



**UNIKLINIK  
KÖLN**

**Wie hätten Sie es gemacht?  
Besprechung interessanter  
pathologischer Fälle**

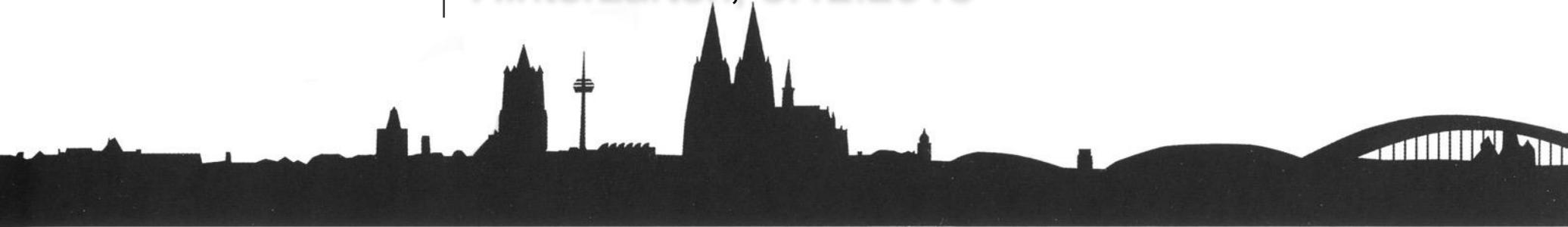
**PD Dr. Jan Becker**

**Prof. Dr. Christine Kurschat**

Institut für Pathologie und

Klinik II für Innere Medizin, Uniklinik Köln

Hinterzarten, 8.12.2018



**Fall 1**

# Fall 1

**Patient U.T, 58 Jahre alt**

## **Vorgeschichte:**

- renale Grunderkrankung: p-ANCA-positive Vaskulitis  
ED 11/2004
- HD ab 2007
- Z.n. **Nierentransplantation** 1.12.2016  
Verstorbenenenspende, Rescue-Angebot von ET, MM 1-2-0  
- bestes Kreatinin auf **220**  $\mu\text{mol/l}$  (**2.5** mg/dl)

# Fall 1

**Patient U.T, 58 Jahre alt**

## **Verlauf:**

- **V.a. Nierenarterienstenose** bei Z.n. akutem Transplantatversagen unter ACE-Hemmergabe und Hypertonie
  - PTA der Transplantatarterie ohne Erfolg
  - Re-Implantation der Nierenarterie nach Kürzung 7/2018
- **CMV-Kolitis** bei CMV-Risikokonstellation D+R- nach Beendigung der Valganciclovirprophylaxe, seitdem mehrfache CMV-Reaktivierungen, Valganciclovir und Cytotect, ausgeprägte Leukopenie

# Fall 1

**Patient U.T, 58 Jahre alt**

## **Medikation:**

- Advagraf 3 mg-0-0 mg
- Prednisolon 5 mg 1-0-0
- MMF 500 mg-0-250 mg
- Torasemid 20 mg 1-0-0
- Felodipin 5 mg 1-0-0
- Ramipril 2.5 mg 1-0-0

# Fall 1

## Patient U.T, 58 Jahre alt

### Verlauf:

- Seit März 2017 de novo-DSA Anti-DR53, MFI 272, nicht komplementfixierend, im Verlauf konstant 11/17
- **November 2017**: Kreatininanstieg von **200**  $\mu\text{mol/l}$  (**2.28** mg/dl) auf **316**  $\mu\text{mol/l}$  (**3.59** mg/dl) unklarer Genese

# Fall 1

## Patient U.T, 58 Jahre alt

### Verlauf:

- Seit März 2017 de novo-DS komplementfixierend, im Ve
- **November 2017**: Kreatinin auf **316**  $\mu\text{mol/l}$  (**3.59** mg/dl)

### Laborwerte:

- Kreatinin: **316**  $\mu\text{mol/l}$  (**3.59** mg/dl)
- Proteinurie: 369 mg/g Kreatinin
- Albuminurie 162 mg/g Kreatinin
- Hämaturie

# Fall 1

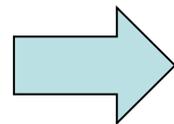
**Patient U.T, 58 Jahre alt**

## Verlauf:

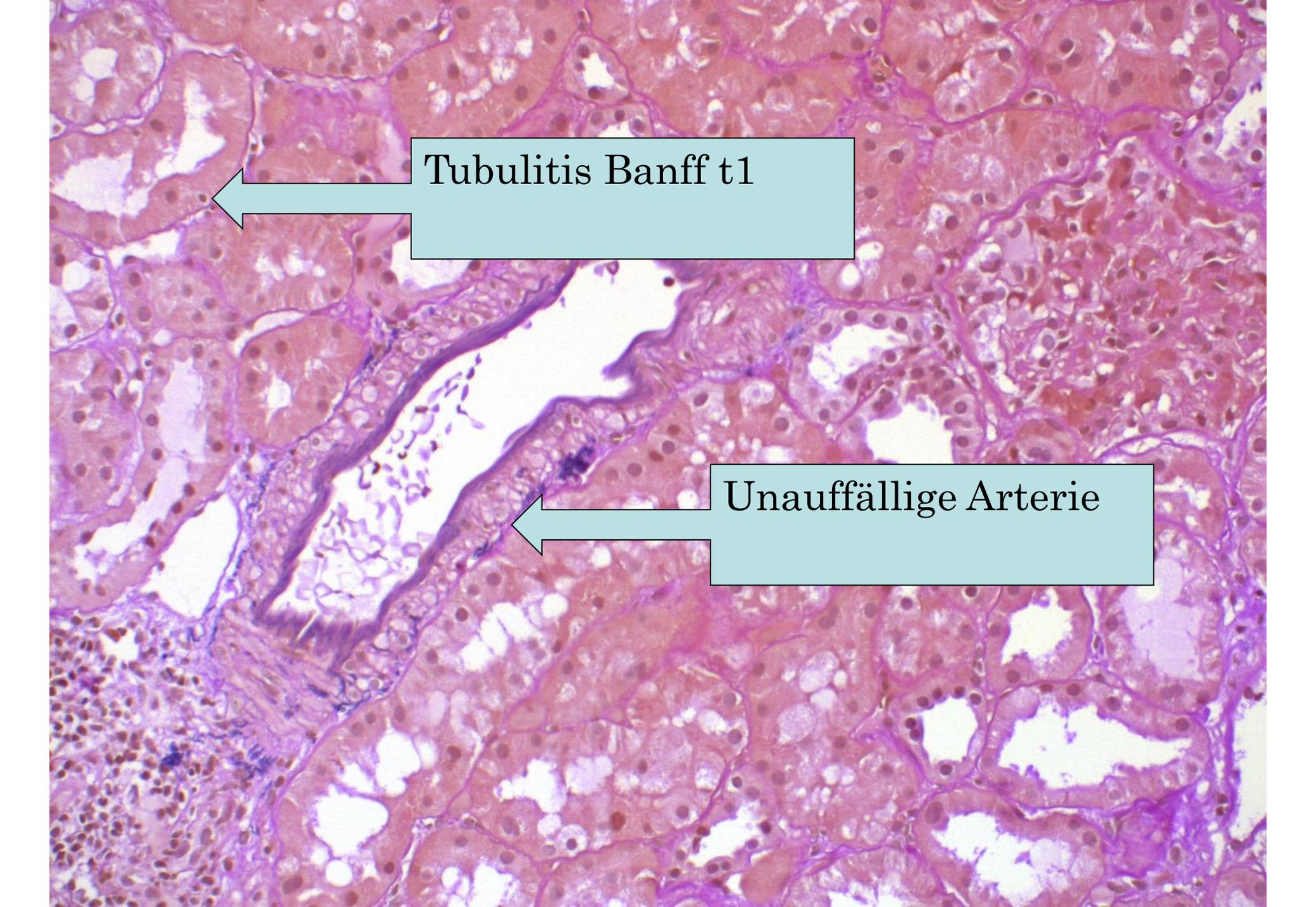
- Seit März 2017 de novo-DS komplementfixierend, im Ve
- **November 2017**: Kreatinin auf **316**  $\mu\text{mol/l}$  (**3.59** mg/dl)

## Laborwerte:

- Kreatinin: **316**  $\mu\text{mol/l}$  (**3.59** mg/dl)
- Proteinurie: 369 mg/g Kreatinin
- Albuminurie 162 mg/g Kreatinin
- Hämaturie



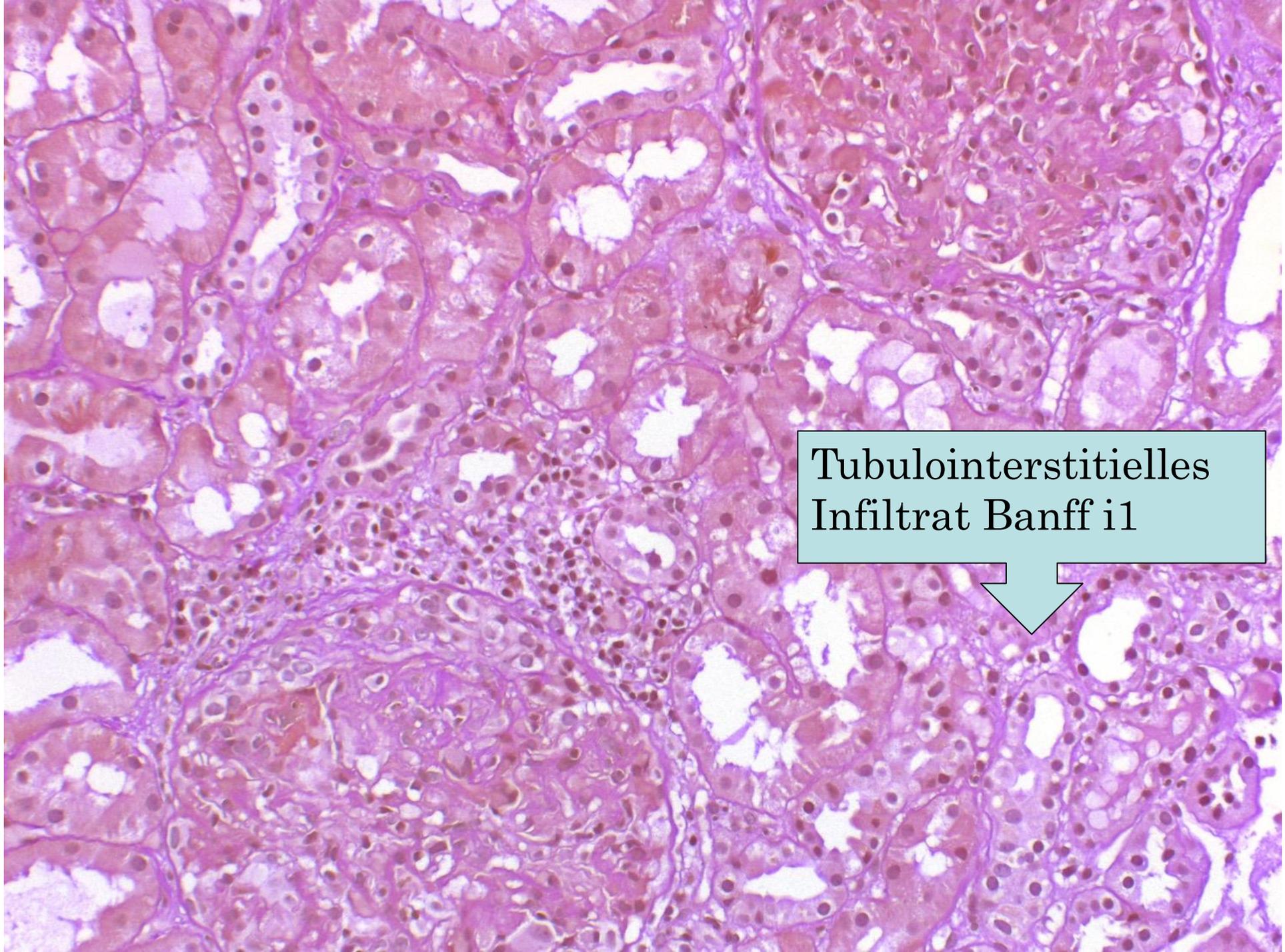
**Biopsie**



Tubulitis Banff t1

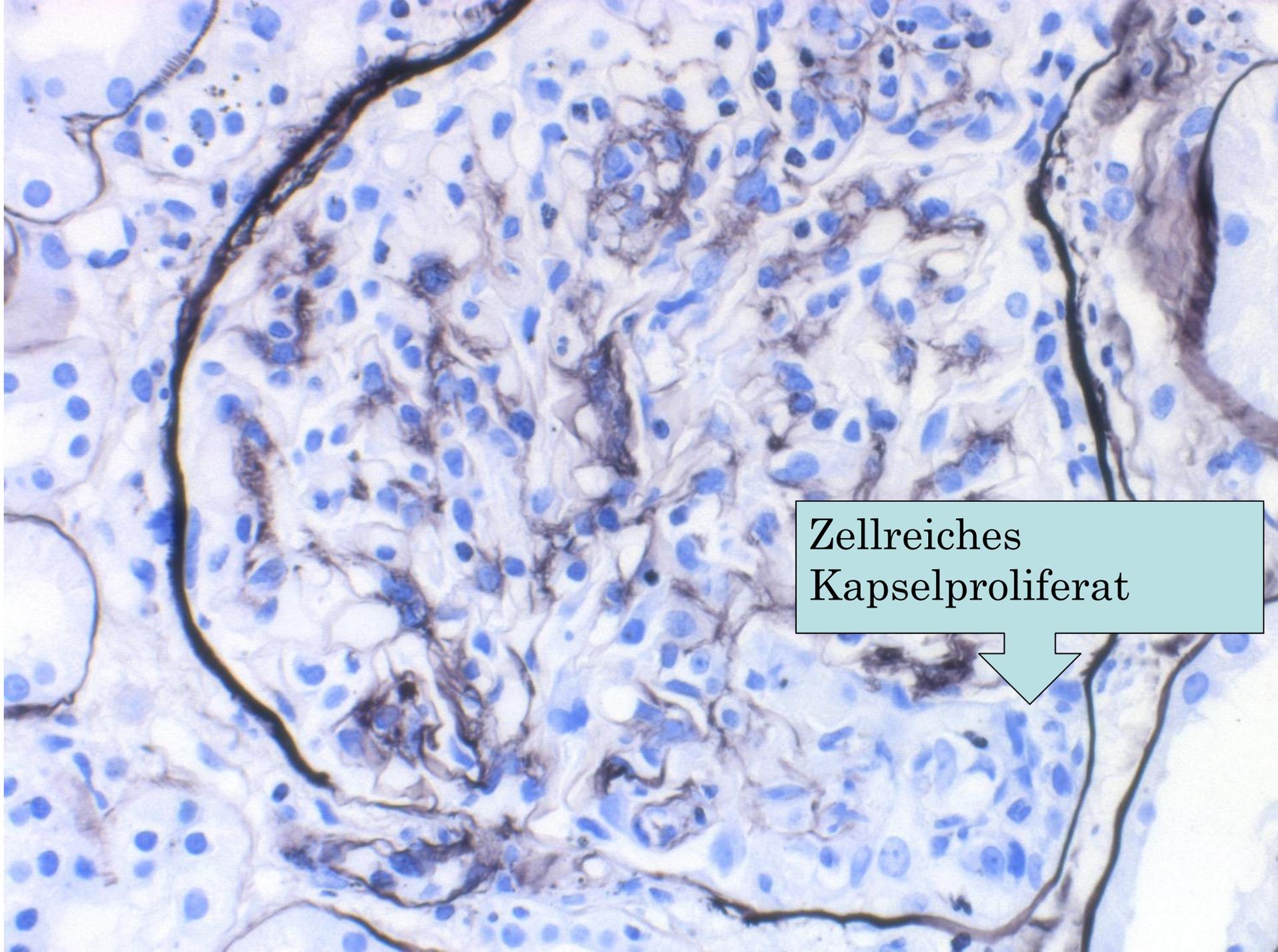
This histological image shows a section of kidney tissue stained with hematoxylin and eosin (H&E). The tissue displays numerous renal tubules with varying degrees of cellular infiltration. A prominent feature is the presence of tubulitis, where inflammatory cells have infiltrated the tubular walls. A large, clear space in the center represents a dilated tubule or a cyst. A blood vessel, identified as an artery, is visible in the lower-middle section, showing a thick, muscular wall and a clear lumen. The overall architecture is somewhat disorganized due to the inflammatory process.

