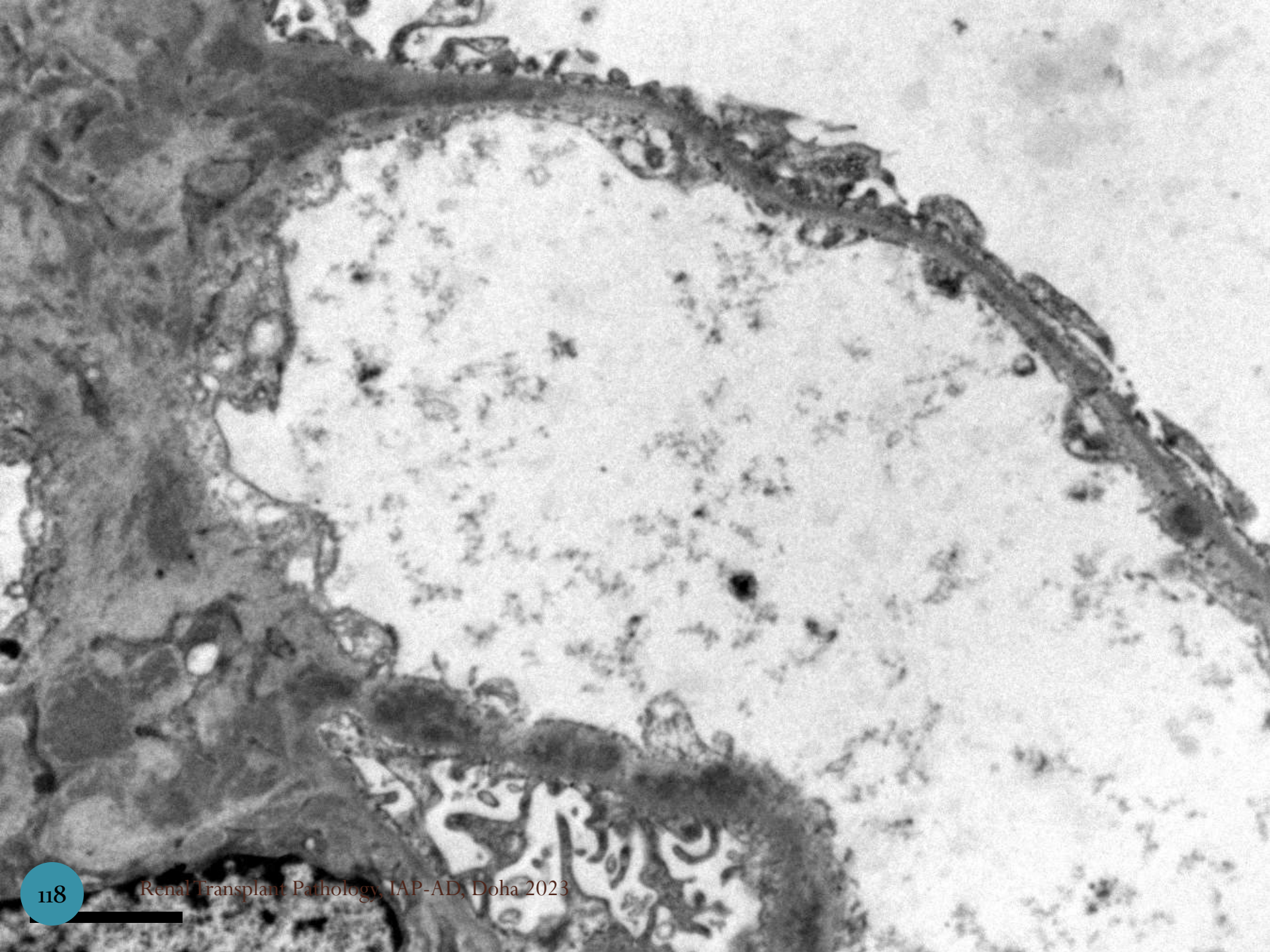


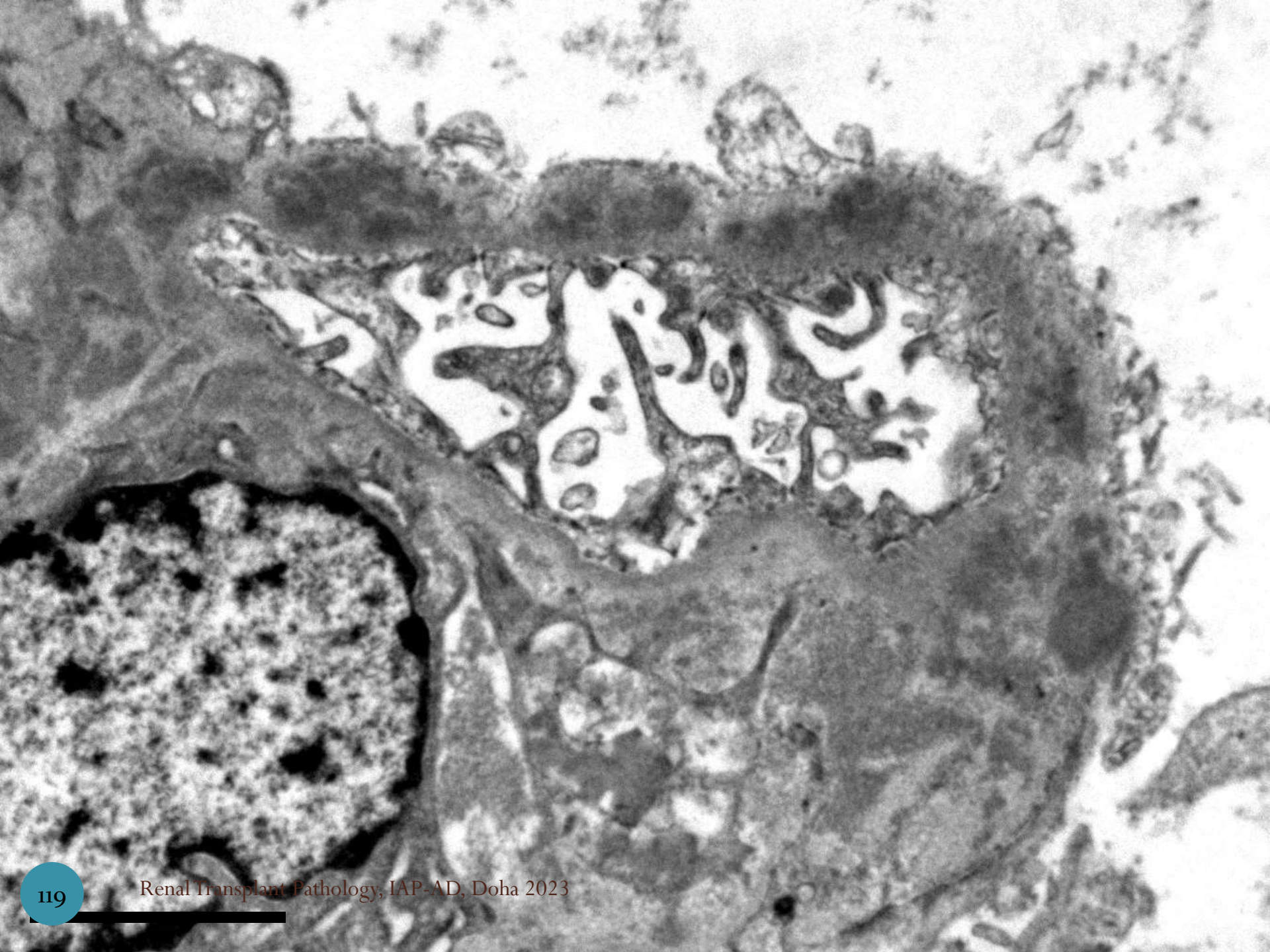
SV-40

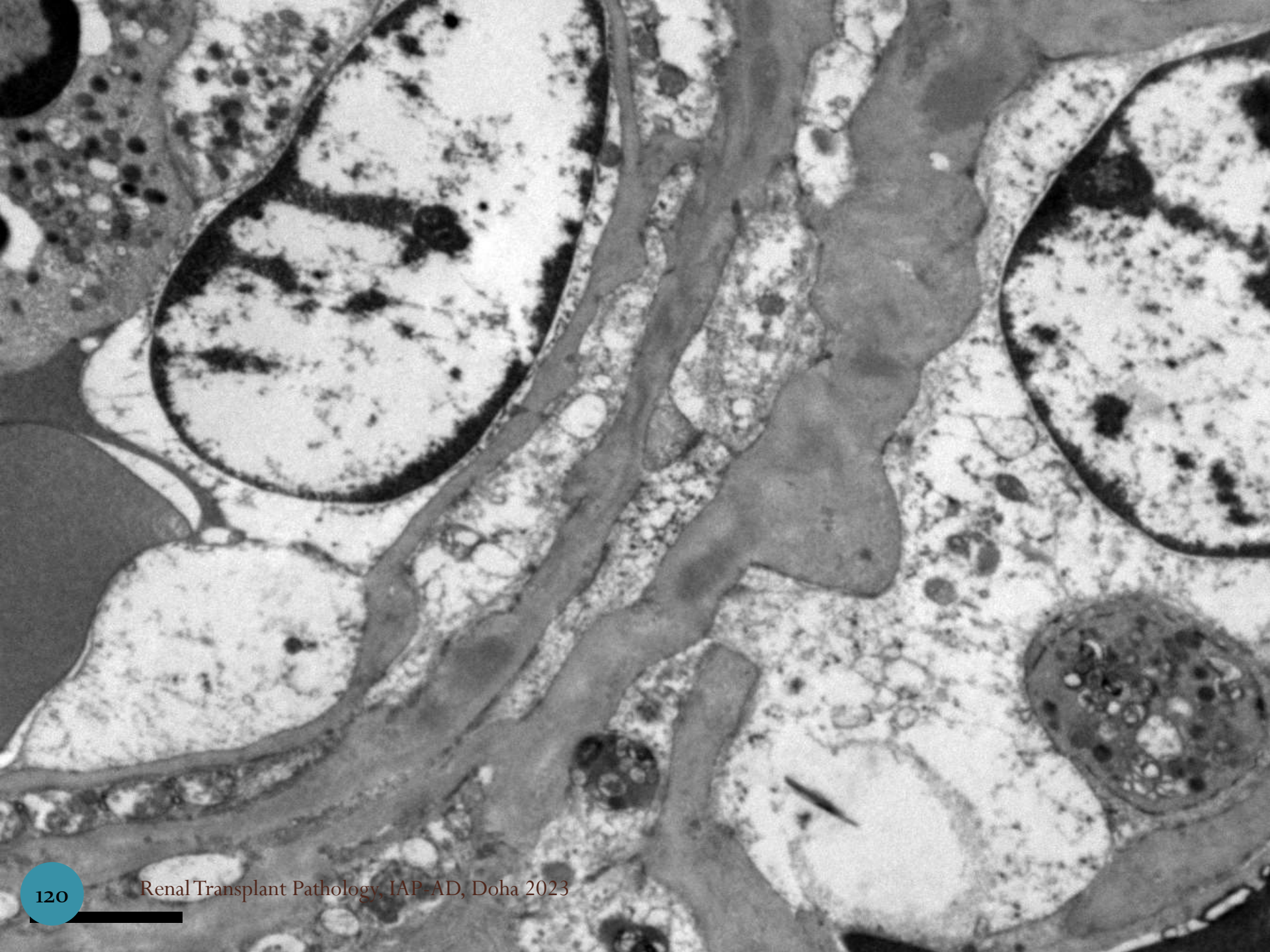
Case 4

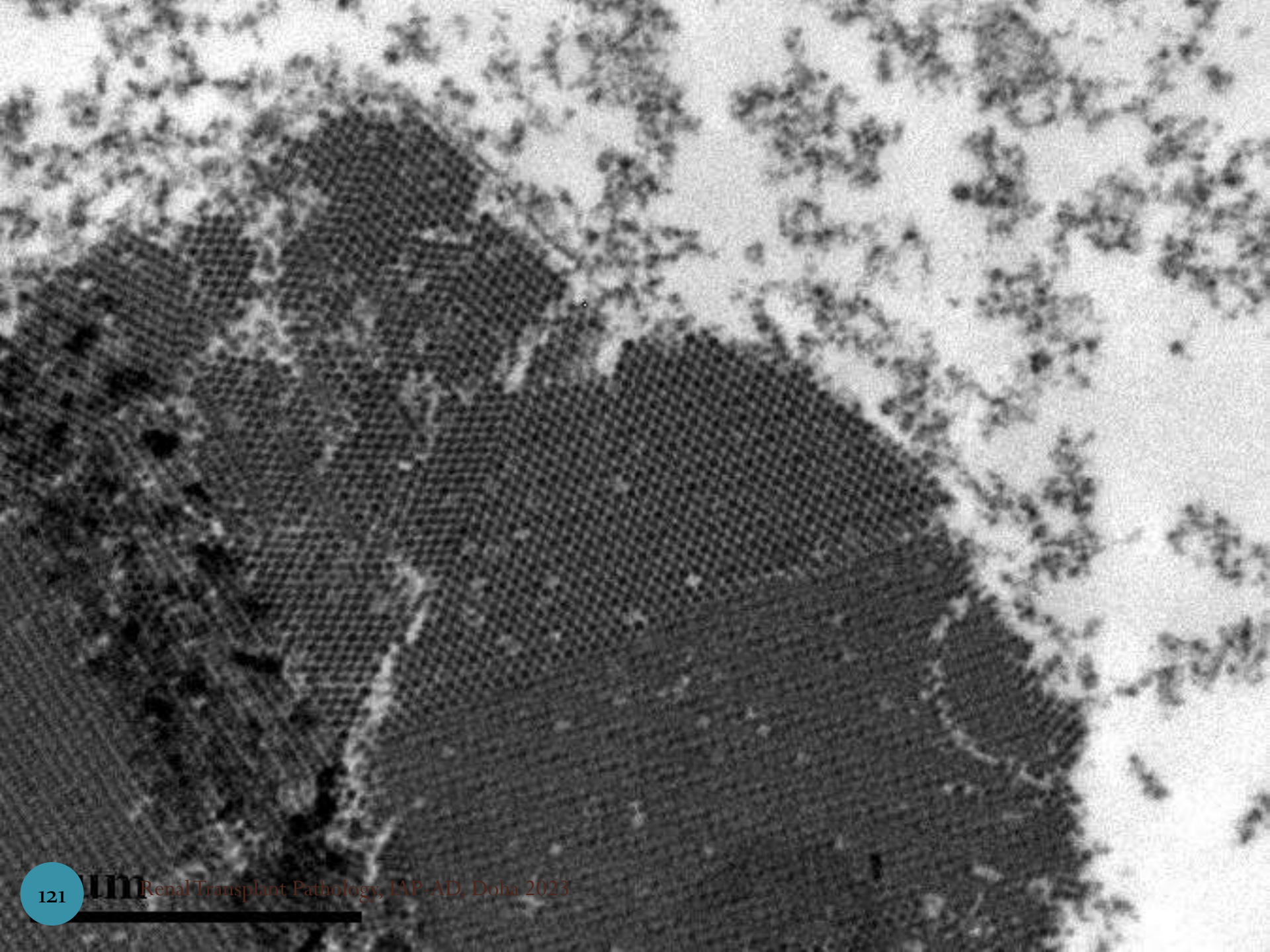
- DIF:
  - 3 glomeruli.
  - Diffuse and global coarse granular mesangial and capillary staining for C3 (3+)
  - Staining for IgG and Kappa and Lambda light chains (1+).
  - No staining for IgM, IgA, C4 and C1q.

