
Fibrillary Glomerulonephritis

A clinicopathologic diagnosis based on organized glomerular deposits

Light microscopy · immunofluorescence · electron microscopy · DNAJB9

Dr Abu Suraih Sakhri

MBBS, MD (Pathology)

www.abusuraihsakhri.com

Learning goals: Recognize, distinguish, integrate

- Define fibrillary glomerulonephritis (FGN) and the location of its deposits.
- Explain the characteristic light-microscopic and immunopathologic findings.
- Interpret the diagnostic roles of Congo red, DNAJB9, and ultrastructure.
- Distinguish FGN from amyloid, immunotactoid and C3-dominant diseases.
- Link biopsy findings to proteinuria, hematuria and renal function.

FGN is defined by organized glomerular fibrils

A pathologic entity, not a light-microscopic pattern alone

Where

Mesangial regions and
glomerular capillary walls

What

Nonamyloid-type fibrillar
deposits, typically Congo-
red–negative

How identified

DNAJB9 tissue staining with
IF and ultrastructural
correlation

Clinical syndrome and biopsy must be integrated

Proteinuria, hematuria or
declining kidney function



Kidney biopsy with LM, IF
and EM



DNAJB9-positive organized
deposits support FGN

FGN is uncommon among native kidney biopsies

A rare glomerular disorder

A 2019 review reports FGN in fewer than 1% of native kidney biopsies; Rarity increases the value of an integrated biopsy diagnosis.

Etiology remains incompletely established

What is established

- FGN contains fibrillary glomerular deposits.
- Deposits commonly contain immunoglobulin and complement.
- DNAJB9 is strongly associated with deposits.

What remains uncertain

- The initiating molecular event.
- Whether DNAJB9 is causal or a recruited component.
- Mechanisms governing the rate of renal progression.