Unauffällige Arterie



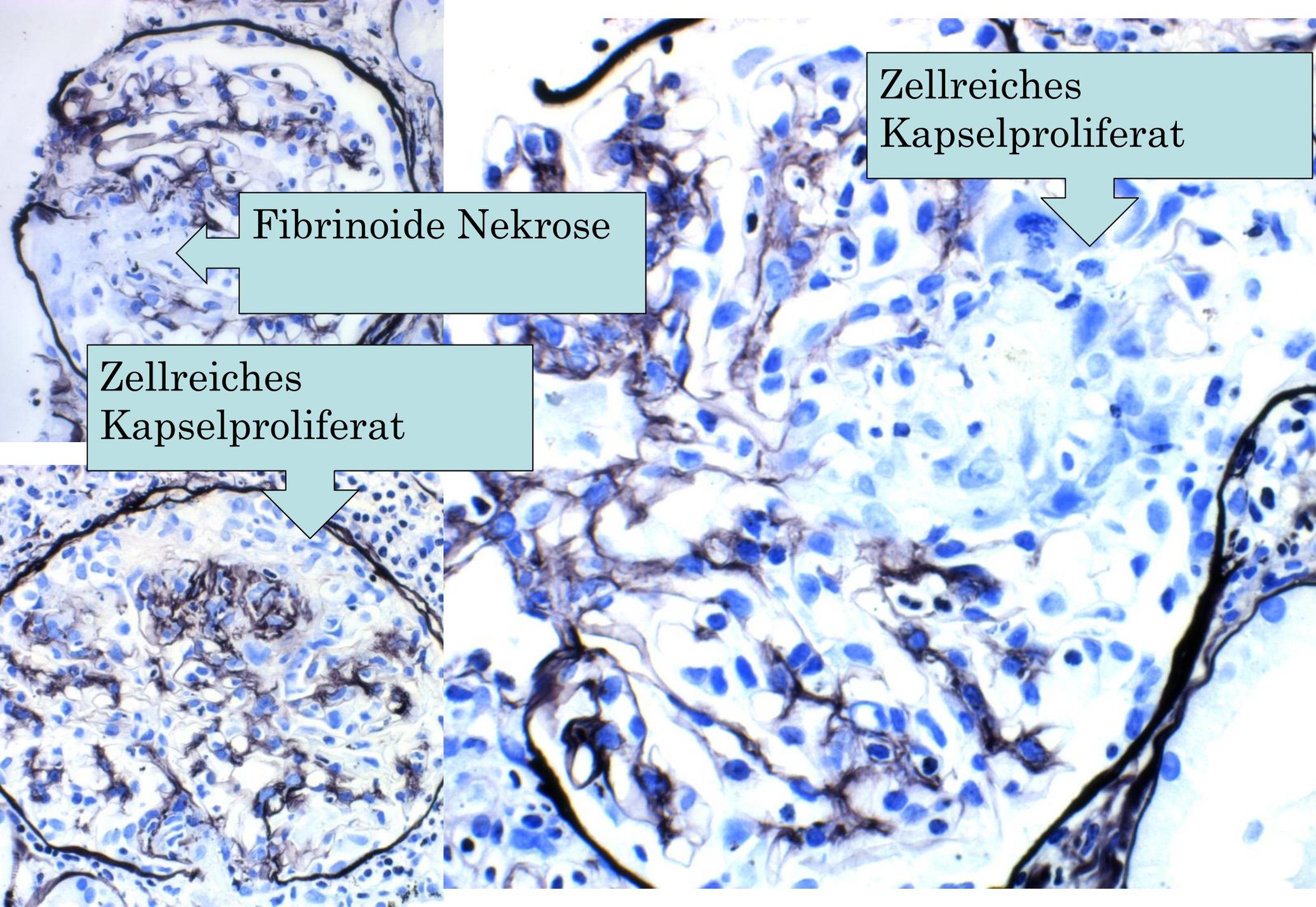
Tubulointerstitielles  
Infiltrat Banff i1





Zellreiches  
Kapselproliferat

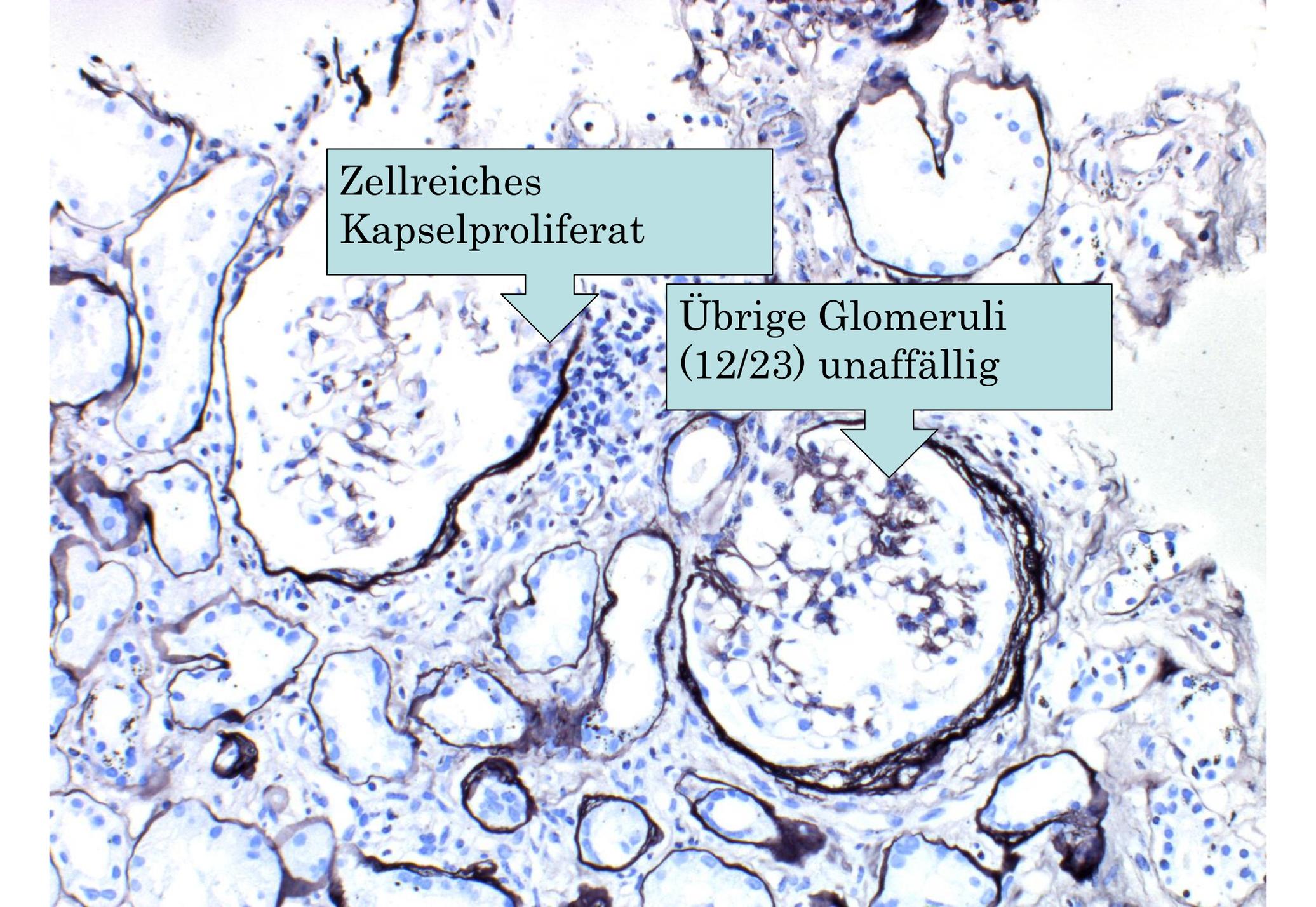




Fibrinoide Nekrose

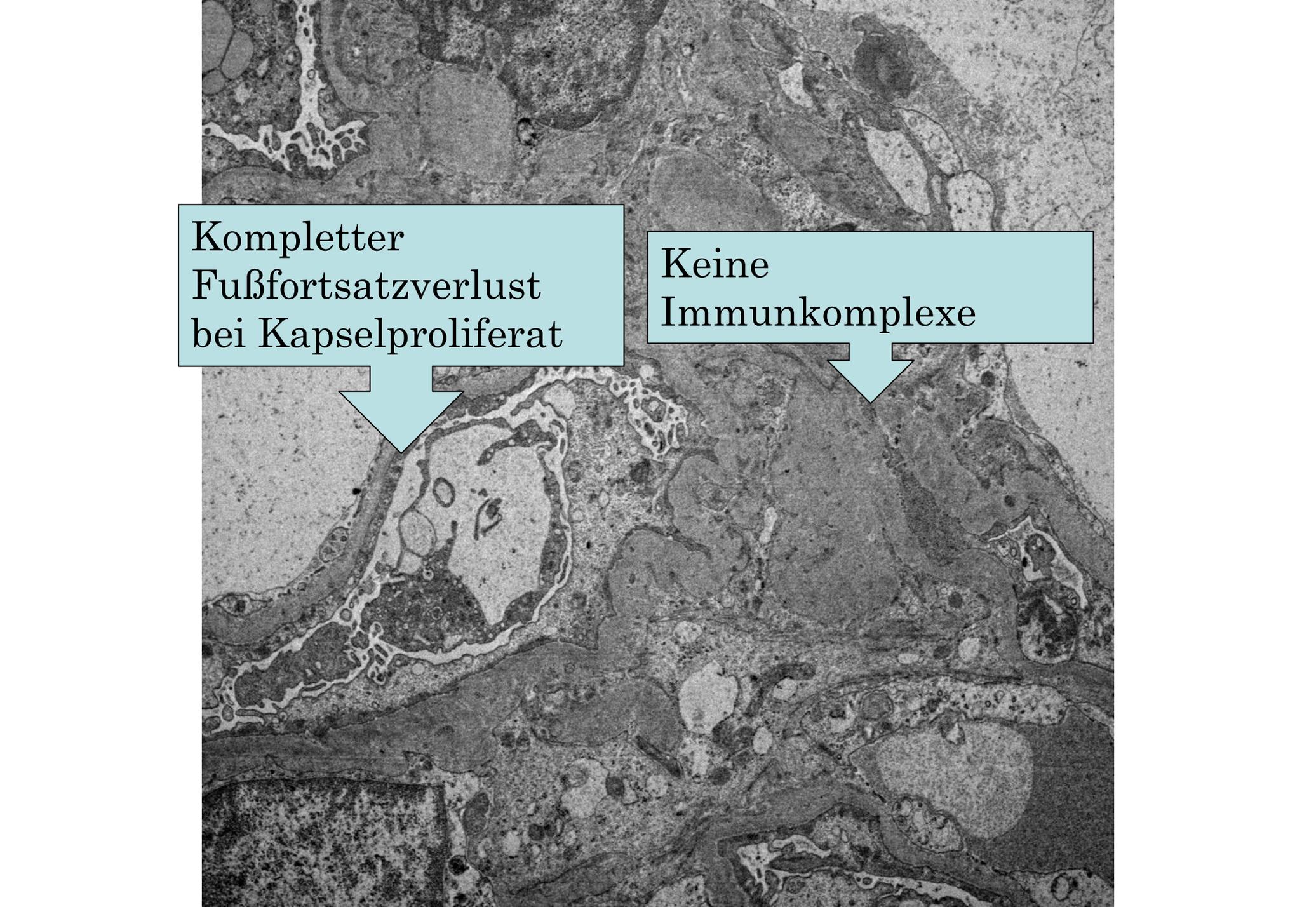
Zellreiches Kapselproliferat

Zellreiches Kapselproliferat



Zellreiches  
Kapselproliferat

Übrige Glomeruli  
(12/23) unauffällig



Kompletter  
Fußfortsatzverlust  
bei Kapselproliferat

This electron micrograph shows a cell junction. A light blue box on the left contains the text 'Kompletter Fußfortsatzverlust bei Kapselproliferat'. A light blue arrow points from this box to a specific area of the cell membrane where the foot processes are absent. Another light blue box on the right contains the text 'Keine Immunkomplexe'. A light blue arrow points from this box to a region of the cytoplasm where no immune complexes are visible.

Keine  
Immunkomplexe

# Histologische Diagnose

Pauciimmune Glomerulonephritis

Fokal frisch nekrotisierend und extrakapillär proliferativ  
(11/23)

Geringe floride interstitielle Begleitnephritis (rein formal  
Banff Borderline)

Mäßiger akuter Tubululusschaden, keine IFTA

Geringe Arteriosklerose, geringe benigne Nephrosklerose

Banff Lesion Scores:

i1, t1, v0, g0, ptc0, C4d0, ci0, ct0, cv1, cg0, mm0, ah1, ti1, i-IFTA1

**Fall 2**

# Fall 2

**Patient R.H., 68 Jahre alt**

## **Vorgeschichte:**

- präemptive **AB0-inkompatible Nierentransplantation** am 17.5.18,  
Spenderin: Ehefrau
  - IgG-Liss 1:64, IgM-NaCL 1:16, Anti-A2
  - prä-OP Rituximab, Plasmaseparation und Immunadsorption  
→ Ziel-Titer 1:4
- Immunsuppression mit Simulect, Tacrolimus, MMF, Prednison  
MM HLA-A 1; HLA-B 1, HLA-DR 1
- Grunderkrankung: Harnaufstau bds. 2/15, Kreatinin **830** µmol/l (**9.42** mg/dl)
- Gewicht: 98 kg

# Fall 2

**Patient R.H., 68 Jahre alt**

## **Kreatininverlauf:**

- prä-OP **830**  $\mu\text{mol/l}$  (**9.42** mg/dl)
- 1. Tag post-OP **256**  $\mu\text{mol/l}$  (**2.91** mg/dl)
- 2. Tag post-OP **312**  $\mu\text{mol/l}$  (**3.55** mg/dl), parallel Anti-A2-IgG 1:8  
→ sofortiger **Beginn Immunadsorption** nach SOP ( $\geq 1:8$ )
- 4. Tag post-OP **480**  $\mu\text{mol/l}$  (**5.46** mg/dl)
- 16. Tag post-OP **609**  $\mu\text{mol/l}$  (**6.93** mg/dl): Krea max.

# Fall 2

**Patient R.H., 68 Jahre alt**

## **Titerverlauf AB0-Titer:**

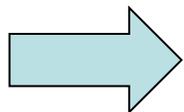
- initial Anti-A2 IgG-Liss **1:64**, IgM-NaCL **1:16**
- nach 2 Plasmapheresen und 8 Immunadsorptionen  
Titer prä-OP: IgG **1:4**, IgM **1:2**
- 2. postoperativer Tag Anstieg des AB0i-Titers auf 1:8 (IgG),  
daher sofortiger Beginn der erneuten Immunadsorption  
nach SOP, insg. 2xPE, 5xIA
- dadurch Rückgang des Titers auf **1:4**, dann **<1:2**
- **Kein Nachweis eines Anti-HLA DSA**

# Fall 2

**Patient R.H., 68 Jahre alt**

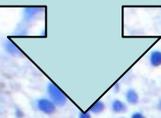
## **Klinischer Verlauf:**

- nach Beginn IA/PS/Steroide → 1. Nierenbiopsie
  - zusätzlich Gabe von ATG
- bei weiter erhöhtem Kreatinin → 2. Nierenbiopsie
- als rescue:
  - Gabe von **Eculizumab** 900 mg 2 x
  - Kreatinin **446** µmol/l (**5.07** mg/dl)