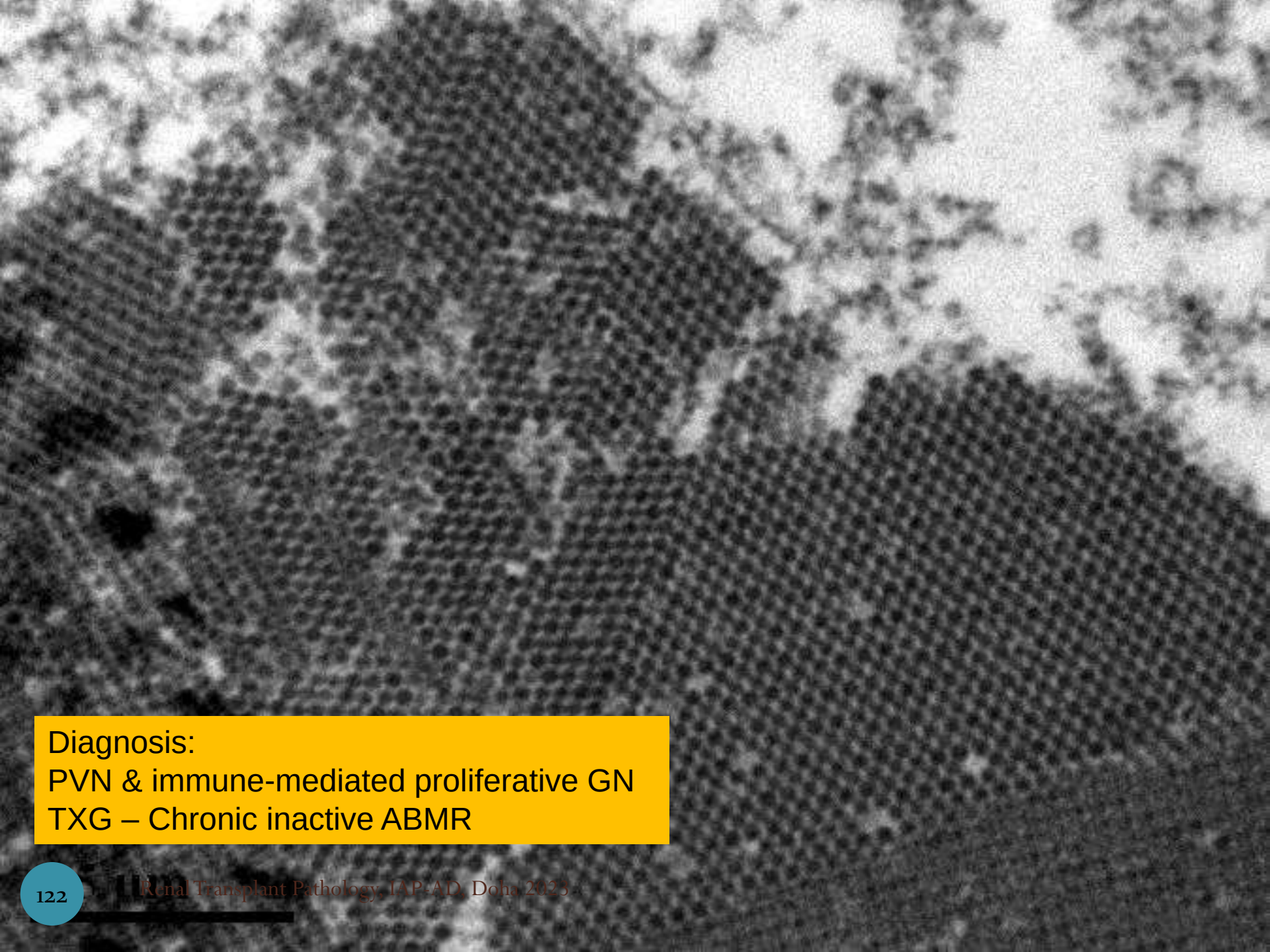








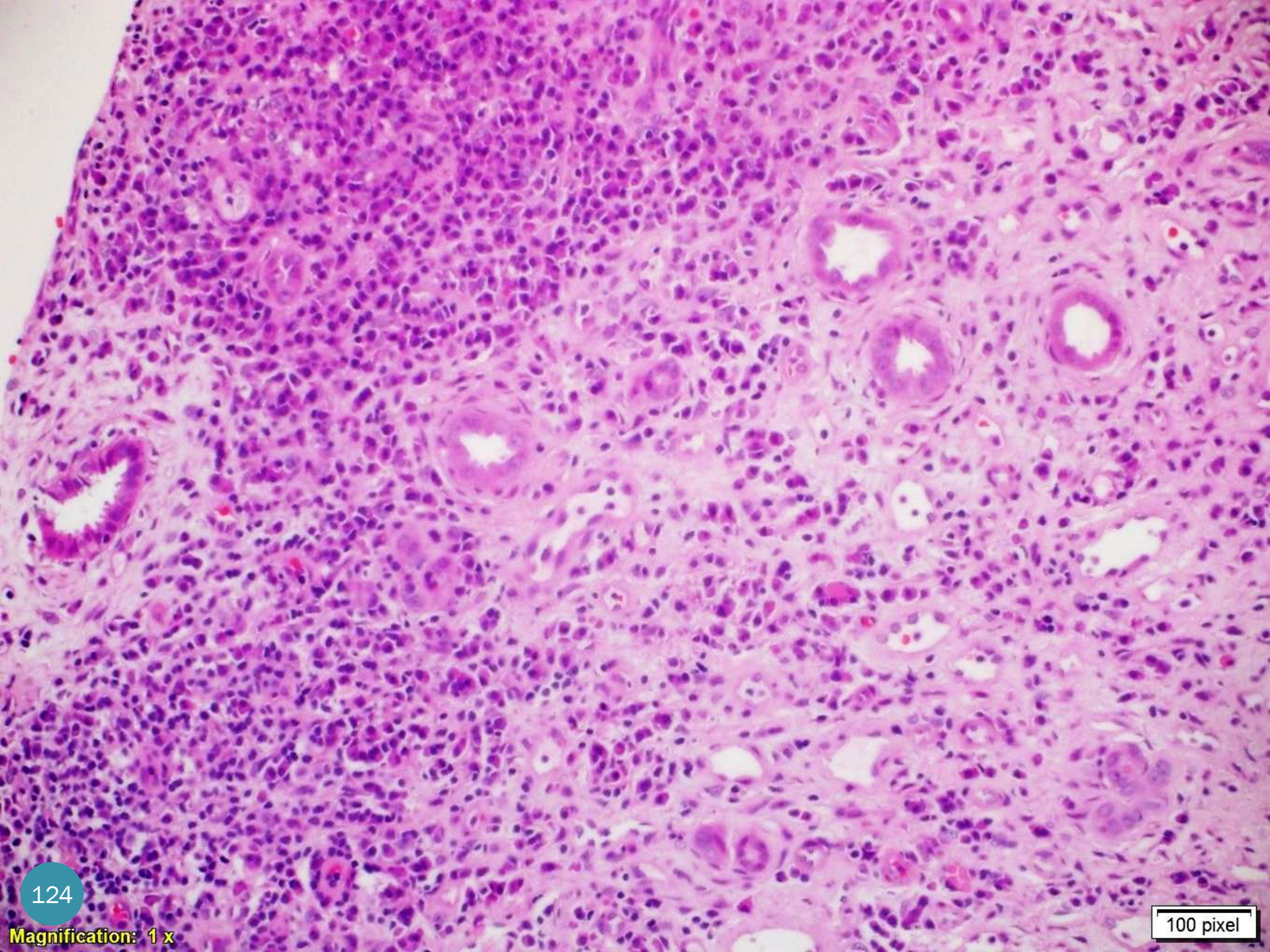




Diagnosis:
PVN & immune-mediated proliferative GN
TXG – Chronic inactive ABMR

Case 5

- 30-year-old woman, S/P living non-related kidney transplant 9 years ago for ESKD secondary to hypoplastic kidney.
- History of multiple episodes of acute cellular rejection.
- Presented with increased serum creatinine.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Magnification: 1 x