FGN sits within the glomerular disease framework

Injury site

Glomerular tuft and filtering
capillary walls

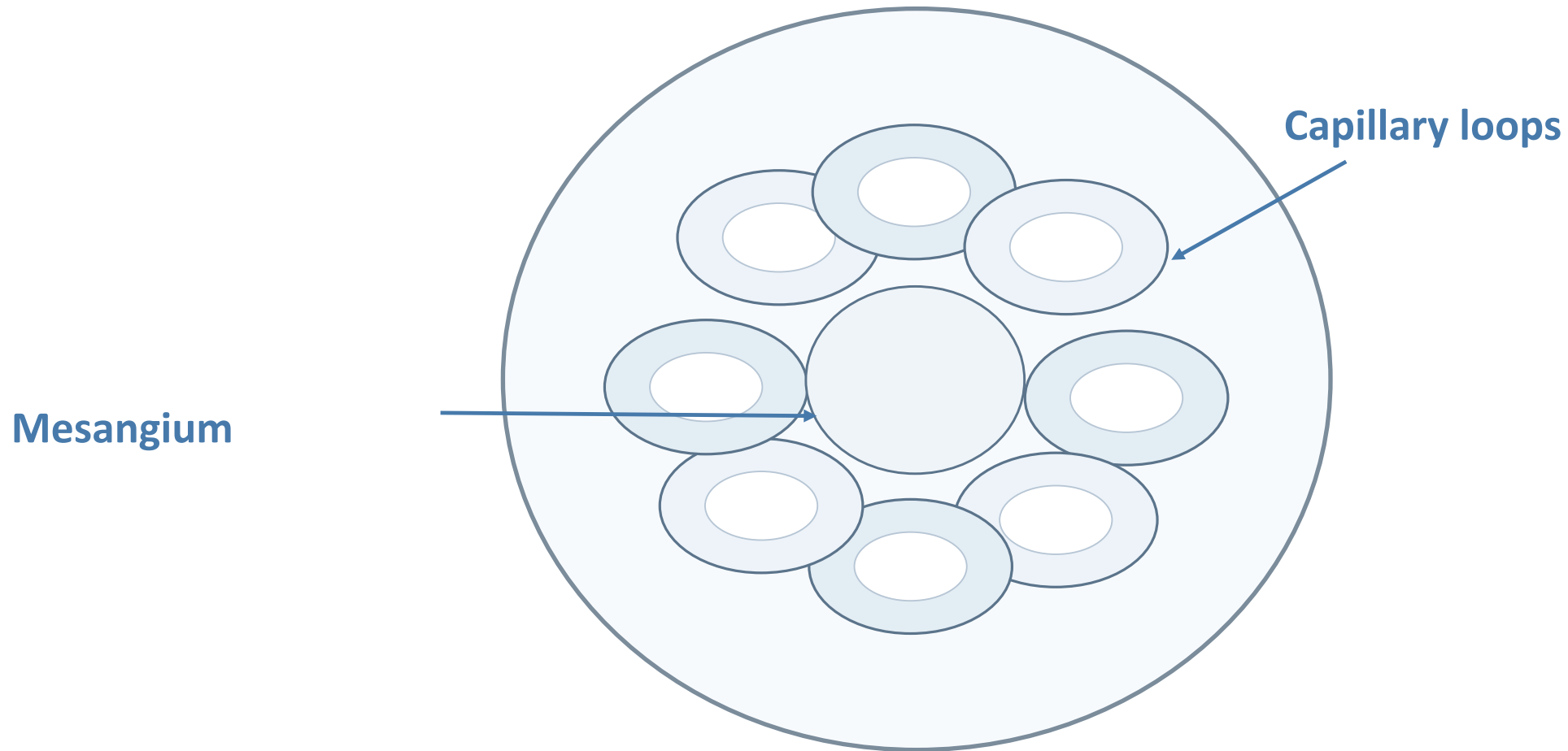
Pattern

May produce mesangial,
MPGN or crescentic
changes

Syndrome

Can produce nephrotic and
nephritic manifestations

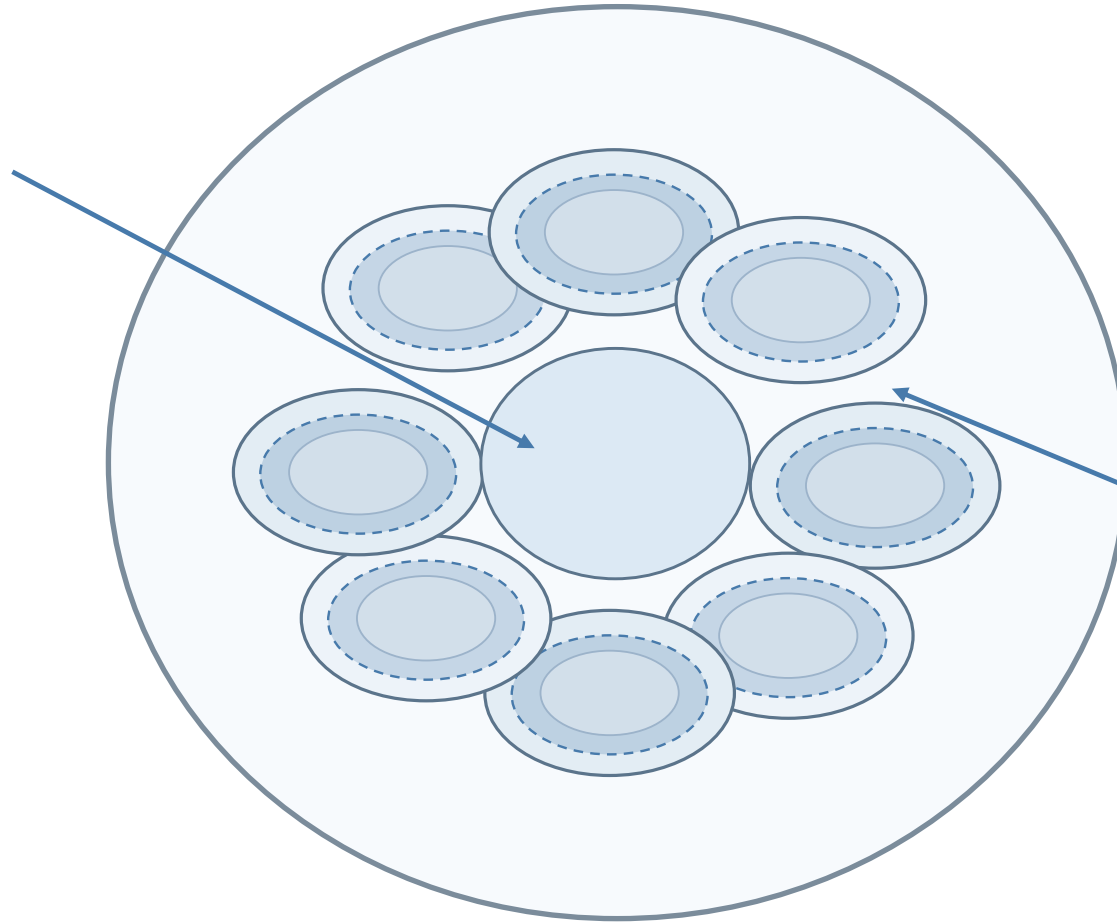
A glomerulus has distinct sites of injury