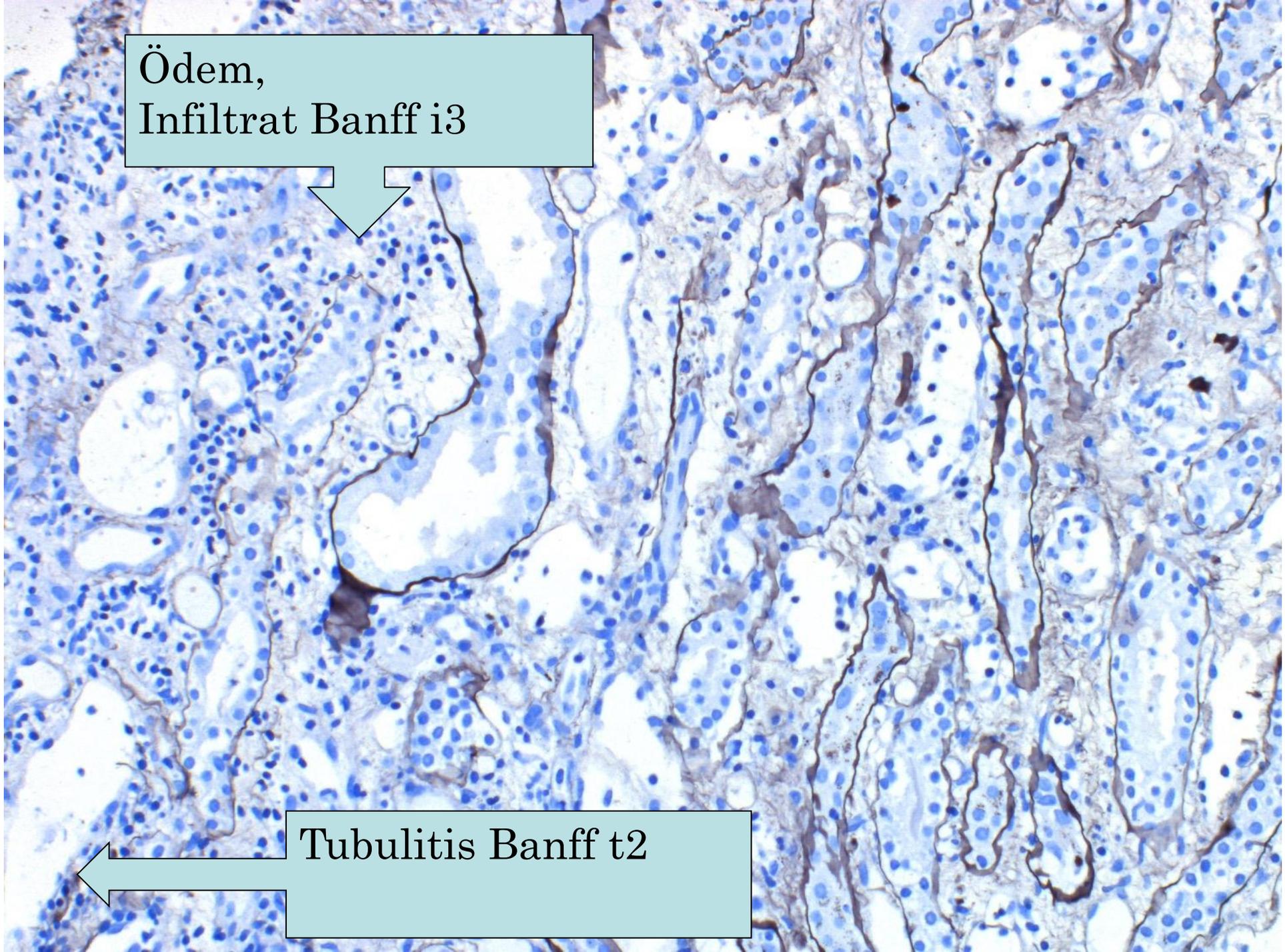


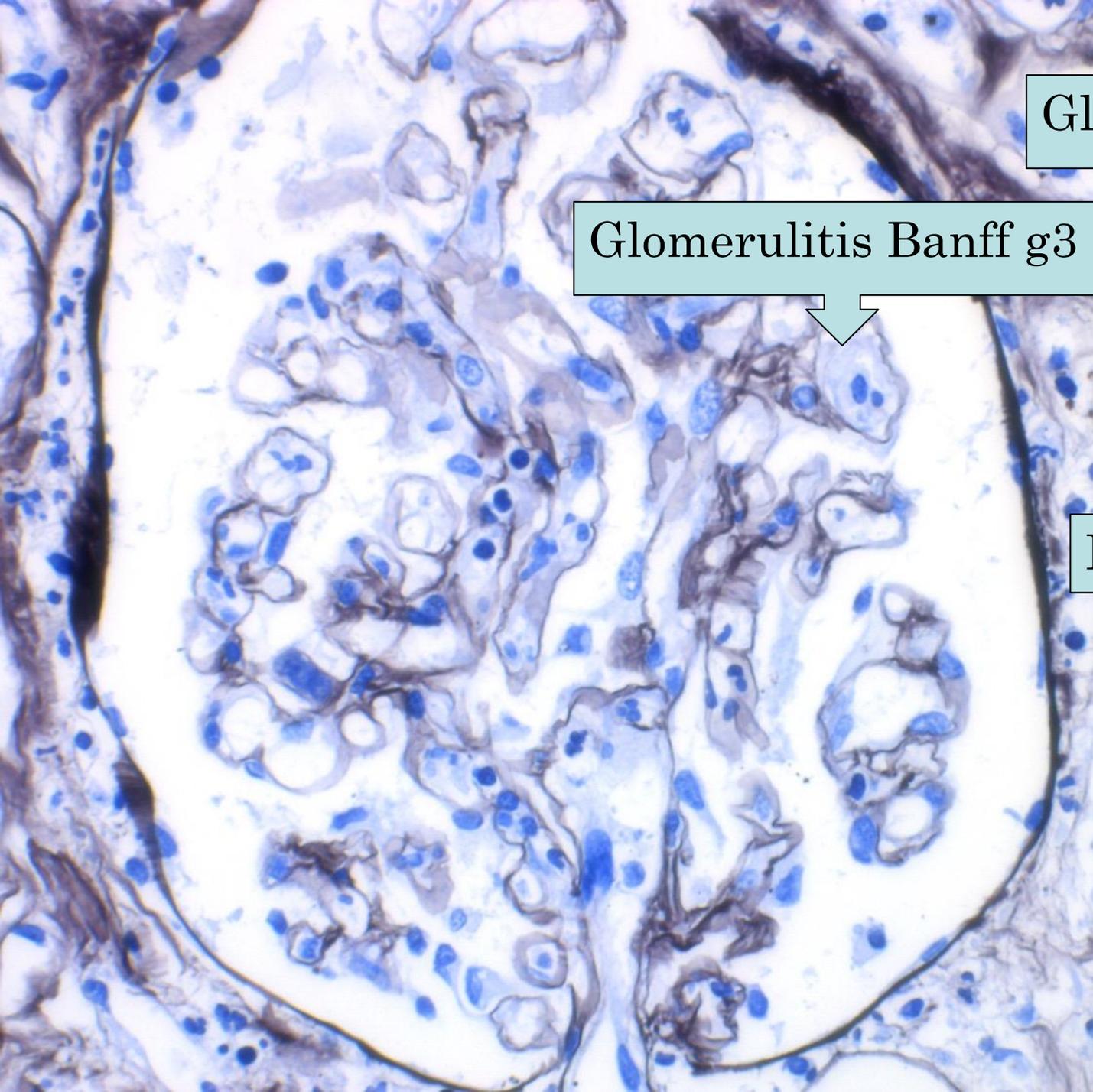
**aktuelle Nierenfunktion:** Kreatinin **224-240** µmol/l (**2.55-2.73** mg/dl)

Ödem,  
Infiltrat Banff i3



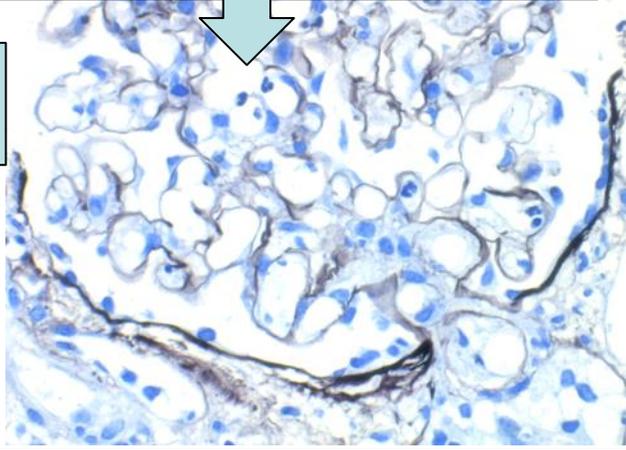
Tubulitis Banff t2



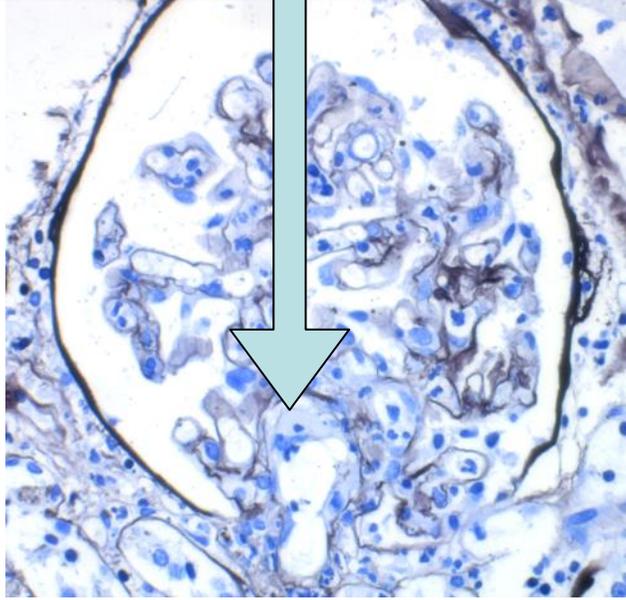


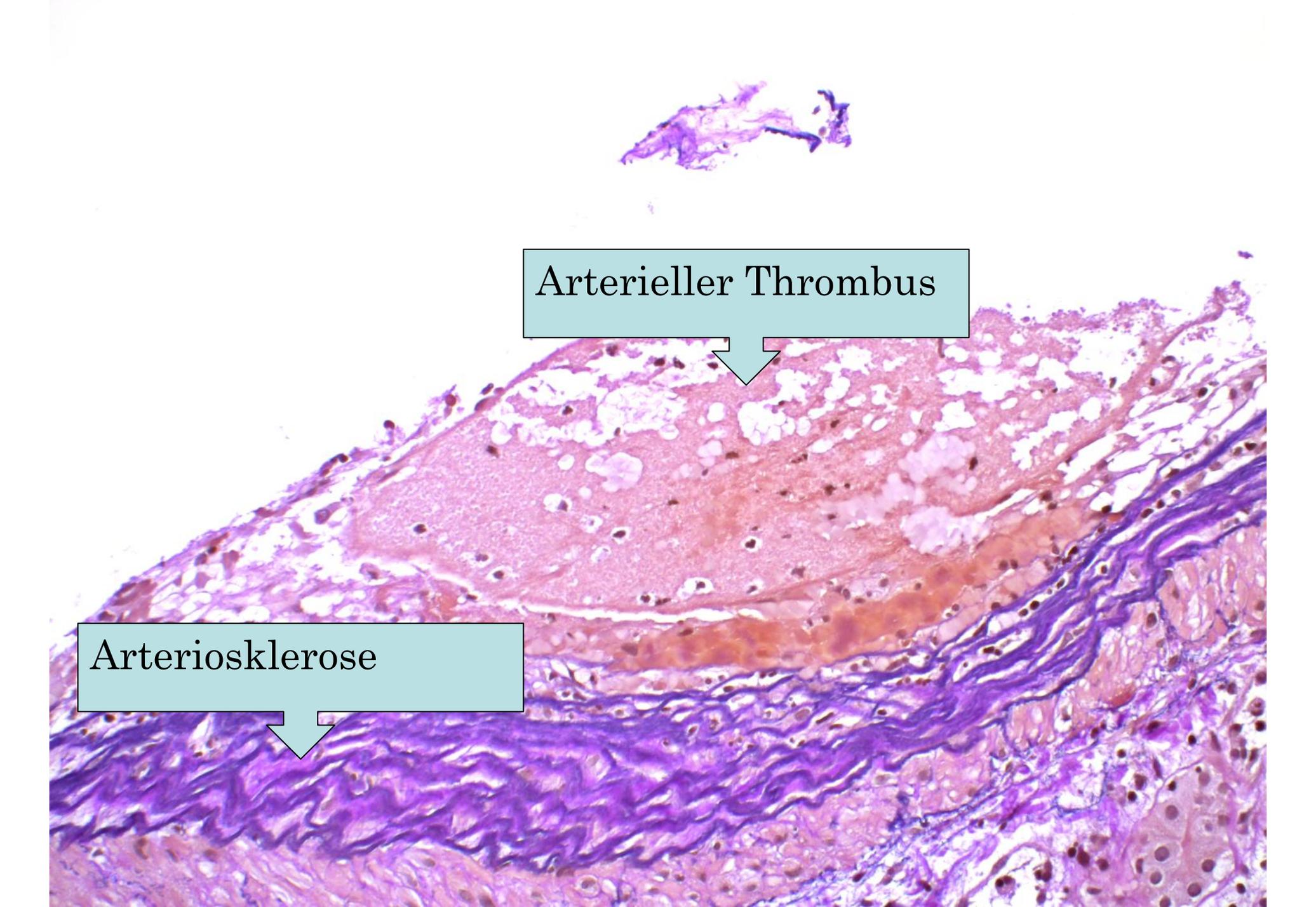
Glomerulitis Banff g3

Glomerulitis Banff g3



Plus Mikrothrombus

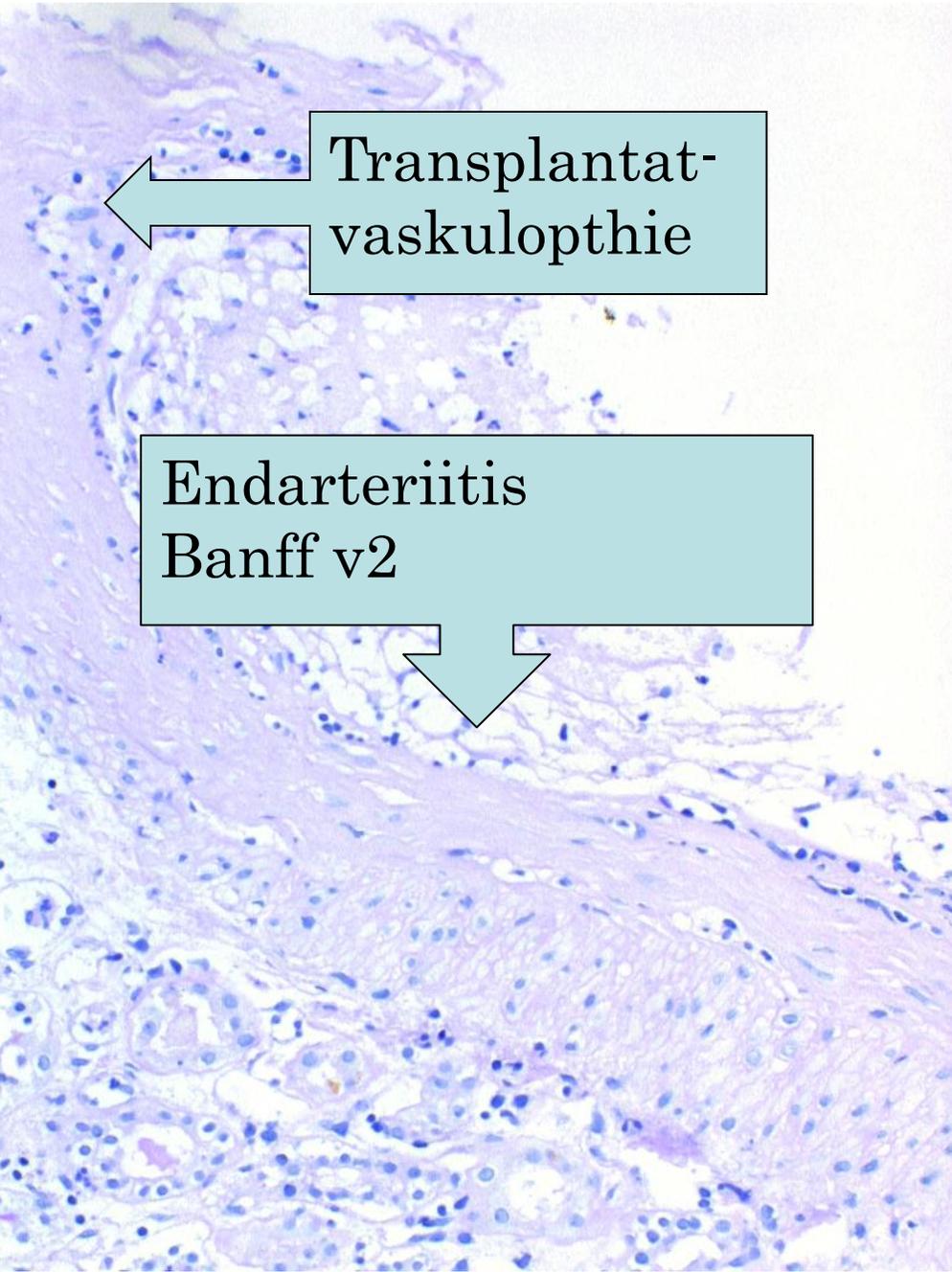




Arterieller Thrombus

This histological image shows a cross-section of an artery. The lumen is partially filled with a thrombus, which is a mass of blood components that has clotted. The thrombus is composed of red blood cells, white blood cells, and fibrin. The arterial wall shows signs of arteriosclerosis, characterized by thickening of the intima and narrowing of the lumen. The image is stained with hematoxylin and eosin (H&E), showing pink cytoplasm and purple nuclei.

Arteriosklerose

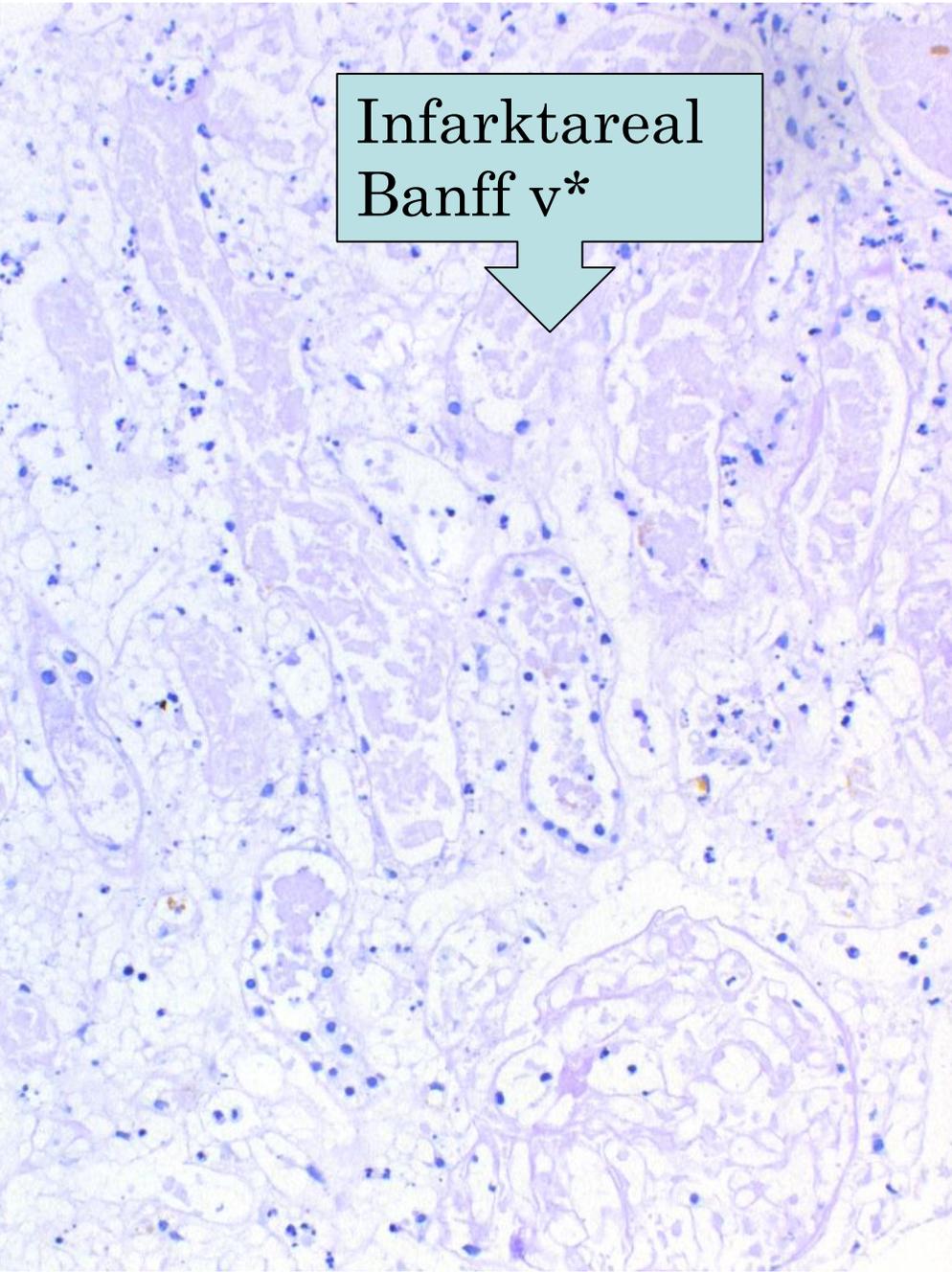


Transplantat-  
vaskulopathie

This histological image shows a blood vessel with significant changes characteristic of transplant vasculopathy. The vessel lumen is severely narrowed by a dense, eosinophilic (pink) mass of proliferating smooth muscle cells and extracellular matrix. The vessel wall is thickened, and the normal architecture is largely obscured by this proliferative process. A light blue arrow points from the text box to the vessel.