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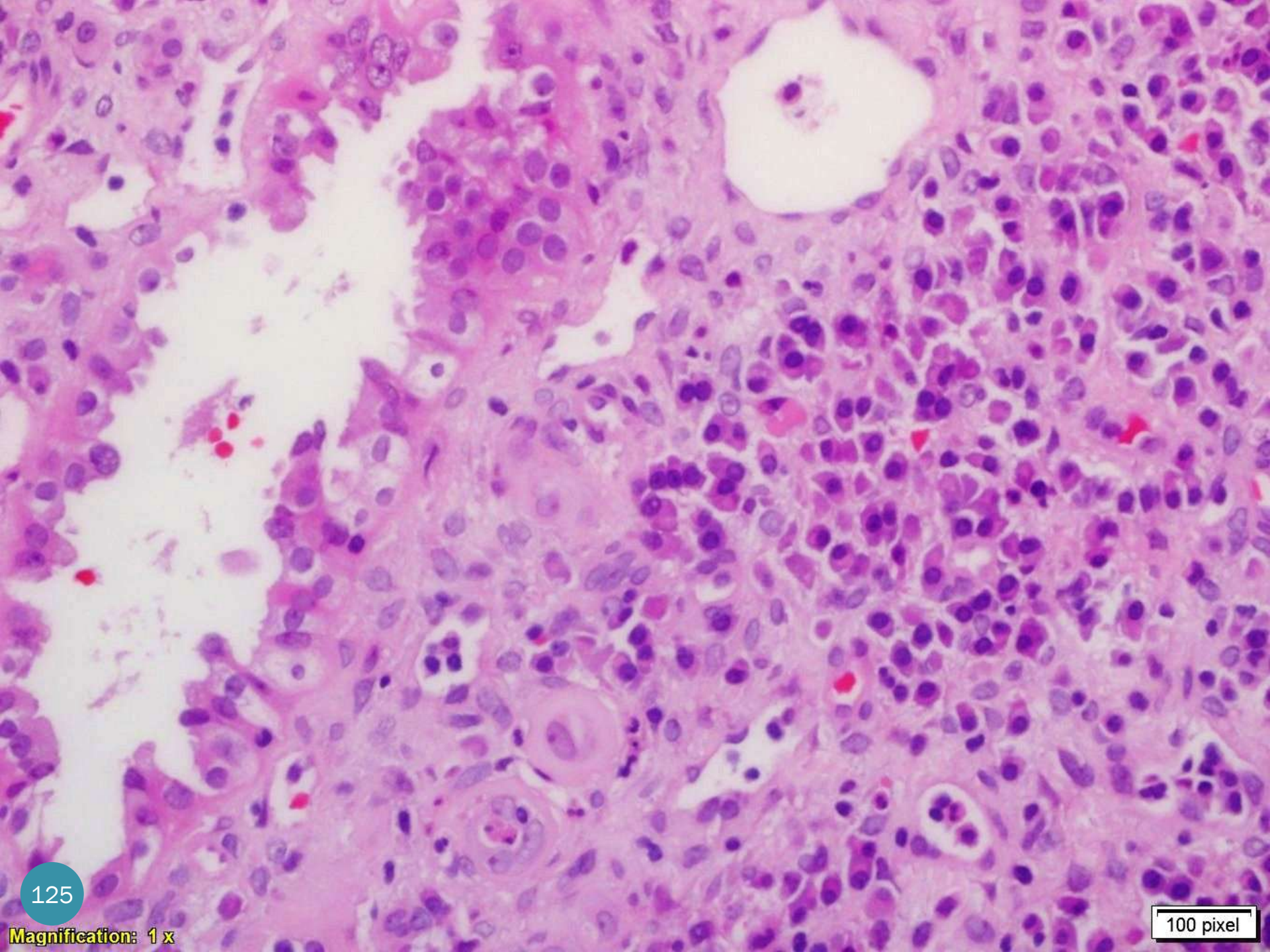
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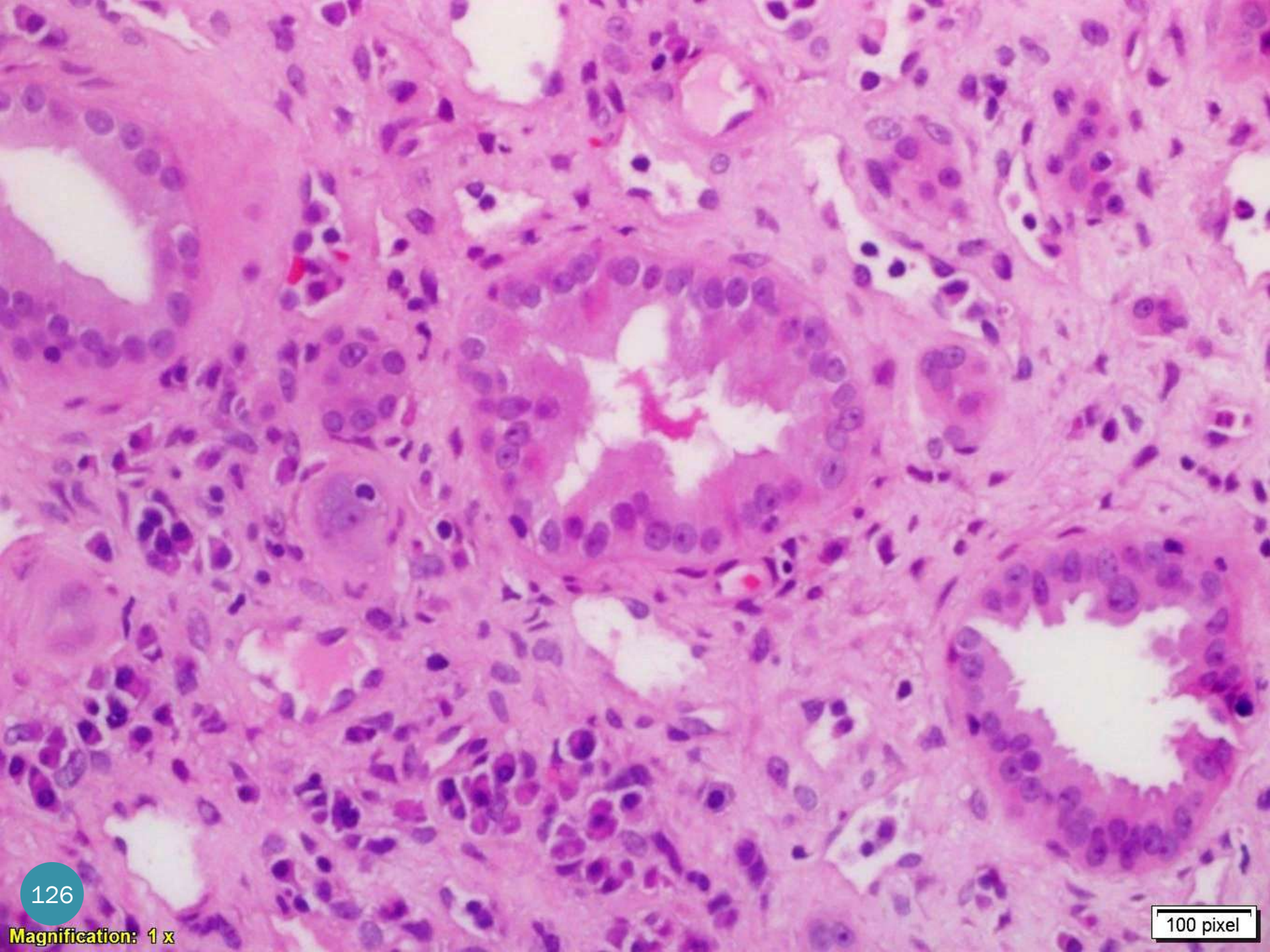
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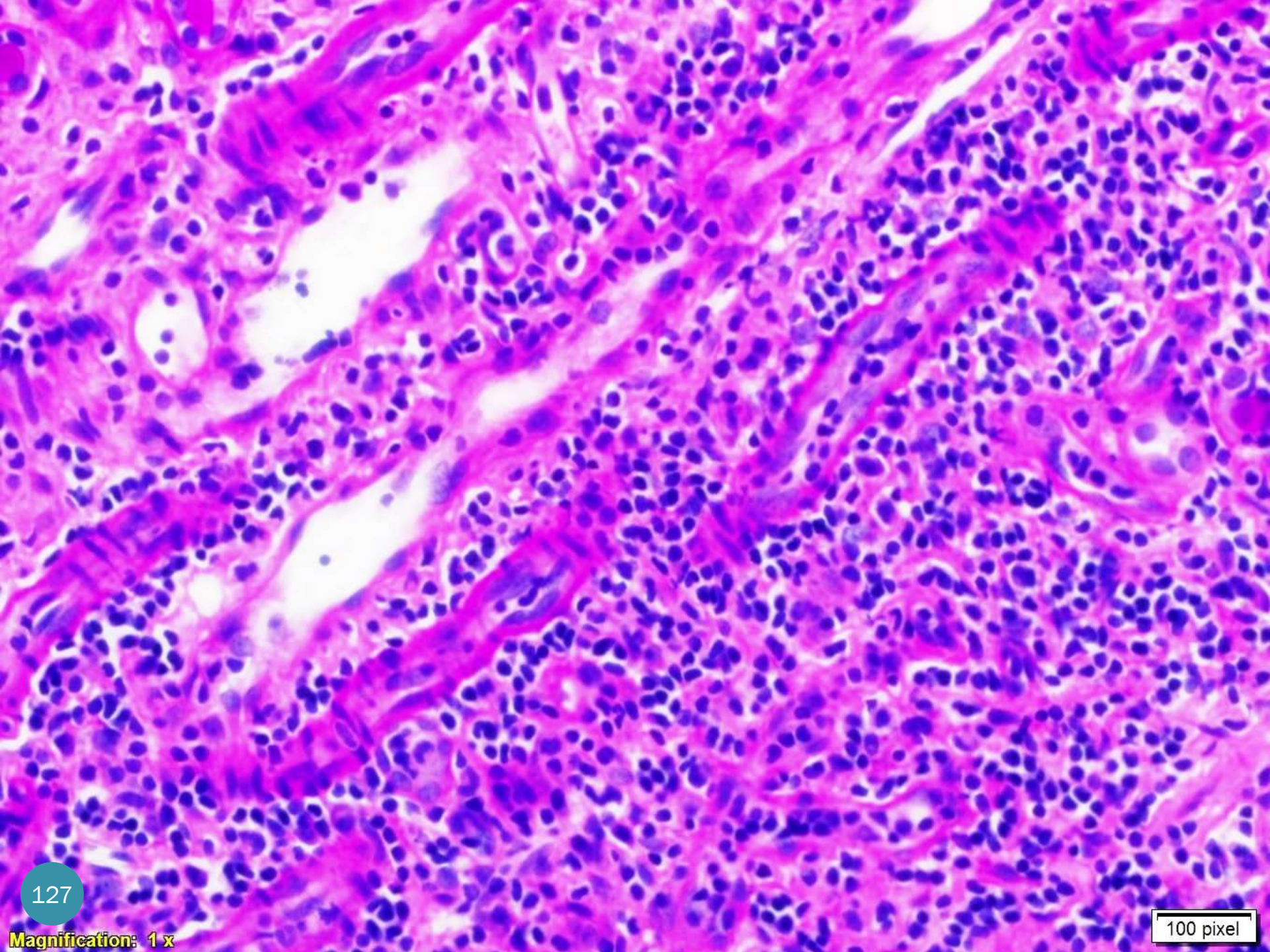
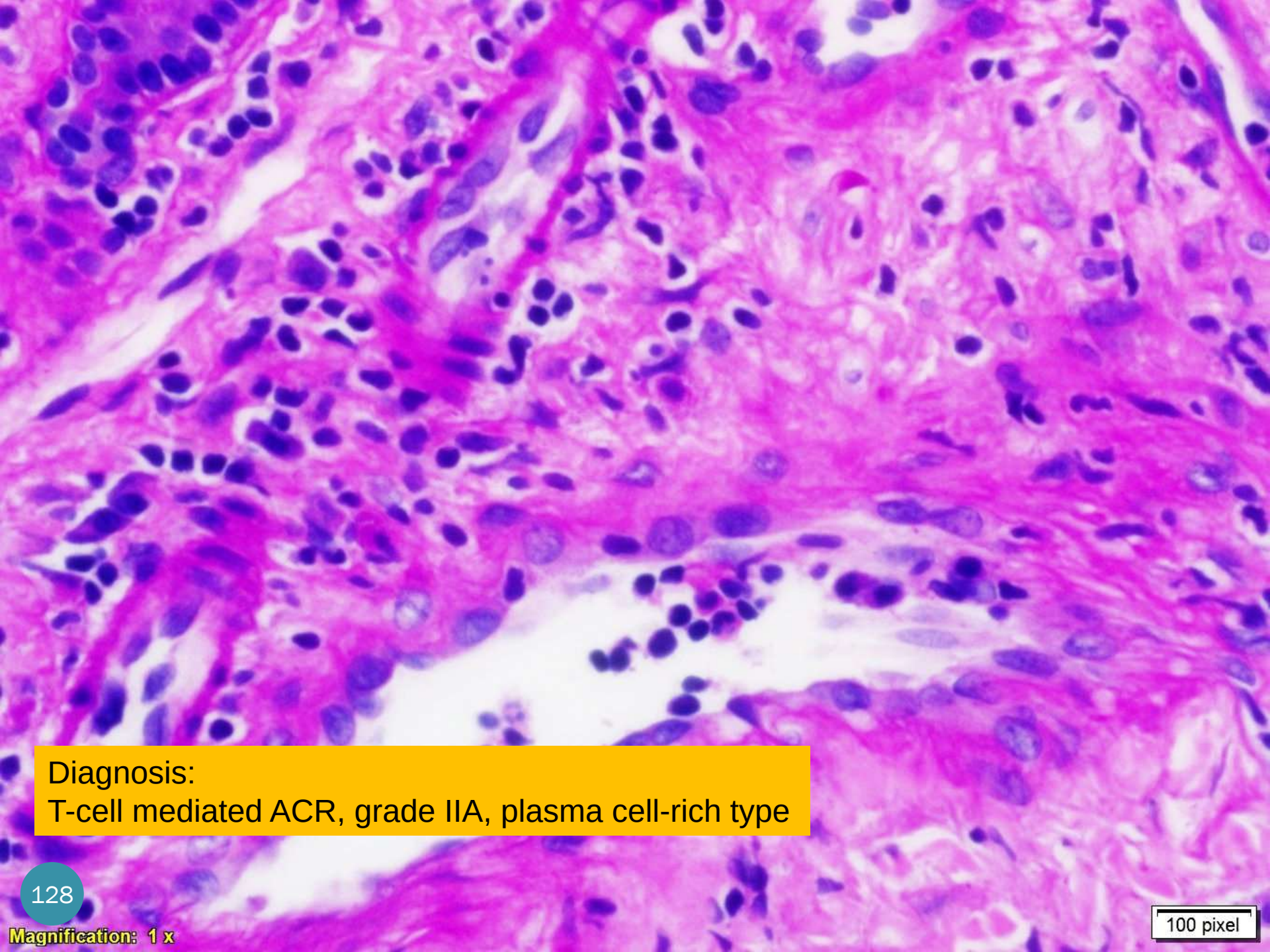
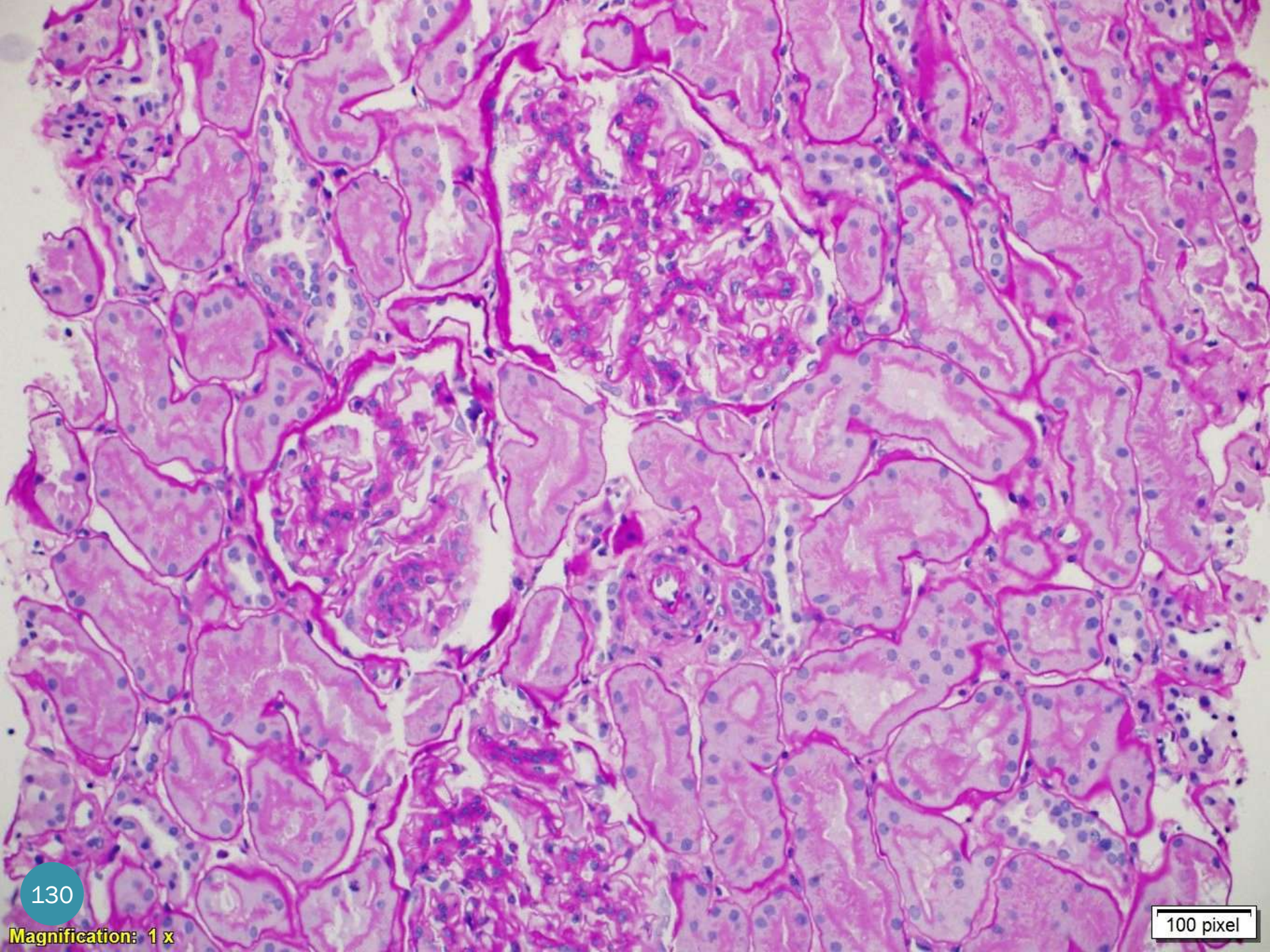

