

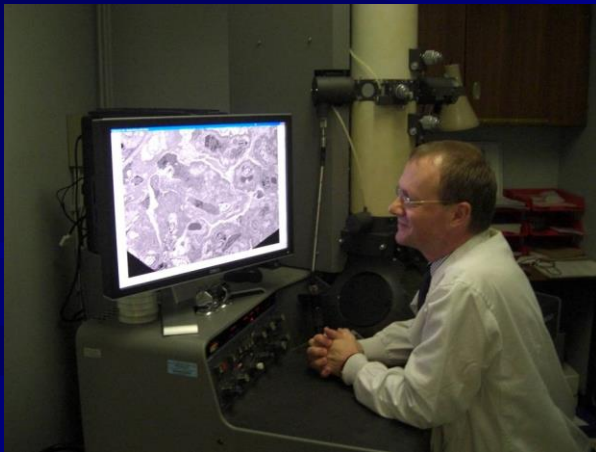
Basic Renal EM workshop

Southampton

September 30th 2011

Renal Ultrastructural Pathology

Lecture 3 My - S



Histopathology Department
Northern General Hospital

Bart E Wagner
BSc CSc FIBMS Dip Ult Path
Chief Biomedical Scientist
Electron Microscopy Section
Histopathology Department
Northern General Hospital
Sheffield
South Yorkshire
UK
S5 7AU
bart.wagner@sth.nhs.uk
Tel+44(0)114-27 14154



Renal ultrastructural pathology

Lecture 3 - Topics

1. Myeloma kidney
2. Post infectious Glomerulonephritis
3. Systemic Lupus Erythrematosus (SLE)

Myeloma

Myeloma

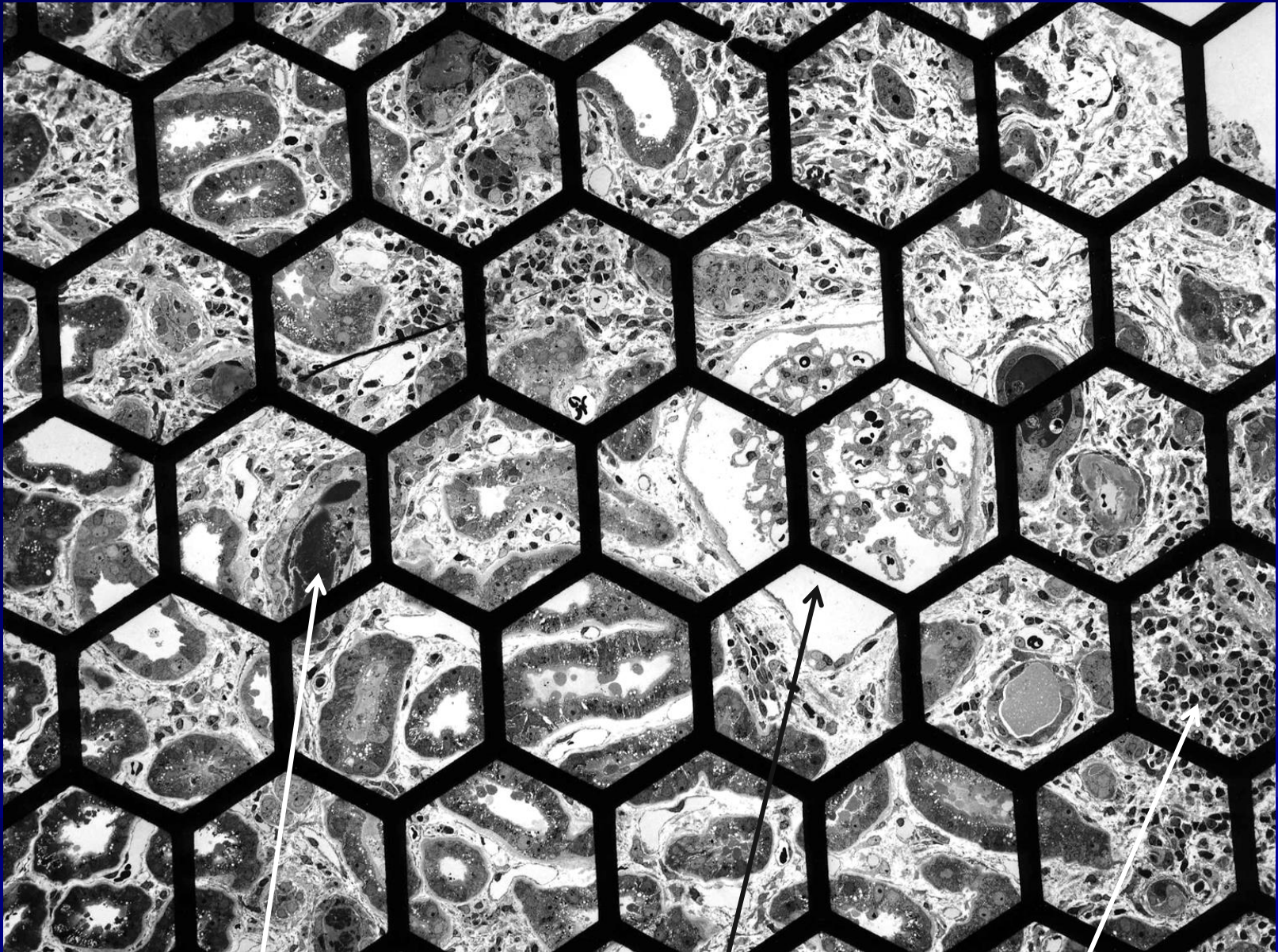
- Amyloid – already looked at – usually lambda light chain
- Cryoglobulinaemic GN – already looked at – usually IgM kappa
- Classical cast nephropathy – usually kappa light chain
- Crystalline cast nephropathy – usually kappa light chain
- Monoclonal Immunoglobulin Deposition Disease MIDD – usually kappa light chain
- Can get combinations of these in same biopsy

Myeloma

- Immunofluorescence may be negative if antibody doesn't attach to abnormal myeloma protein
- In early stages of cast nephropathy, may overlook single tubule with cast and macrophages
- All cases of tubulointerstitial nephritis (TIN) should be examined carefully for evidence of cast nephropathy
- In cases of TIN should check semithin toluidine blue section for evidence of dense staining of basement membranes – indicating MIDD.