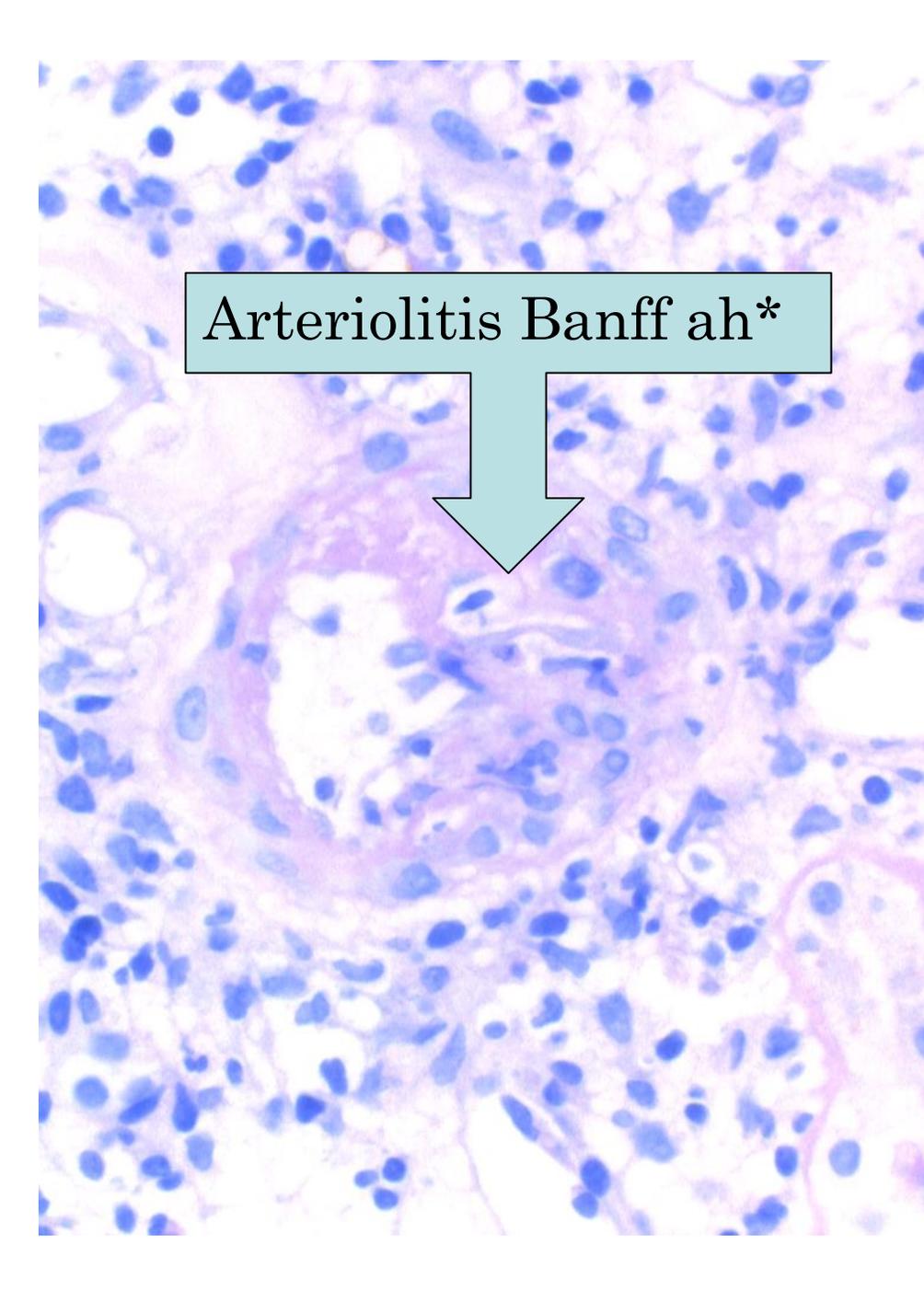
Endarteriitis  
Banff v2

This histological image shows a vessel with endarteritis, a form of transplant vasculopathy. The vessel lumen is almost completely occluded by a dense, eosinophilic mass of proliferating smooth muscle cells. The vessel wall is thickened, and the normal architecture is largely obscured by this proliferative process. A light blue arrow points from the text box to the vessel.



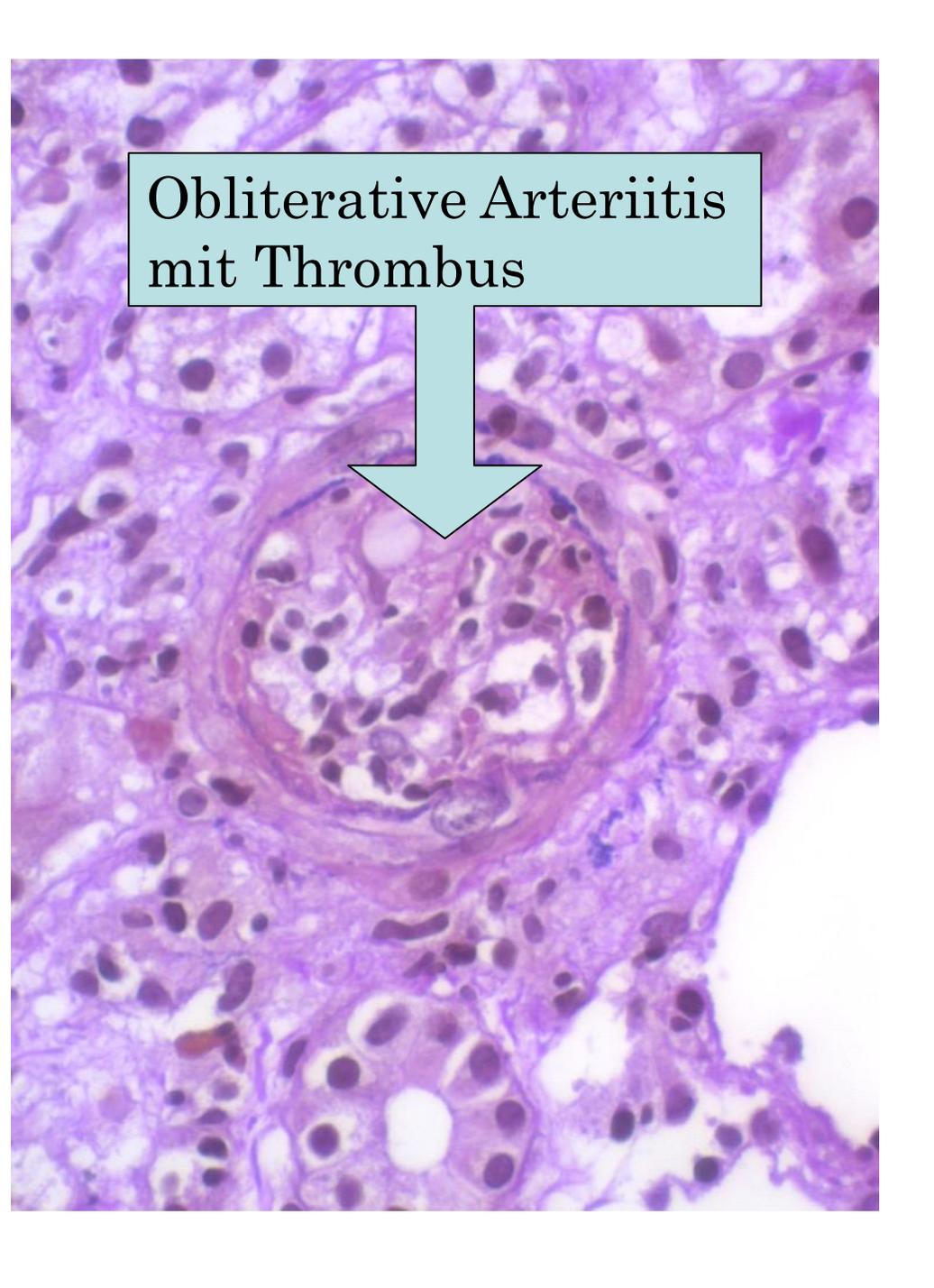
Infarktareal  
Banff v\*

This histological image shows an infarcted area of tissue. The tissue is characterized by a dense, eosinophilic (pink) mass of proliferating smooth muscle cells and extracellular matrix, which is typical of transplant vasculopathy. The vessel lumen is severely narrowed, and the vessel wall is thickened. A light blue arrow points from the text box to the vessel.



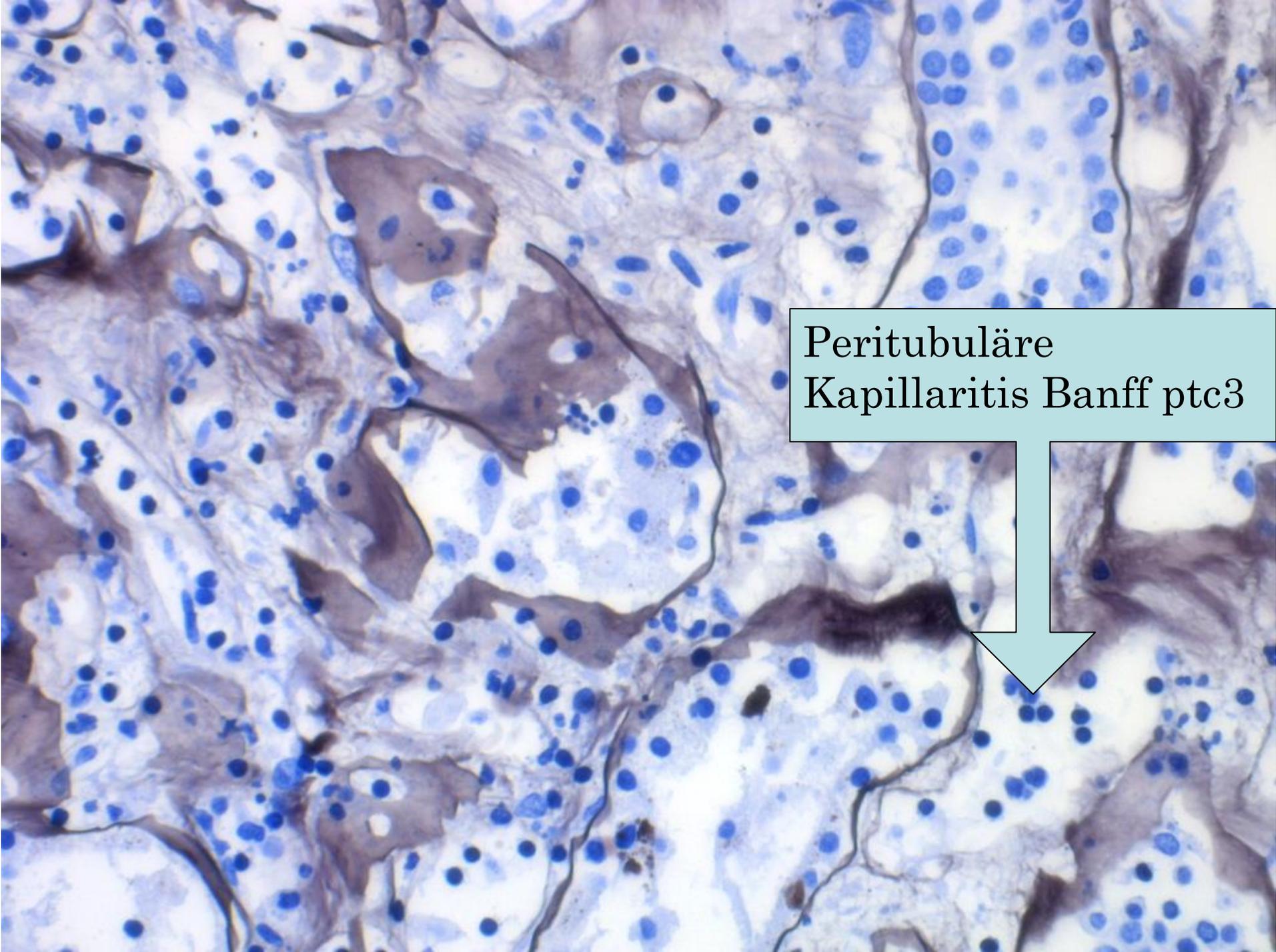
Arterirolitis Banff ah\*

This histological image shows a cross-section of an artery with a thickened wall and a dense infiltrate of inflammatory cells, characteristic of arteriolitis. A teal arrow points from the text box to the affected vessel.



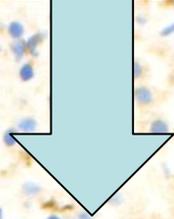
Obliterative Arteriitis  
mit Thrombus

This histological image shows a cross-section of an artery with a thickened wall and a dense infiltrate of inflammatory cells, characteristic of obliterative arteriitis. A teal arrow points from the text box to the affected vessel, which contains a thrombus.

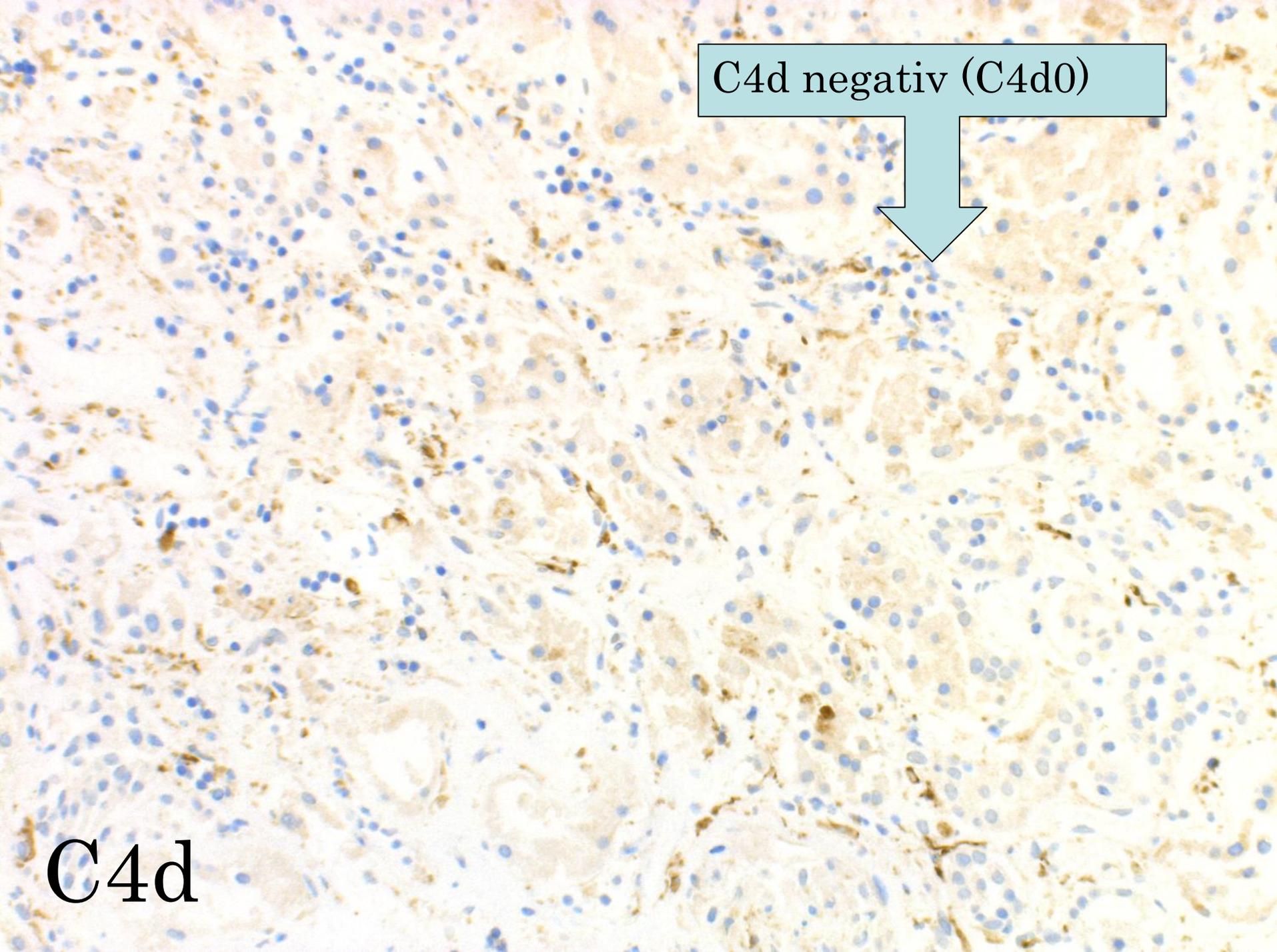


Peritubuläre  
Kapillaritis Banff ptc3

C4d negativ (C4d0)