Simplified glomerular schematic — not histology

FGN deposits occupy two critical compartments

Mesangial deposits



Capillary wall deposits

Simplified glomerular schematic — not histology

The capillary wall is a three-layer filter

Capillary lumen

Fenestrated endothelium

Glomerular basement membrane

Podocyte foot processes

Urinary space

Glomerular barrier damage leads to proteinuria

Deposits and glomerular
capillary injury



Increased passage of plasma
proteins

Proteinuria; Nephrotic
syndrome may develop

Inflammatory injury can produce hematuria

Glomerular inflammation or
capillary injury



Erythrocytes escape into
urinary space



Hematuria ± red-cell casts in
nephritic syndromes

A pathologic pattern is not a single etiology

Membranoproliferative pattern

- Describes mesangial proliferation and capillary-wall remodeling.
- Can be produced by distinct disease mechanisms.
- An appearance, not itself proof of FGN.

Fibrillary glomerulonephritis

- A deposit-defined glomerular entity.
- May exhibit an MPGN pattern on LM.
- Requires immunopathologic identification.

FGN frequently has an MPGN-type lesion

- Light microscopy may show a membranoproliferative configuration.
- Mesangial expansion/proliferation and altered capillary loops can coexist.
- GBM remodeling is a tissue response to underlying glomerular injury.
- An MPGN biopsy pattern should prompt etiologic classification.

Double contours indicate capillary-wall remodeling

Subendothelial deposits /
endothelial insult



New basement-membrane
material and interposition



A double-contour “tram-
track” pattern

Mesangial changes can reshape the tuft

Cellularity

Mesangial proliferation
increases tuft cellularity

Matrix

Expanded matrix
emphasizes mesangial
regions

Lobulation

Capillary-loop architecture
may become accentuated

Crescents are another possible FGN pattern

Severe glomerular capillary injury



Leakage of fibrin and inflammatory mediators



Extracapillary cellular crescent formation

A crescent is a response, not a unique diagnosis

What a crescent means

- Severe capillary-wall injury.
- Cell accumulation in Bowman space.
- Possible rapidly progressive course.

What it does not mean

- Not exclusively FGN.
- Not sufficient to classify immune mechanism.
- Not a replacement for IF, EM and clinical workup.