Classical Cast Nephropathy

Cast nephropathy

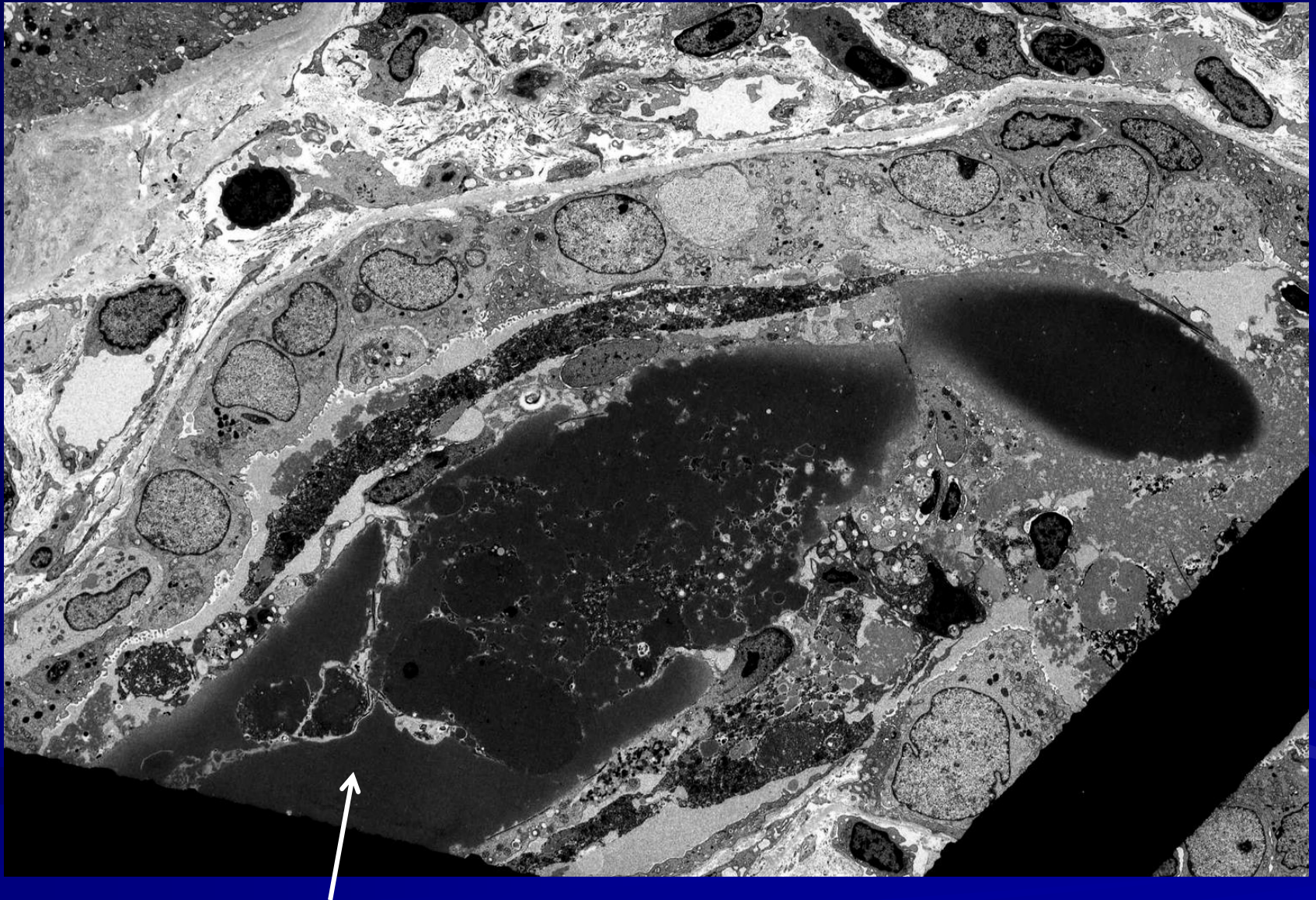


Myeloma protein cast in tubular lumen

Normal glomerulus

Interstitial inflammation

Cast nephropathy

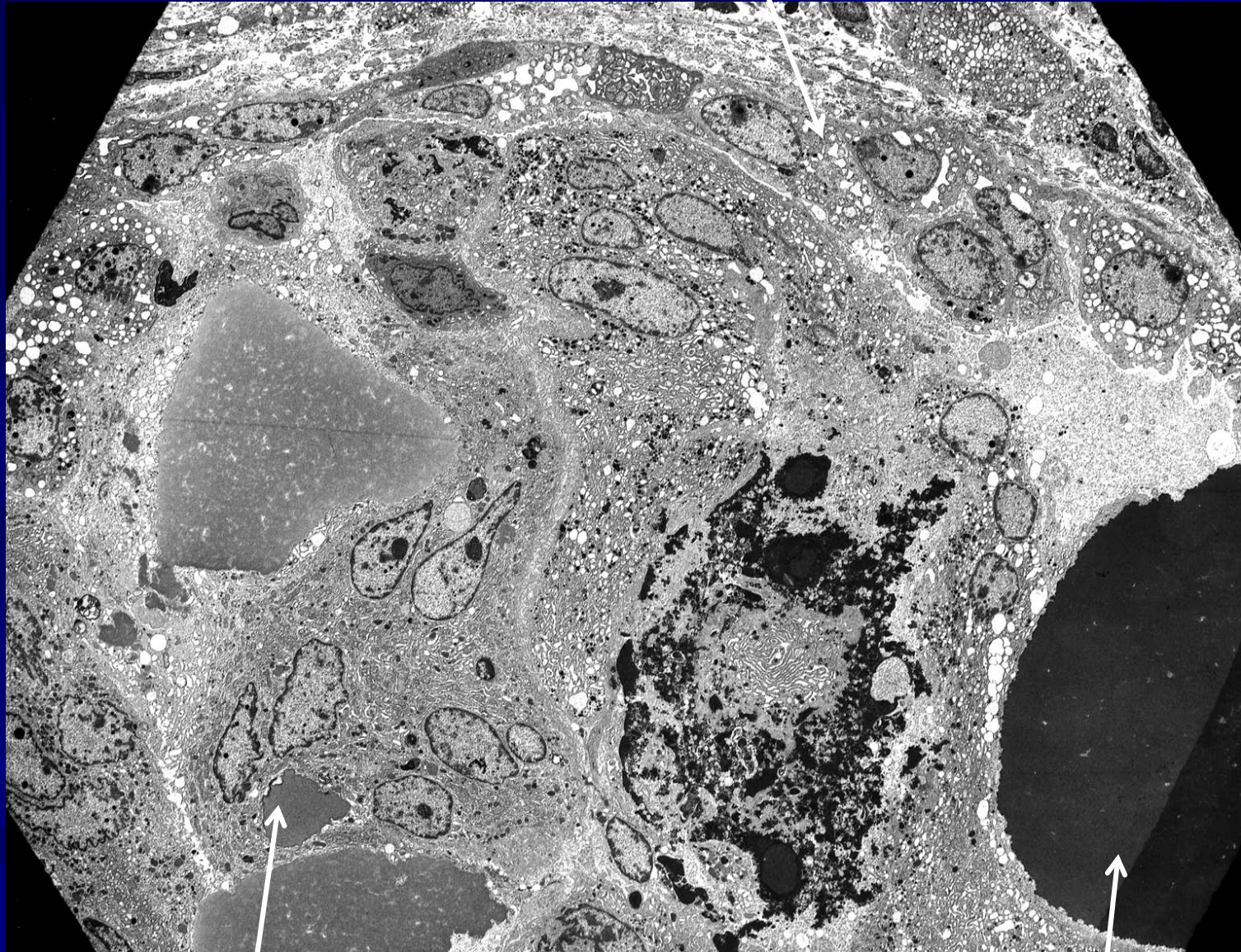


Myeloma protein

Higher magnification of previous slide

Different case to previous

Distal convoluted tubule epithelial cells

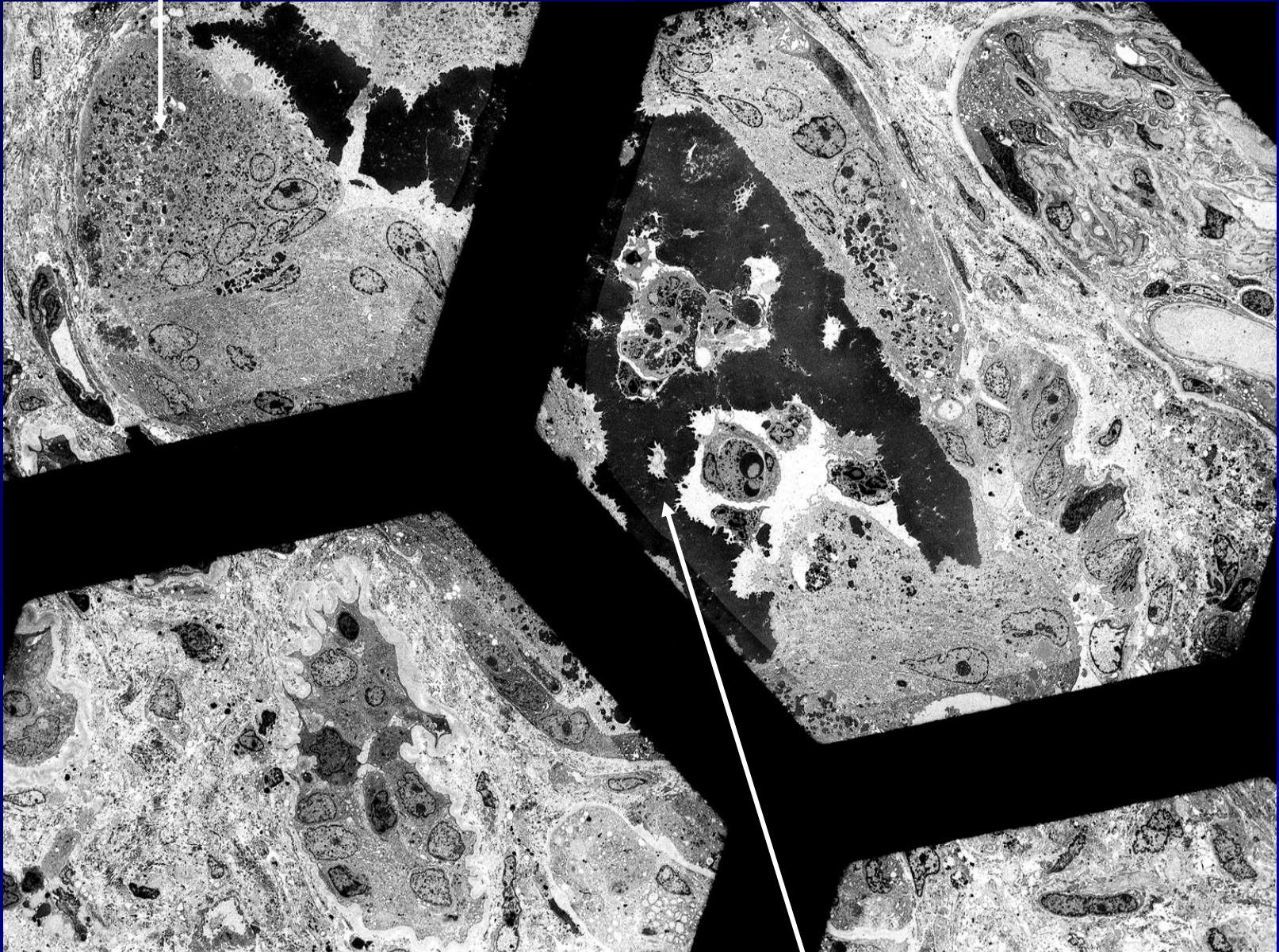


Multinucleated giant cell phagocytosing cast protein

Myeloma protein

Multinucleate macrophage giant cell

Cast nephropathy



Myeloma protein in lumen of tubule

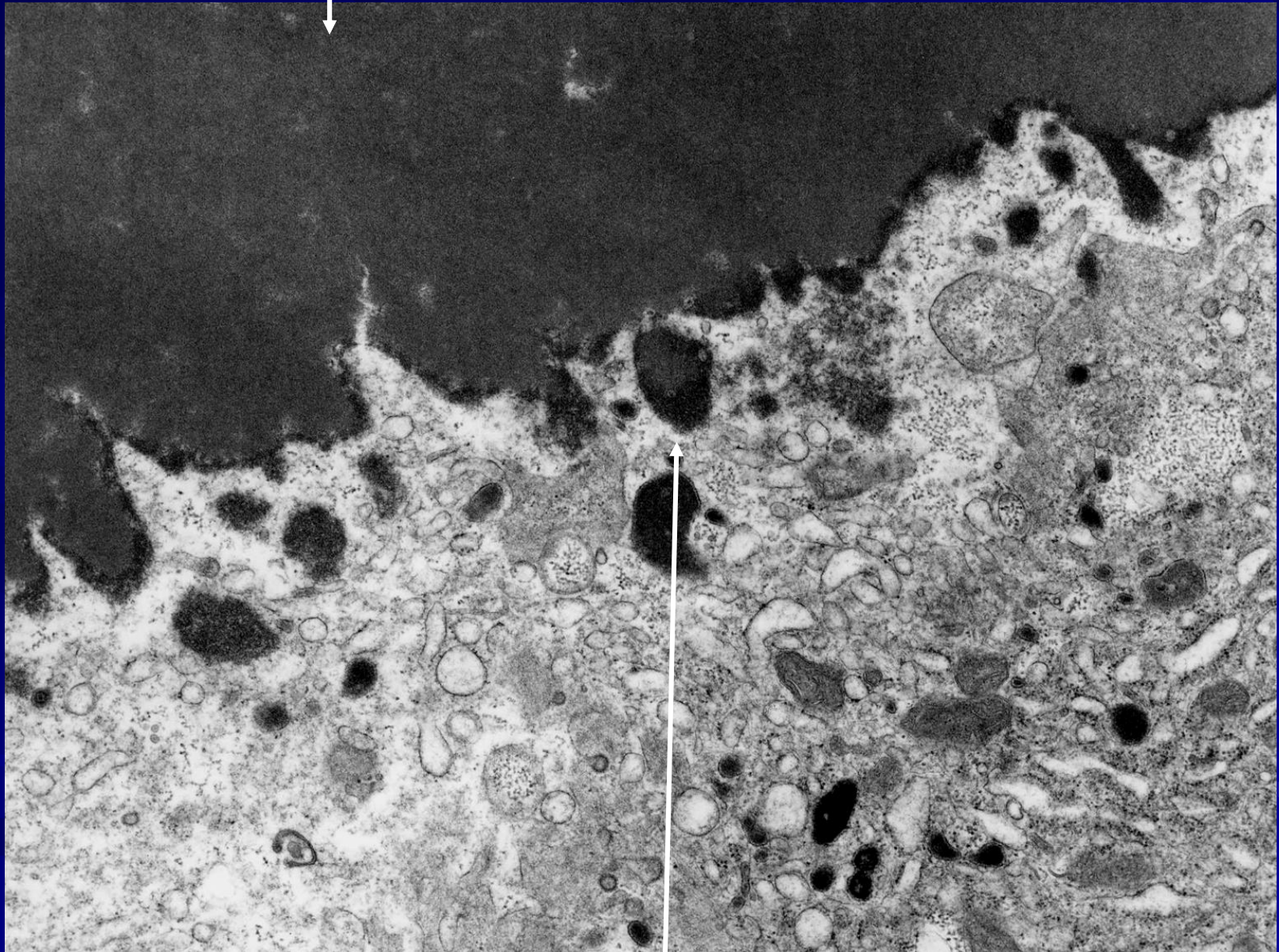
Myeloma protein



Higher magnification of previous slide

Multinucleate macrophage giant cell

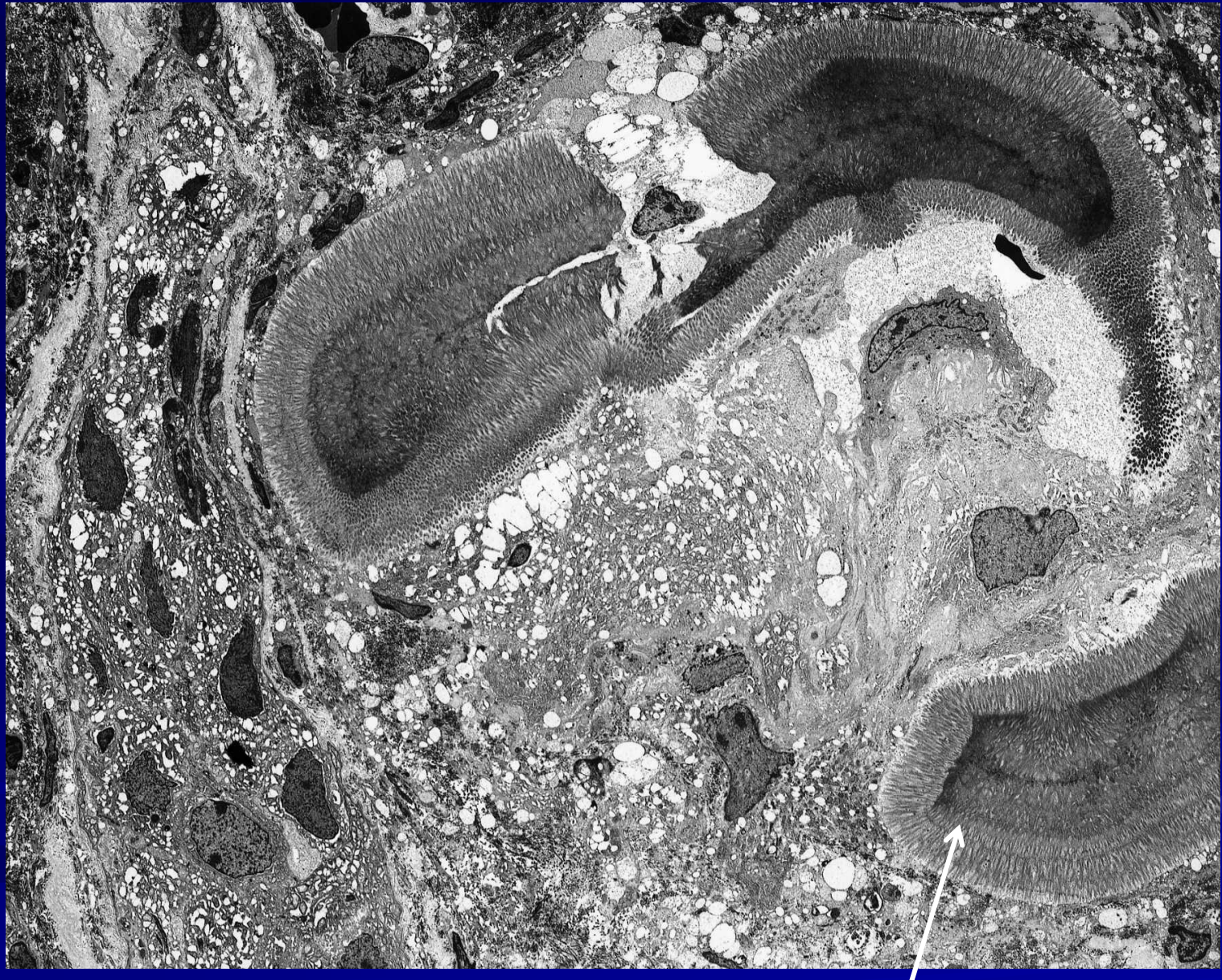
Myeloma protein



Higher magnification of previous slide

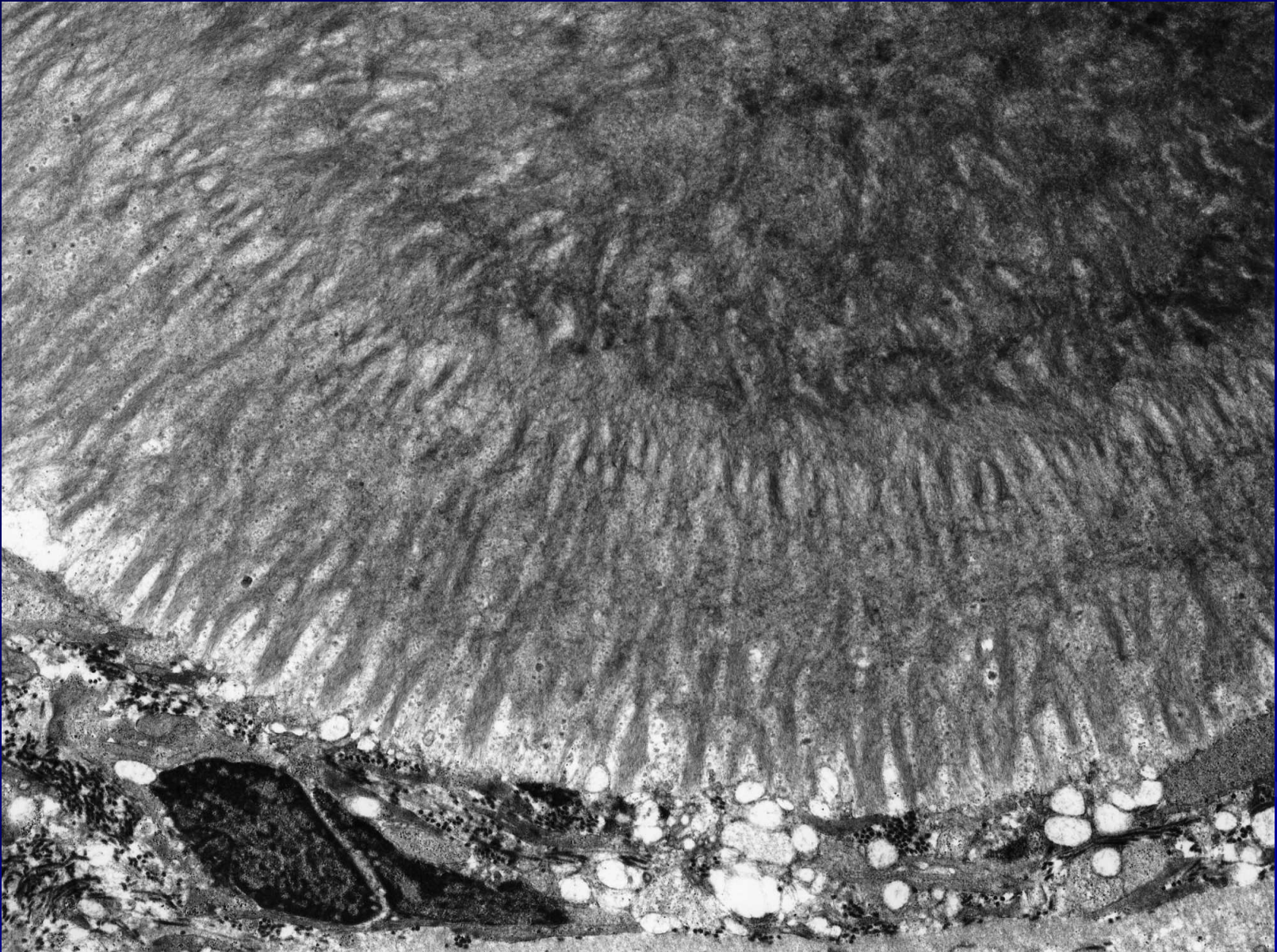
Intralysosomal myeloma protein

Different case to previous slide



Laminated cast

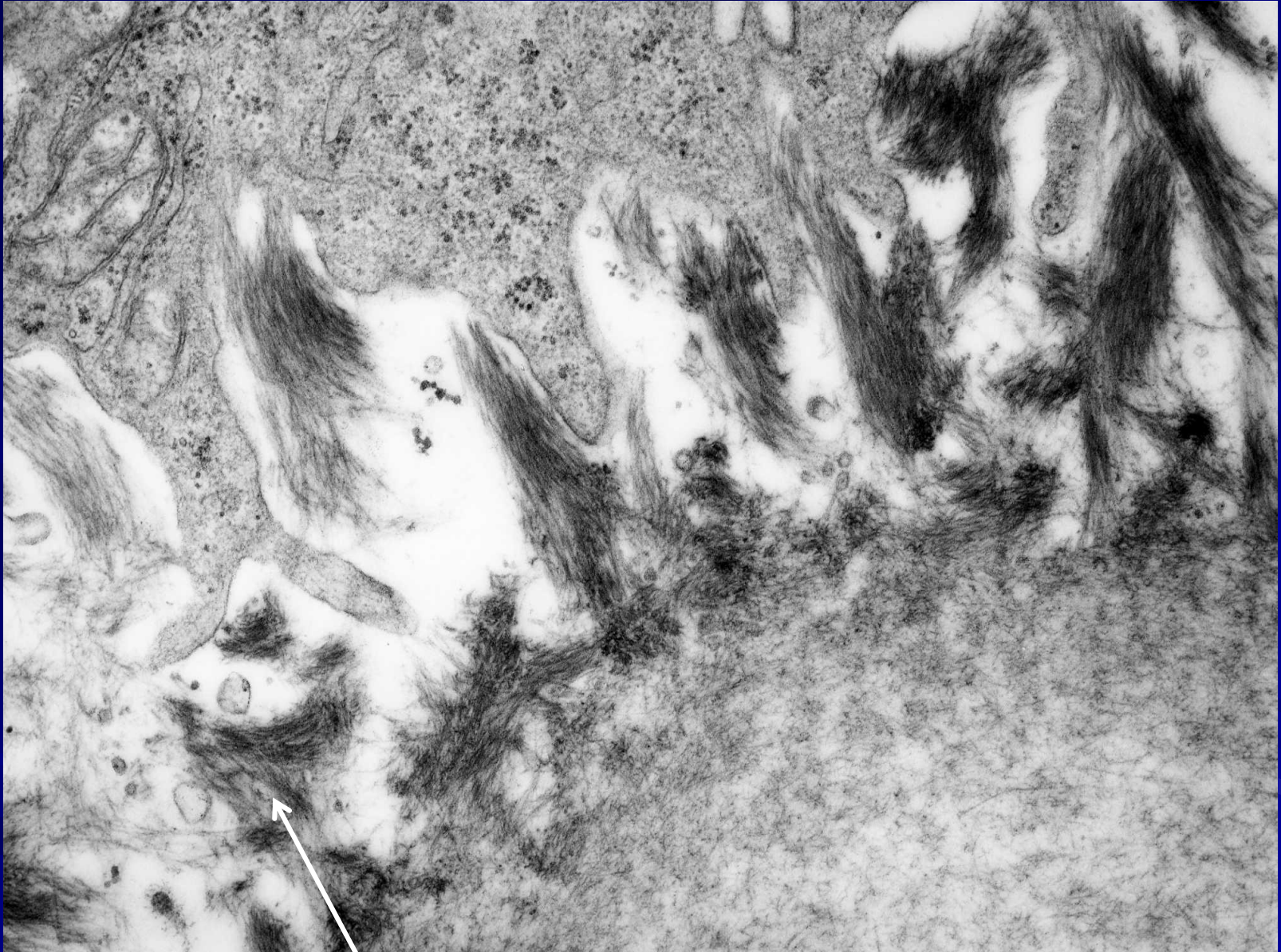
Laminated cast



Higher magnification of previous slide

Sirius red positive cast protein

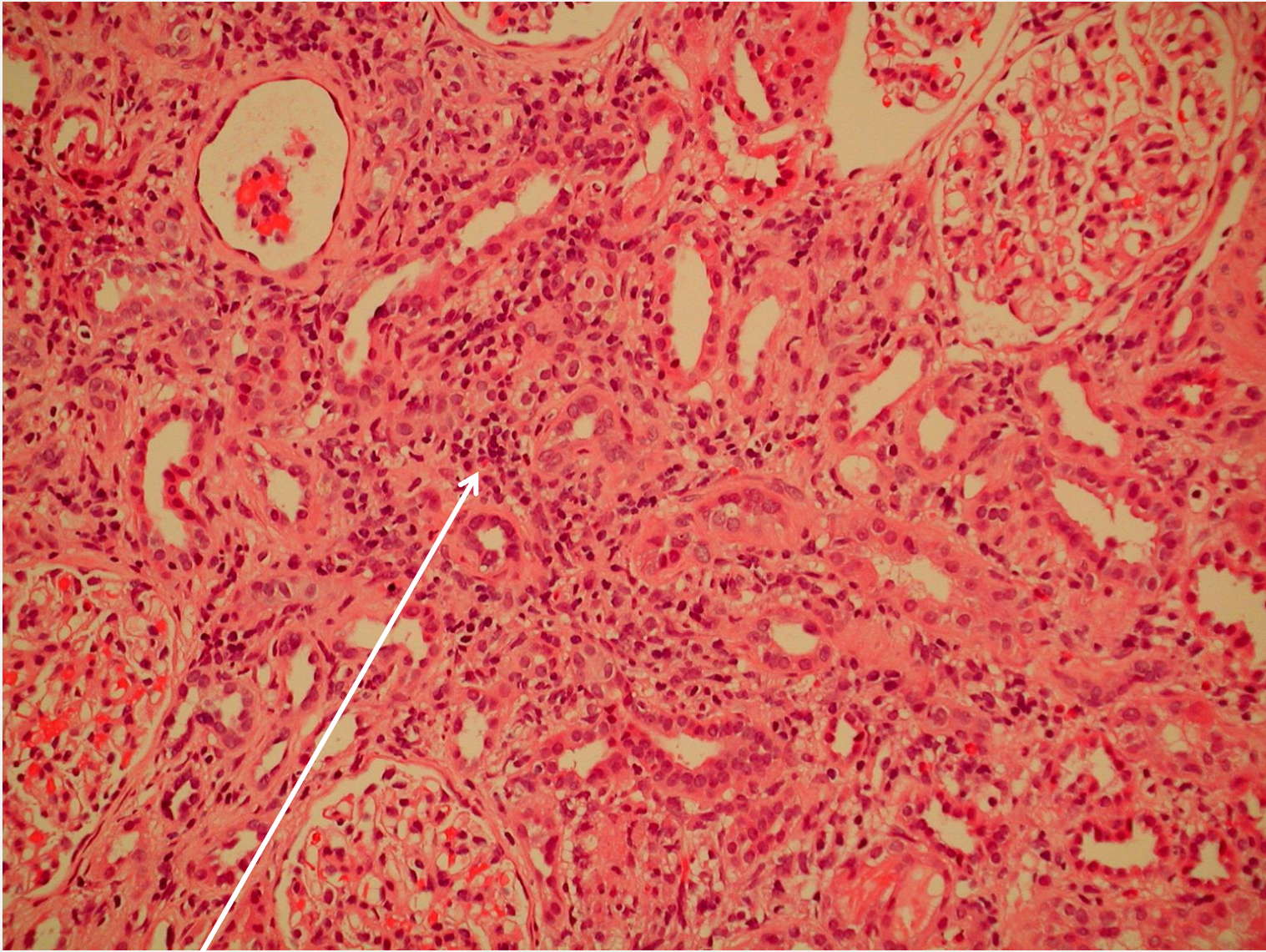
Different case to previous slide



Edge of cast Sirius Red positive

Crystalline cast nephropathy

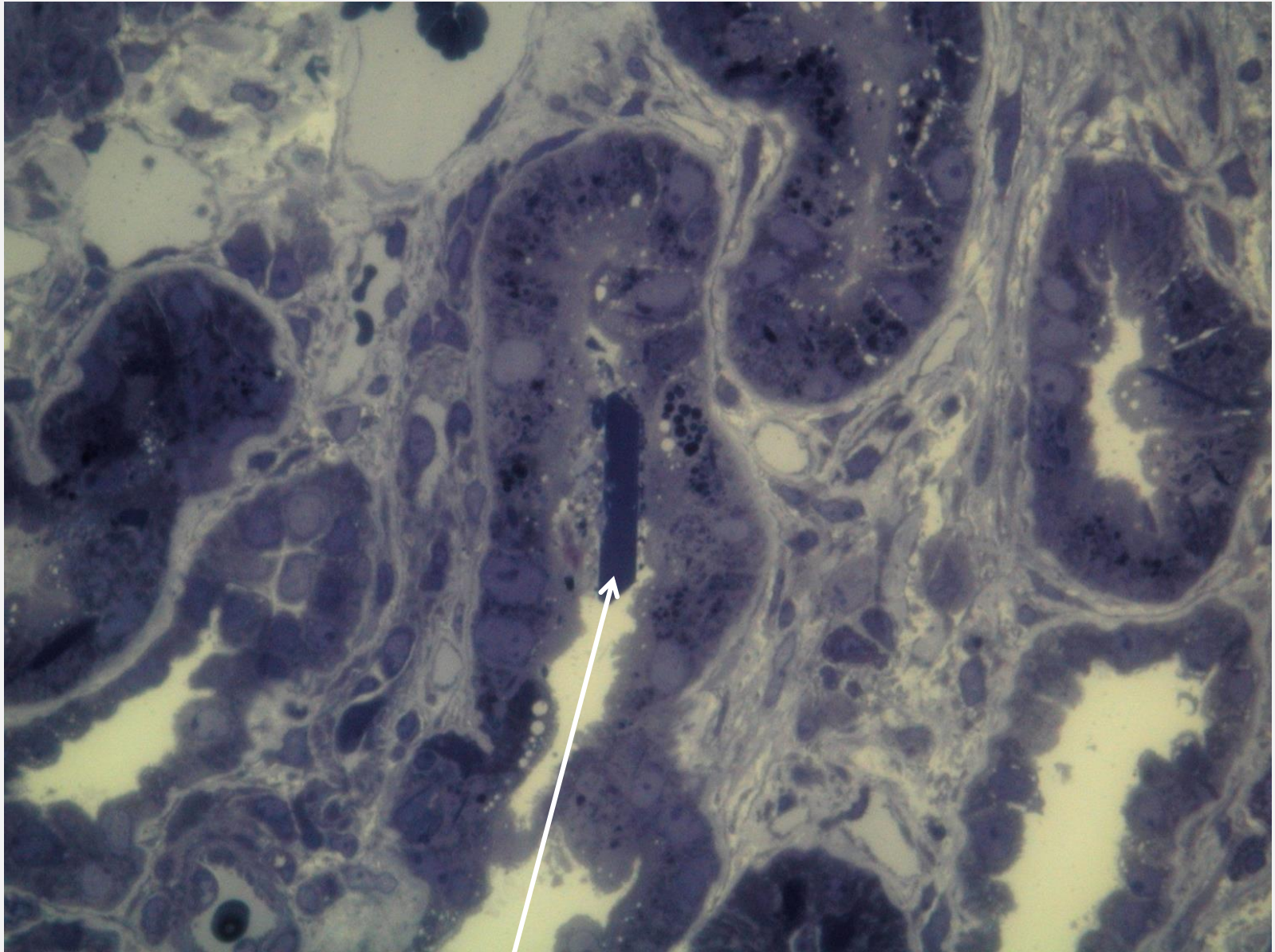
H&E crystalline cast nephropathy



H&E - tubulointerstitial nephritis

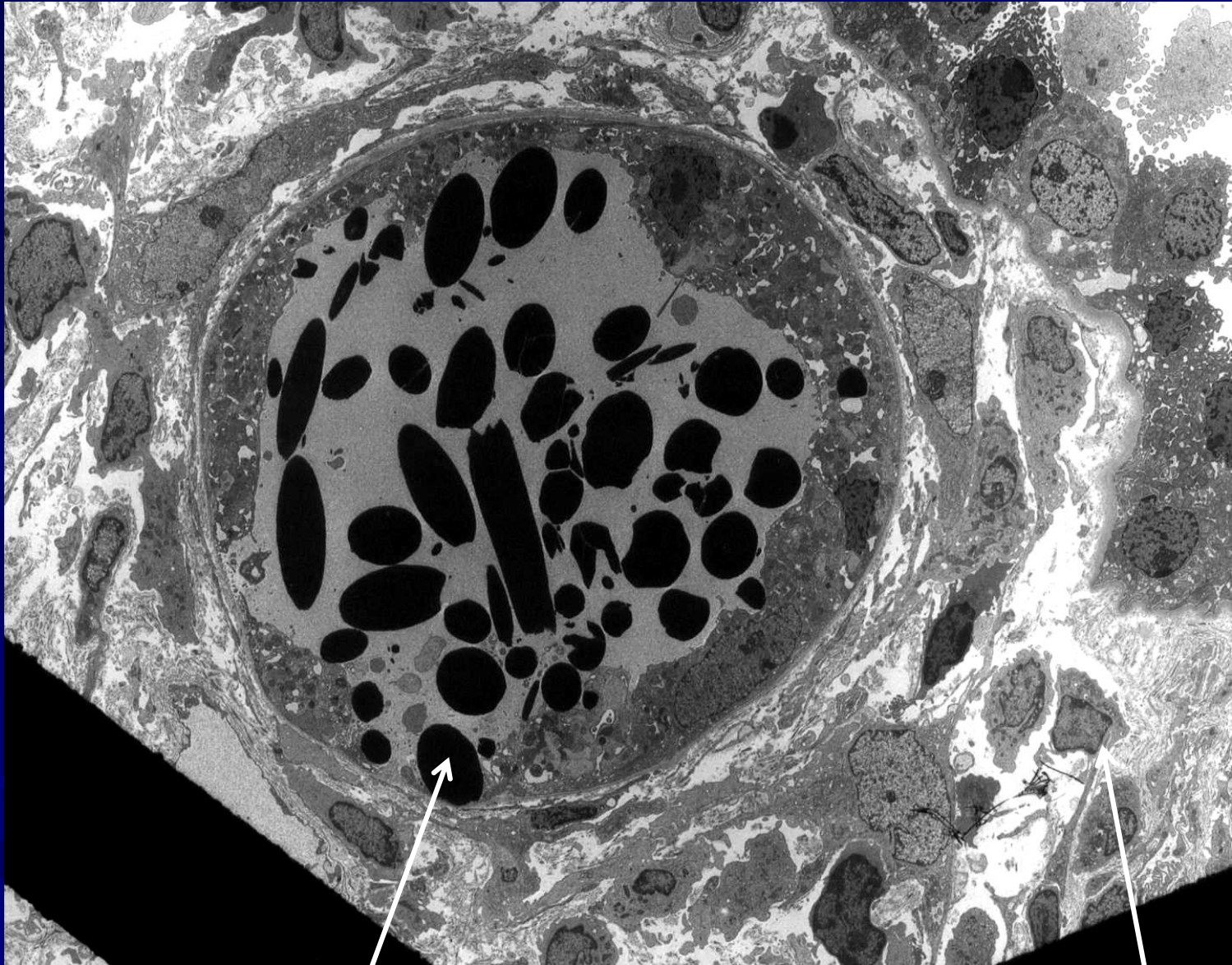
Casts negative by immunofluorescence
Casts not noticed on histology but noticed on resin tol blue