C4d



# Histologische Diagnose

Beginnend chronifizierte aktive humorale Abstoßung

Akute TCMR Banff IIA, schwere Arteriolitis

Floride thrombotische Mikroangiopathie

Schwere Transplantatglomerulitis

Schwere diffuse peritubuläre Kapillaritis

Fokaler frischer Infarkt

Geringe Arteriosklerose

Ca. 10% IFTA, schwerer akuter Tubulusschaden

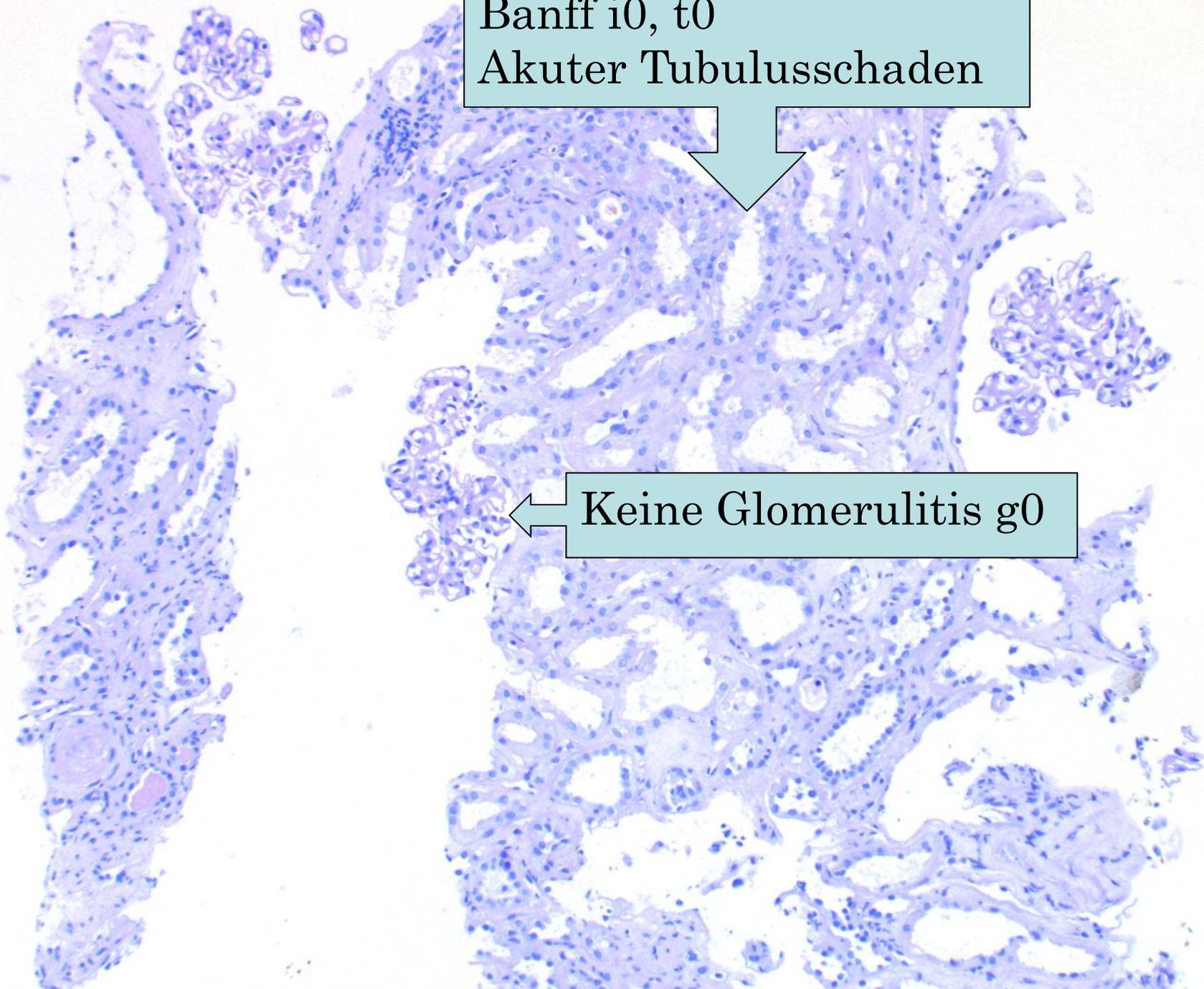
Banff Lesion Scores:

i3, t2, v2\*, g3, ptc3, C4d0, ci1, ct1, cv1, cg0, mm0, ah0\*, ti3,  
i-IFTA1

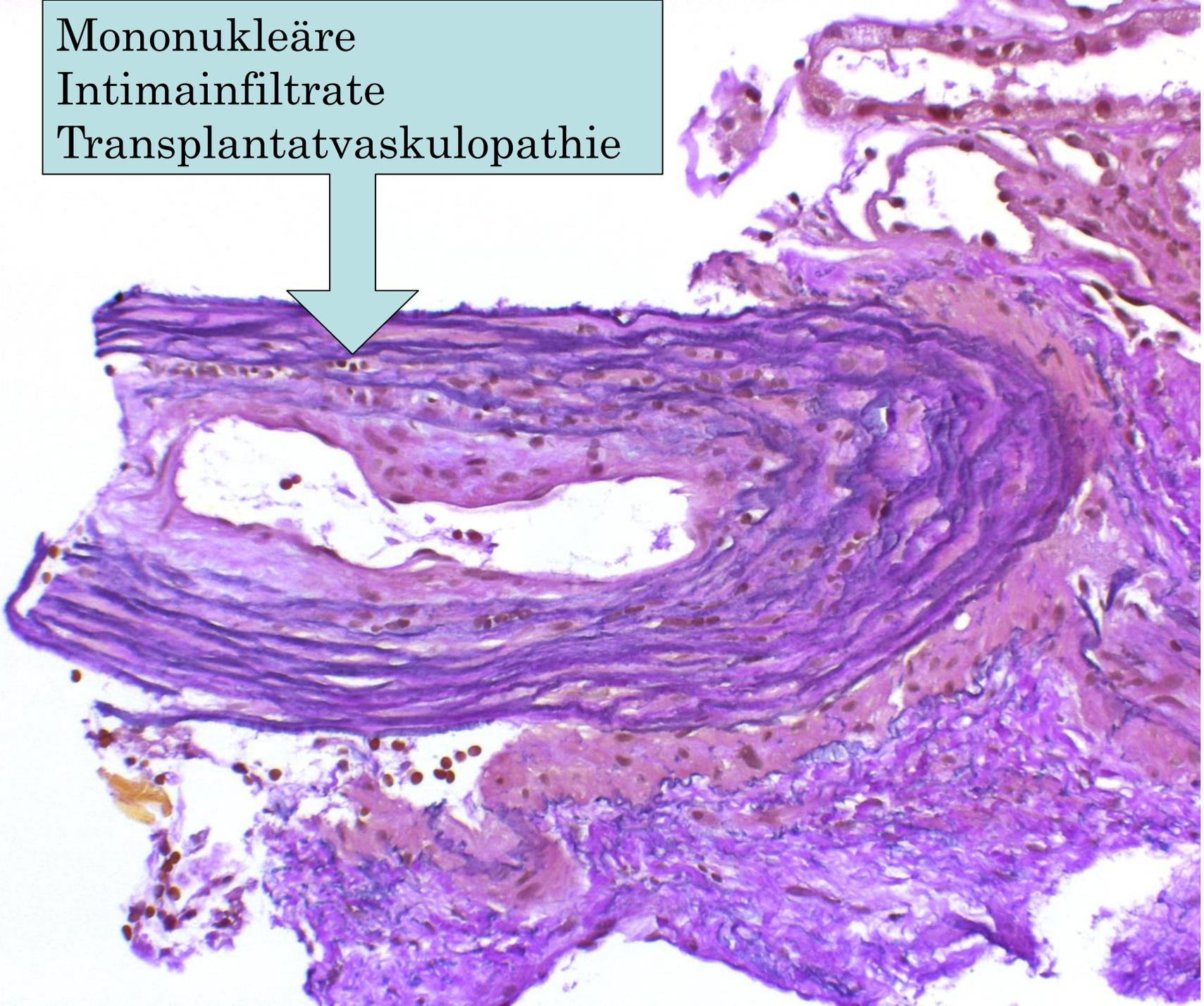
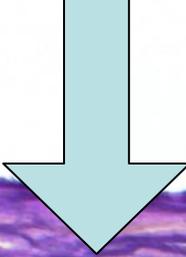
## 2. Biopsie 19.06.2018

Banff i0, t0  
Akuter Tubulusschaden

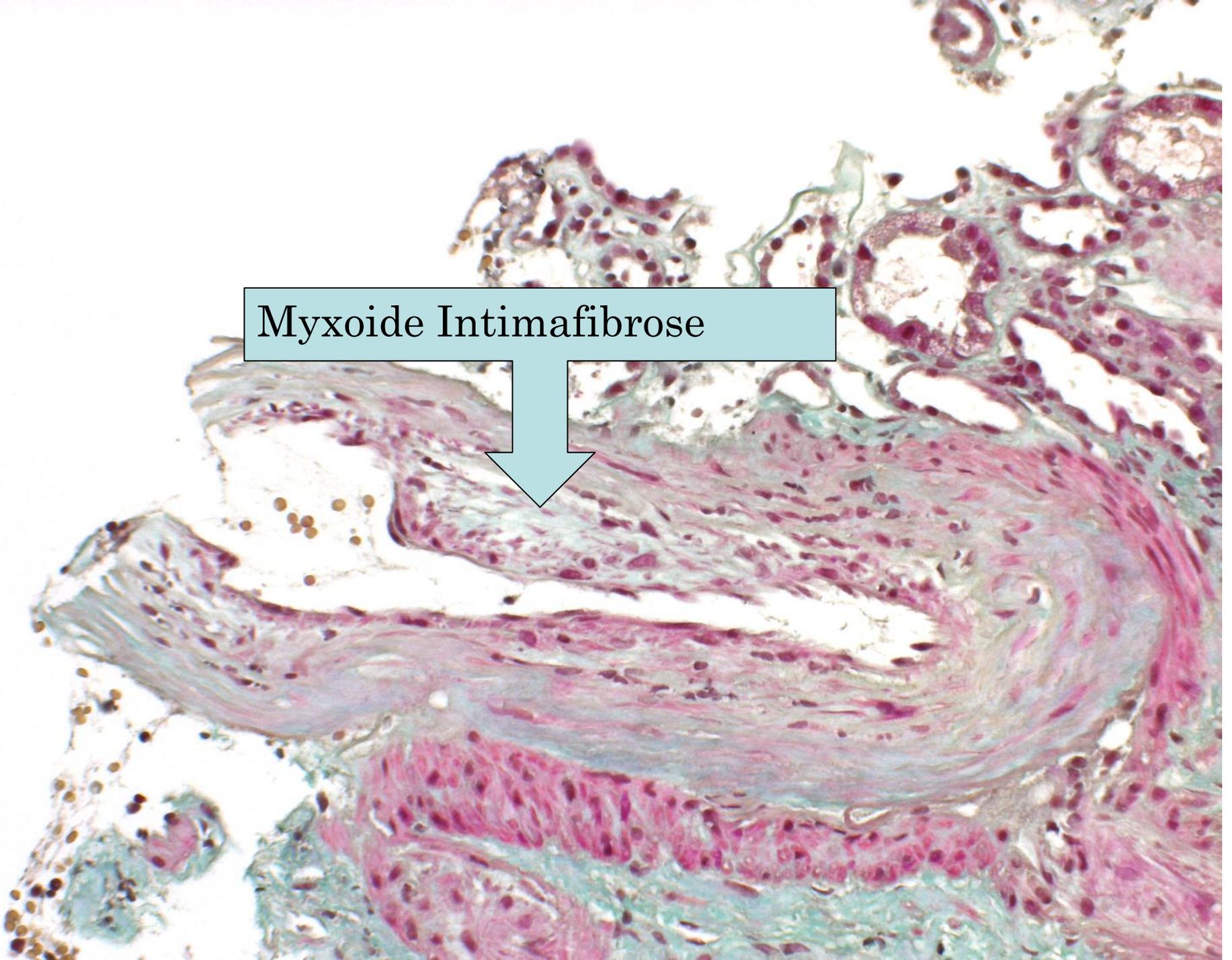
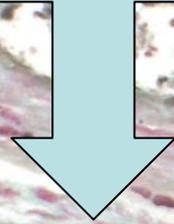
Keine Glomerulitis g0



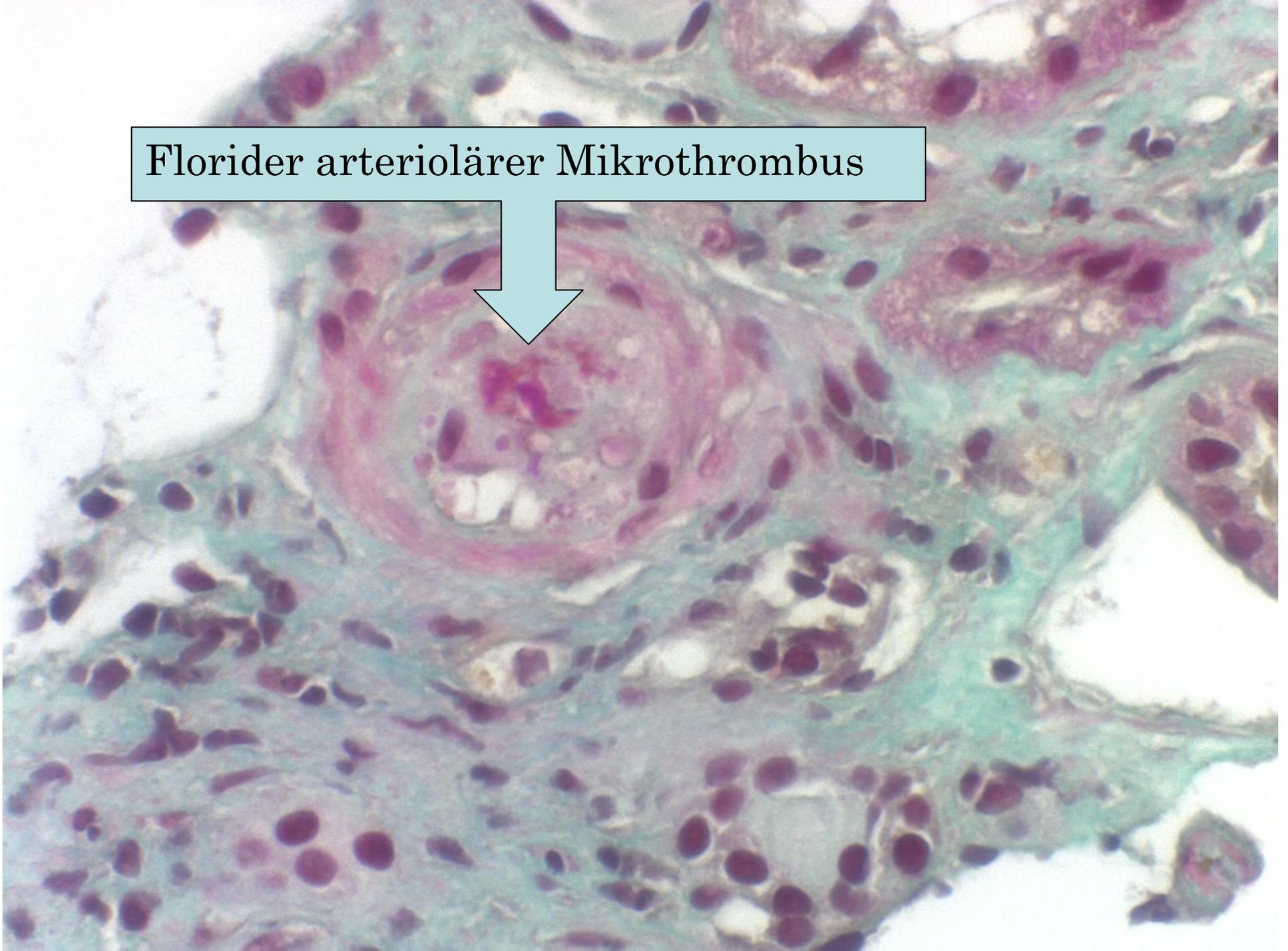
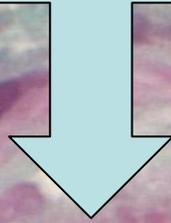
Mononukleäre  
Intimainfiltrate  
Transplantatvaskulopathie