Light microscopy does not establish FGN alone

Mesangial injury

Can occur in other immune-mediated glomerular diseases

MPGN pattern

Shared by immunoglobulin-related and complement-related disorders

Crescents

Shared by several rapidly progressive glomerulonephritides

The biopsy is interpreted by three modalities

Light microscopy

Defines the pattern and severity of glomerular injury

Immunofluorescence

Identifies immunoglobulins, light chains and C3

Electron microscopy

Characterizes fibril organization and location

Congo red is usually negative in FGN

Characteristic result

- Typical FGN deposits lack Congo-red positivity.
- This is a useful distinction from amyloid.
- Interpret together with ultrastructure.

Diagnostic limitation

- A negative stain does not prove FGN.
- Rare congophilic variants are described in reviews.
- DNAJB9 and deposit morphology remain important.

The Congo-red result is one diagnostic dimension

Fibrillary deposits detected



Congo red typically negative



DNAJB9, Ig profile and EM
establish identity

Immunofluorescence usually identifies IgG

- Deposits typically react for IgG.
- The staining reflects material in mesangial and capillary-wall regions.
- An immunoglobulin-positive pattern must be interpreted alongside EM.
- IgG deposition alone is not specific for FGN.

IgG4 is frequently represented in deposits

Subclassification finding

- IgG4 often predominates among IgG subclasses.
- The observation helps characterize the deposits.
- FGN remains a tissue-level diagnosis.

Avoid overinterpretation

- IgG4 is not a standalone diagnostic test.
- Subclass patterns vary across cases.
- IgG4 positivity does not explain all disease mechanisms.