Semi-thin section toluidine blue stained



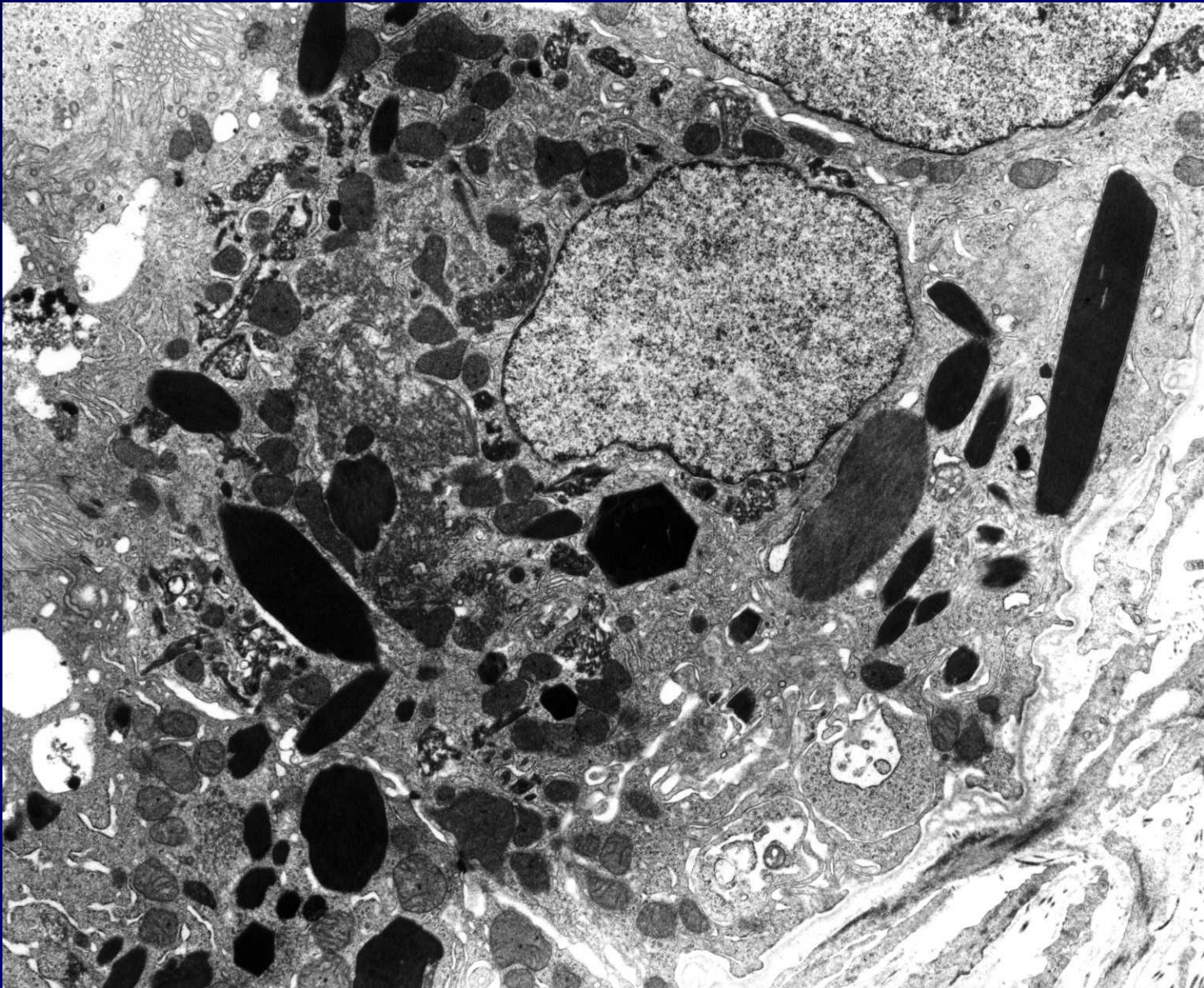
Crystalline cast

Crystalline cast nephropathy



BJ protein crystals

Mononuclear cell infiltrate in interstitium



Crystalline myeloma protein within proximal tubular epithelial cell lysosomes

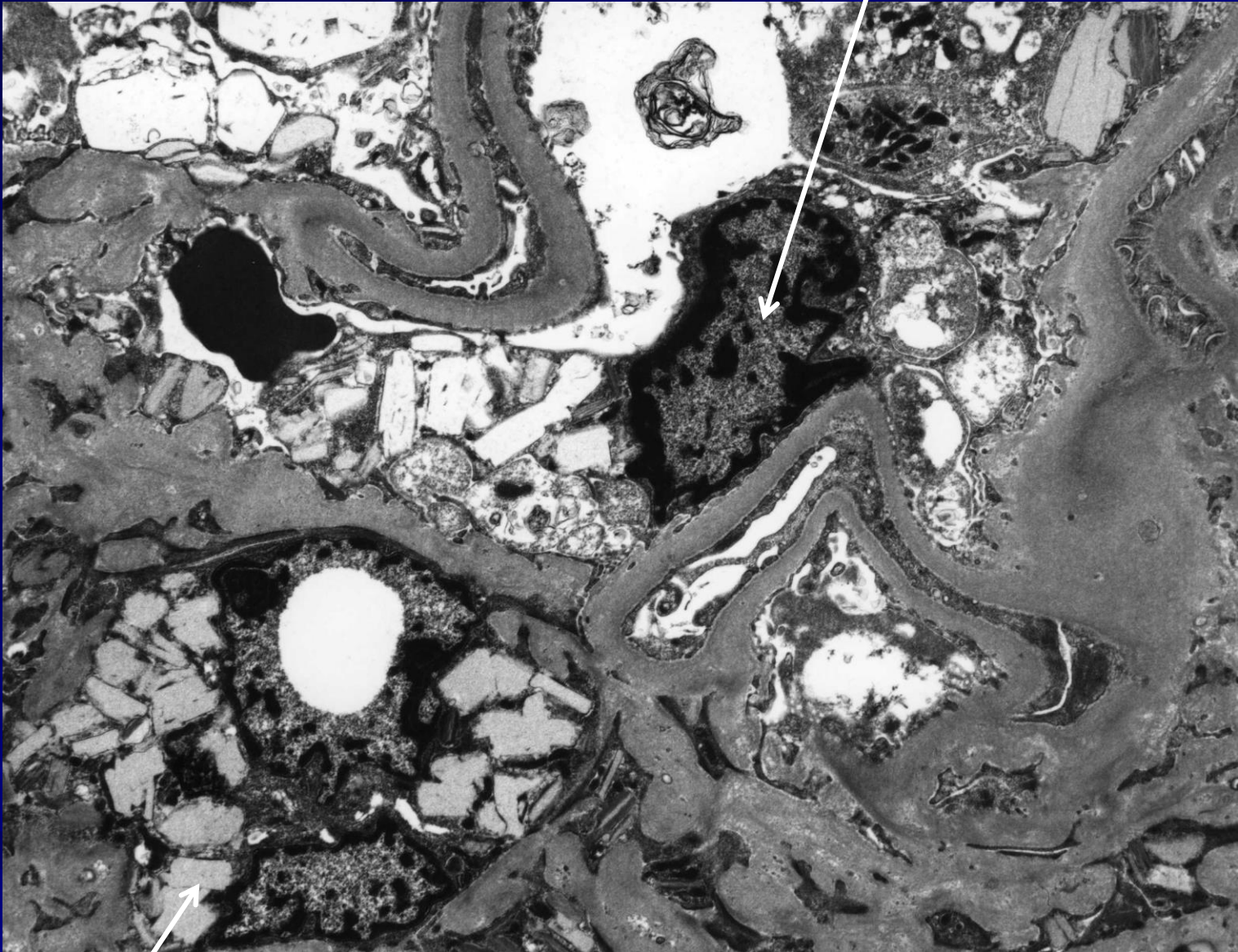
Crystalline myeloma

(another case)

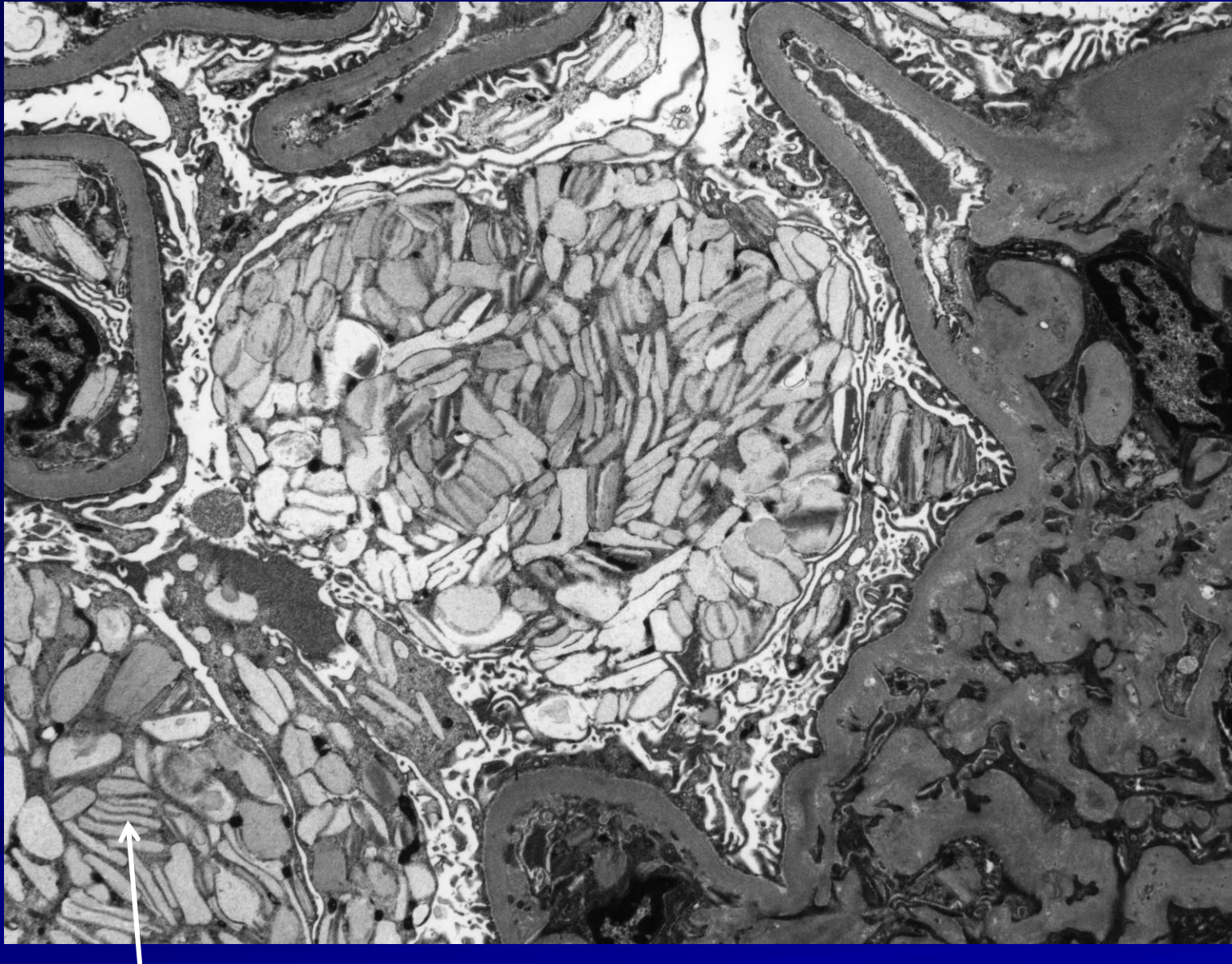
this one from Birmingham QE Hospital

Myeloma protein in lysosomes

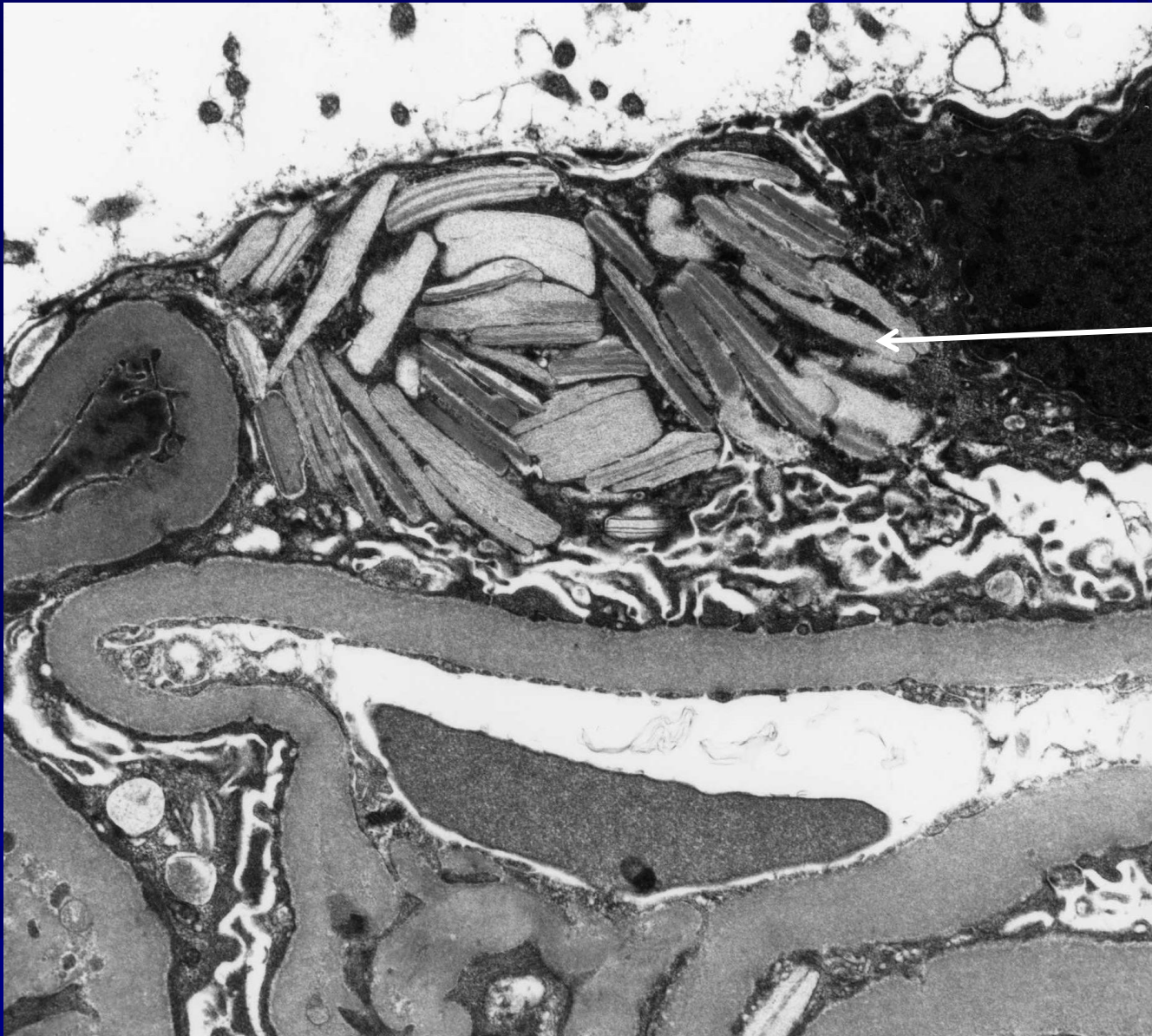
Podocyte



Mesangial cell

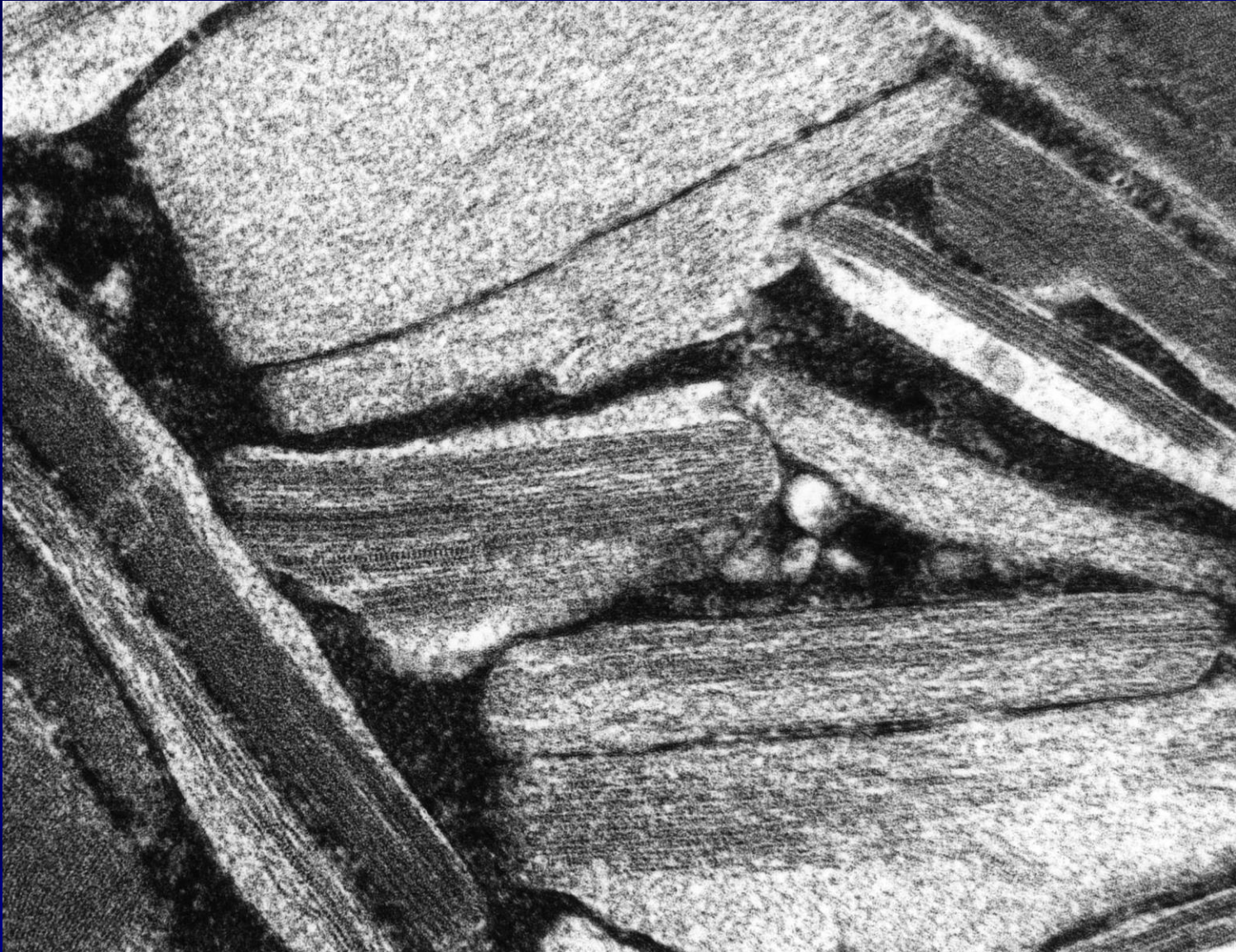


Podocyte lysosomes increased in number and filled with myeloma protein



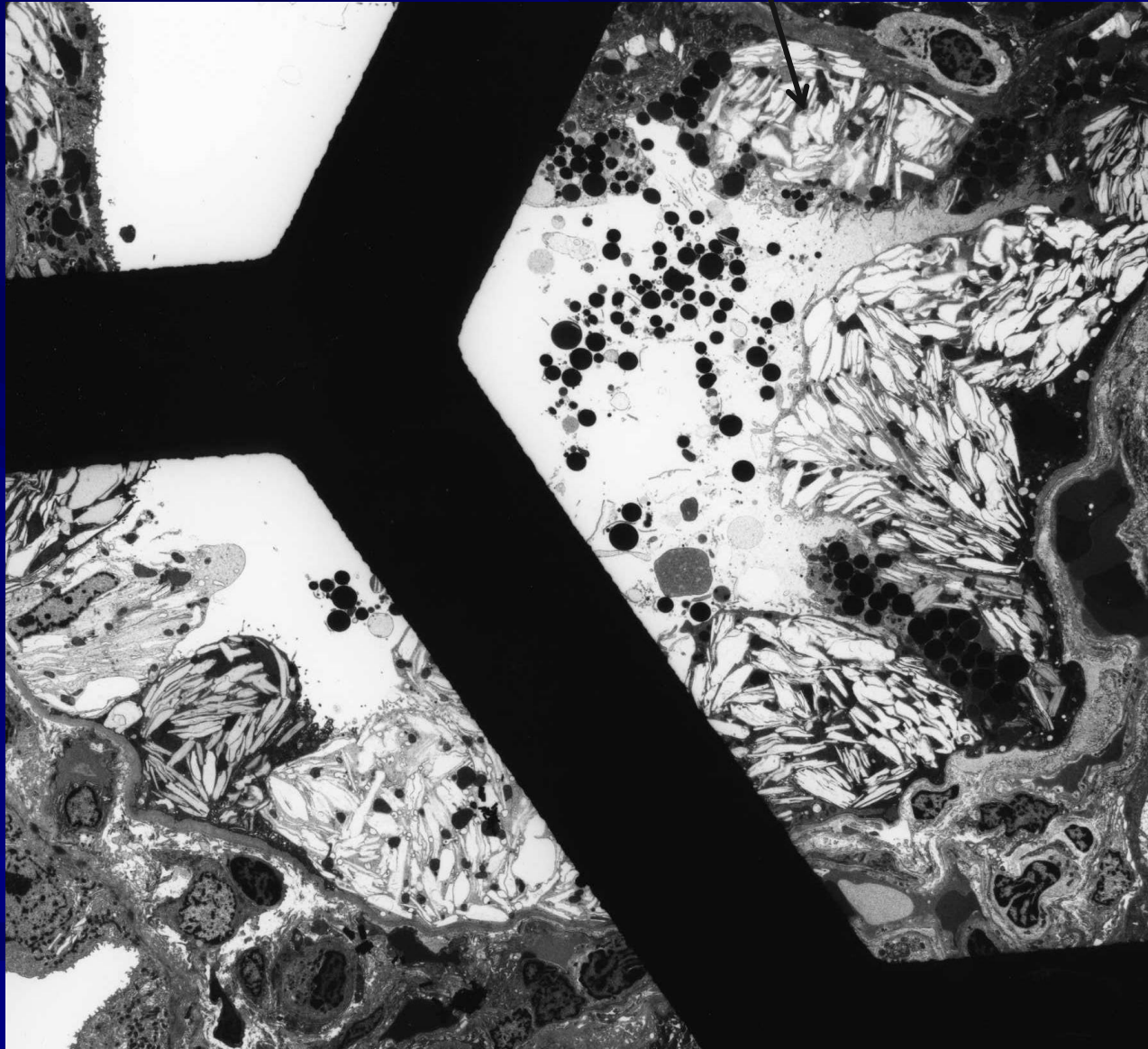
Podocyte
lysosomes
filled with B2
protein