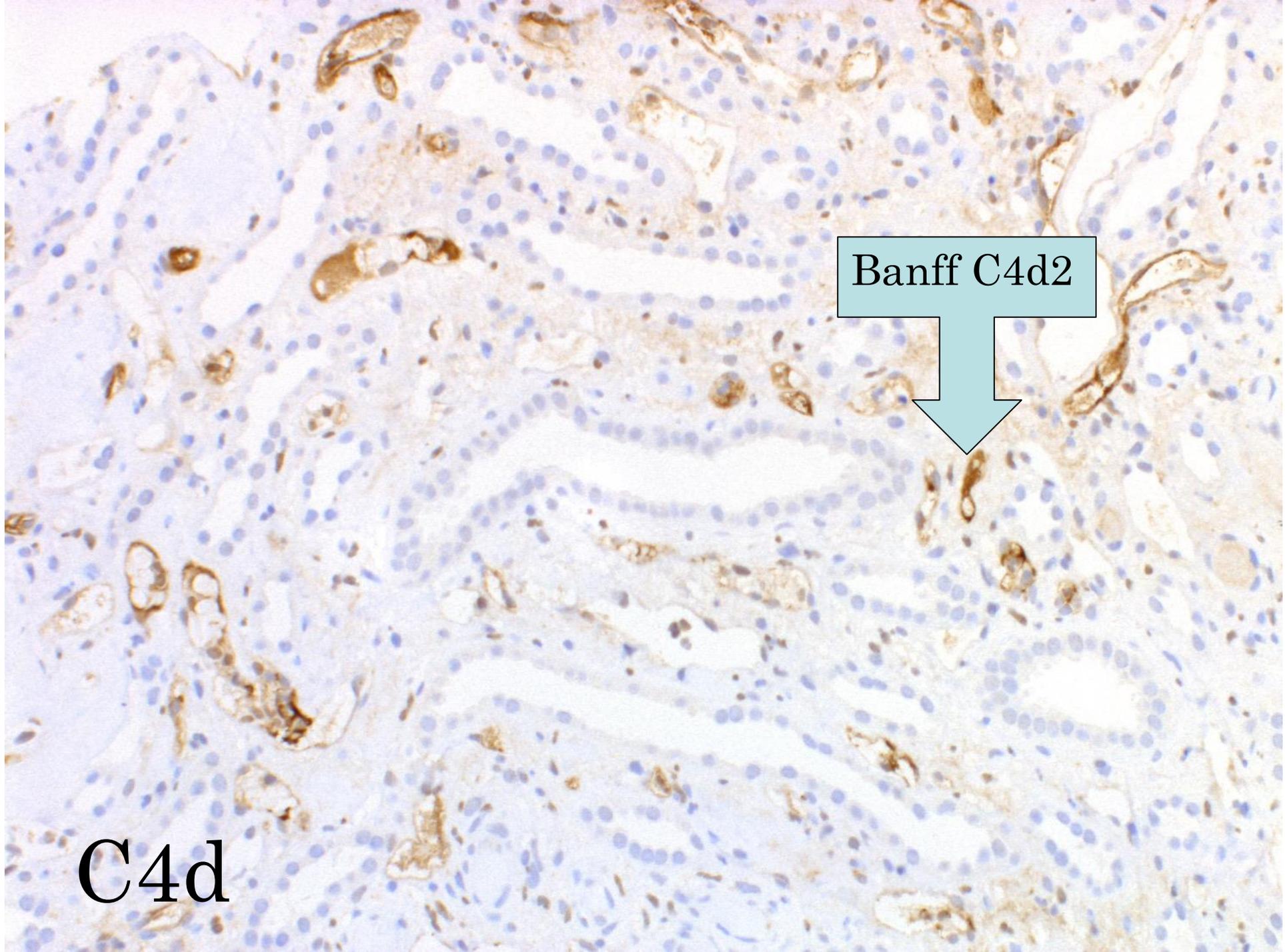


Myxoide Intimafibrose



Florider arteriolärer Mikrothrombus





Banff C4d2

C4d

# Histologische Diagnose

Chronifizierte aktive humorale Abstoßung  
Schwere Transplantatvaskulopathie  
Floride arterioläre TMA  
Geringe Arteriosklerose  
Mäßiger akuter Tubulusschaden

Banff Lesion Scores:

i0, t0, v0, g0, ptc0, C4d2 (*i*AB0), ci0, ct0, cv3, cg0, mm0, ah0, ti3, i-  
IFTA0

**Fall 3**

# Fall 3

**Patientin S.A., 34 Jahre alt**

## **Vorgeschichte:**

- Dialysepflichtige Niereninsuffizienz bei membranöser GN,  
1. HD 2003  
auffälliger Augenbefund (Katarakt)  
Großeltern konsanguin (Cousins)
- **1. Nierentransplantation** LSP durch Vater 2003,  
TX-Versagen 2007
- **2. Nierentransplantation** 2/2010 (Verstorbenenenspende)  
HU bei fehlenden Zugangsmöglichkeiten  
MM 1-1-1

# Fall 3

**Patientin S.A., 34 Jahre alt**

## **Vorgeschichte:**

- Wiedervorstellung mit **Zwillingsschwangerschaft** in der 12. SSW nach IVF 2014

zusätzlich damals ED HOCM und pulmonal-arterielle Hypertonie, PAP sys 34 mmHg und höhergradige Mitralklappeninsuffizienz

- Sectio der Zwillinge in der 30.SSW, 29.12.2014; Babys wohlauf

# Fall 3

**Patientin S.A., 34 Jahre alt**

## **Kreatininverlauf:**

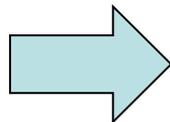
- Bestes Kreatinin 2010: **77**  $\mu\text{mol/l}$  (**0.88** mg/dl)
- 3/16 **135**  $\mu\text{mol/l}$  (**1.54** mg/dl), **rez. Harnwegsinfekte 3 MRGN**
- 3/17 plötzlicher Kreatininanstieg auf **430**  $\mu\text{mol/l}$  (**4.89** mg/dl)  
→ Nierenbiopsie, Steroidstoß
- 5/17: Kreatinin **150**  $\mu\text{mol/l}$  (**1.71** mg/dl)
  
- aktuelles Kreatinin: **204**  $\mu\text{mol/l}$  (**2.32** mg/dl)

# Fall 3

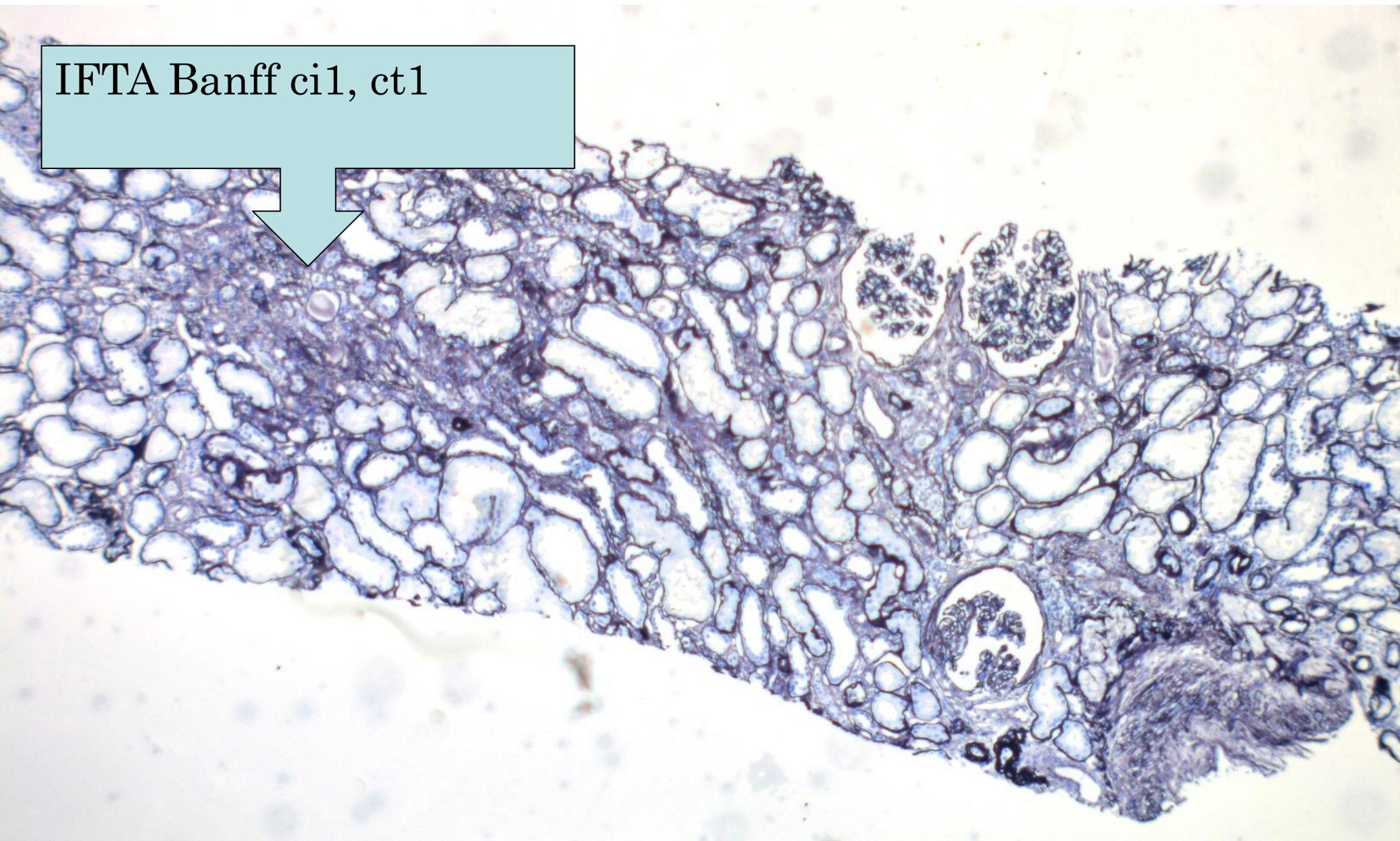
**Patientin S.A., 34 Jahre alt**

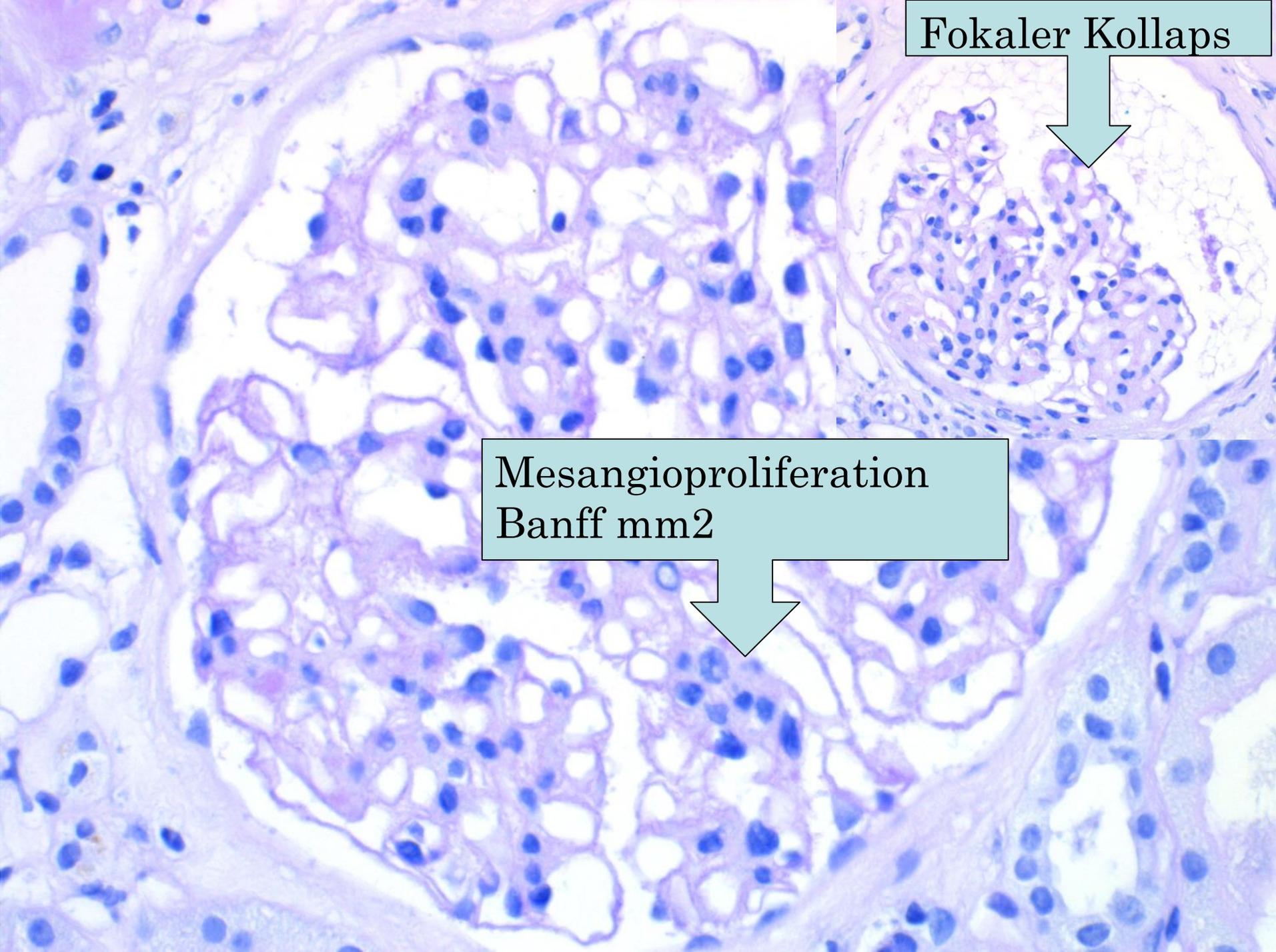
## **Vorgeschichte:**

- 3 Jahre später: Verschlechterung der Transplantatfunktion 3/17  
Kreatinin **430**  $\mu\text{mol/l}$  (**4.89**  $\text{mg/dl}$ )

 **Biopsie**

IFTA Banff ci1, ct1

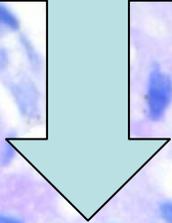




Fokaler Kollaps

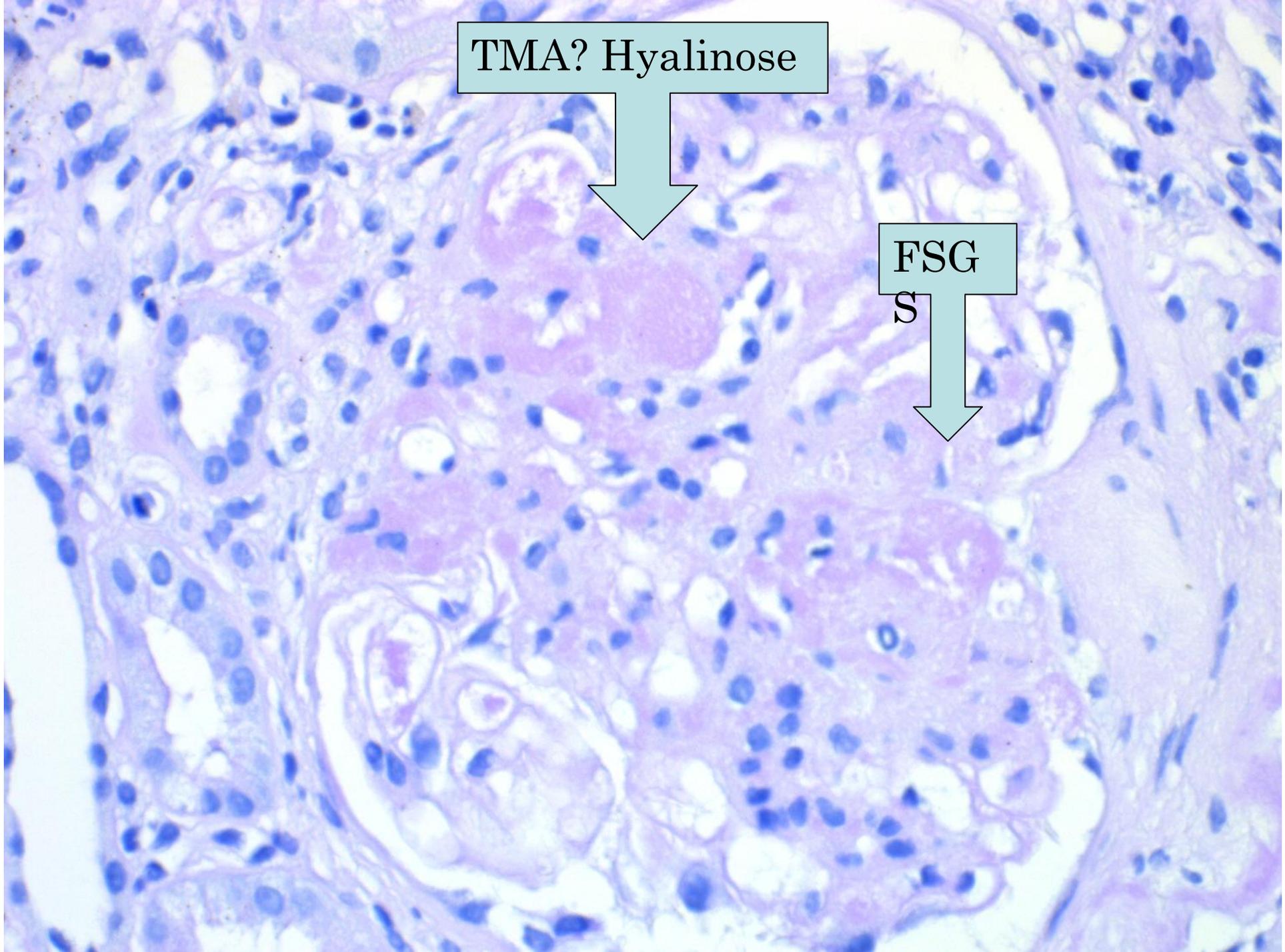
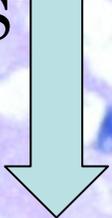
Mesangioproliferation  
Banff mm2