Complement C3 commonly accompanies IgG

Glomerular IgG deposition



C3 may be detected in the same involved compartments



An IgG/C3 pattern supports an immune-deposit process

Both light chains are usually detectable

κ light chain

Often detectable within
glomerular deposits

λ light chain

Often detectable within the
same deposits

Interpretation

Concordant detection
supports a polytypic pattern

Monotypic-appearing deposits need verification

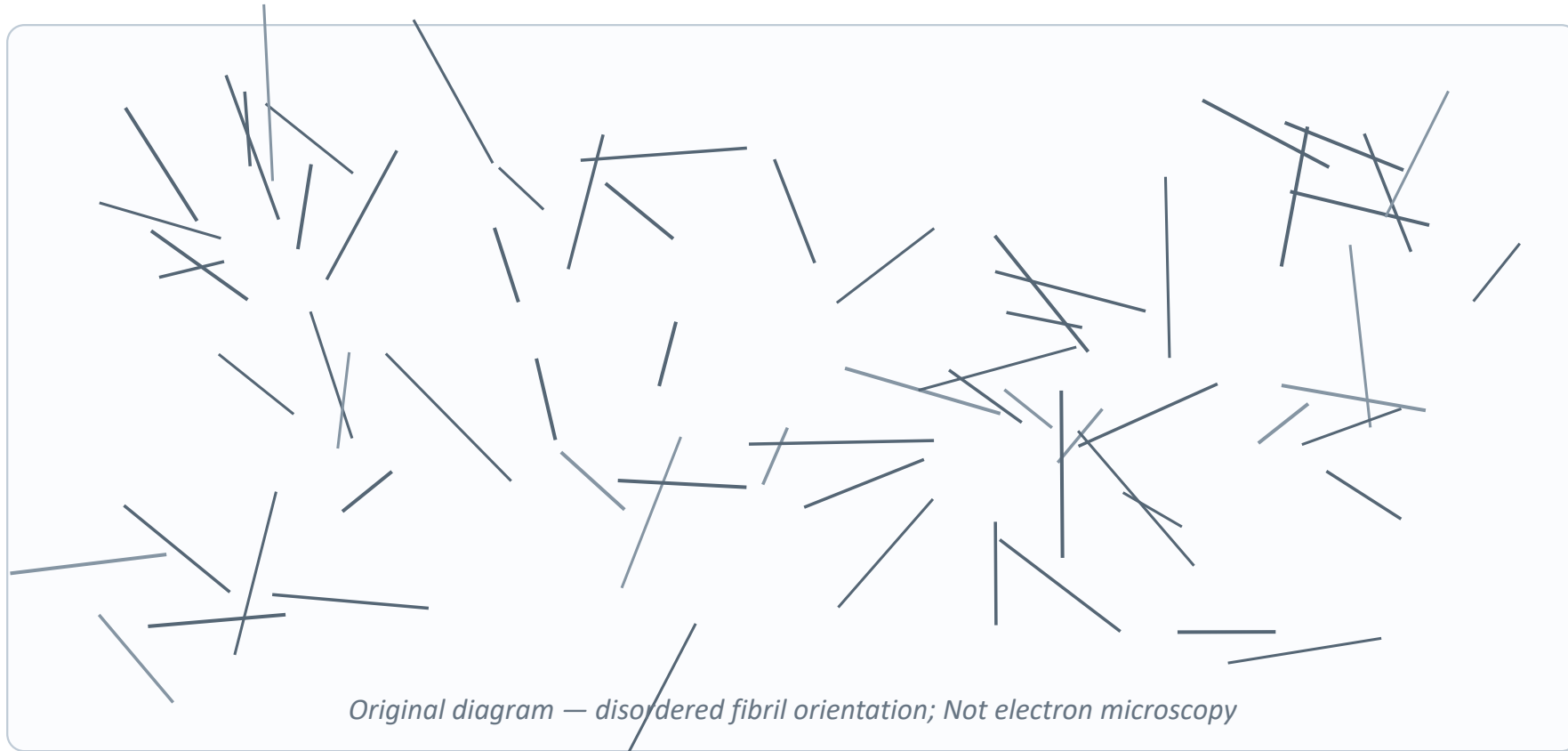
Why the issue arises

- FGN is often polyclonal but exceptions exist.
- Apparent light-chain restriction complicates classification.
- Single observations can be misleading.

Practical response

- Correlate with DNAJB9 and ultrastructure.
- Consider additional tissue studies as appropriate.
- Do not equate restriction with systemic malignancy.

Electron microscopy reveals disordered fibrils



FGN fibrils are nonbranching and randomly oriented

- Fibrils lie without a uniform parallel arrangement.
- The fibrils do not form regular hollow-core microtubules.
- This ultrastructural organization helps distinguish other deposit diseases.
- Electron microscopy assesses both deposit type and localization.

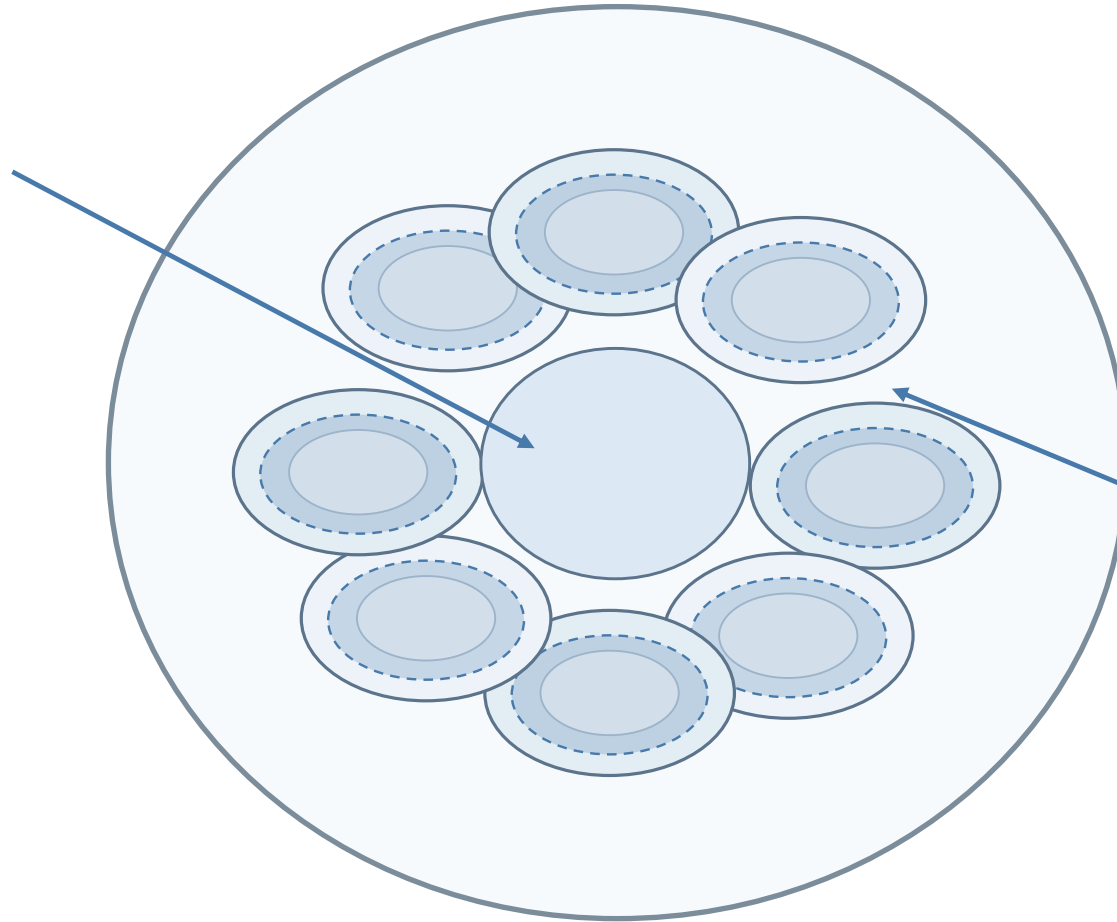
FGN fibrils have a characteristic size range