Crystalline myeloma in podocyte lysosomes

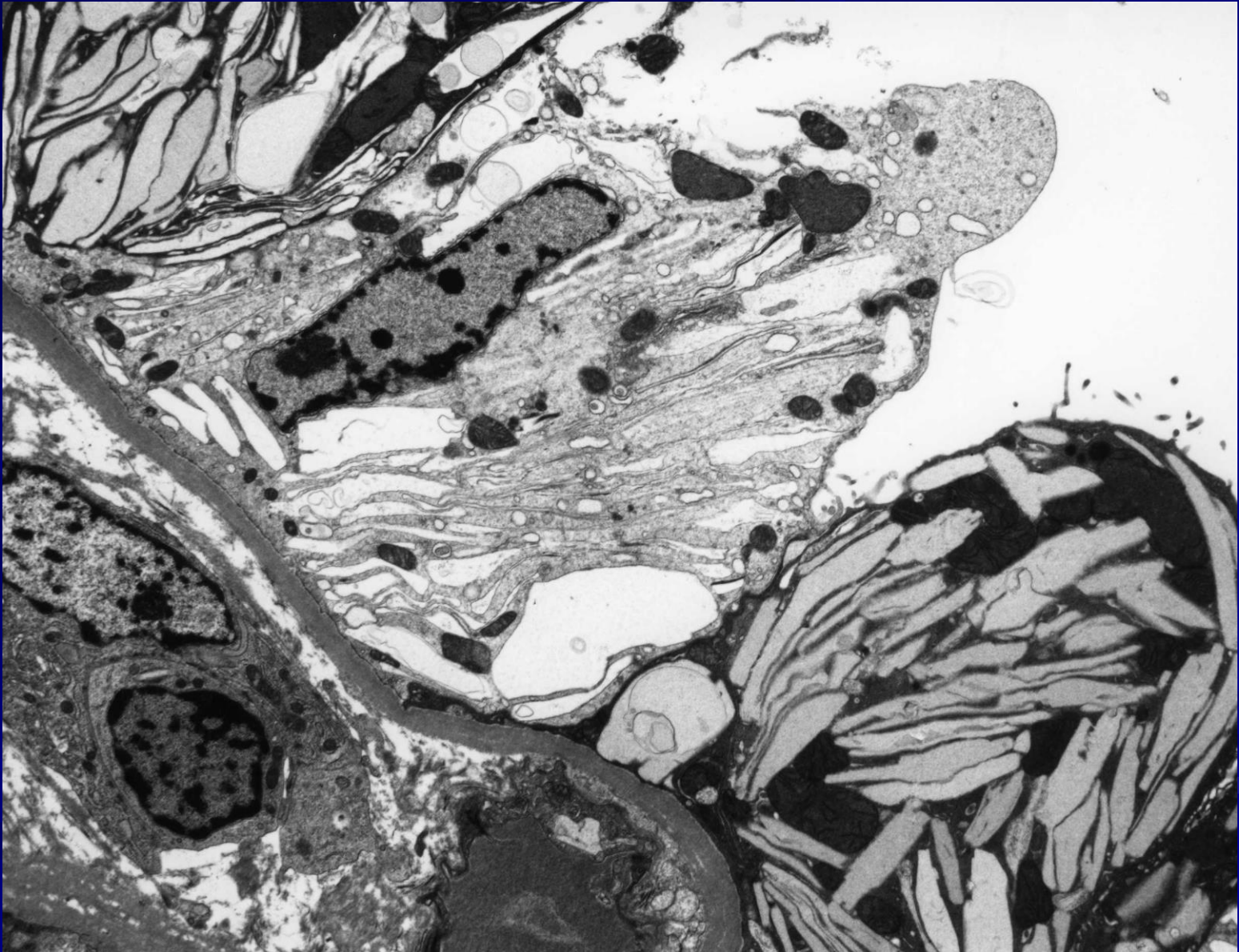


Higher magnification of previous slide

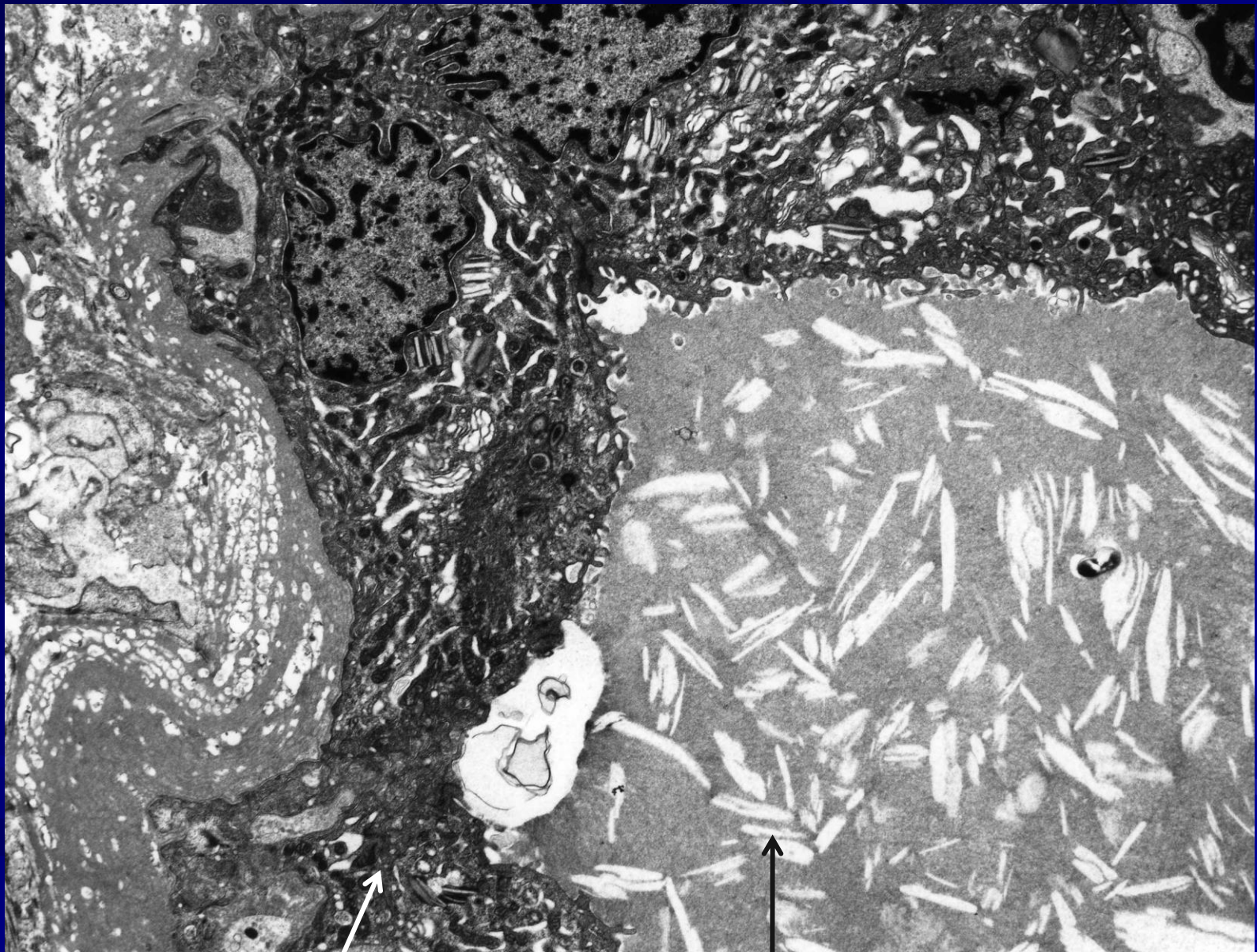
Distal convoluted tubular epithelial cells



Lysosomes all filled with crysatilline myeloma protein



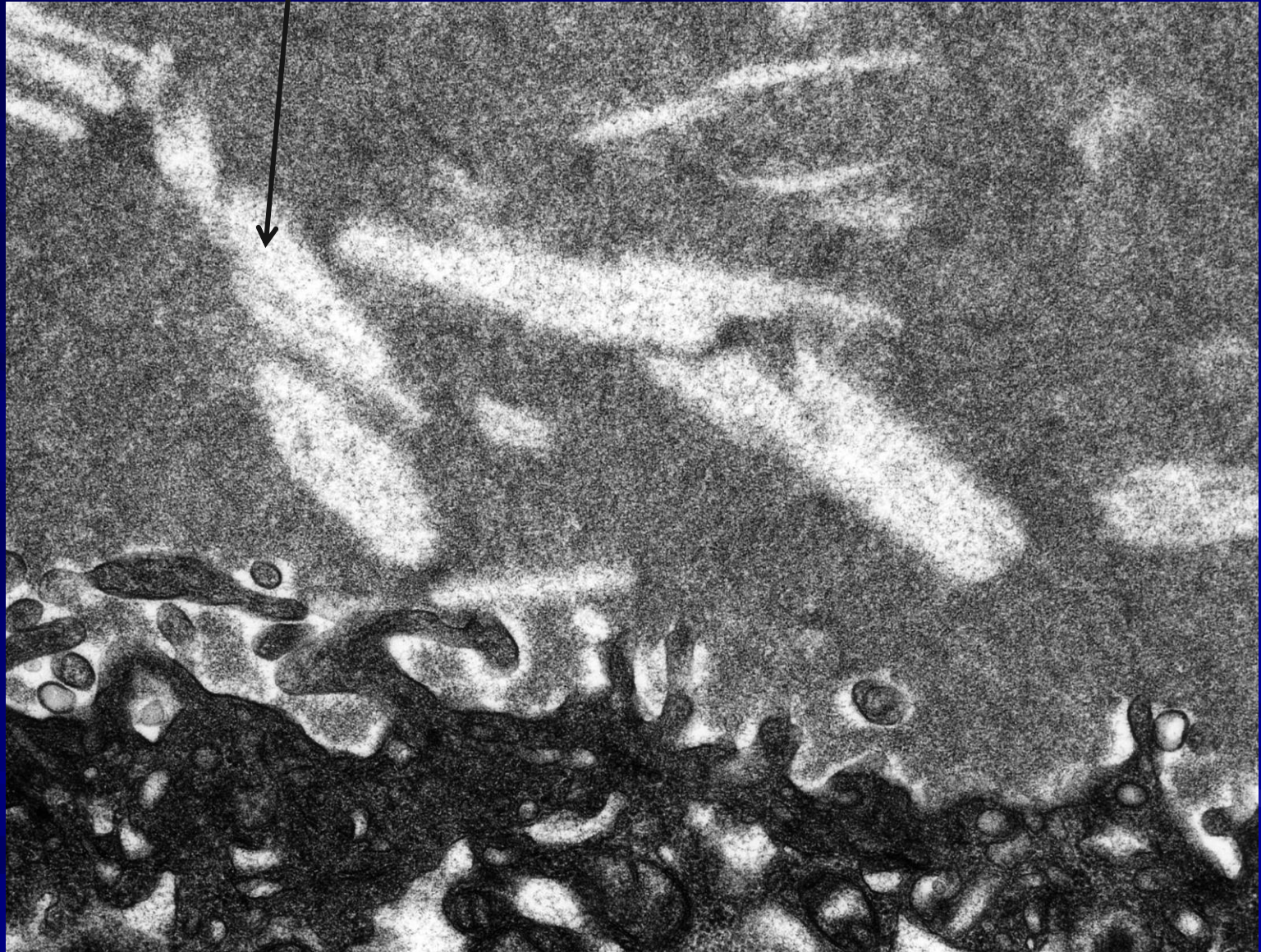
Higher magnification of previous slide



Distal convoluted tubule cells

Myeloma protein in tubular lumen

Myeloma protein crystals



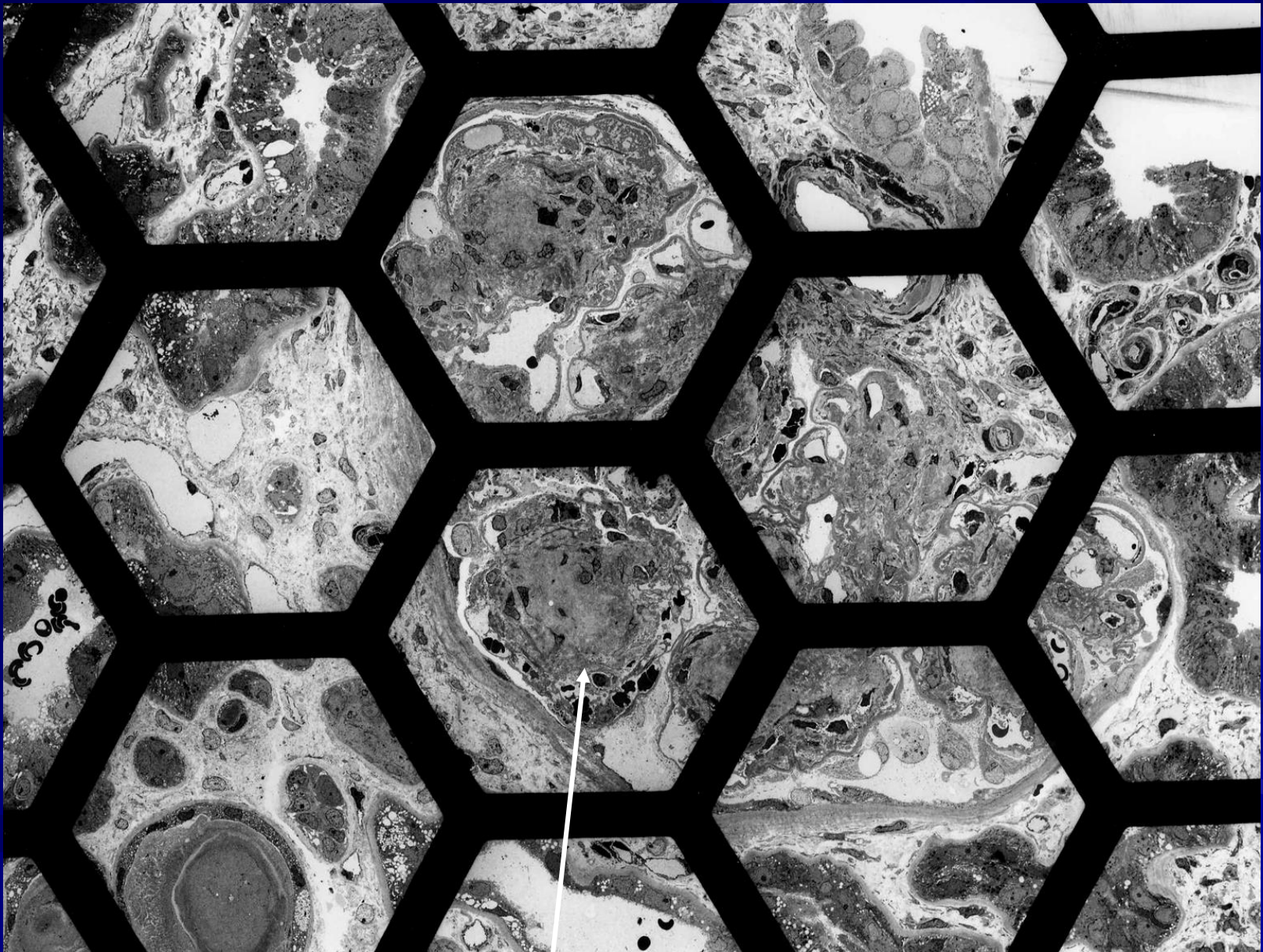
Higher magnification of previous slide



Lymphocyte intralysosomal crystals

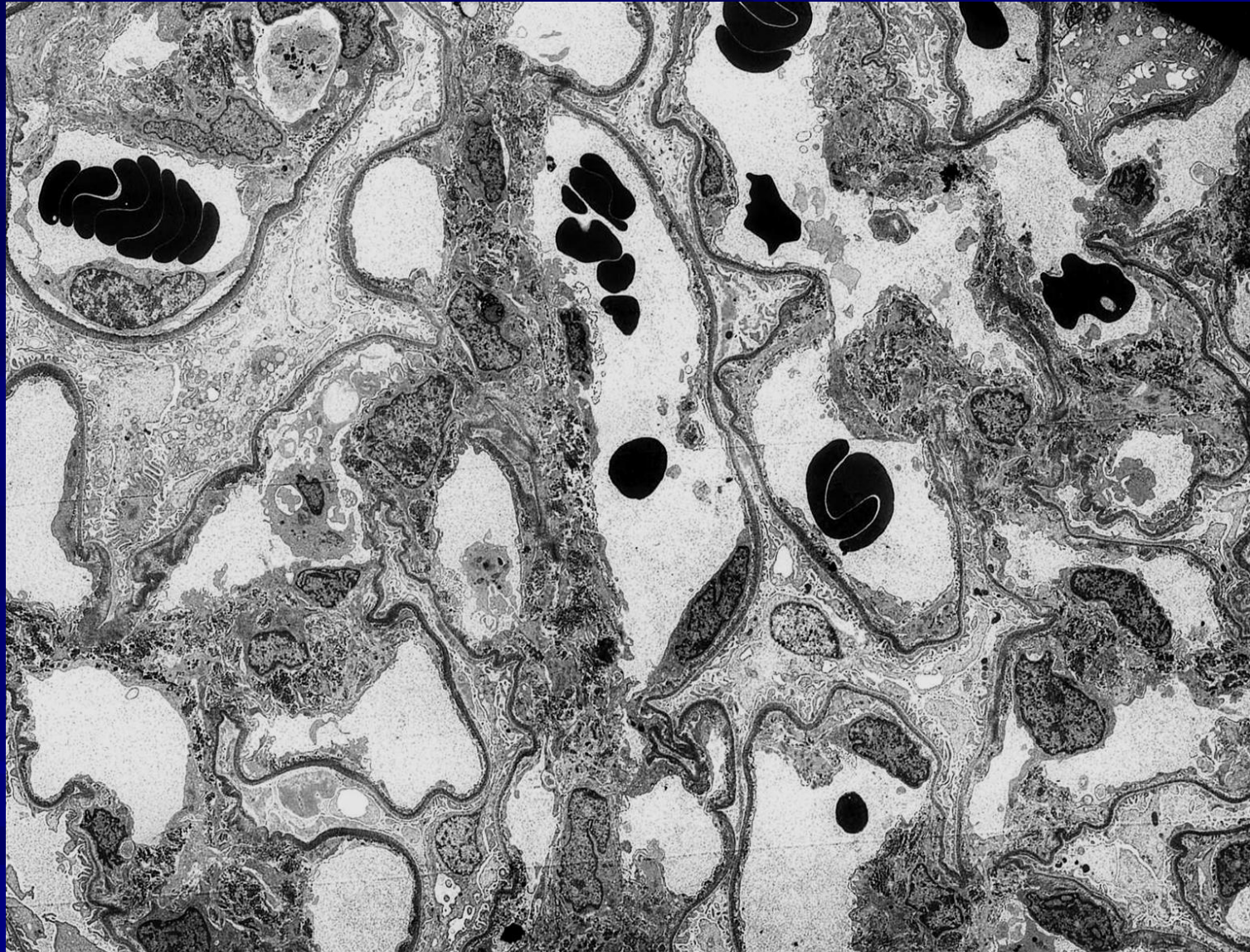
Monoclonal Immunglobulin Deposition Disease MIDD

Monoclonal immunoglobulin deposition disease MIDD



Nodular glomerulosclerosis

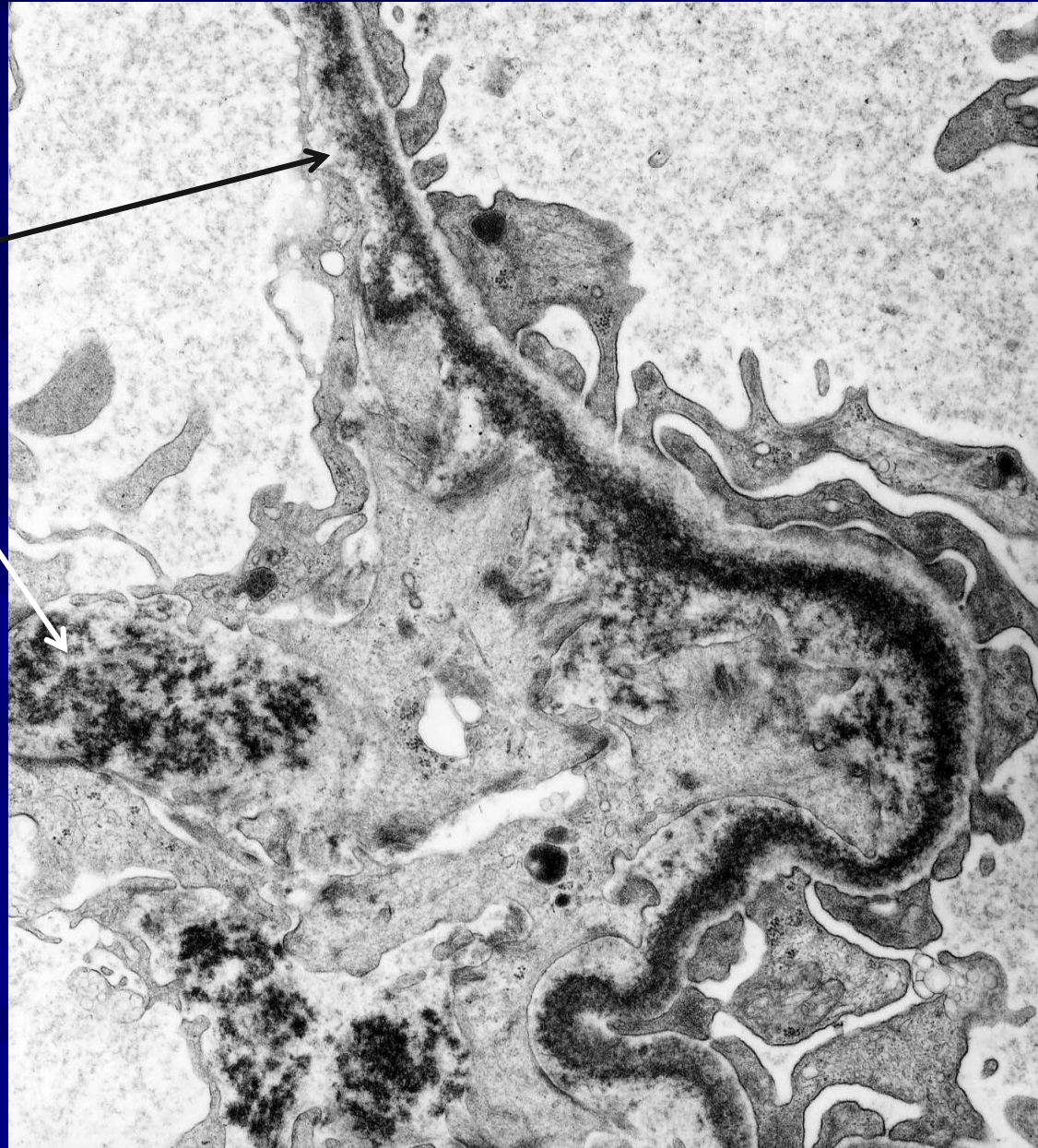
Light chain deposition along GBM and in mesangial matrix

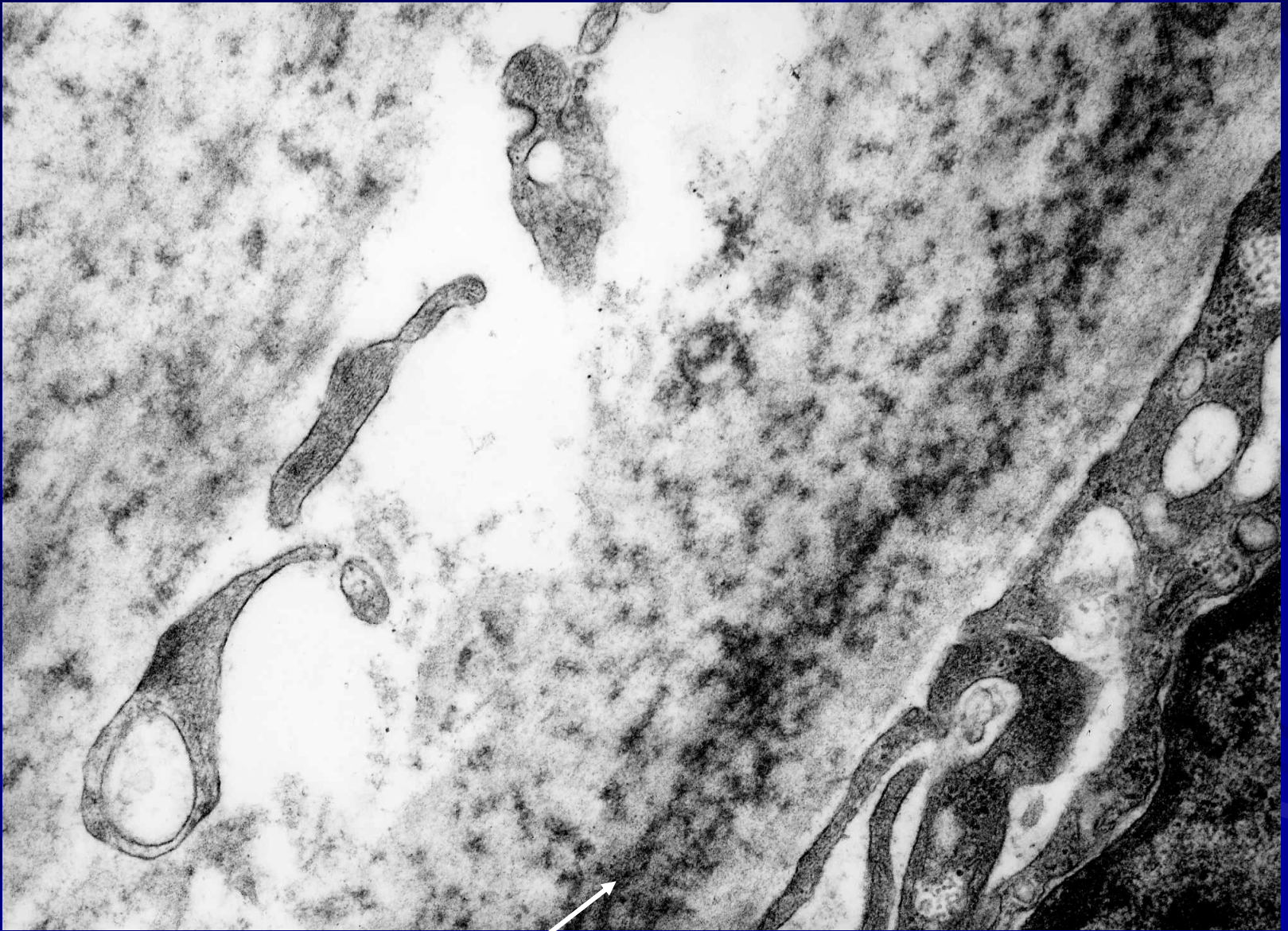


All GBM's appear more electron dense than usual.