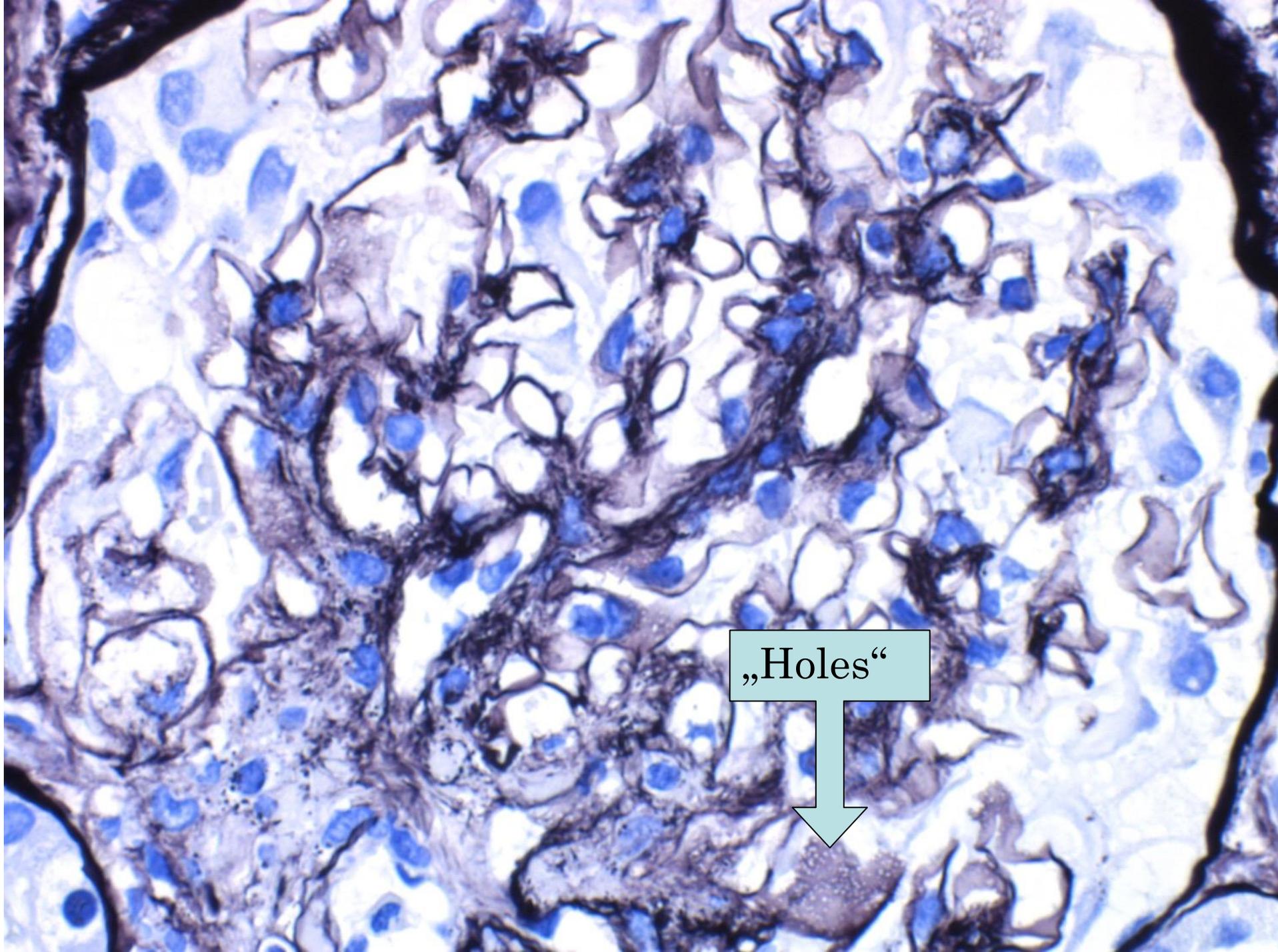
TMA? Hyalinose



FSG

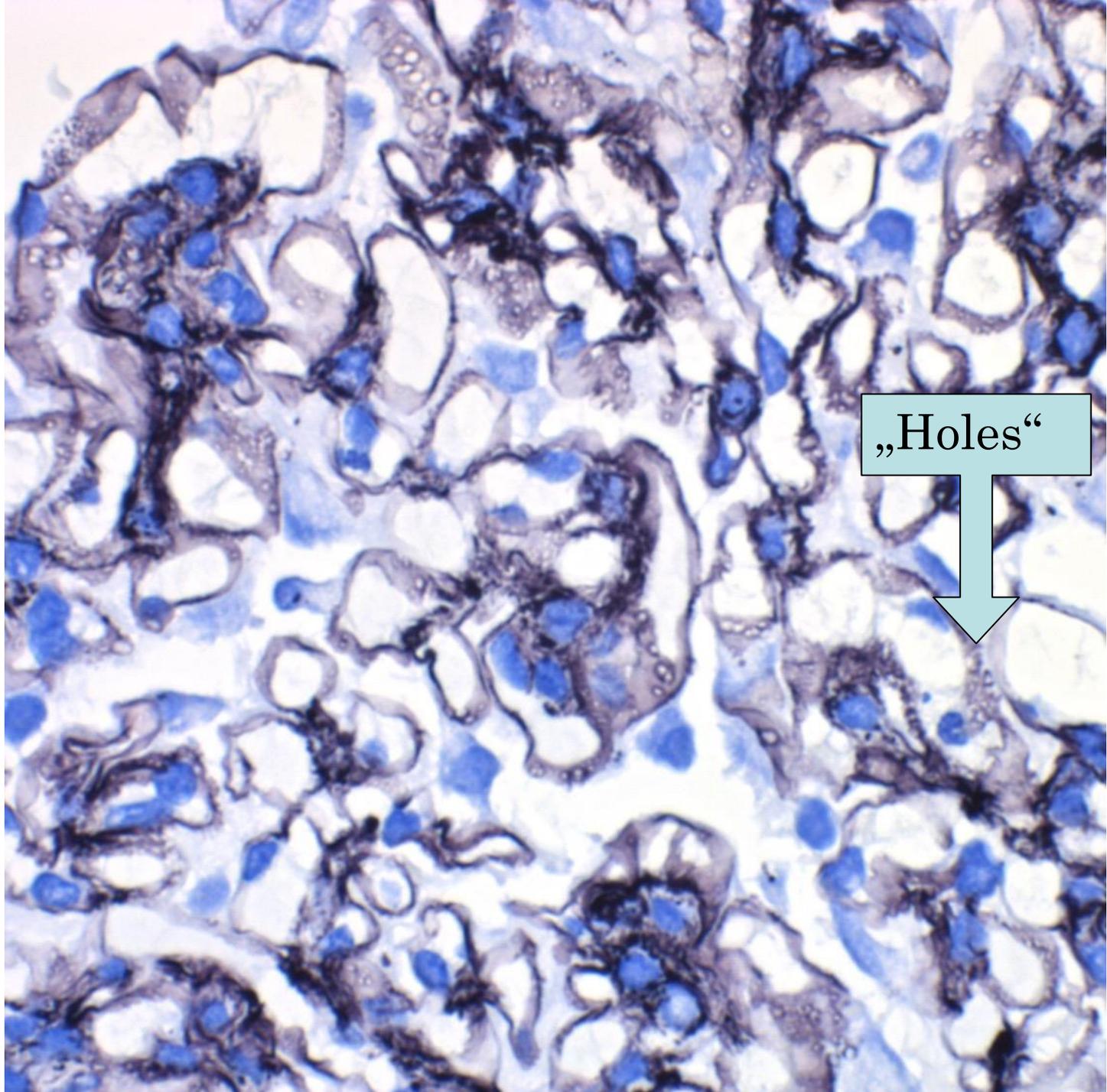
S



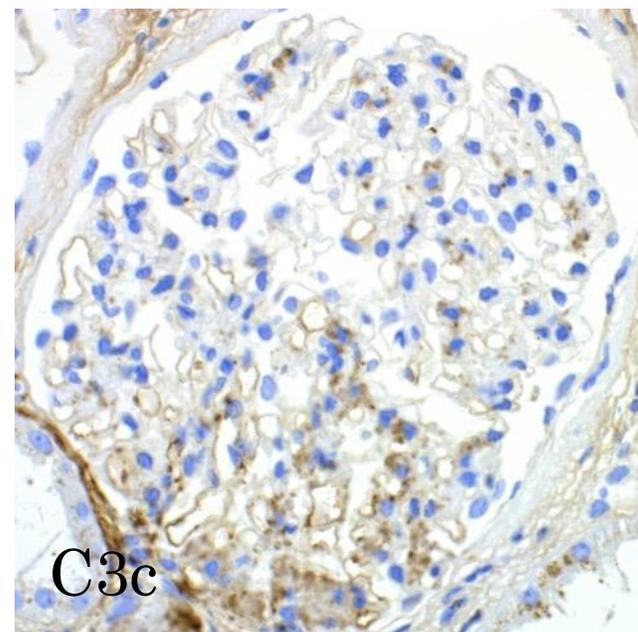
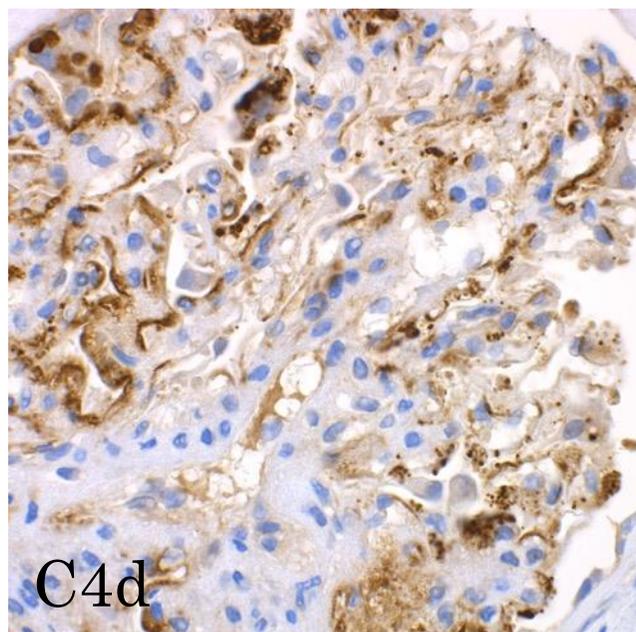
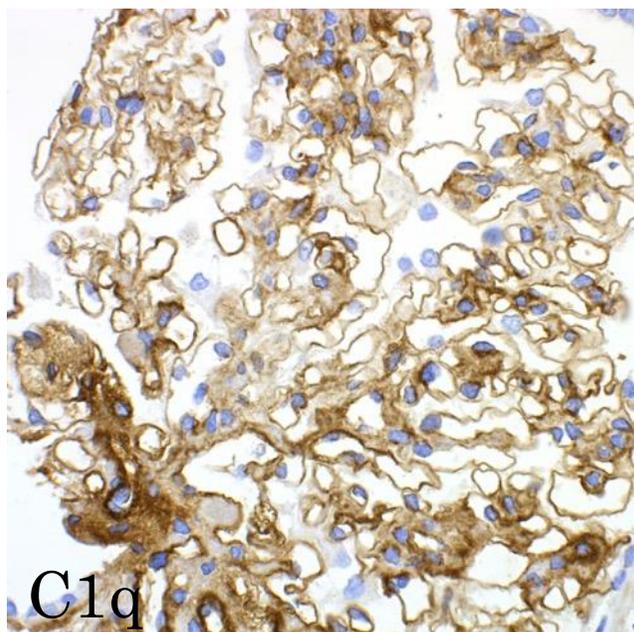
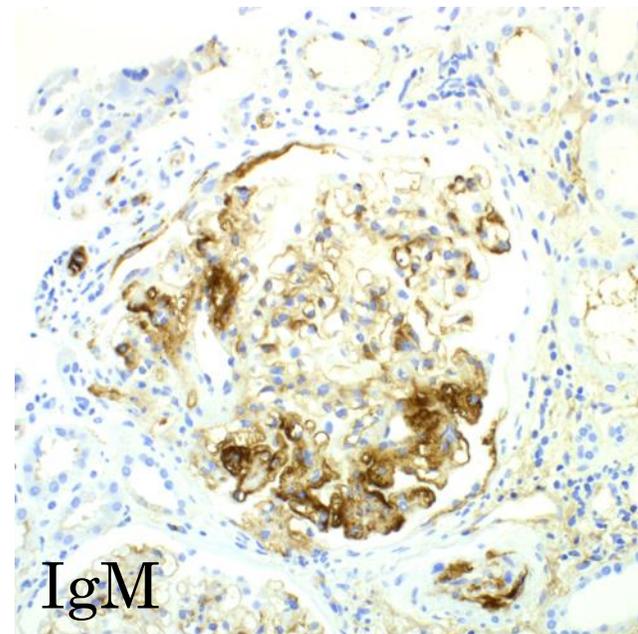
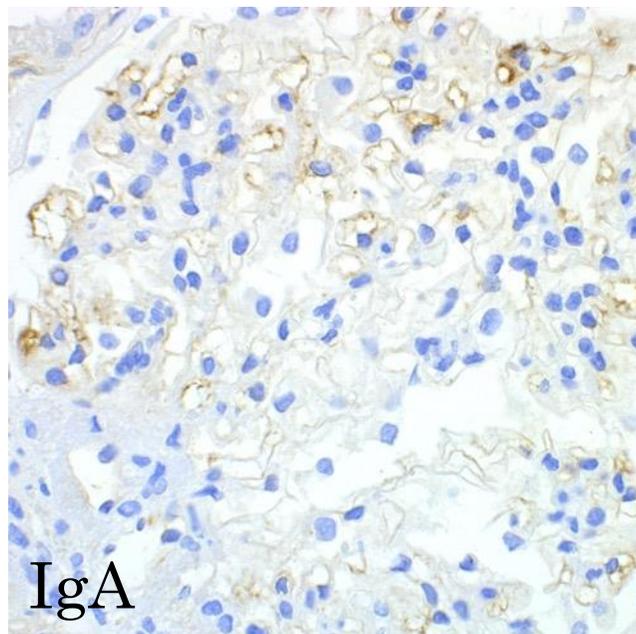
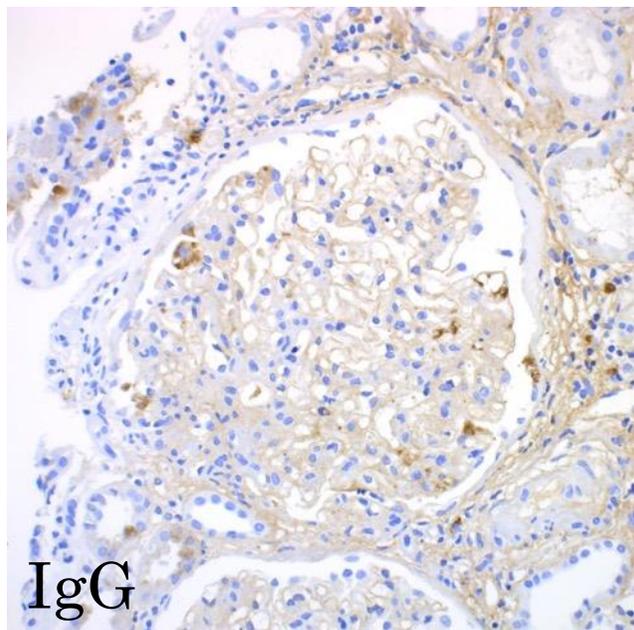


