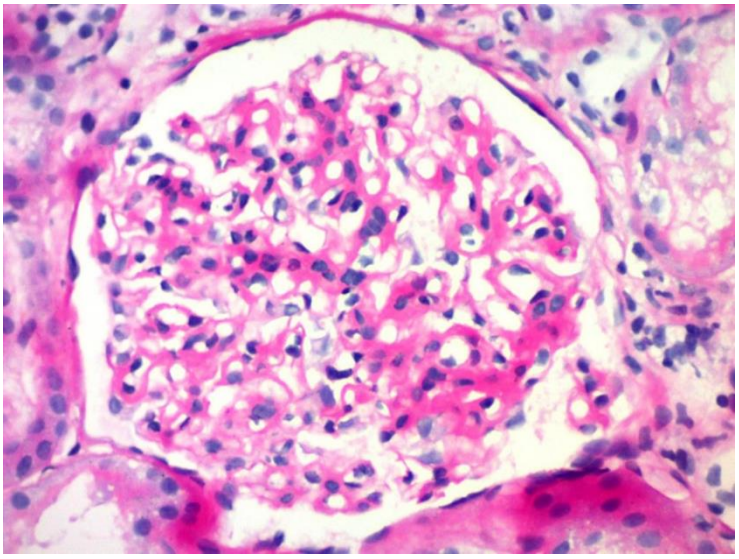
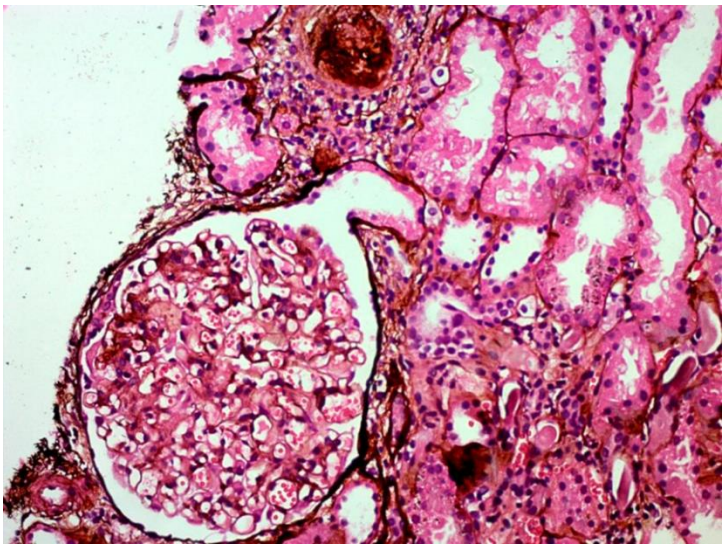
CASE PRESENTATION

CASE HISTORY

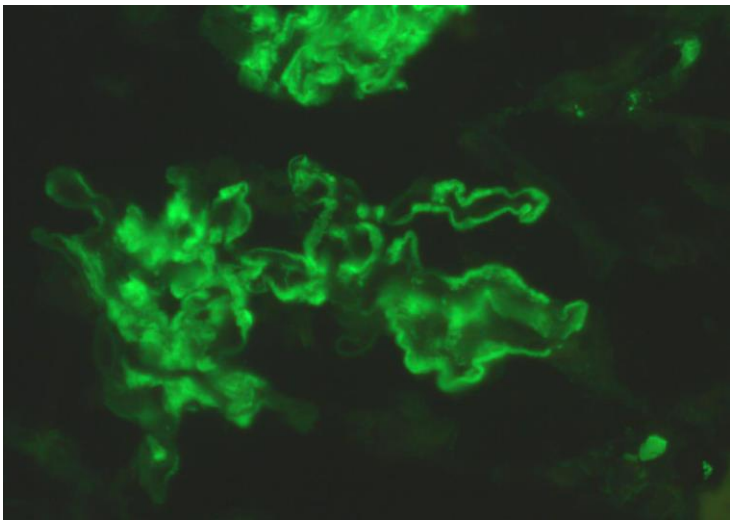
- F/54 years
- C/o dyspnea on exertion, on and off pedal oedema and generalized weakness since 1 month
- K/c/o HT, Hypothyroidism since 4-5 years – on regular treatment
- No other major illness like Diabetes
- Investigations - Hb 8.1, normal WBC and platelet count, Insidiously rising S Creat (presently 2.0), Urine routine +4 protein, absent RBCs, casts ++, Urine protein 9.2 gm/ gm Creat, S. Chol 143.5, Normal S. Protein, Albumin, Normal C3, ANA negative, HIV/HbsAg/HCV negative
- Biopsy for proteinuria and renal dysfunction



PAS, x400



Silver, x200



DIF IgG x400

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CASE PRESENTATION

MCQs

1. Based on the above, what further would you like to do to make the diagnosis?

   A. More History
   B. Further Stains / Immunofluorescence
   C. Immunohistochemistry
   D. Electron Microscopy

2. What are probable differential diagnosis?

   A. IgA nephropathy
   B. Infection associated glomerulonephritis
   C. Deposition diseases (amyloid/fibrillary/immunotactoid)
   D. Lupus nephritis