Approximately 15–25 nm in diameter

Reported in a 2019 review (mean near 20 nm). Size is a diagnostic clue, not a substitute for full ultrastructural interpretation.

Electron-dense fibrils involve mesangium and wall

Mesangial deposits



Capillary wall deposits

Simplified glomerular schematic — not histology

Amyloid is the primary fibrillar alternative

Feature	FGN	Amyloidosis
Congo red	Usually negative	Typically positive
Fibrils	Larger, disordered	Typically thinner fibrils
Immunophenotype	Usually IgG/C3 with DNAJB9	Variable by amyloid type
Confirmatory step	DNAJB9 + EM	Amyloid typing and morphology

Immunotactoid deposits show another architecture

Finding	FGN	Immunotactoid GN
Ultrastructure	Random fibrils	Organized microtubules
Hollow center	Not characteristic	May be evident
Fibril dimensions	Generally smaller	Generally larger structures
DNAJB9	Usually positive	Typically negative

DNAJB9 is a tissue biomarker of FGN

Identity

DnaJ heat-shock protein
family member B9

Location

Present within characteristic
glomerular deposits

Practical value

Immunohistochemical
staining helps identify FGN

DNAJB9 immunohistochemistry strengthens diagnosis

- DNAJB9 has high diagnostic sensitivity and specificity in studied biopsy series.
- Strong glomerular deposit staining supports FGN in the correct setting.
- The assay is particularly helpful when deposit morphology is difficult to classify.
- Interpret antibody staining with light microscopy and immunofluorescence.

DNAJB9 is diagnostic, not necessarily pathogenic

Supported

- DNAJB9 accumulates in FGN deposits.
- Tissue immunostaining is diagnostically informative.
- It belongs to a stress-response protein family.

Not established

- That DNAJB9 triggers initial injury.
- That tissue positivity defines treatment response.
- A proven DNAJB9-targeted therapy.