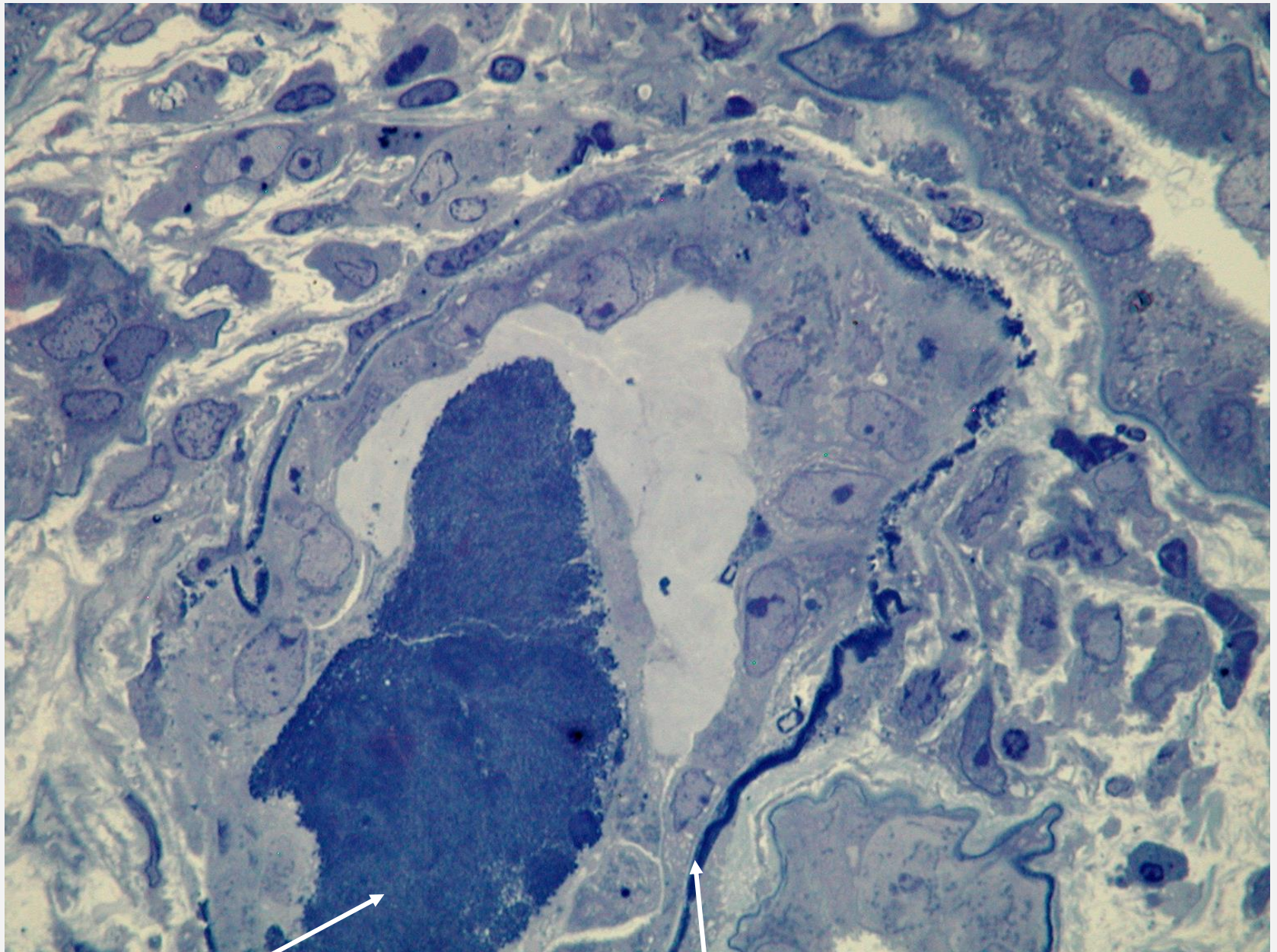
Different case to previous slide

Electron dense
granular myeloma
protein on GBM
and in mesangium



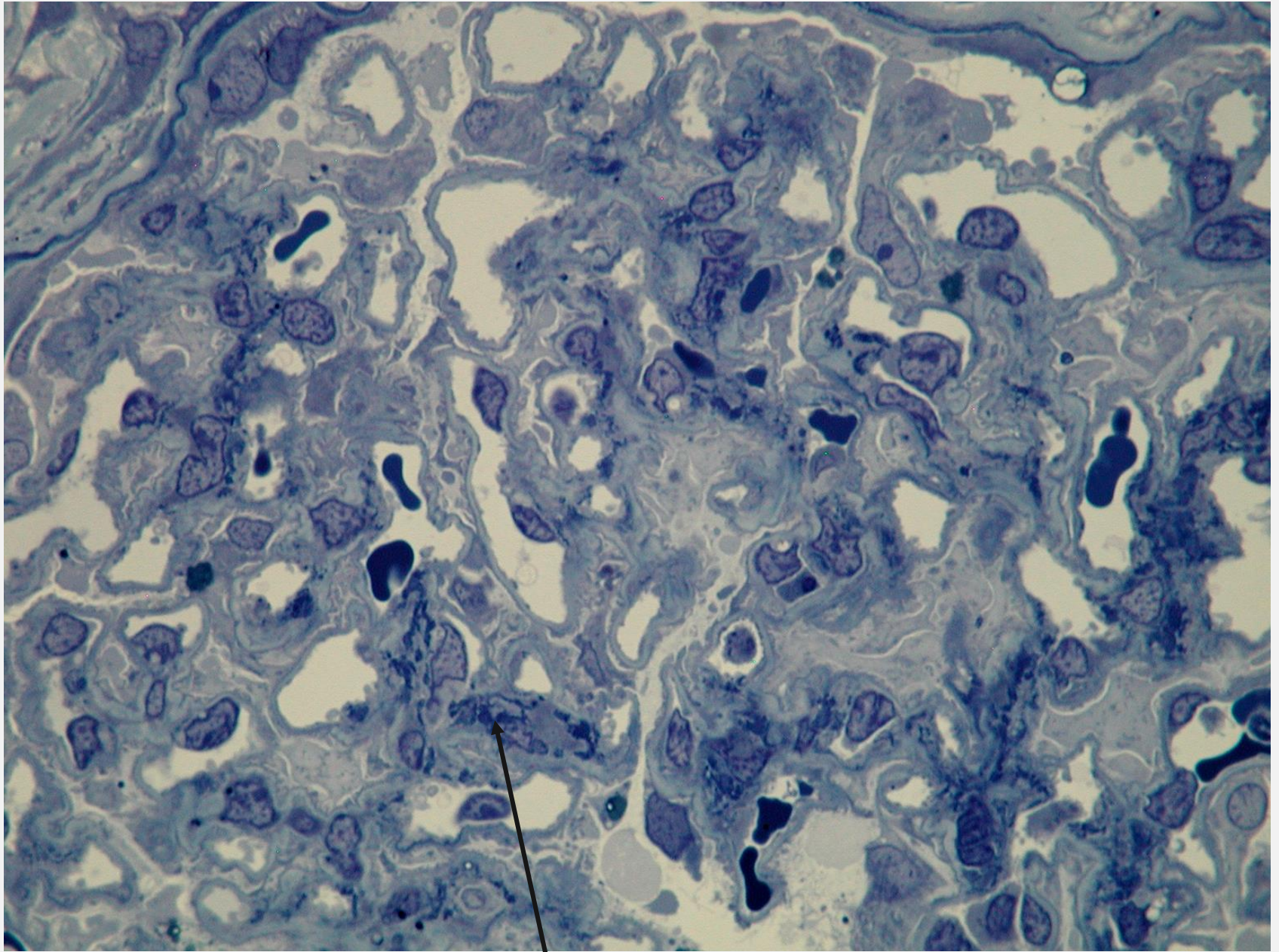


Finely granular electron dense myeloma protein on Bowman's capsule



Myeloma protein cast

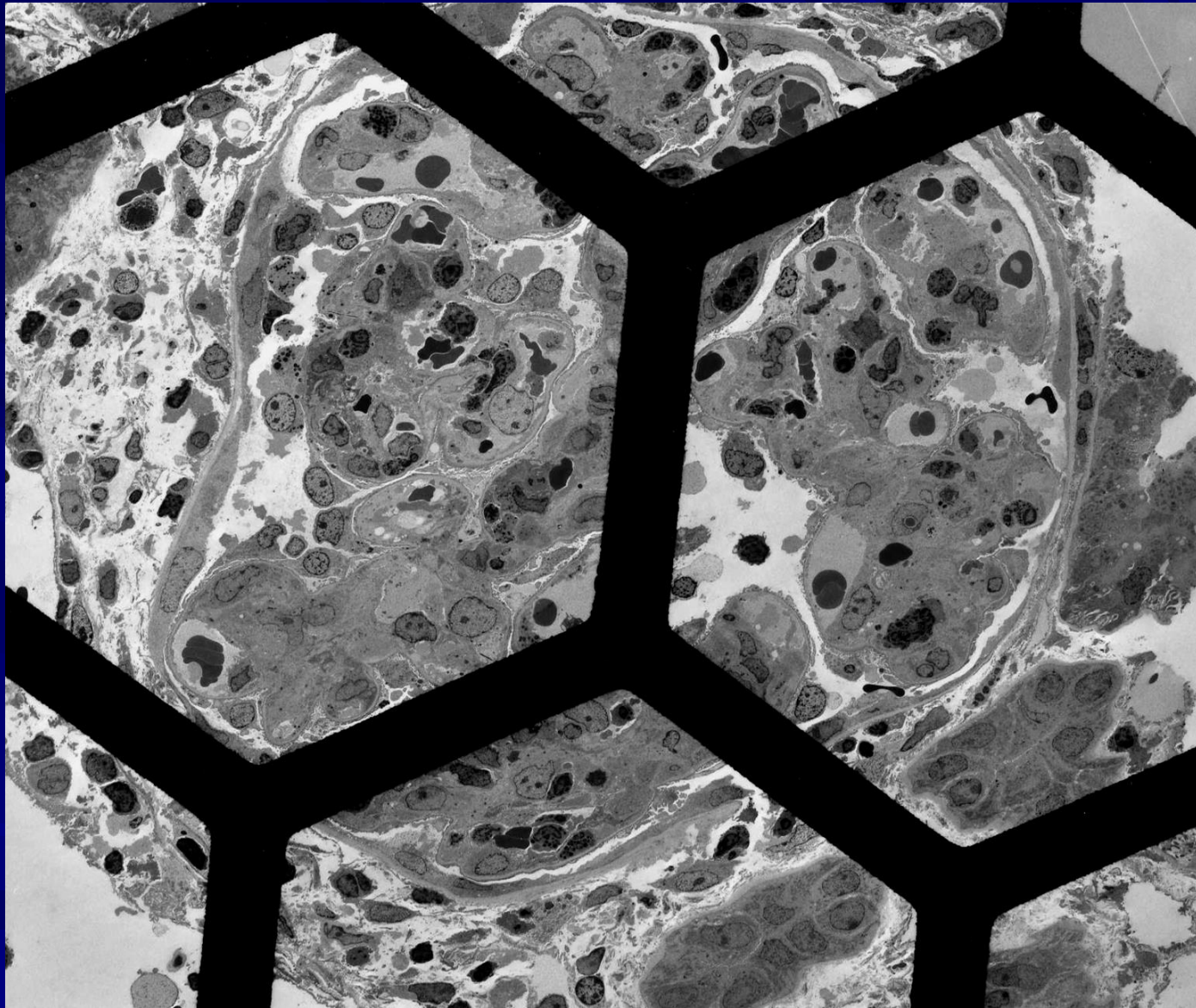
Monoclonal protein on tubular basement membrane



Light chain in mesangium

Post infectious GN

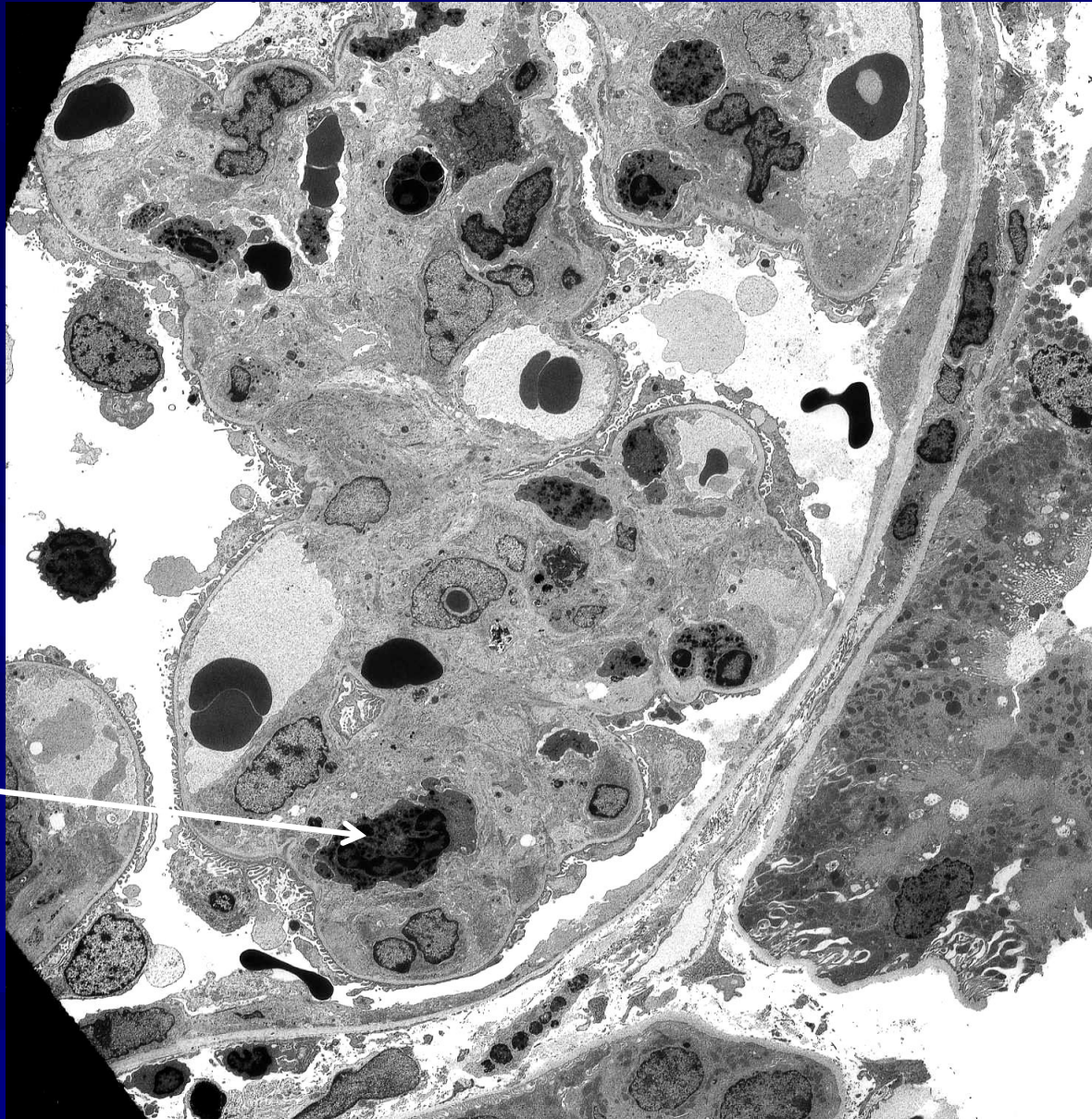
Acute



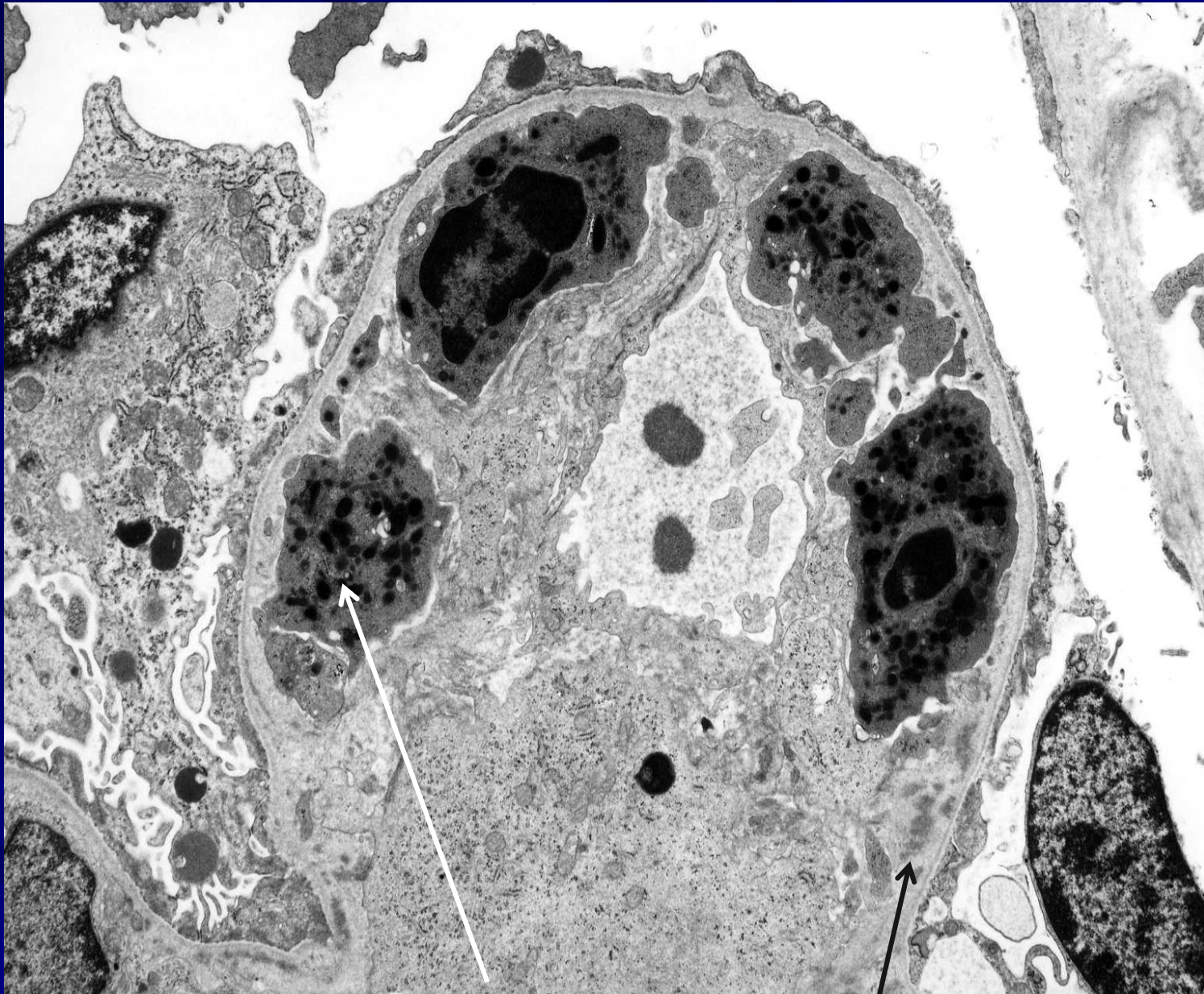
Acute proliferative glomerulonephritis with numerous neutrophils