127
Magnification: 1 x
100 pixel


Diagnosis:
T-cell mediated ACR, grade IIA, plasma cell-rich type
128
Magnification: 1 x
100 pixel

Case 6

- 49-year-old man, S/P living non-related kidney transplant 6 years ago for ESKD secondary to lupus nephritis.
- No previous renal allograft biopsy.
- Presented with nephrotic range proteinuria.


130
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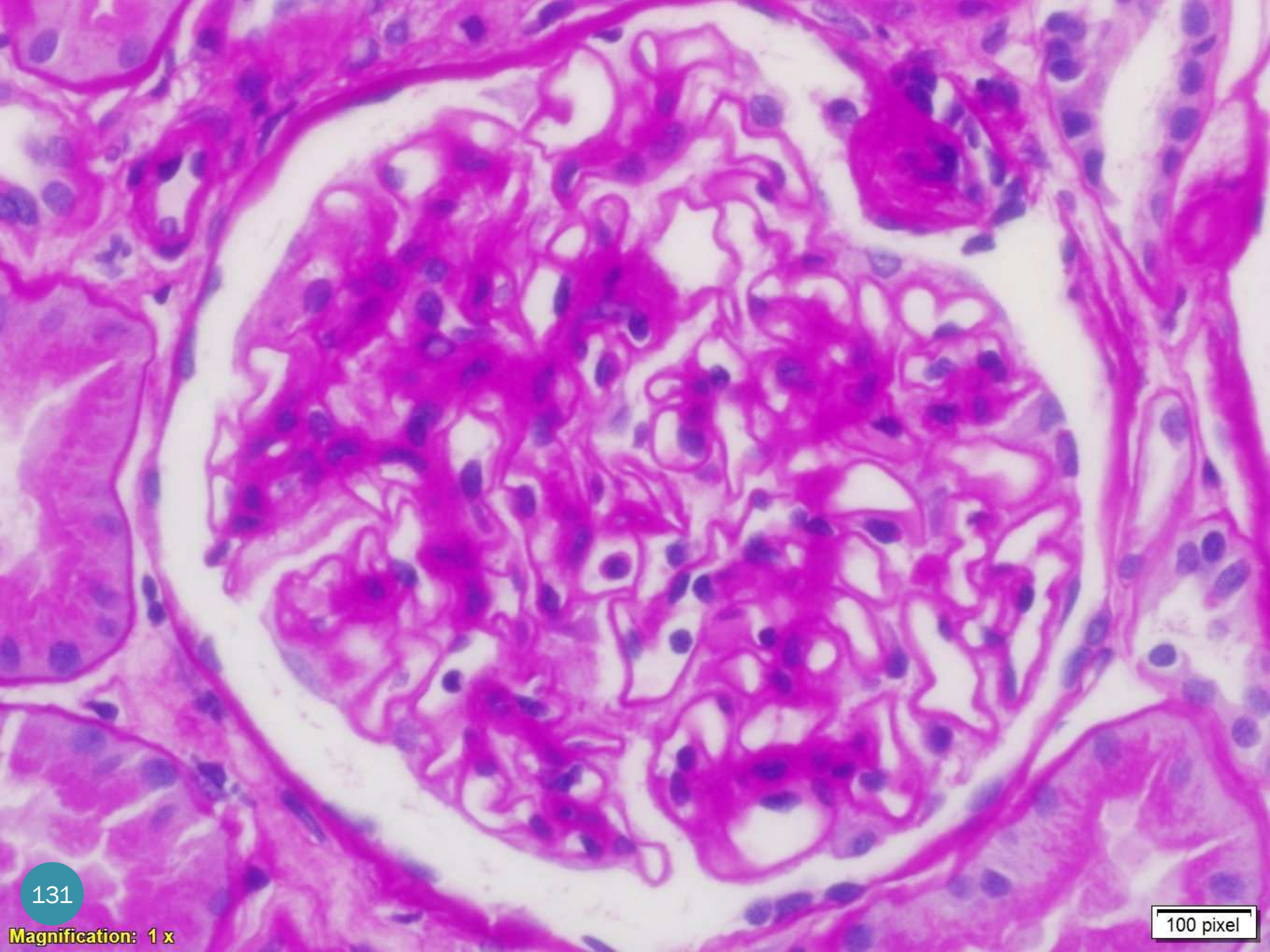
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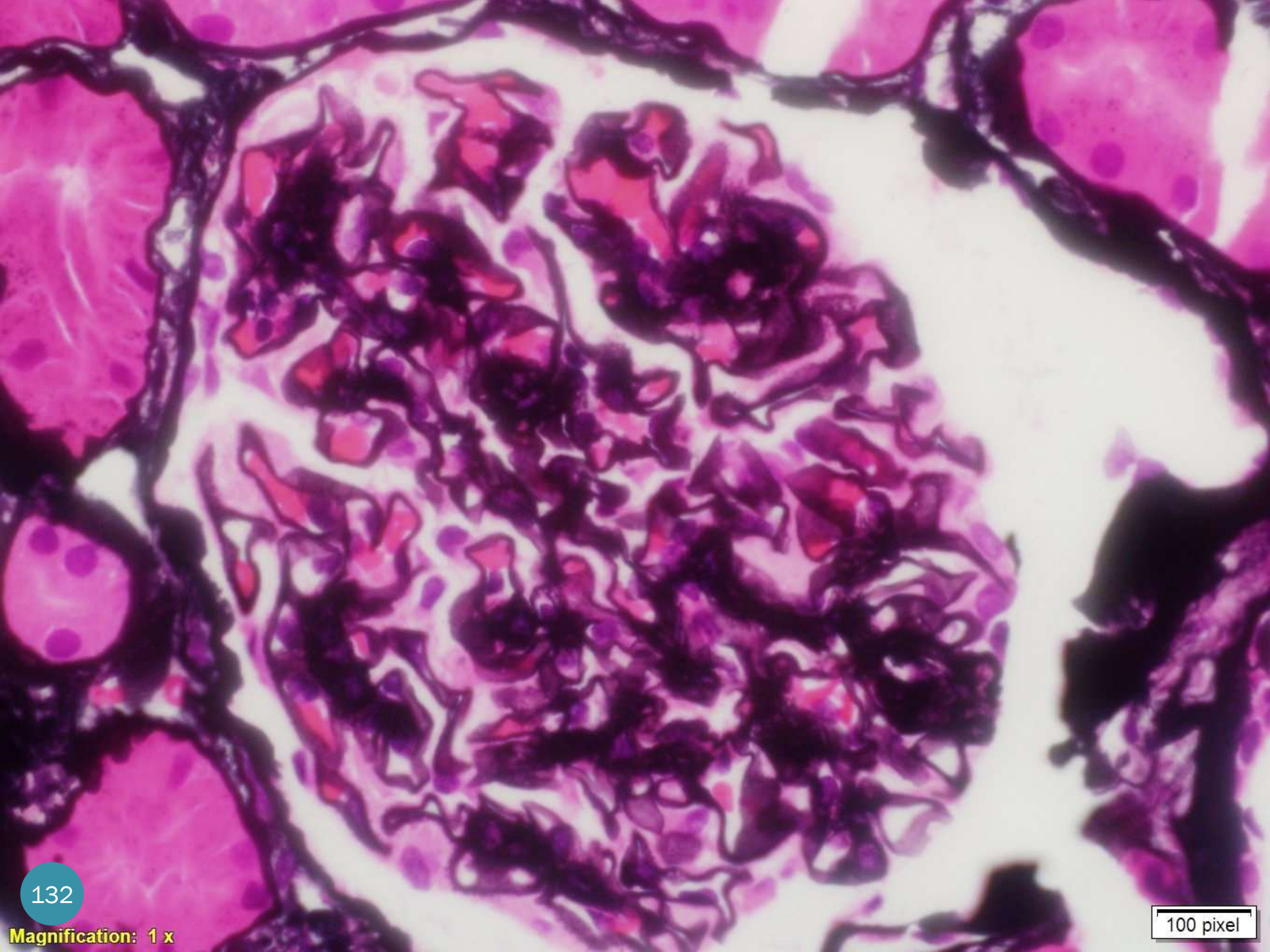
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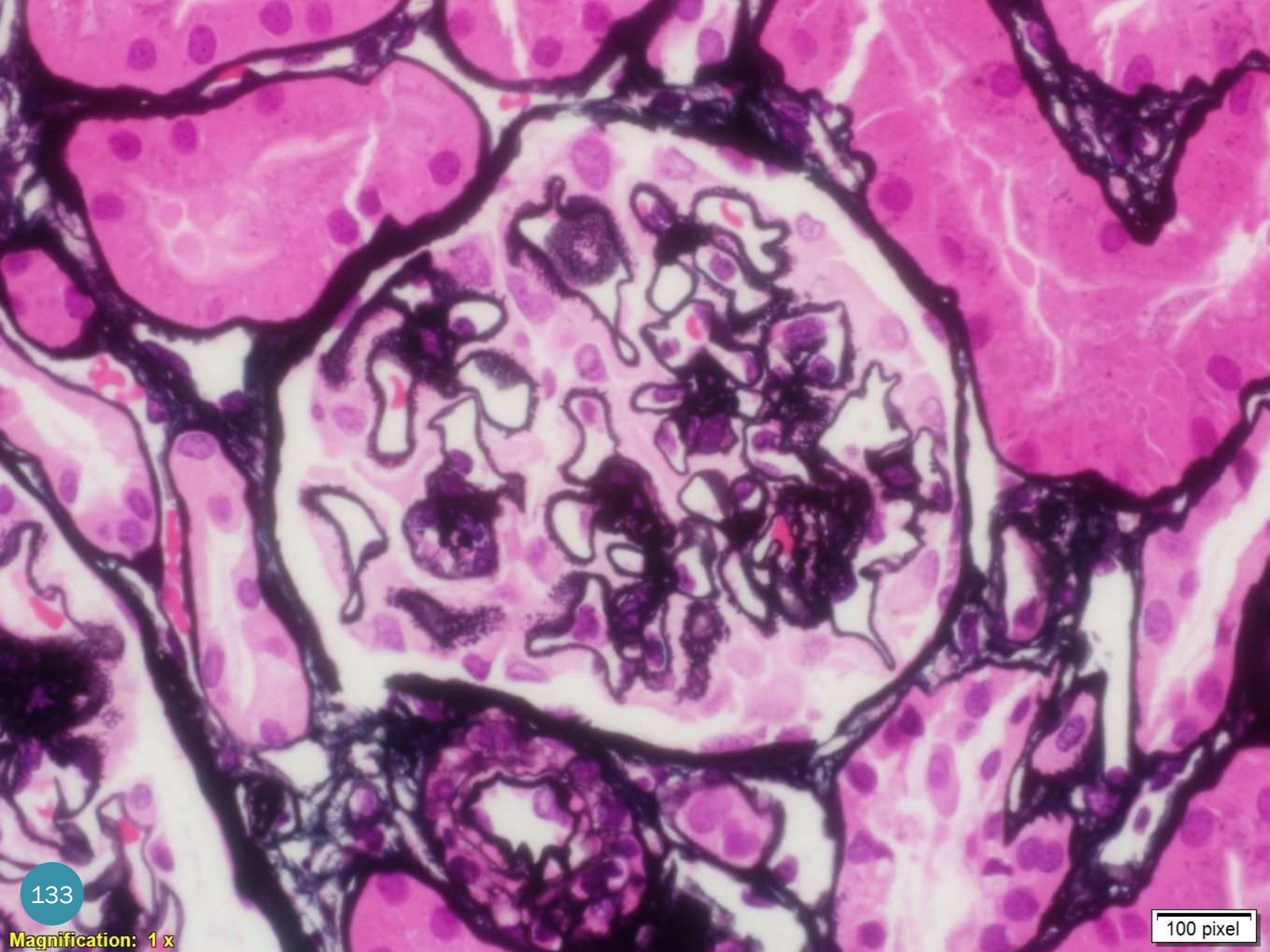
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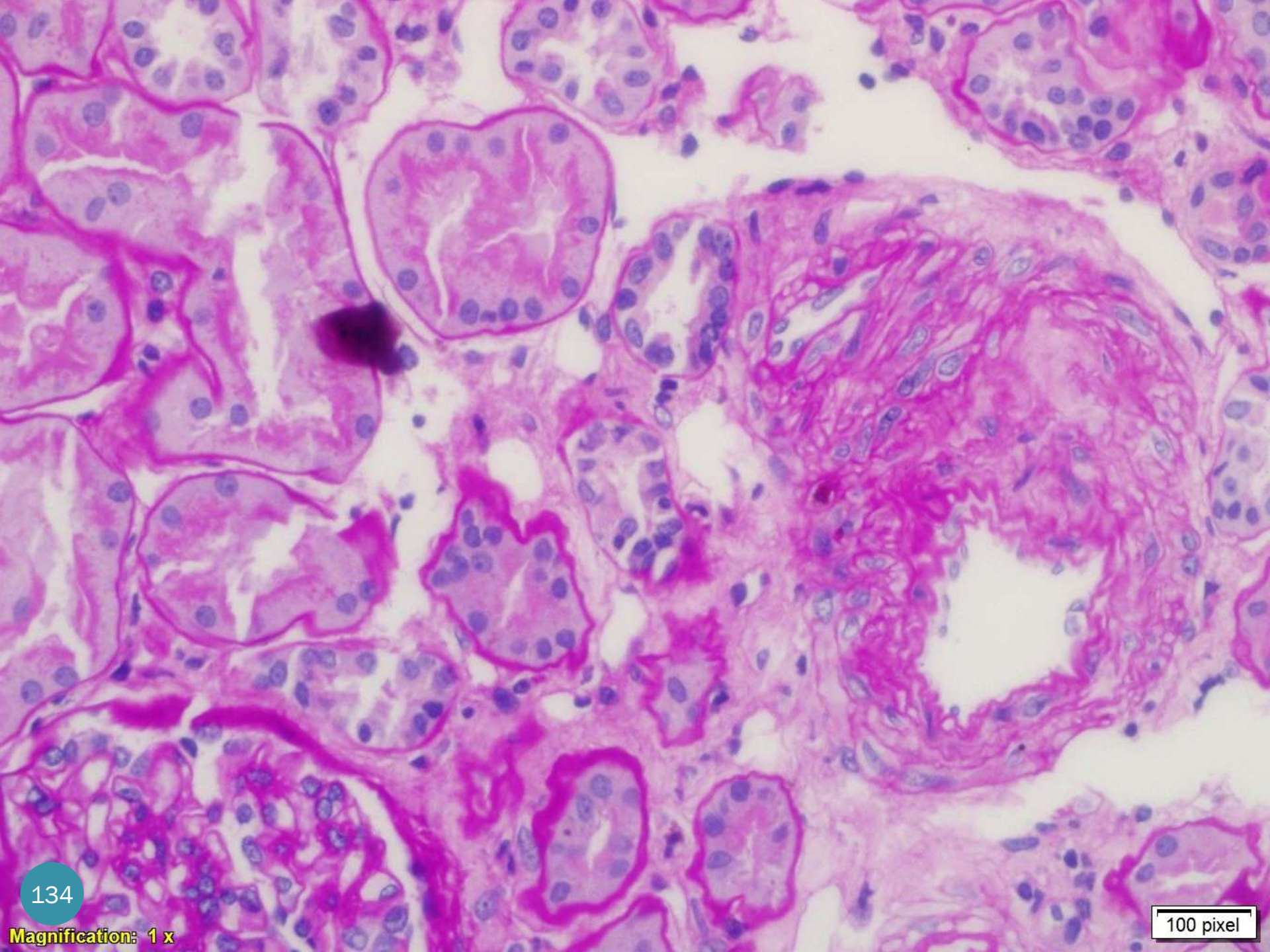
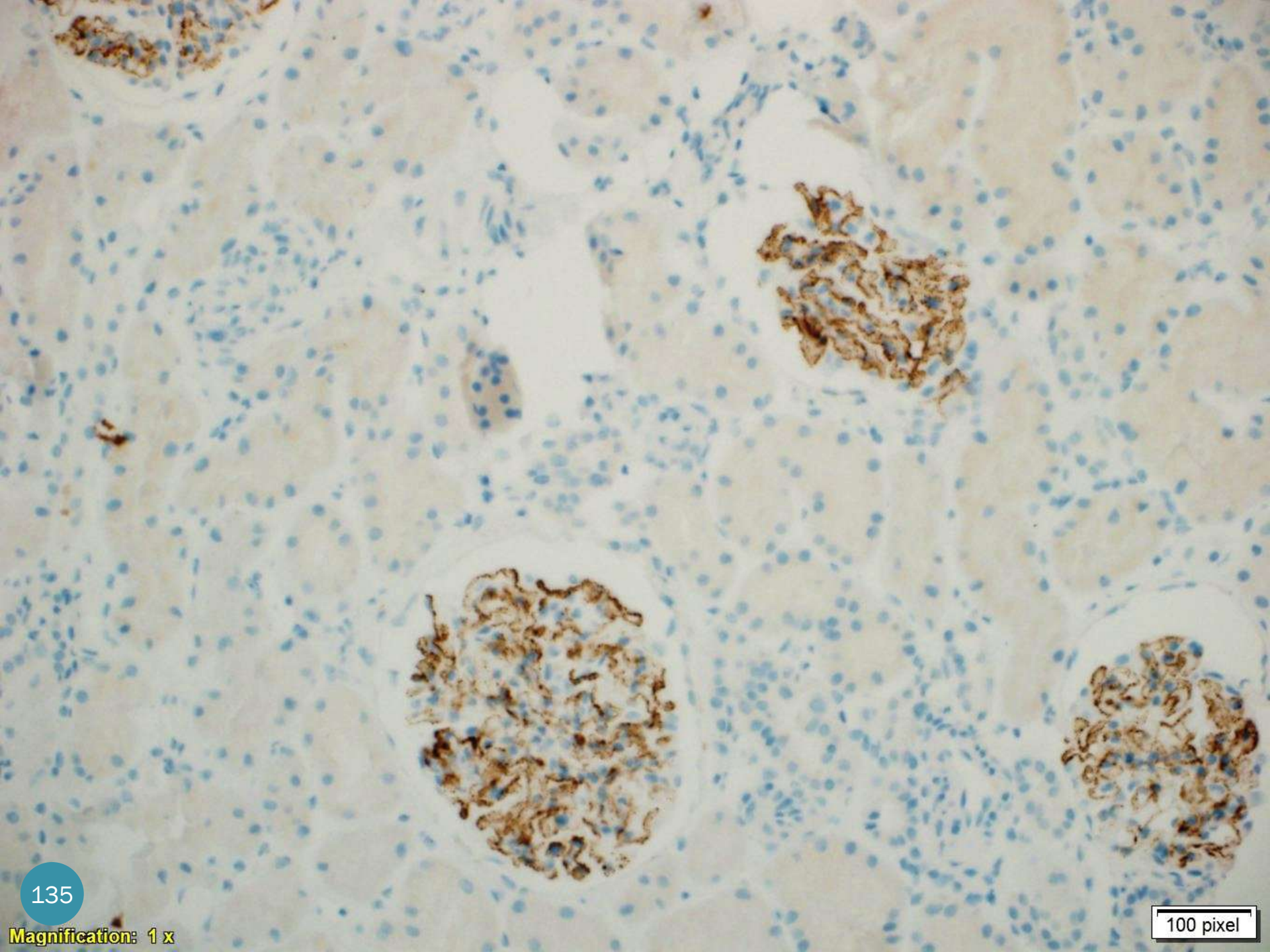