EM and DNAJB9 give complementary information

Question	Electron microscopy	DNAJB9 IHC
Are fibrils present?	Directly characterizes them	Does not visualize fibrils
How are deposits arranged?	Shows orientation/location	Shows tissue localization
Is this likely FGN?	Morphology supports identity	Biomarker supports identity
Can tests replace context?	No	No

Integrated diagnosis follows evidence in sequence

Identify lesion pattern on light microscopy



Characterize IgG, C3 and κ/λ by immunofluorescence



Assess Congo red and DNAJB9 staining



Use electron microscopy to evaluate organized fibrils



Correlate with clinical findings and competing diagnoses

Pitfall: Reporting MPGN without its cause

Incomplete report

- “Membranoproliferative GN” describes architecture.
- It does not specify deposit composition.
- It may obscure a treatable alternate process.

More informative report

- Describe the MPGN pattern.
- Add IF, DNAJB9 and EM characterization.
- Classify the underlying glomerulopathy.

Pitfall: A Congo-negative stain is nonspecific

Unjustified leap

- Congo red negative → FGN.
- Overlooks other Congo-negative deposits.
- Misses required immunopathologic context.

Preferred reasoning

- Look for organized fibrils.
- Assess immunoglobulin/C3 pattern.
- Confirm with DNAJB9 and EM where available.

Pitfall: Apparent monoclonality is complex

- Some reported FGN cases display monotypic deposits.
- Light-chain restriction should prompt careful technical review.
- Potential systemic paraprotein disease requires clinical correlation.
- The finding does not automatically establish a monoclonal gammopathy.

Pitfall: Interpretation without electron microscopy

What can be established

- LM shows a glomerular injury pattern.
- IF defines IgG/C3 and light chains.
- DNAJB9 strongly supports FGN.

What remains less direct

- Fibril architecture is not visualized.
- Atypical deposits may require EM.
- Do not claim unseen ultrastructural findings.

Differentiate C3-dominant glomerulopathy

Feature	FGN	C3 glomerulopathy
IF emphasis	IgG plus C3 common	C3-dominant staining
Core mechanism	Pathogenesis unresolved	Alternative complement dysregulation
Deposits	Fibrillary, DNAJB9-associated	C3-rich deposits
Workup focus	DNAJB9/EM/deposit type	Complement studies + EM

Differentiate immune-complex MPGN

Feature	FGN with MPGN pattern	Immune-complex MPGN
Light microscopy	May show MPGN	Shows MPGN
Deposit structure	Characteristic fibrils	Typically nonfibrillar dense deposits
IF	IgG, C3 often present	IgG, C3 often present
Discriminator	DNAJB9 and fibrillar EM	Etiology + nonfibrillar EM

Differentiate crescentic anti-GBM disease

Feature	Crescentic FGN	Anti-GBM GN
Crescents	Possible	Commonly prominent
IgG pattern	Deposit-associated	Linear GBM staining
EM	Fibrillar deposits	Not defined by FGN fibrils
Serology	Correlate clinically	Anti-GBM antibodies relevant

The differential is decided by multiple tests

Amyloid

Congo red, typing, fibril morphology

Immunotactoid disease

Microtubular organization on EM

Complement-mediated GN

C3-dominant immunofluorescence and workup

Nephrotic syndrome can be a clinical presentation

Glomerular filtration barrier
damage



Sustained urinary loss of
proteins



Proteinuria,
hypoalbuminemia and
edema

FGN may cause a nephritic component

- Hematuria reflects glomerular capillary injury.
- More severe inflammatory injury may produce a crescentic pattern.
- Nephritic and nephrotic features can coexist.
- Syndrome designation is not a substitute for histopathologic classification.

Renal insufficiency may progress over time

Persistent glomerular injury



Loss of functioning
glomerular capillaries and
scarring



Progressive decline in kidney
function

Histologic activity and chronic damage differ

Potentially active injury

- Cell proliferation and inflammatory injury.
- Crescents may reflect ongoing severe injury.
- May influence urgency of assessment.

Chronic remodeling

- Mesangial or capillary sclerosis.
- Loss of functioning filtration surface.
- Supports assessment of irreversible damage.

Recurrence after transplantation is recognized

- FGN can recur in kidney allografts.
- Recurrence is established and subsequent reviews.
- Recurrent deposits require accurate morphologic classification.
- The possibility of recurrence does not preclude transplantation.