Higher magnification
of previous slide

Numerous
neutrophils



Higher magnification of 2 slides previous at 12 o'clock



Numerous subendothelial neutrophils

Numerous small mesangial and subendothelial deposits

Neutrophil non-equatorially sectioned

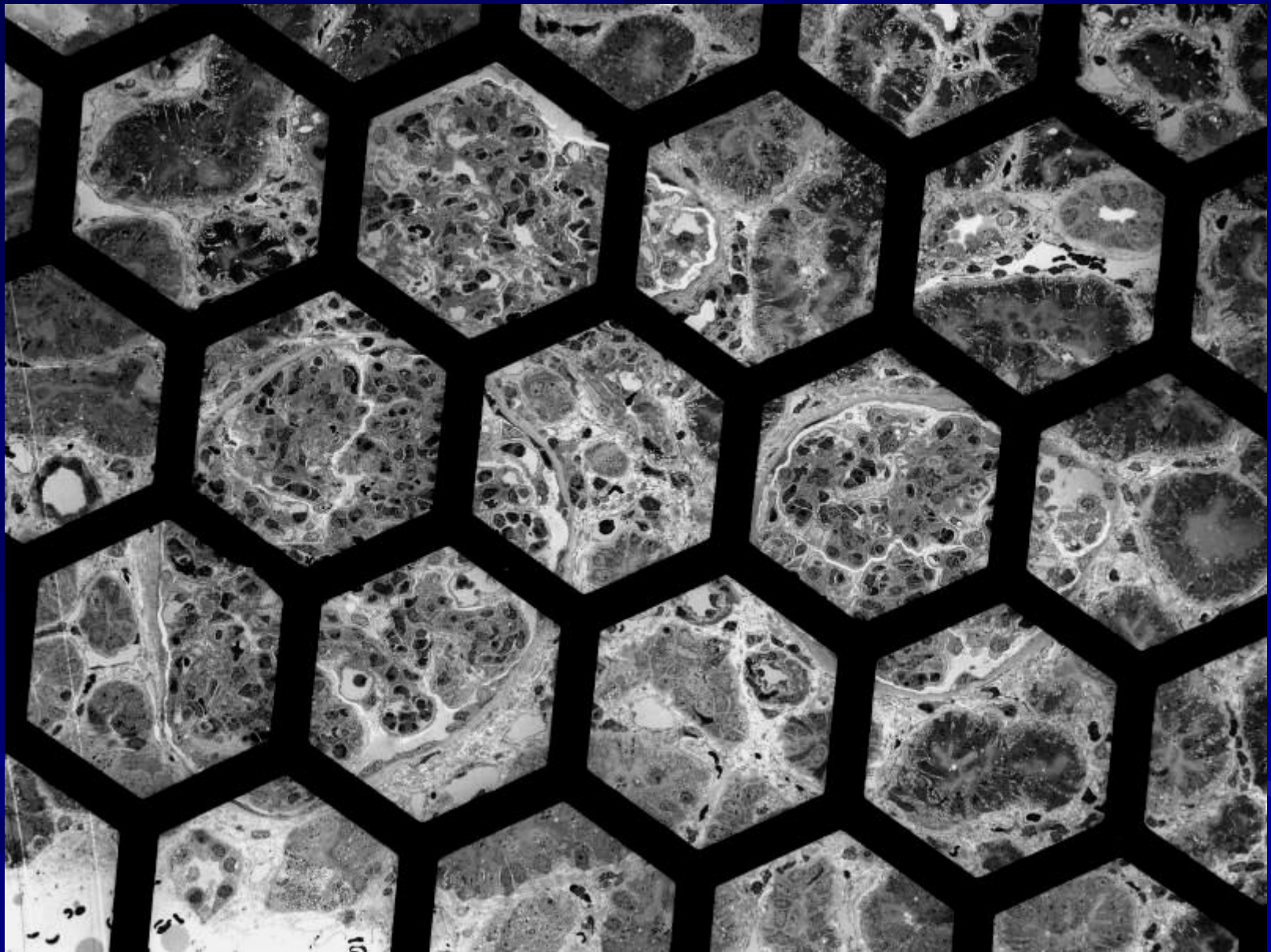


Numerous small subendothelial deposits - by immunofluorescence C3

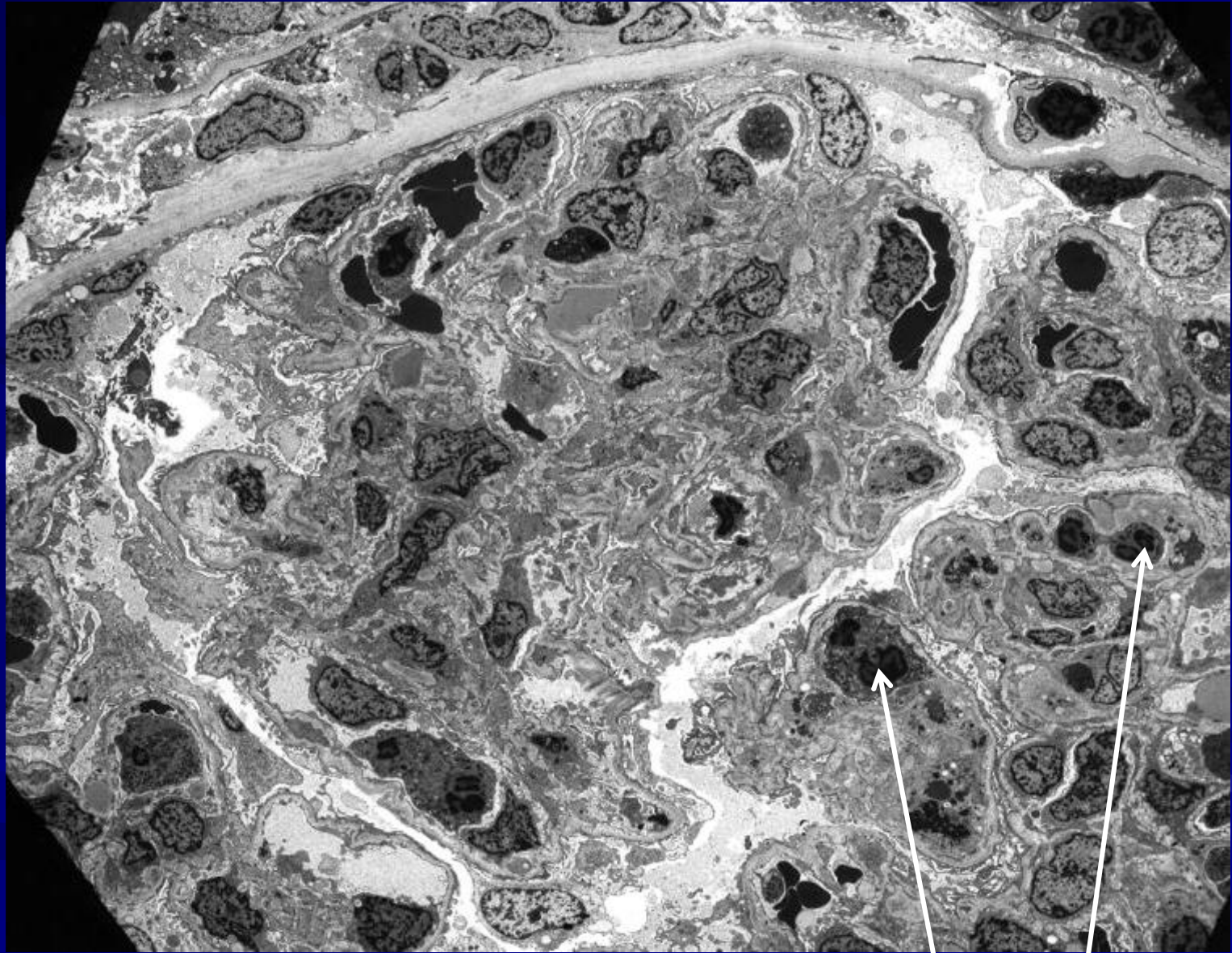
Post-infectious glomerulonephritis subacute

Post-infectious glomerulonephritis subacute

- Immunofluorescence: C3 mainly (can be confused for acute MCGN type 1)
- Histology: Numerous neutrophils in glomerulus (can be confused for acute MCGN type 1)
- EM: Occasional subepithelial humps