134
Magnification: 1 x
100 pixel


135
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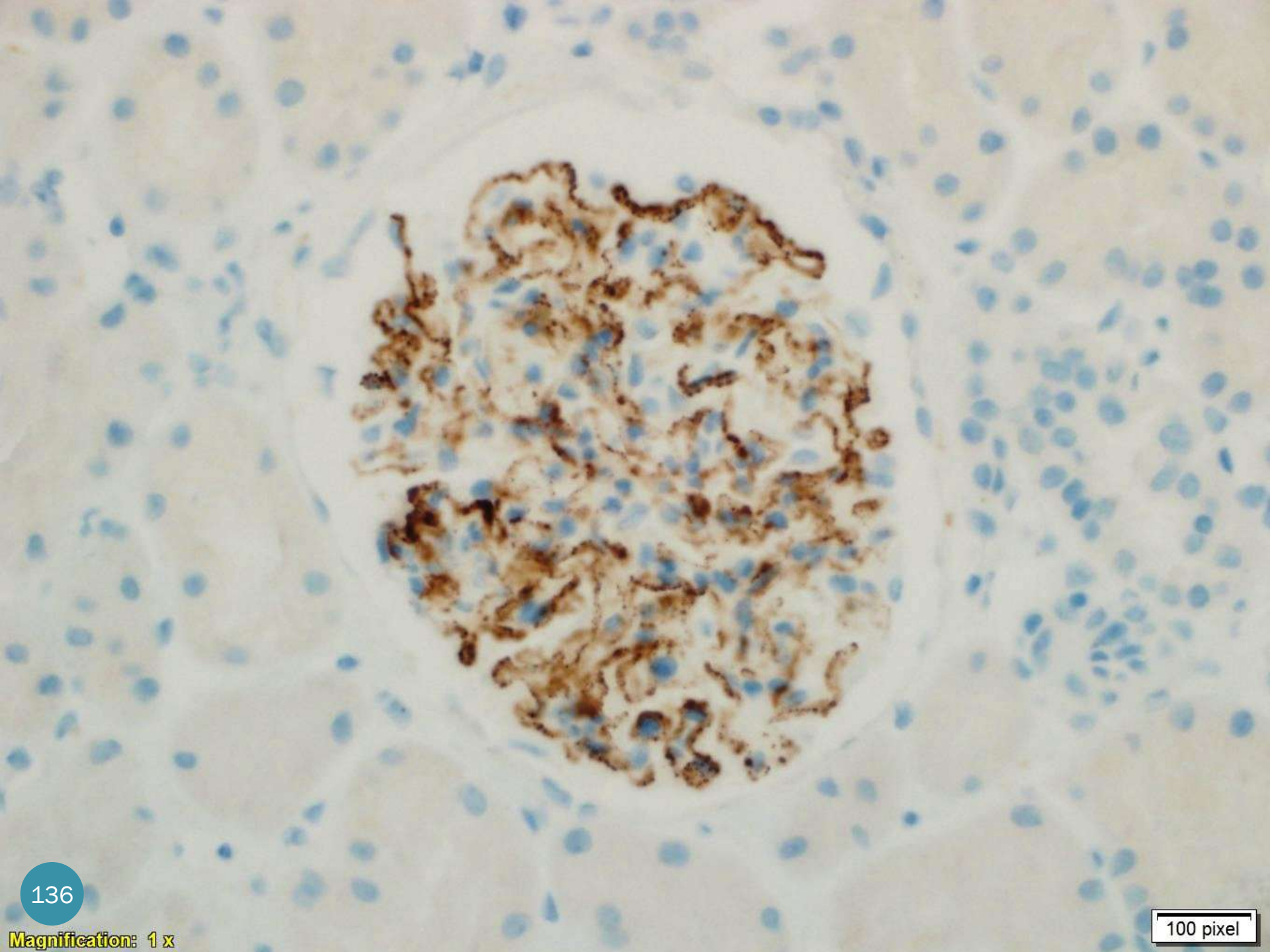
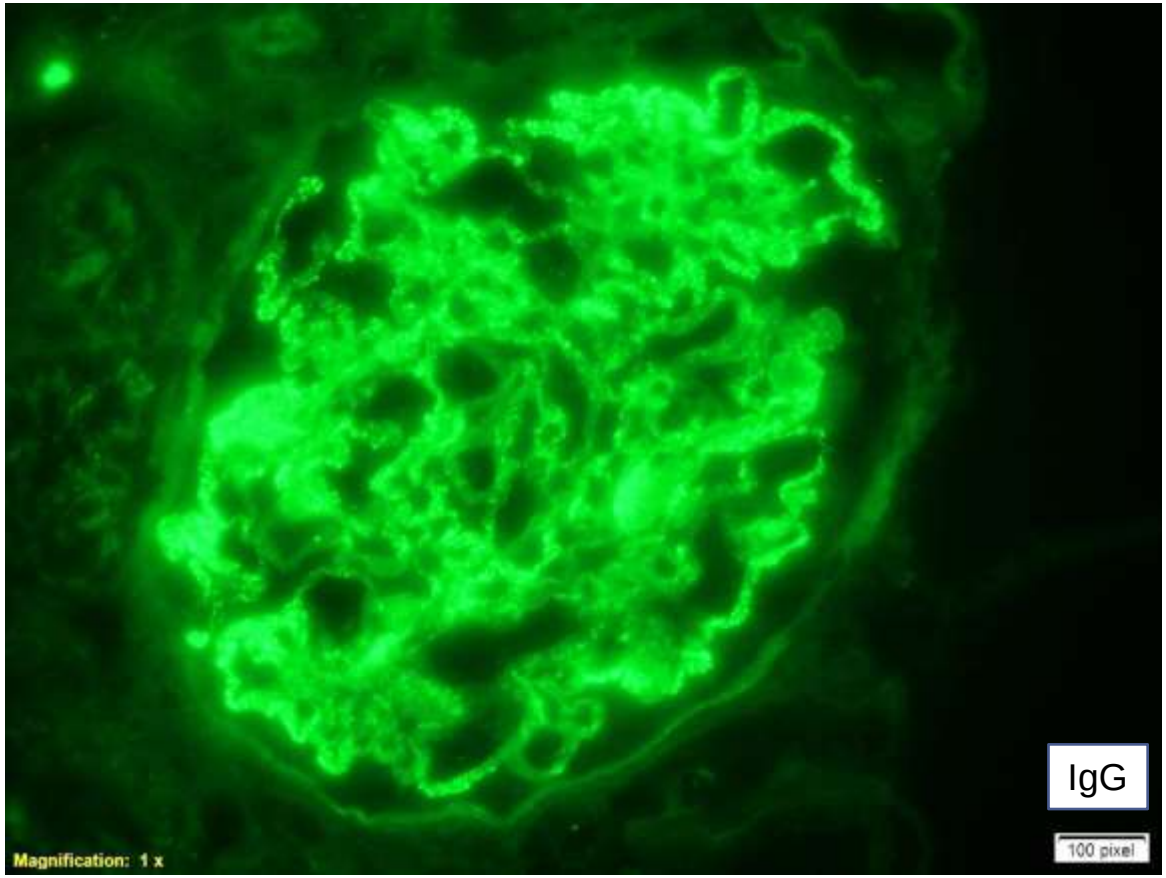
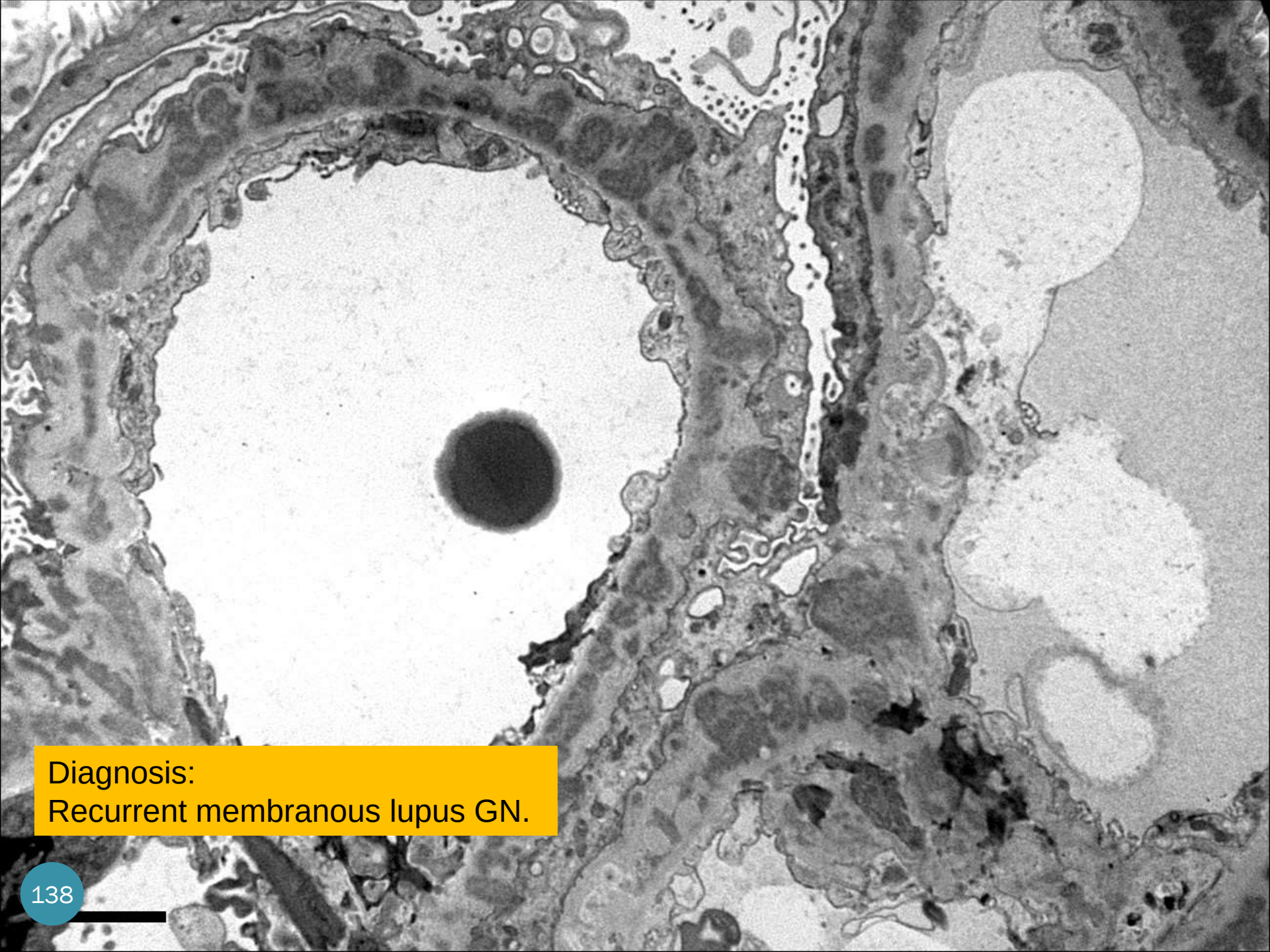

136
Magnification: 1 x
100 pixel

Case 6

- DIF:
  - Diffuse and global granular capillary and mesangial staining for IgG (2+), C1q (3+) and KAPPA (2+) and Lambda (2+) light chains.
  - Nonspecific mesangial staining for IgM and C3.
  - Negative IgA.