Clinical associations are not universal causes

Reported associations

- Autoimmune disease.
- Hepatitis C infection.
- Some malignancies or hematologic disorders.

Critical interpretation

- Association is not proof of causation.
- Many cases lack a proven associated condition.
- Clinical investigation should be individualized.

Therapeutic evidence remains limited

- No universally established disease-specific regimen exists.
- Supportive kidney-protective care addresses blood pressure and proteinuria.
- Immunosuppressive approaches are reported, but outcomes are variable.
- Management decisions require specialist clinical assessment.

Case A: An MPGN pattern with IgG deposits

A patient has proteinuria and hematuria. Renal biopsy shows an MPGN pattern. IF detects IgG and C3.

Which tests would distinguish FGN from other causes of MPGN?

Case A: Determine the deposited material

- Assess DNAJB9 immunohistochemistry.
- Examine the organization and location of deposits by EM.
- Review κ/λ staining and Congo red.
- The MPGN pattern itself cannot complete the diagnosis.

Case B: Congo-red–negative fibrillary deposits

The biopsy contains disordered fibrils in the mesangium and capillary walls.
Congo red is negative.

What additional pattern would strengthen a diagnosis of FGN?

Case B: Recognize the immunopathologic profile

- Polyclonal IgG deposits, often with IgG4 representation.
- Concomitant C3 deposition.
- Both κ and λ light chains usually present.
- DNAJB9 immunostaining supports fibrillary GN.

Case C: Crescents plus abnormal IF staining

A biopsy contains crescents and an unusual glomerular IgG staining pattern.

Why is a crescent count or IgG stain alone inadequate for classification?

Case C: Integrate cause and injury pattern

- Crescents mark severe glomerular injury but are not specific.
- Examine IgG distribution and additional immune reactants.
- Seek fibrillary material, DNAJB9 and EM confirmation when indicated.
- Correlate with the rapidly progressive clinical course and serology.

Case D: New allograft proteinuria

A recipient transplanted for biopsy-proven FGN develops new proteinuria and deterioration of allograft function.

Which prior disease-specific finding should remain in the differential?

Case D: Consider recurrent FGN

- FGN recurrence in kidney transplants is documented.
- Clinical changes are not specific for recurrence.
- Biopsy interpretation again requires LM, IF and deposit characterization.
- DNAJB9 can help assess a suspected recurrent deposit disease.

A complete FGN biopsy report integrates evidence

Describe light-microscopic pattern and chronic damage



Record IgG/C3 and κ/λ immunofluorescence findings



State Congo red and DNAJB9 findings



Describe fibrillar ultrastructure if actually assessed



Provide an integrated diagnosis with limitations

The FGN diagnostic signature

Domain	Most characteristic finding
Deposits	Mesangial + capillary-wall fibrils
Light microscopy	Often MPGN and/or crescentic
Immunofluorescence	Usually polyclonal IgG, C3, κ and λ
Congo red	Typically negative
Tissue marker	DNAJB9 staining supports diagnosis
Clinical course	Proteinuria, hematuria, progressive dysfunction

Questions that remain open in FGN

- What initiates the formation of fibrillar deposits?
- Why does DNAJB9 accumulate within deposits?
- Which pathobiologic mechanisms predict progression?
- Which therapies can reproducibly alter long-term outcomes?

Core references and diagnostic reading

Robbins, Cotran & Kumar. Pathologic Basis of Disease. 11th ed. 2026. Chapter 20, pp. 815–836.

Rosenstock JL, Markowitz GS. Fibrillary Glomerulonephritis: An Update. Kidney Int Rep. 2019;4:917–922.

Nasr SH et al. DNAJB9 Is a Specific Immunohistochemical Marker for FGN. Kidney Int Rep. 2018;3:56–64.

Updates on the Diagnosis and Management of FGN. Adv Kidney Dis Health. 2024;31:374–383.