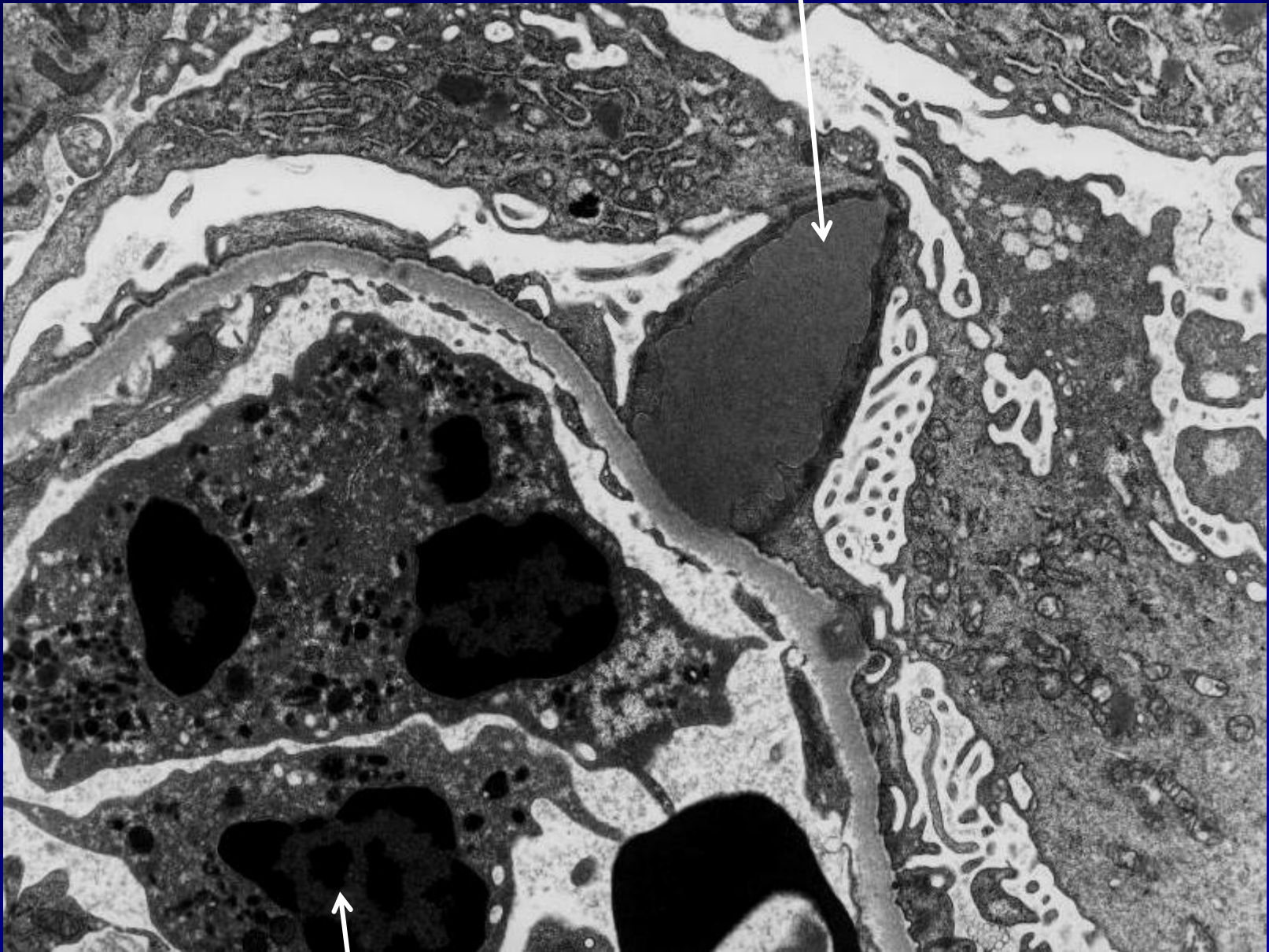
Acute proliferative glomerulonephritis



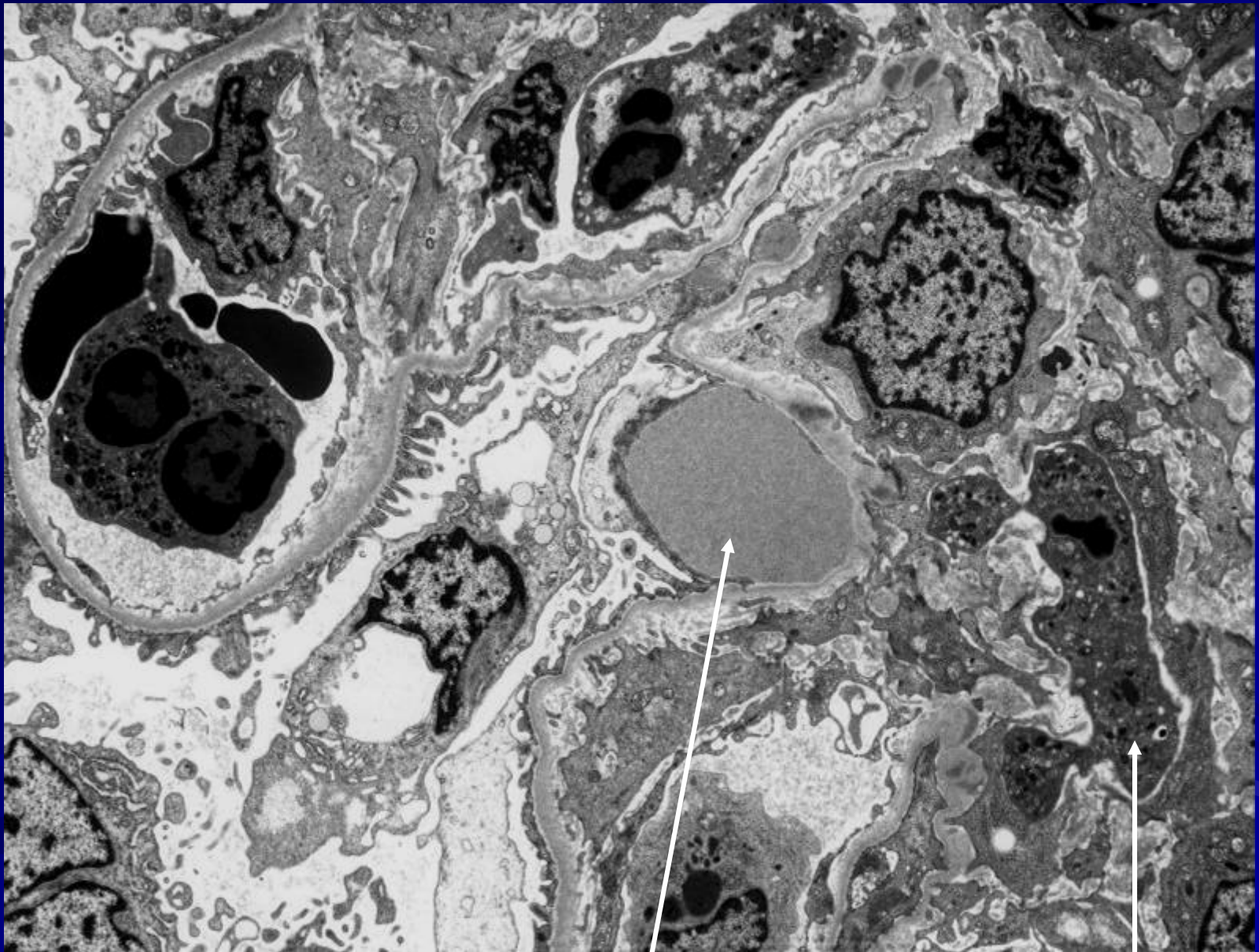
Acute proliferative glomerulonephritis

Numerous neutrophils

Subepithelial hump



Intracapillary luminal neutrophils



Subepithelial hump

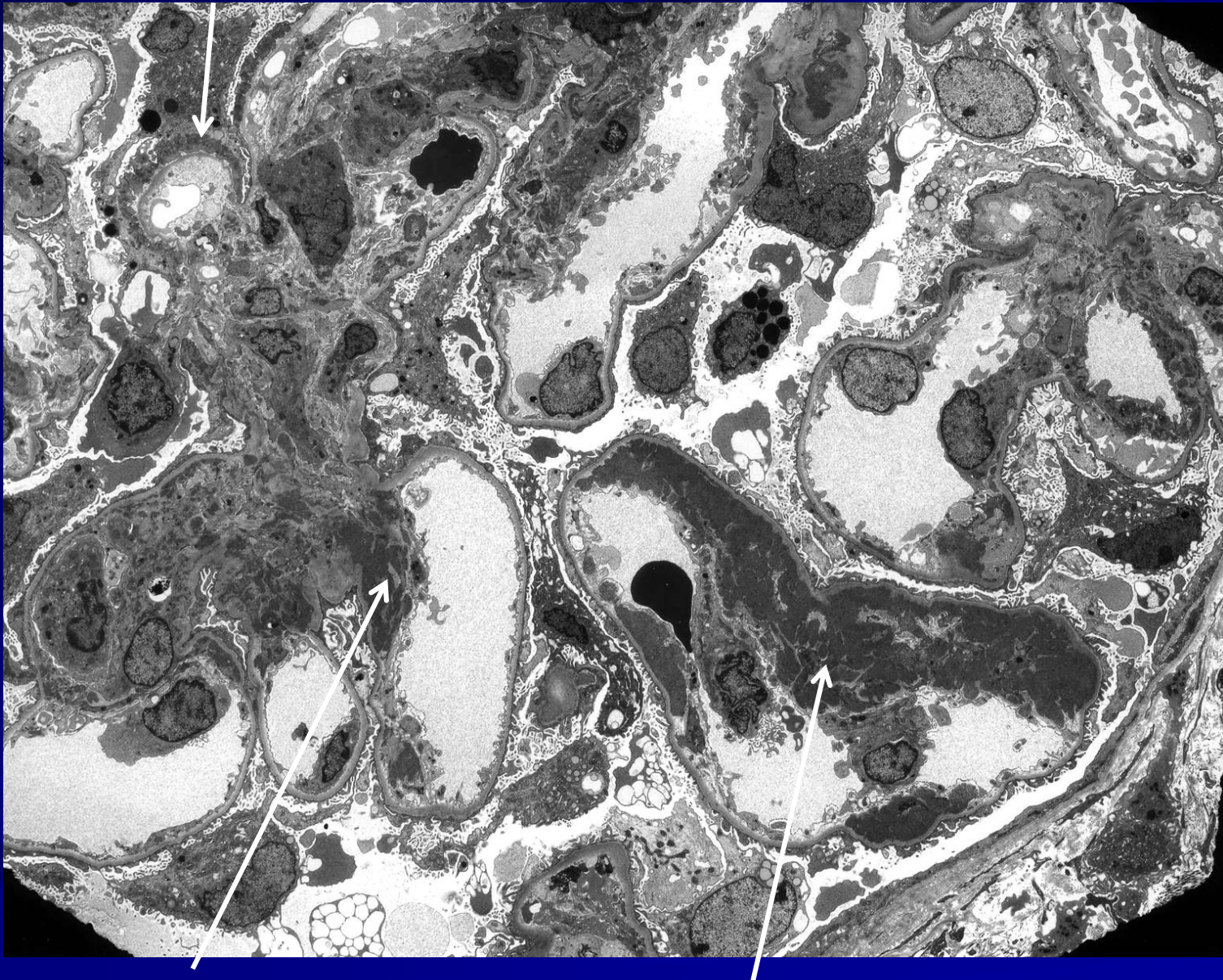
Neutrophil in mesangium

Chronic osteomyelitis case

IF: significant IgG, C3, IgA - trace IgM, C1q

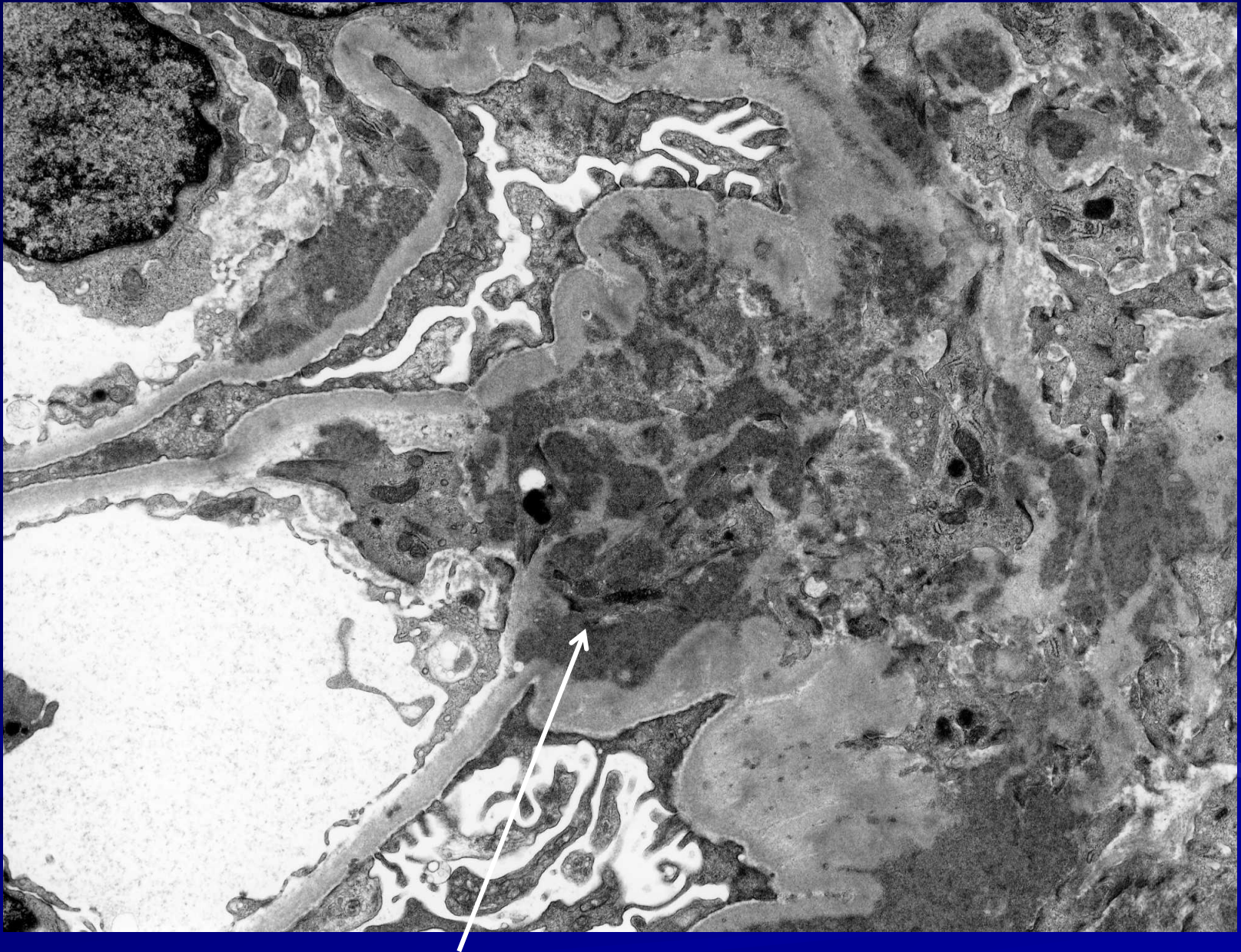
Can be IgA rich if Staph infection

Subepithelial deposits



Large mesangial deposits

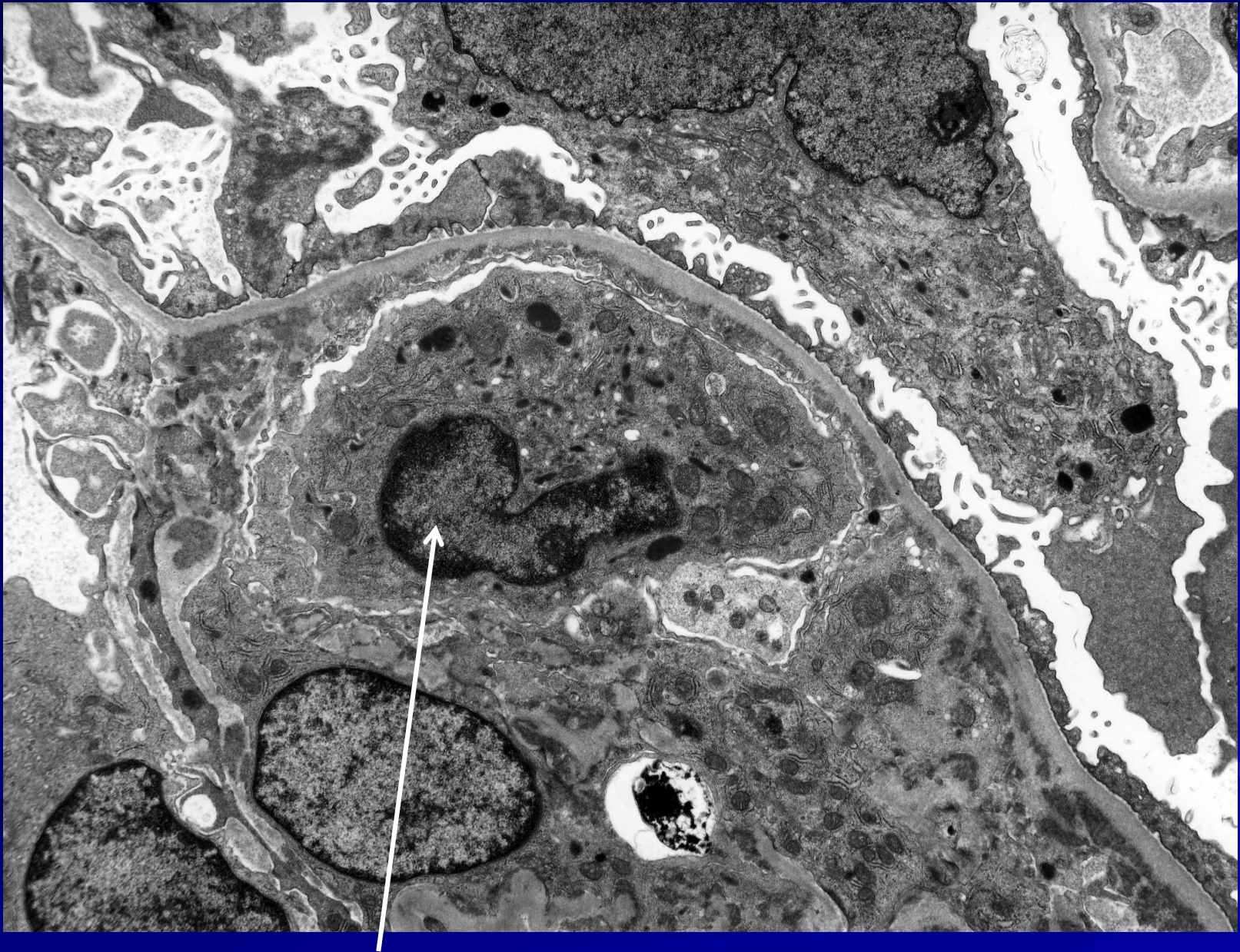
Large subendothelial deposits



Large mesangial deposits



Large subendothelial deposits



Monocyte in capillary loop

Systemic Lupus Erythematosus

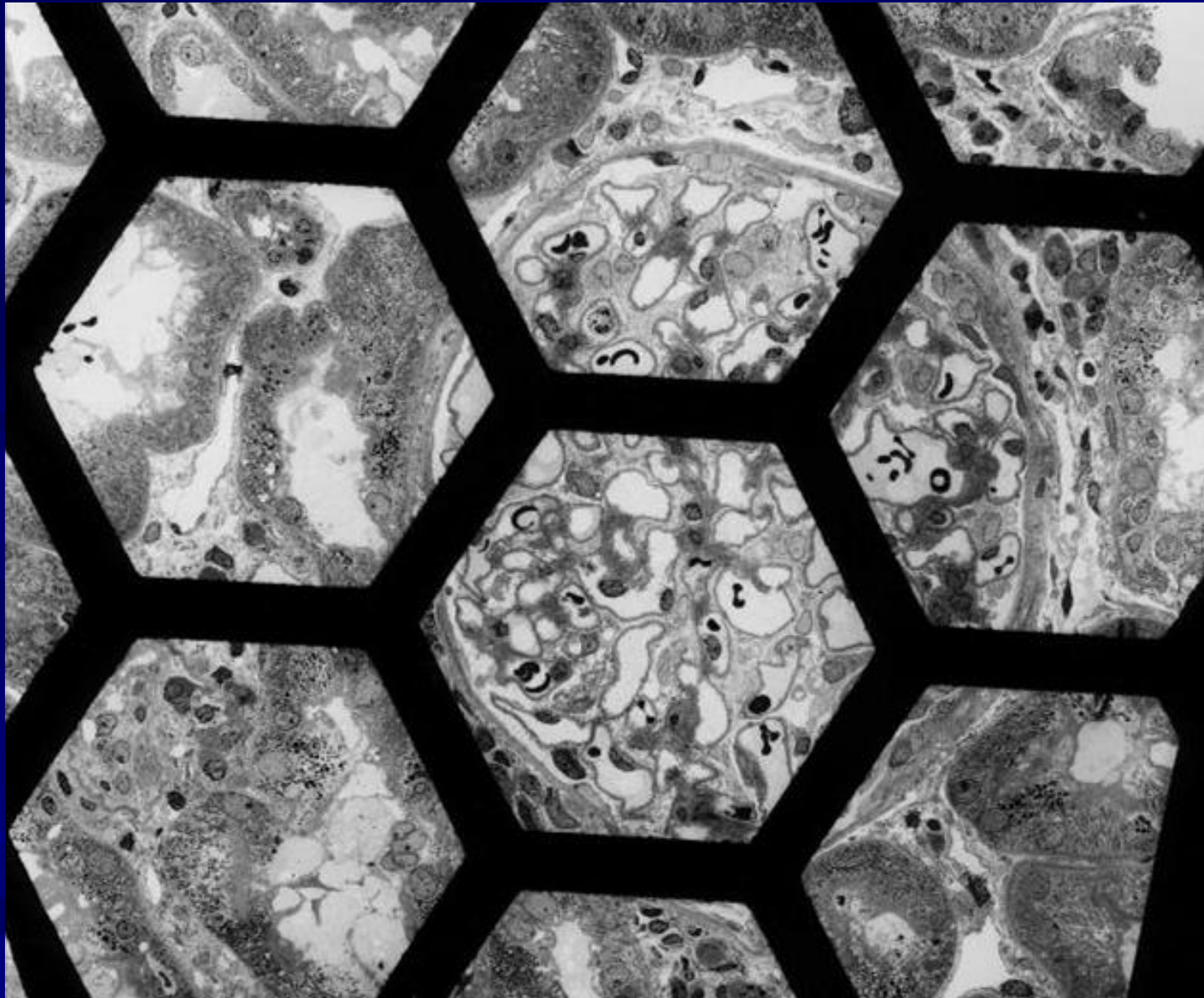
SLE

SLE classification

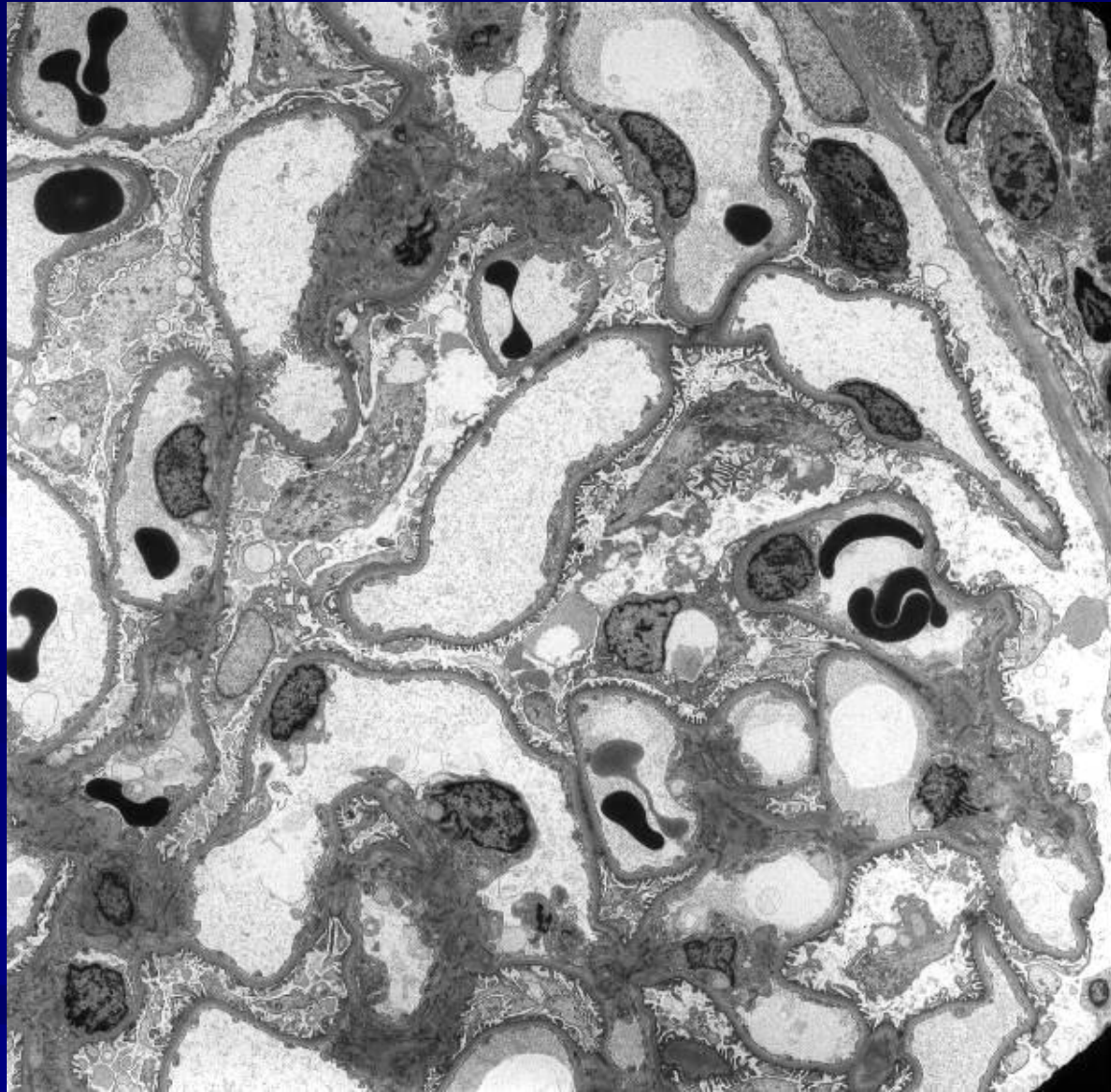
- Class 1: Minimal
- Class 2: Mesangial proliferative
- Class 3: Focal
- Class 4: Diffuse
- Class 5: Membranous
- Class 6: Advanced sclerosing

SLE

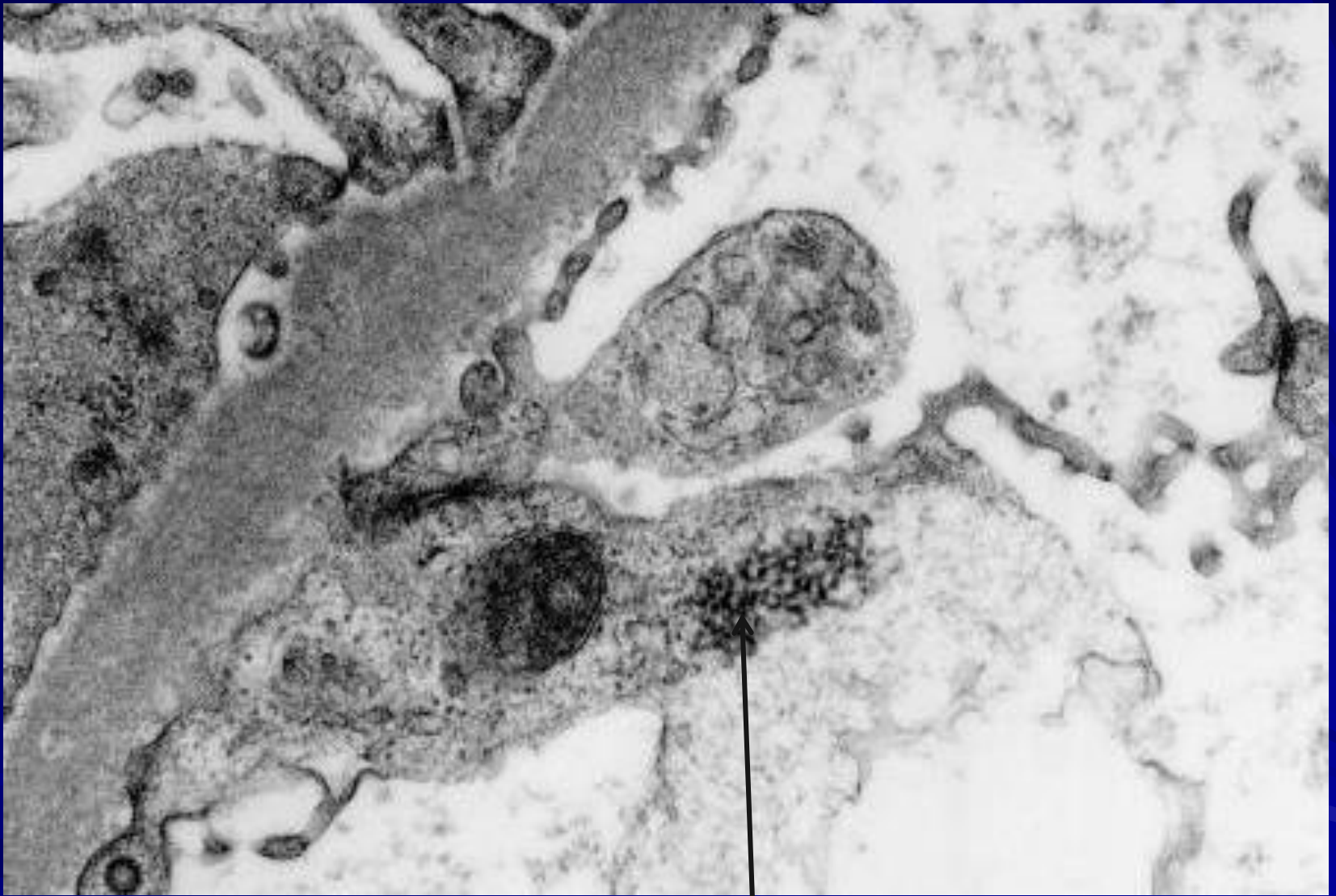
- Immunofluorescence: Always IgG, usually in addition either IgA or IgM, often full house. Both kappa and lambda present. C3 more frequent than C1q.
- Deposits can be found in glomeruli, tubular basement membrane and in vessel wall.



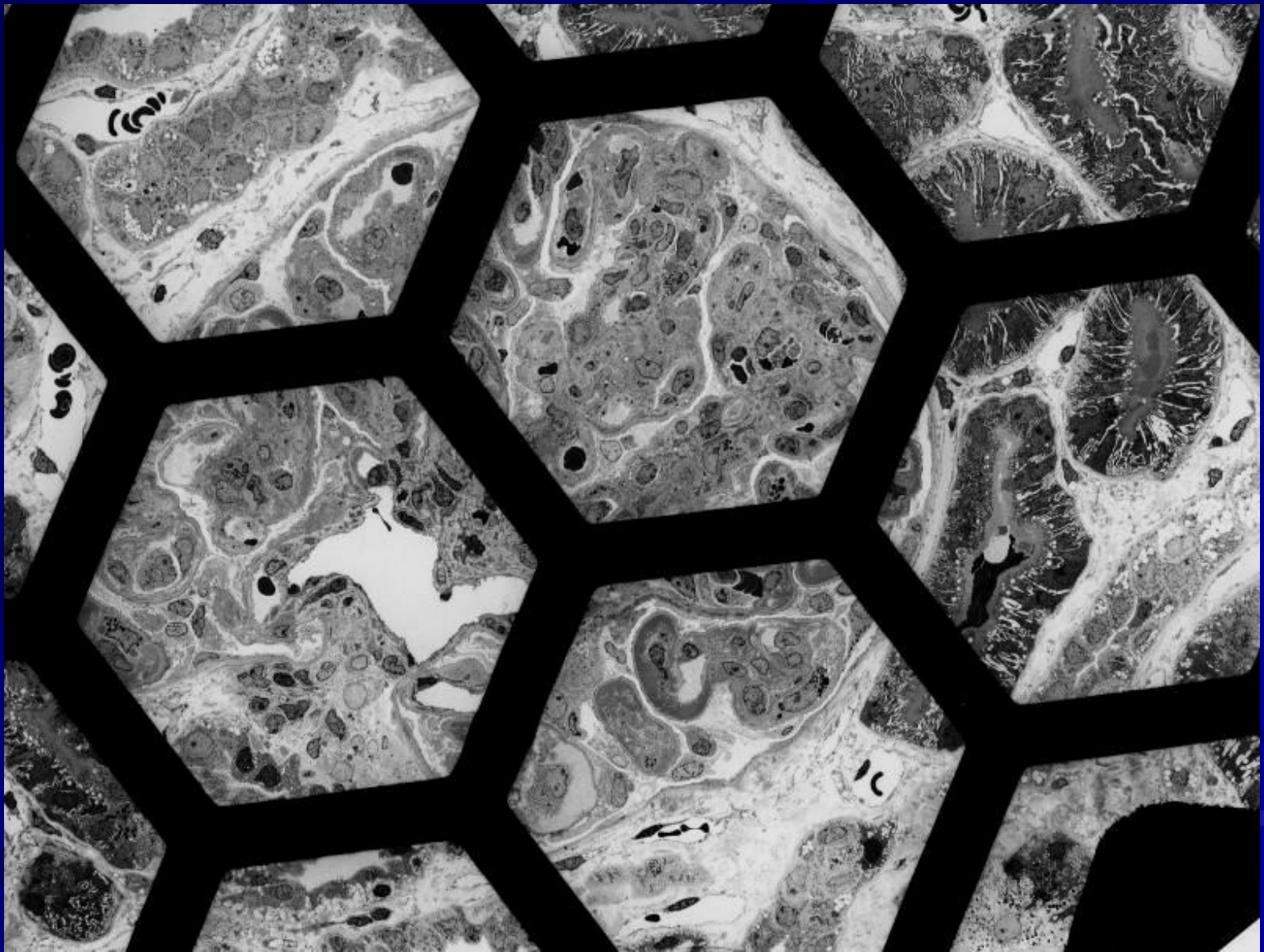
Class 1 – normal histologically



Higher magnification of previous slide

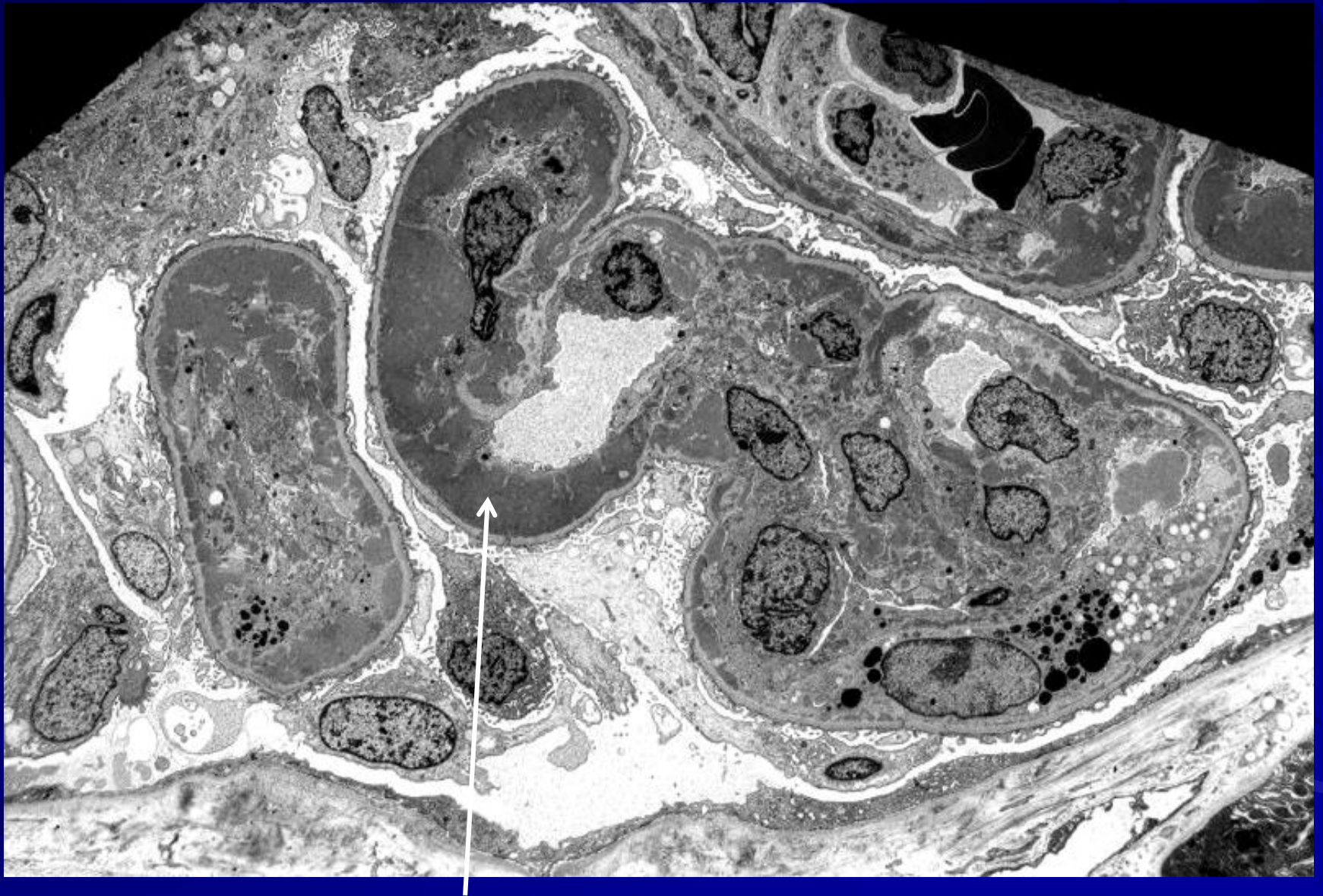


In this case, no deposits but tubuloreticular complexes present



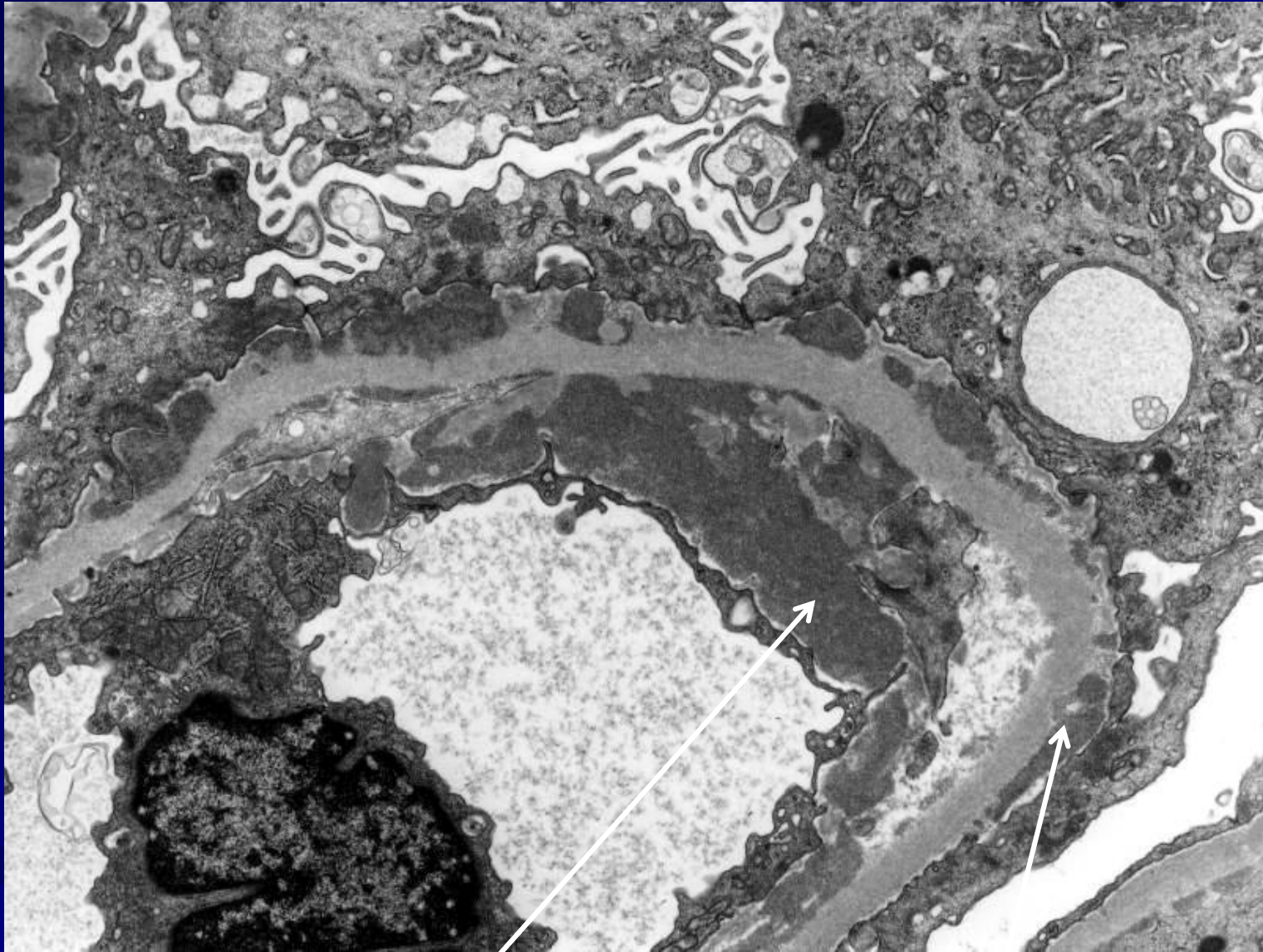
Hypercellular glomerulus – accentuation of lobular architecture