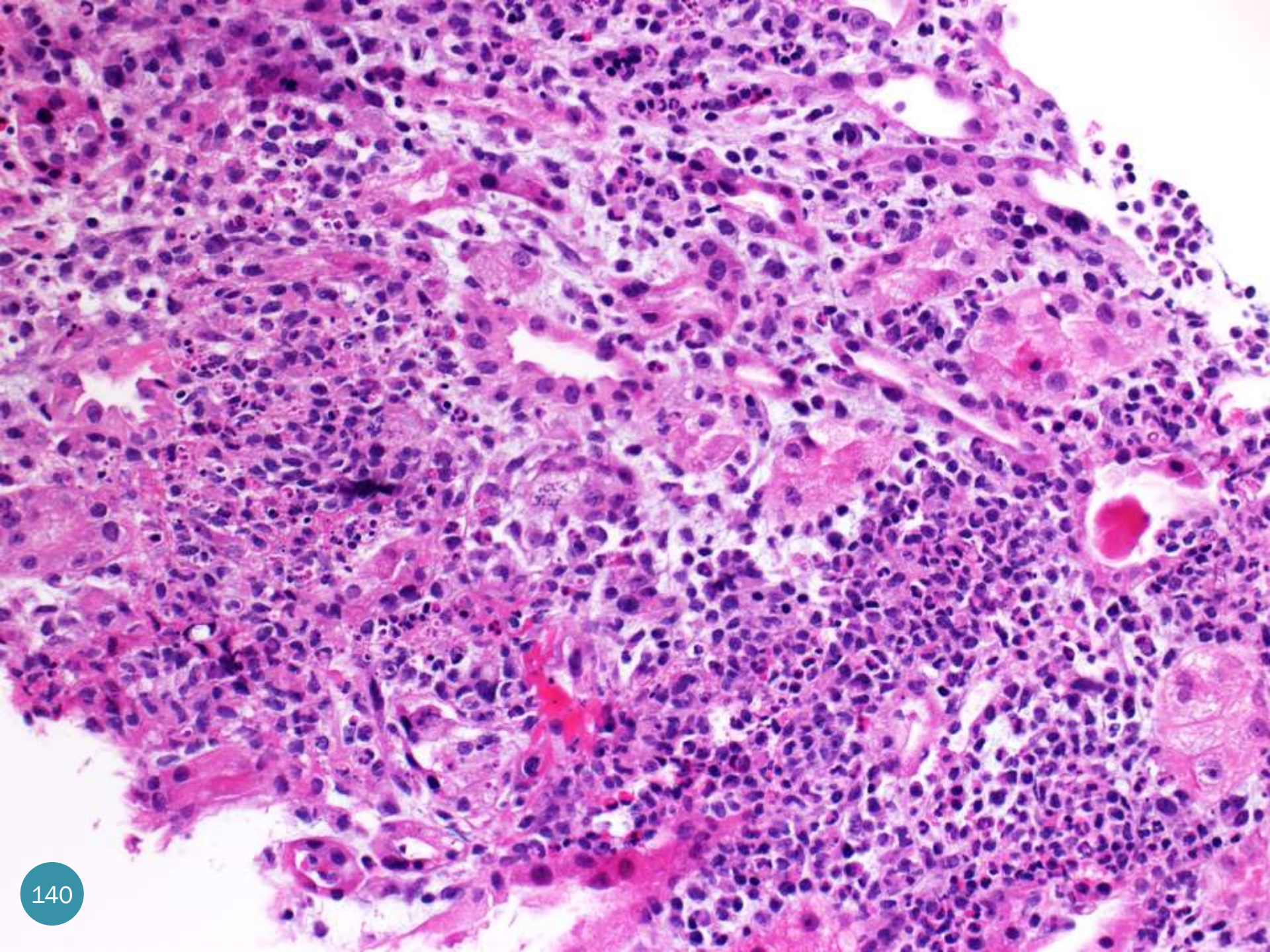


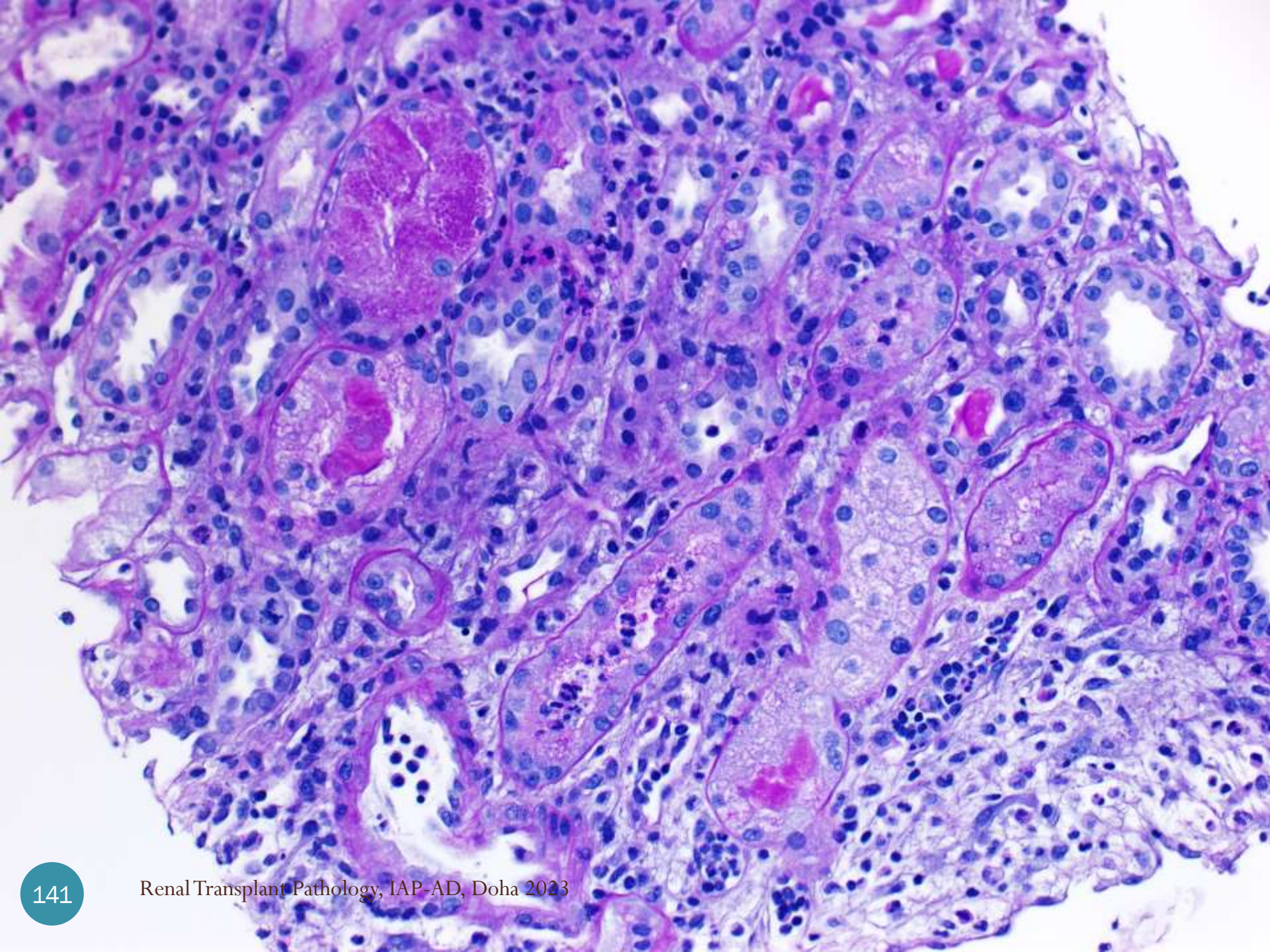
Diagnosis:
Recurrent membranous lupus GN.

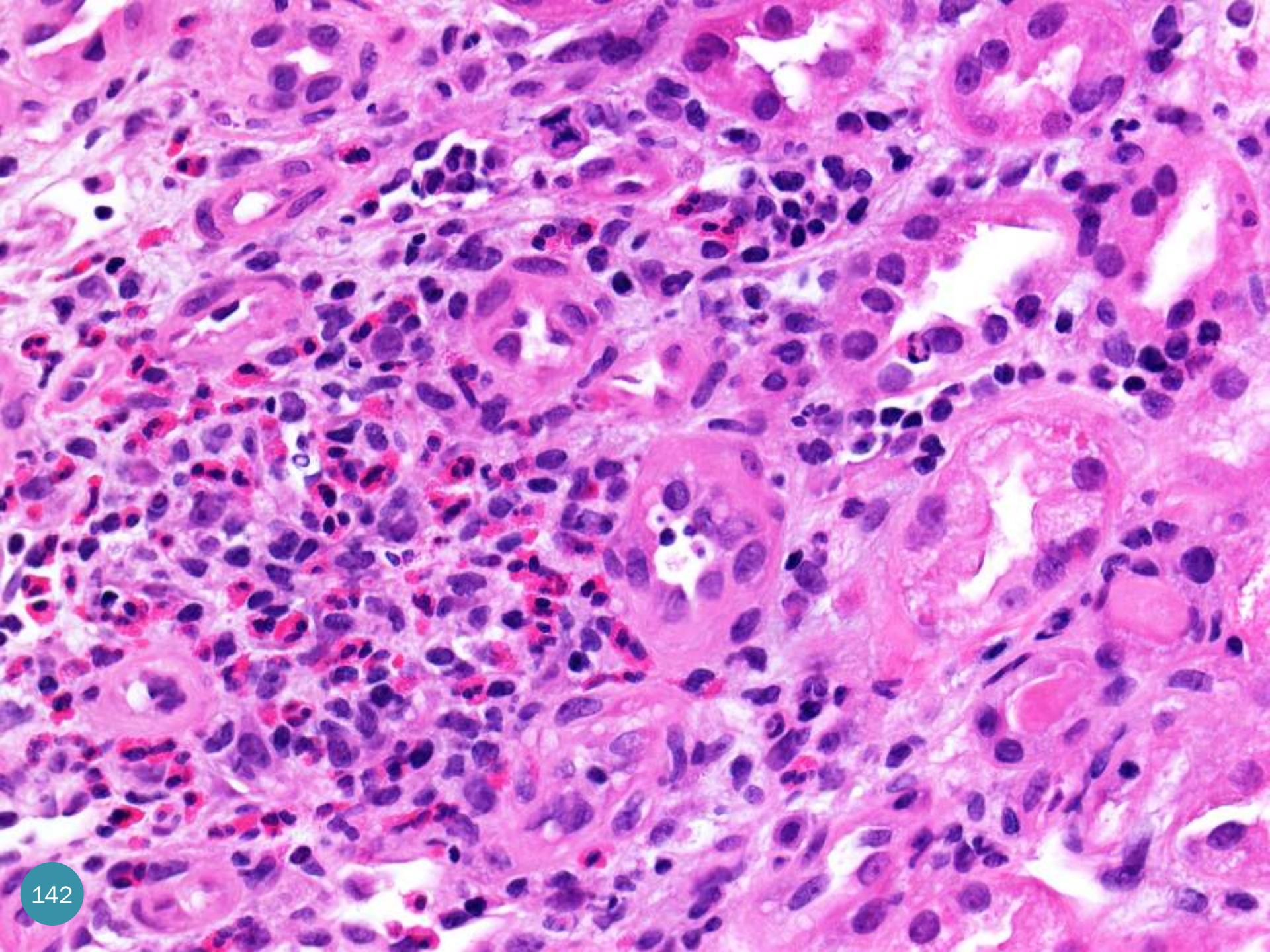
Case 7

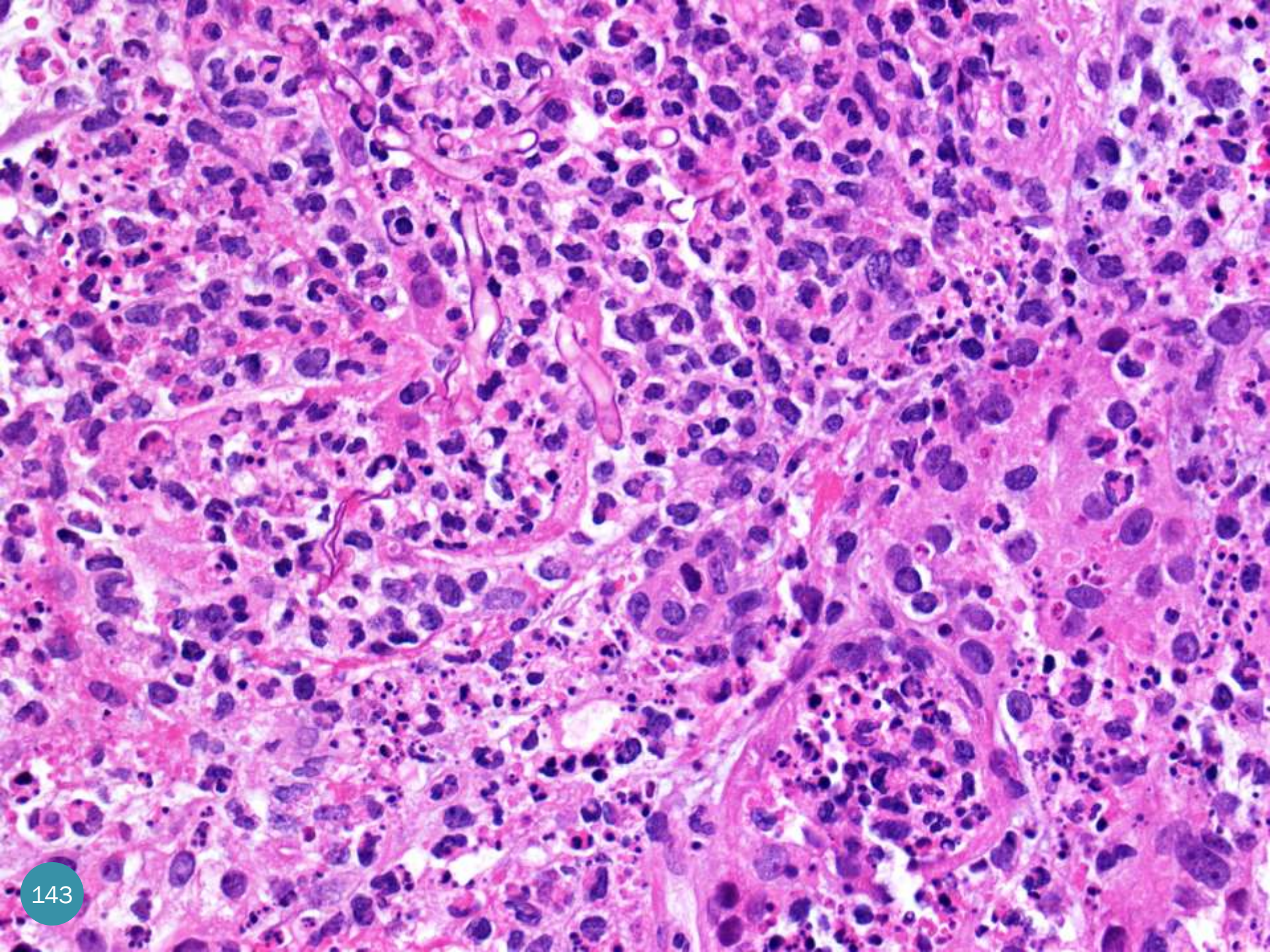
- 57-year-old hypertensive woman with of tuberculosis and 4 moths post living related renal transplant secondary to end stage renal disease of unknown etiology.