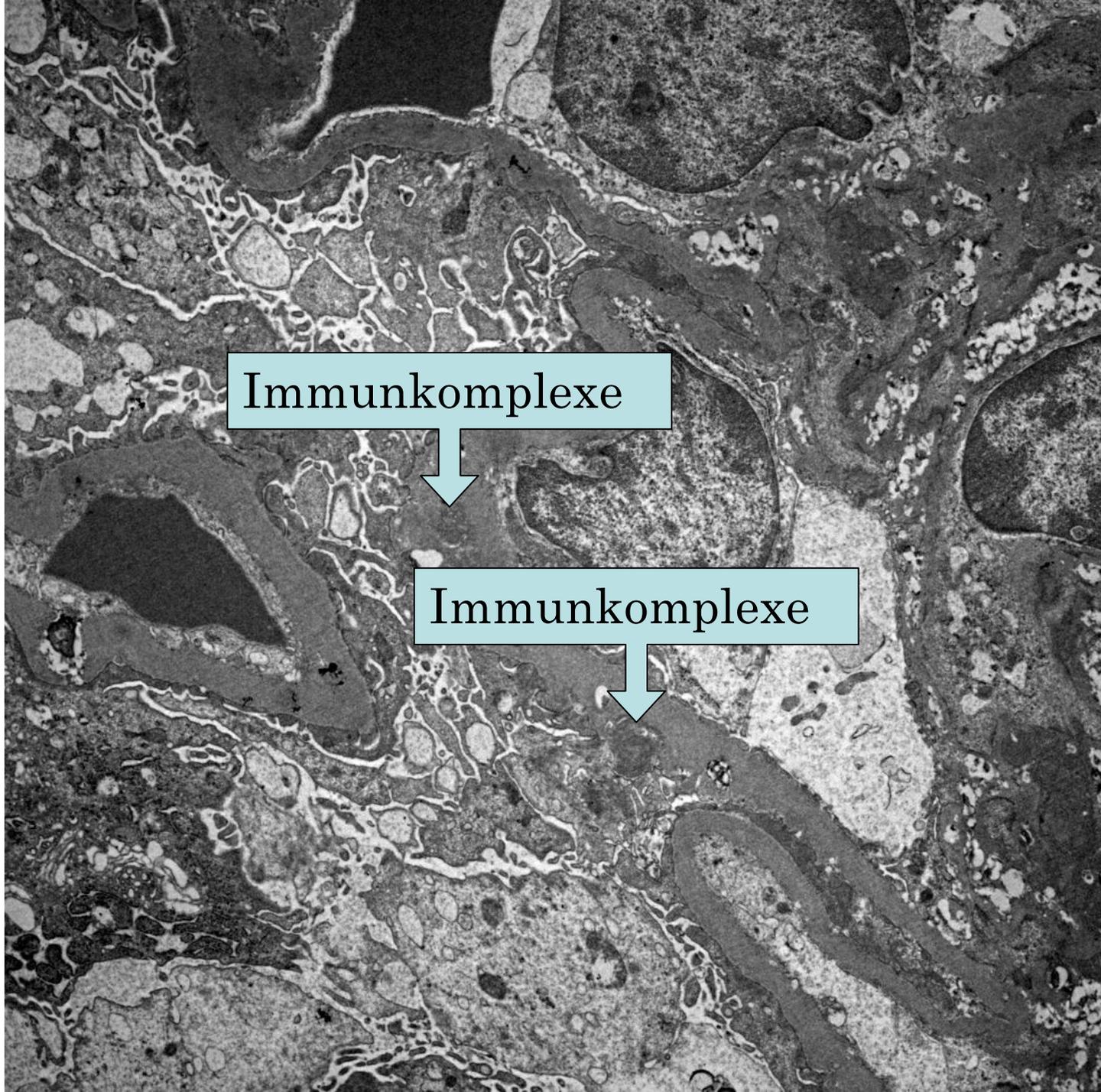
„Holes“





„Holes“

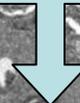




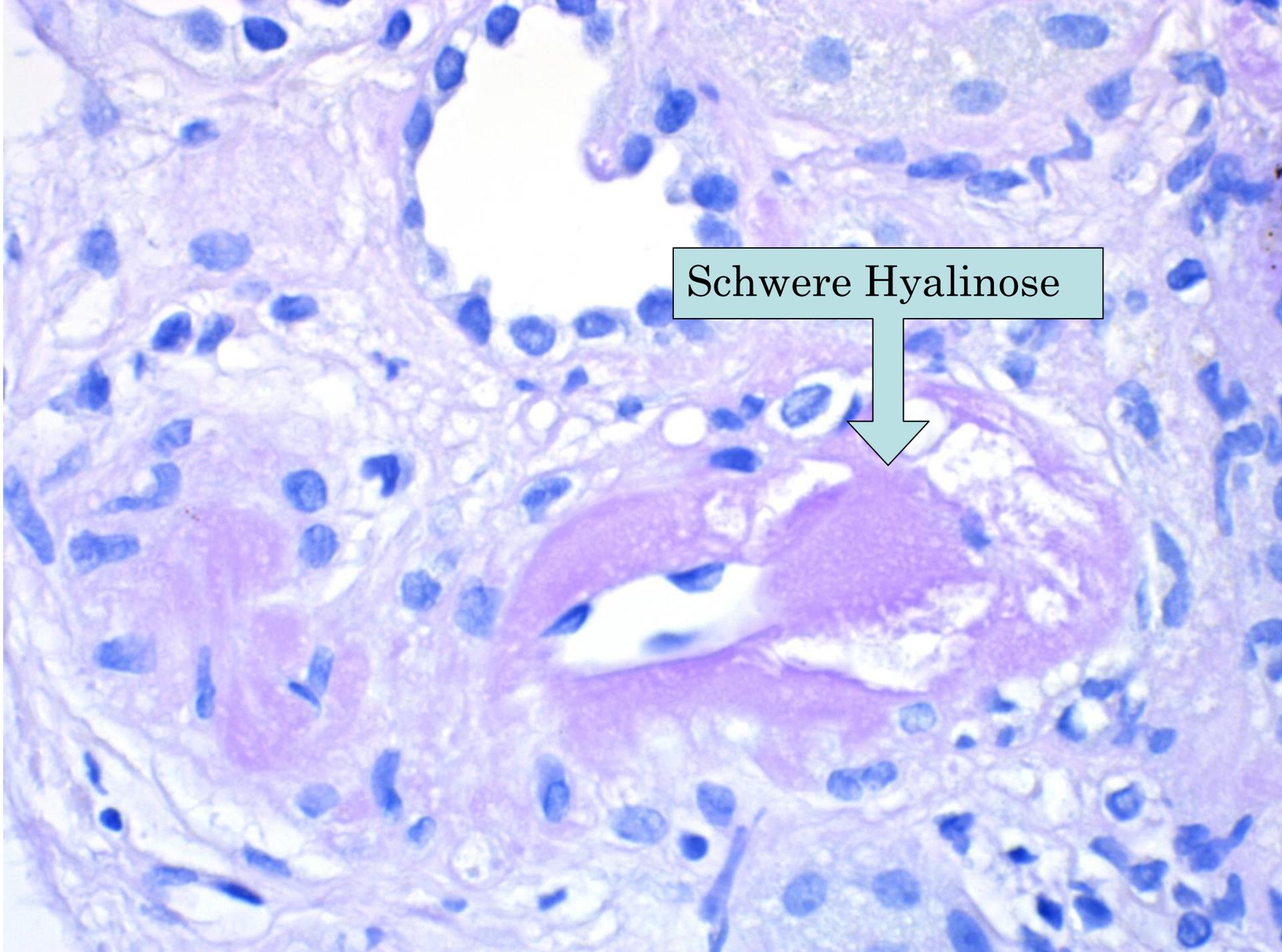
Immunkomplexe

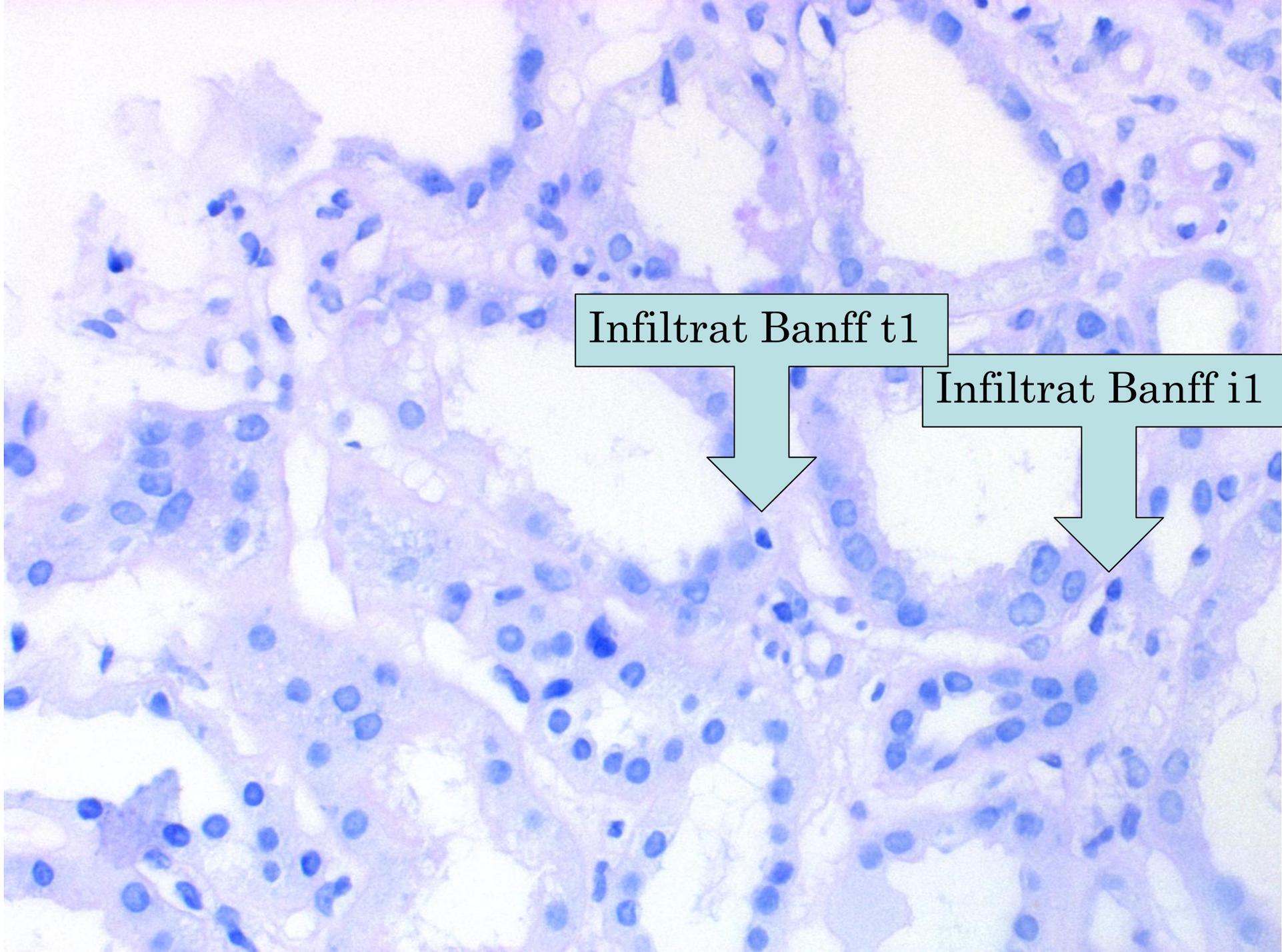


Immunkomplexe

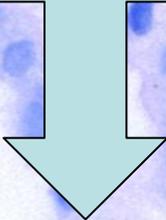


Schwere Hyalinose

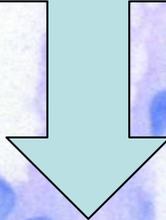




Infiltrat Banff t1



Infiltrat Banff i1



# Histologische Diagnose

Ungewöhnliche membranöse Glomerulonephritis (Rekurrenz)

Borderline akute TCMR

Schwere chronische Calcineurinhemmerarteriopathie

Ca. 10% IFTA, geringer akuter Tubulusschaden

Mäßige Arteriosklerose

Banff Lesion Scores:

i1, t1, v0, g0, ptc0, C4d0, ci1, ct1, cv2, cg0, mm2, ah3, ti3,  
i-IFTA0

# LCAT-Mutation

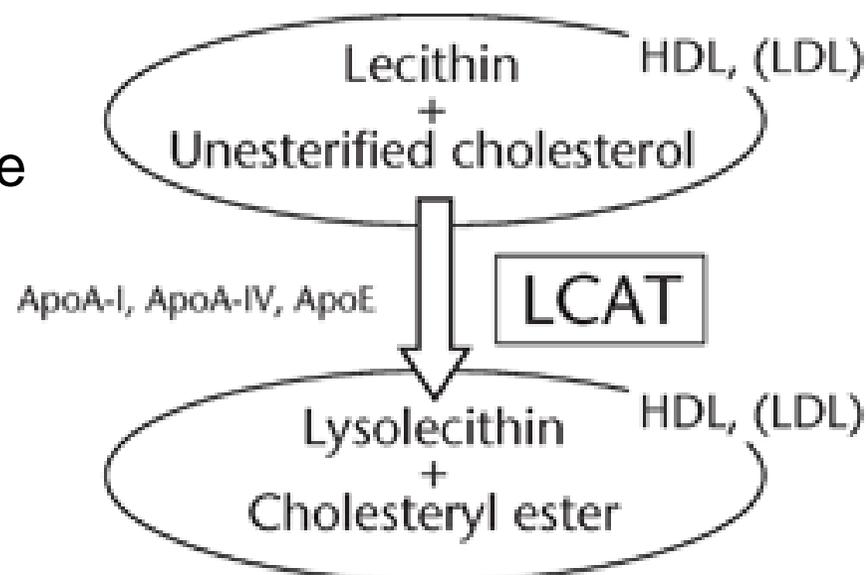
## Molekulargenetische Testung:

- 1. Großeltern konsanguin
- 2. ungewöhnlicher Biopsiebefund

**LCAT** = Lecithin-Cholesterin-Acyltransferase

Lecithin + Cholesterol  
→ Lysolecithin + Cholesterylester

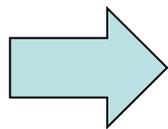
autosomal rezessiv



# LCAT-Mutation

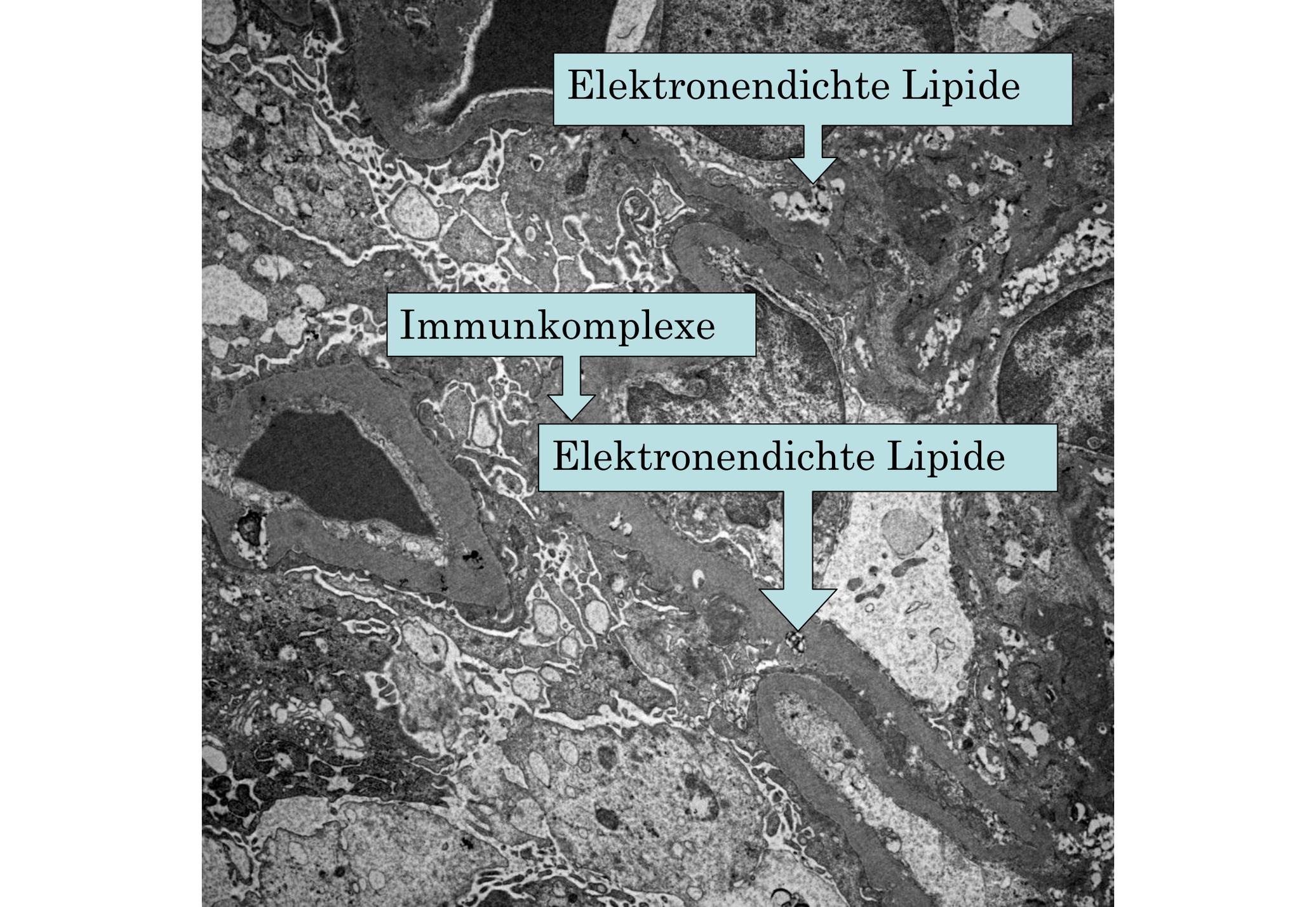
## Klinische Manifestation

- „Fischaugenkrankheit“ → massive Hornhauttrübung (1/3 der Pat.)
- Enzymdefekt 1991 beschrieben:  
schwere HDL-Defizienz  
LCAT in der Leber gebildet
- moderat erhöhtes kardiovaskuläres Risiko
- Proteinurie und Niereninsuffizienz



ggf kombinierte LTX und NTX





Elektronendichte Lipide

This electron micrograph shows a cross-section of a cell with various organelles. Three light blue boxes with black text and arrows point to specific features: 'Elektronendichte Lipide' at the top, 'Immunkomplexe' in the middle, and another 'Elektronendichte Lipide' at the bottom. The background shows a complex network of membranes and granules.

Immunkomplexe

Elektronendichte Lipide

# Histologische Diagnose

**Korrigierte Diagnose: Rekurrenz LCAT-Defizienz im Transplantat**

Borderline akute TCMR

Schwere chronische Calcineurinhemmerarteriopathie

Ca. 10% IFTA, geringer akuter Tubulusschaden

Mäßige Arteriosklerose

Banff Lesion Scores:

i1, t1, v0, g0, ptc0, C4d0, ci1, ct1, cv3, cg0, mm0, ah3, ti3,  
i-IFTA0

**Vielen Dank!**