Higher magnification of previous slide



Very large subendothelial deposits

Class 4 Lupus nephritis



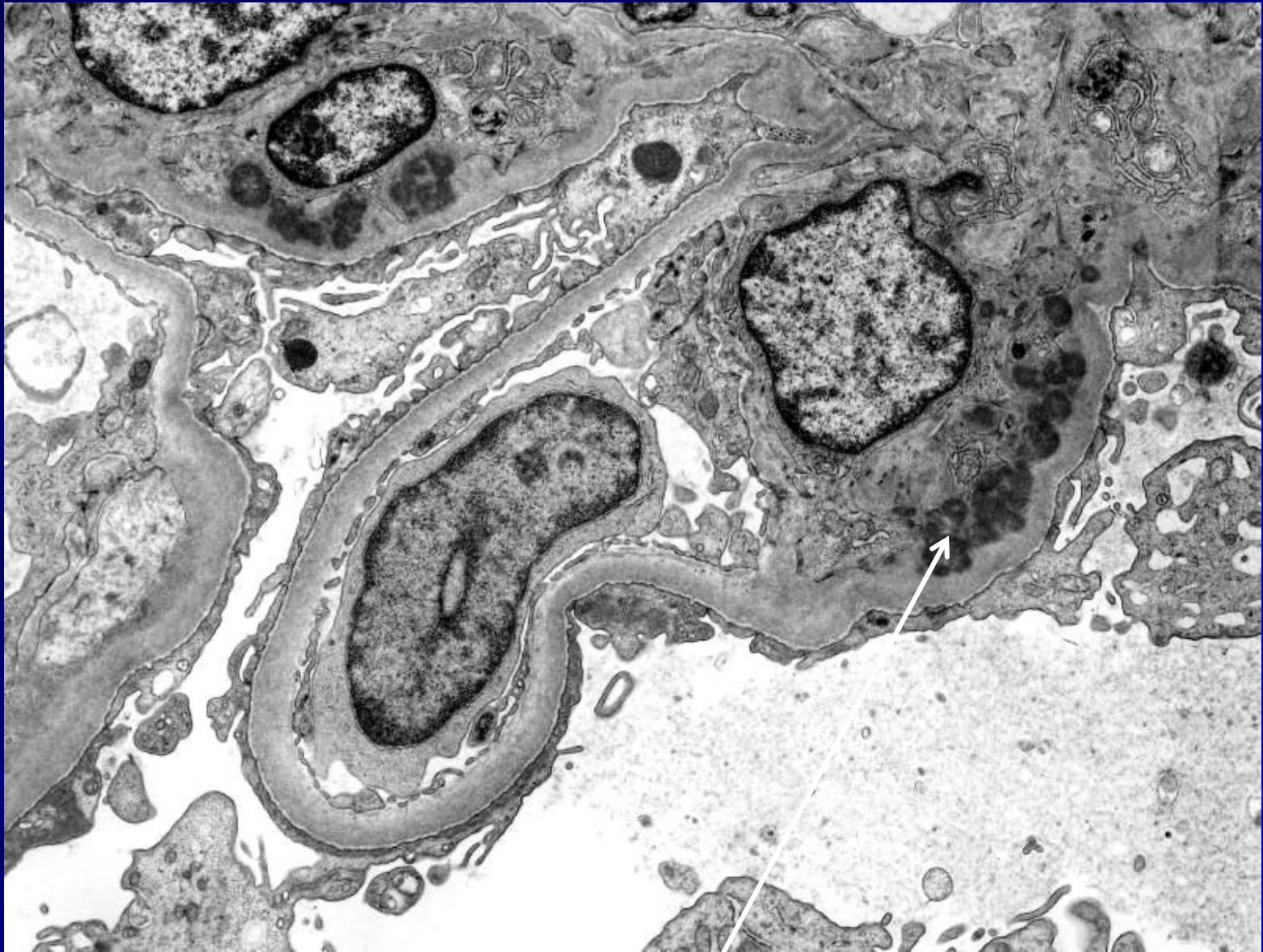
Subendothelial deposits

Subepithelial deposits



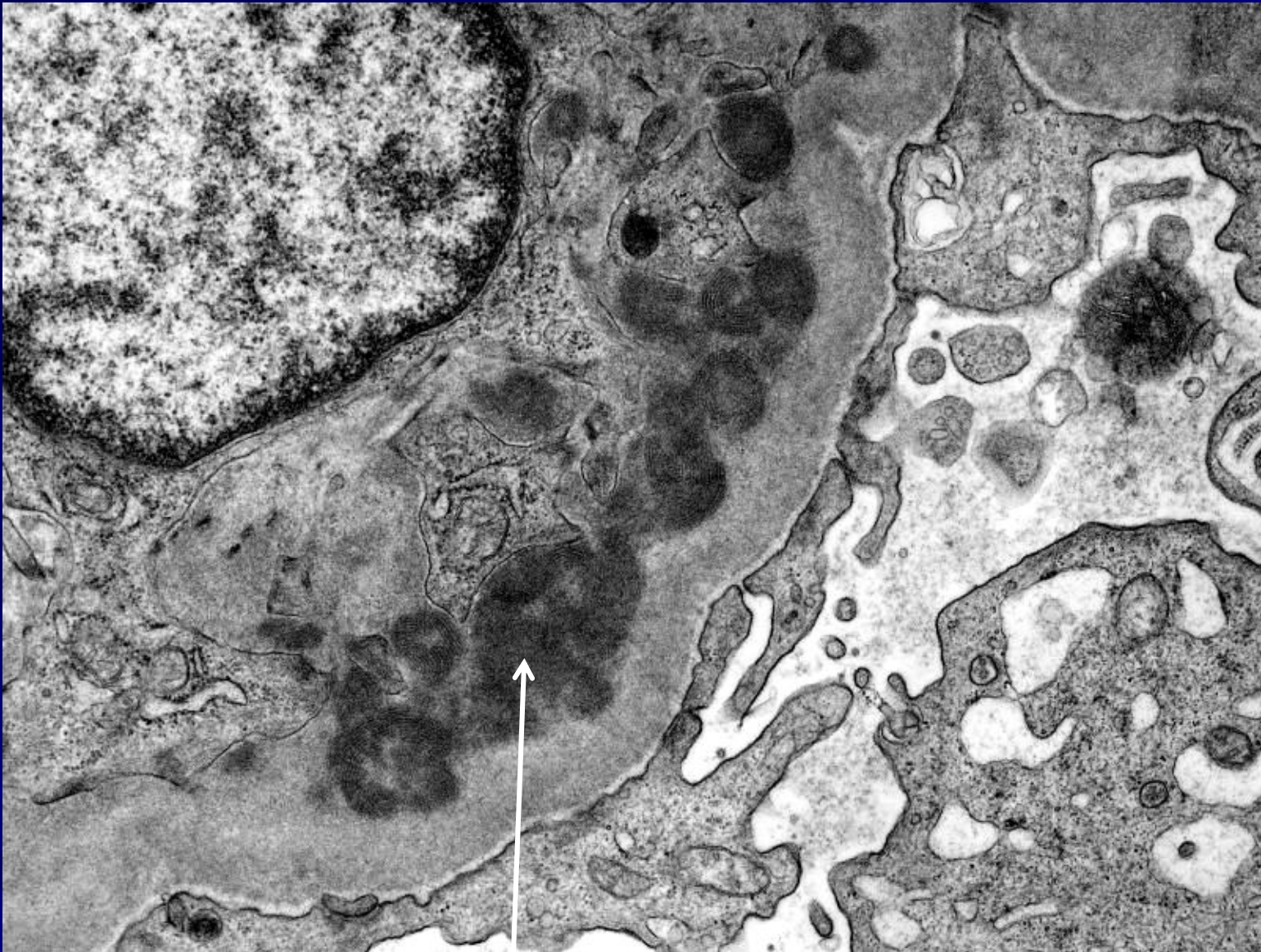
Large endothelial tubuloreticular complex

Different case – with structured deposits



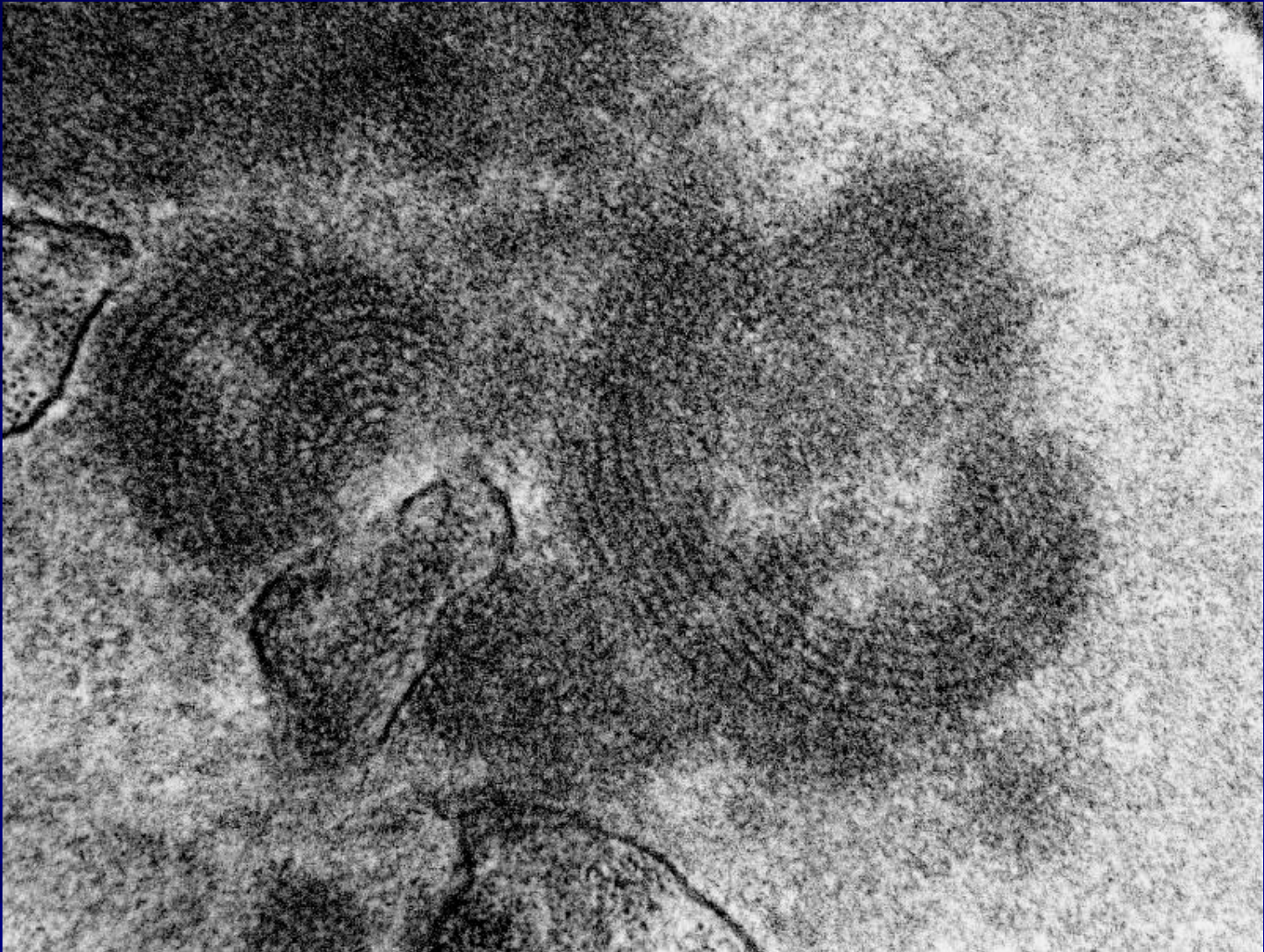
Mesangial deposits

Higher magnification of previous slide



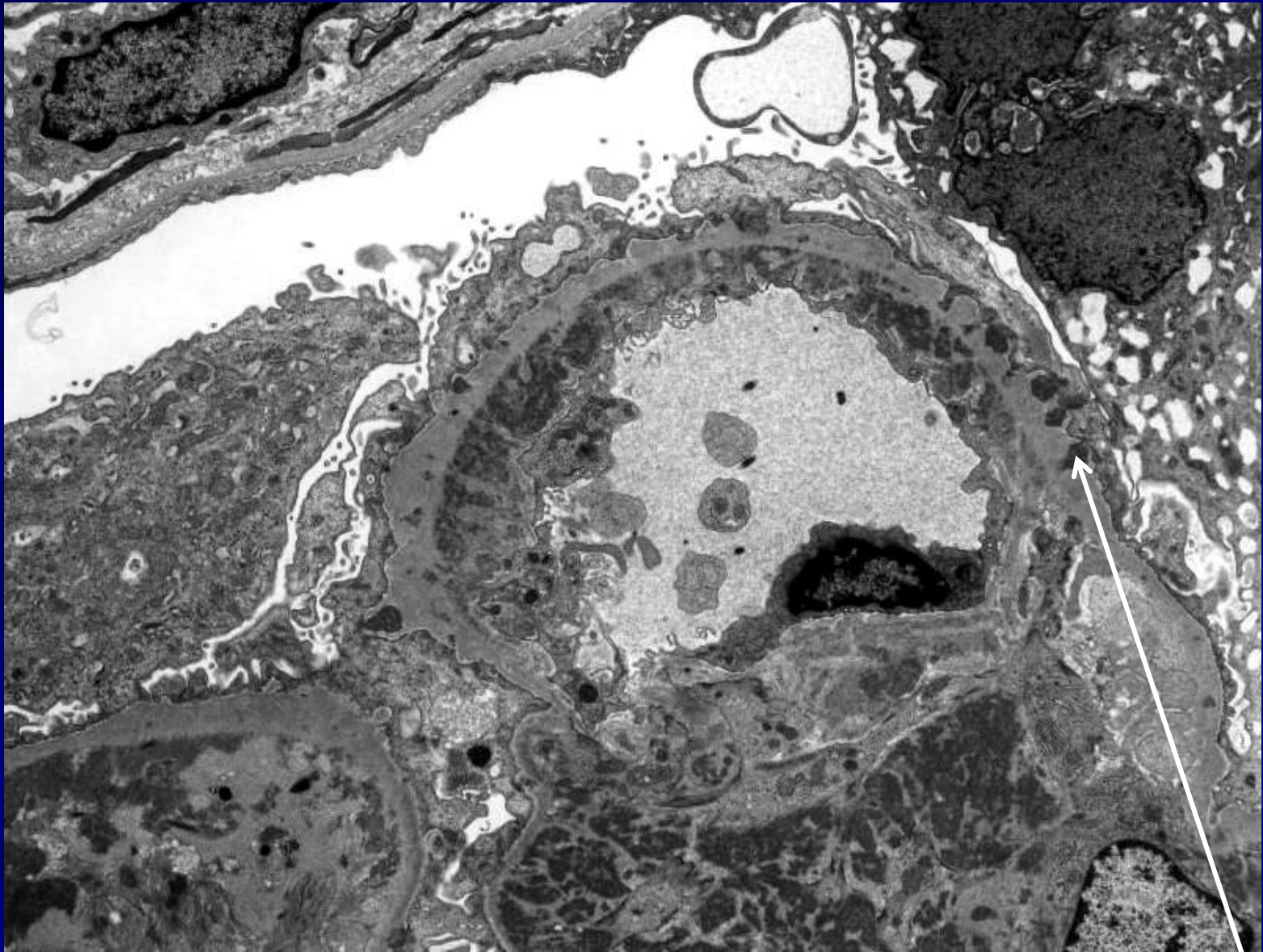
Mesangial deposits

Higher magnification of previous slide



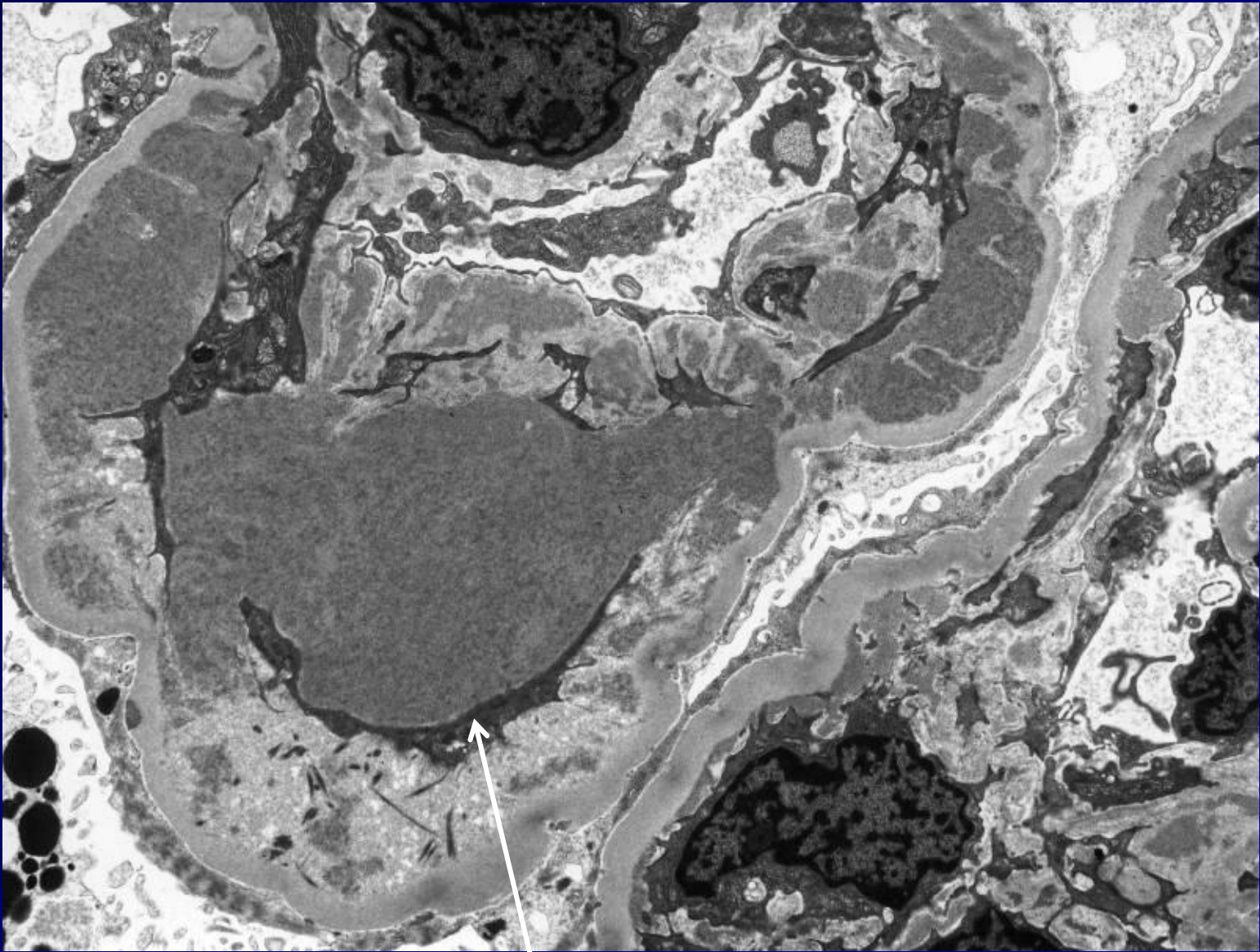
Fingerprint pattern - structured deposit

Full house EM



Mesangial
deposits

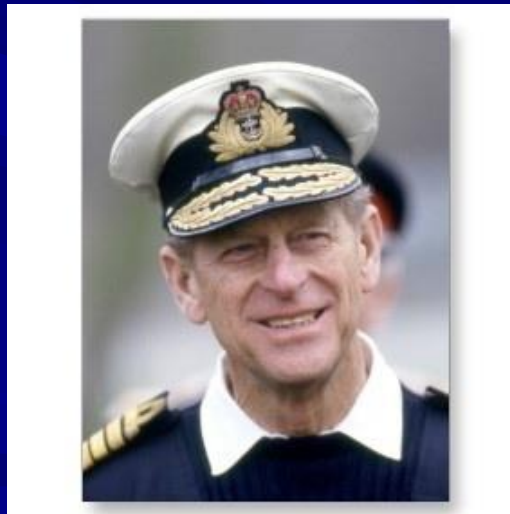
Subepithelial
deposits



Mesangial cell interpositioning

Time for a quick break?

‘The mind cannot absorb what the backside cannot endure’



Prince Philip ,The Duke of Edinburgh.