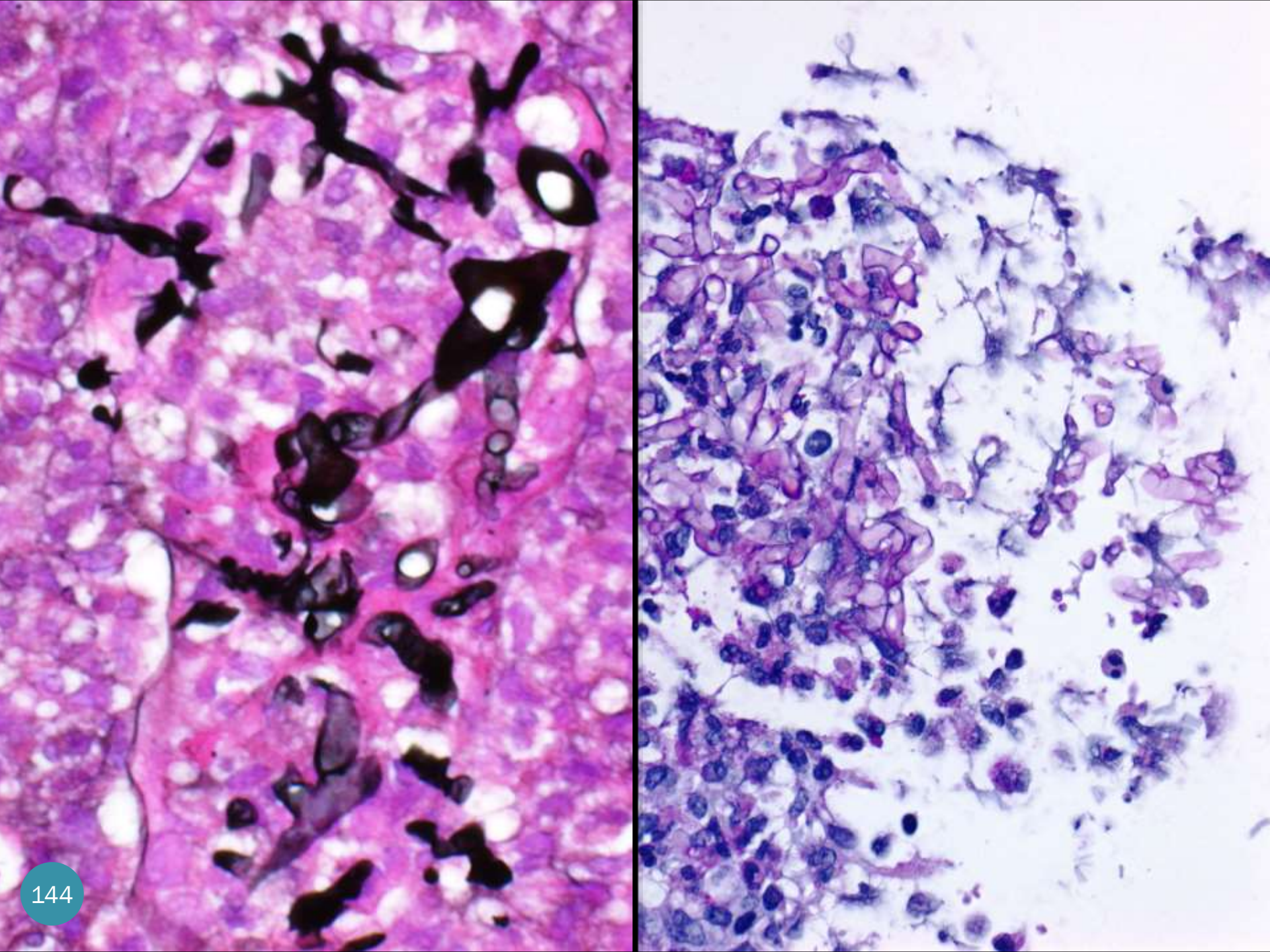
- Admitted as a case of K. Pneumonia and bacteremia, and while hospitalized developed acute renal graft dysfunction.

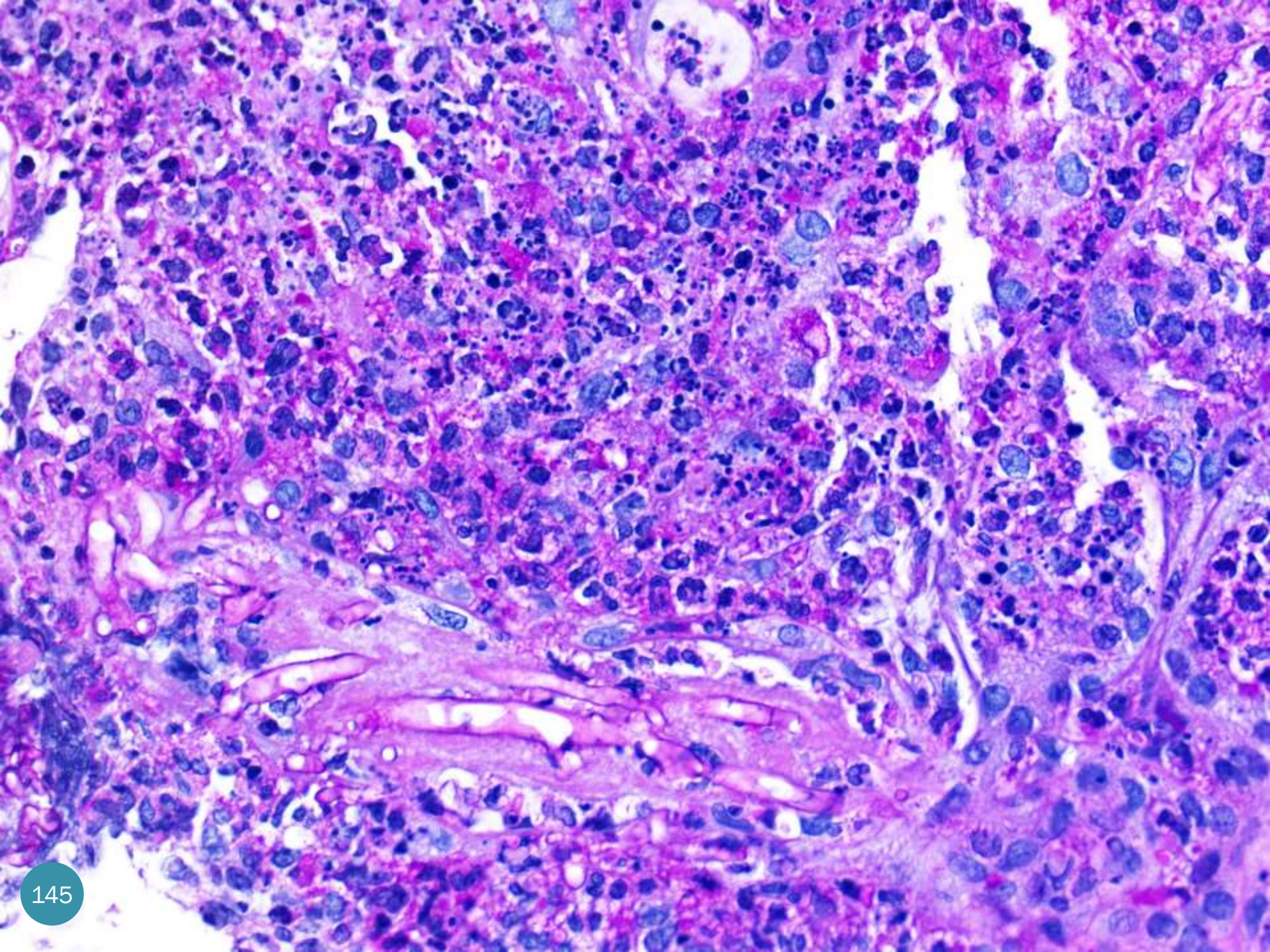


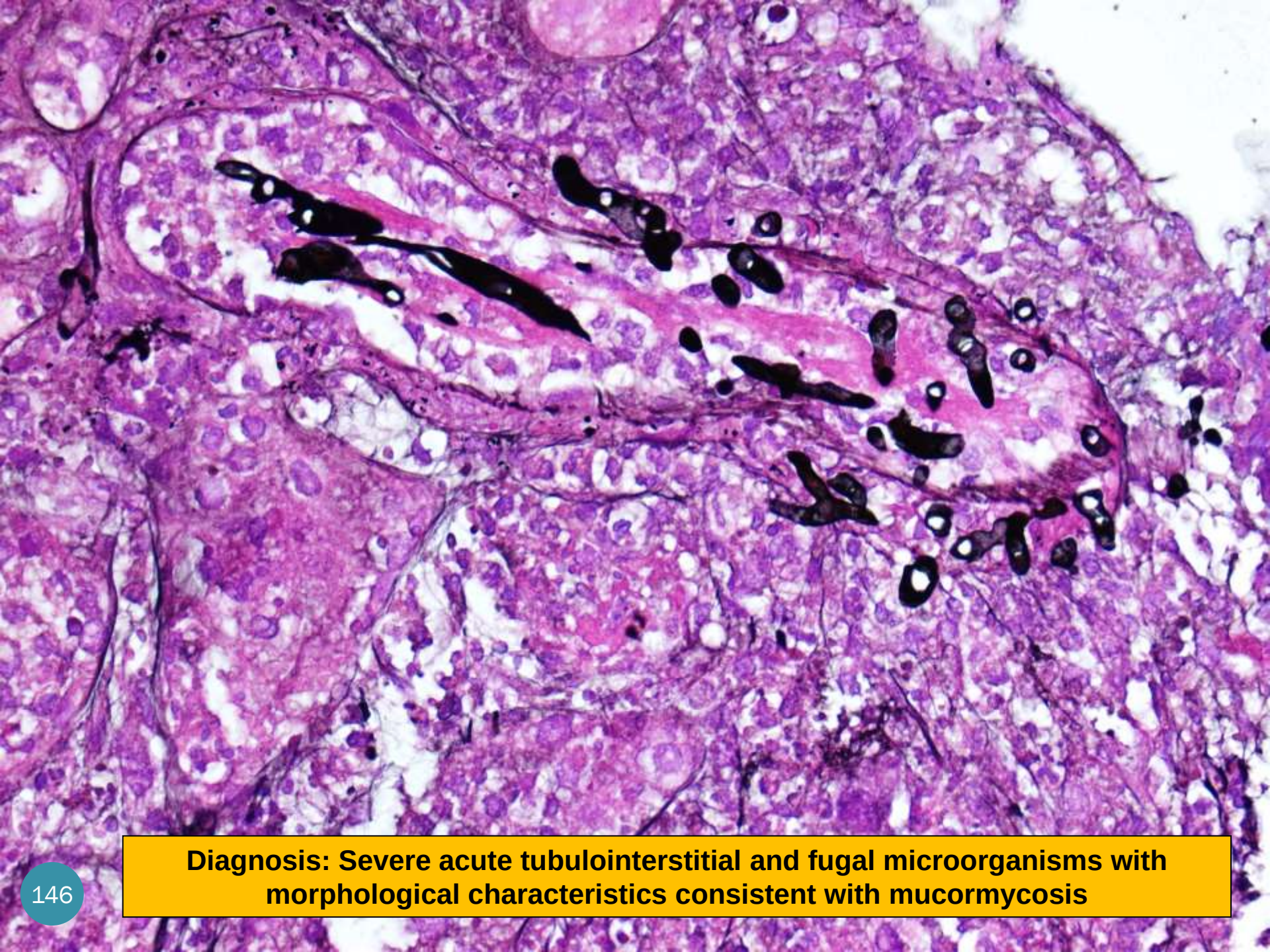












Diagnosis: Severe acute tubulointerstitial and fugal microorganisms with morphological characteristics consistent with mucormycosis

Thank you