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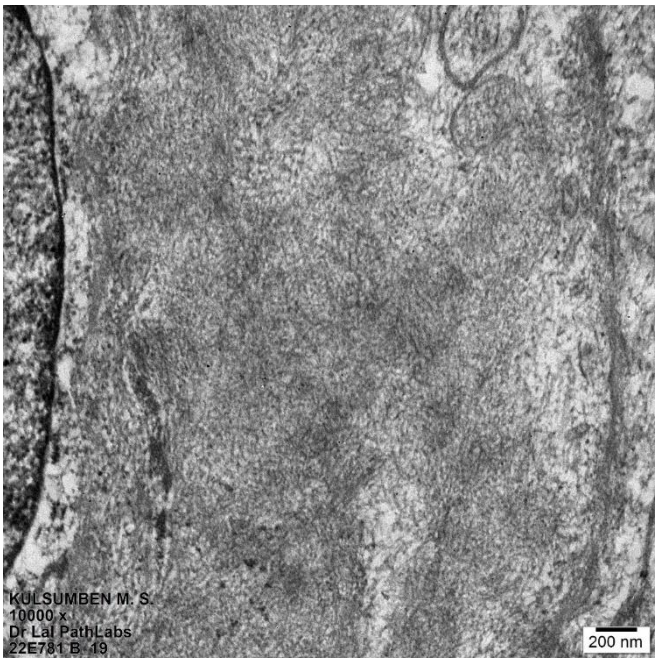
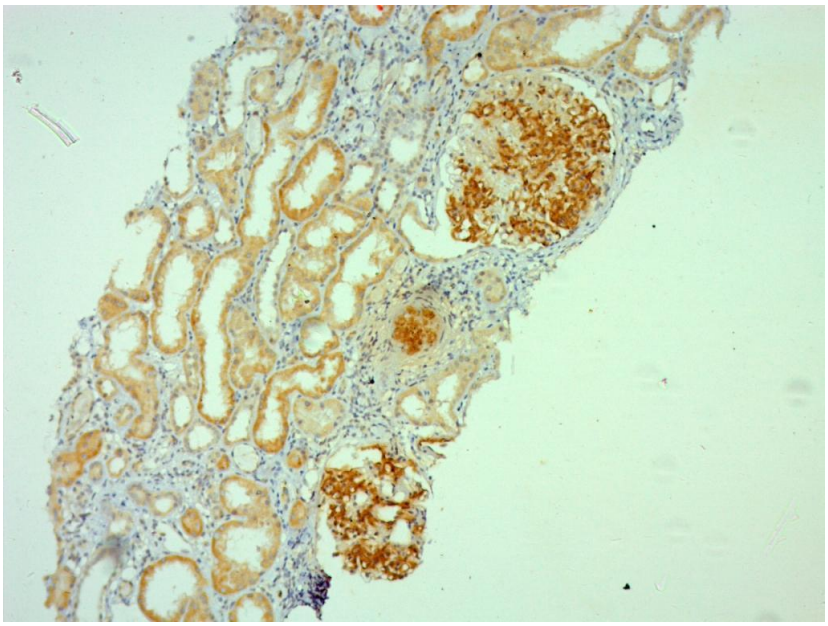
CASE PRESENTATION

DIAGNOSIS – FIBRILLARY GLOMERULONEPHRITIS WITH POLYCLONAL Ig DEPOSITS

Diagnosis was confirmed with help of Electron microscopy and IHC, DNAJB9



EM x10000



IHC DNAJB9 x200

(Courtesy Dr. Alok Sharma, LPL Delhi)

This case was put up to highlight that this diagnosis is now possible without EM also; with the help of IHC (DNAJB9).

The salient pointers in this case for this diagnosis indicators include relevant history, light microscopy and immunofluorescence features.

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CASE PRESENTATION

ANSWER TO MCQs

3. Based on the above, what further would you like to do to make the diagnosis?

    E. More History
    F. Further Stains / Immunofluorescence
    G. Immunohistochemistry
    H. Electron Microscopy

Answer – Until recently (2018), the answer would be D. Electron Microscopy. With the discovery of DNAJB9 in 2018, IHC for the same is also enough for diagnosis of this condition. Thus C. Immunohistochemistry is also correct.

4. What are probable differential diagnosis?

    E. IgA nephropathy
    F. Infection associated glomerulonephritis
    G. Deposition diseases (amyloid/fibrillary/immunotactoid)
    H. Lupus nephritis

Answer – C. Deposition Disease (Fibrillary Glomerulonephritis).

CASE PRESENTATION

DISCUSSION

Fibrillary glomerulonephritis (FGN) is categorized under the category of glomerular disease with organized deposits. It was first described in 1977 with the help of ultrastructural examination by Rosenmann & Eliakim. The term FGN was coined by Alpers et al. Duffy et al. recognized this as a distinct glomerular disease in 1983.

FGN is confined to the kidneys and is found in less than 1 % of native kidney biopsies. It is commonly seen in the **6th decade** with a **female preponderance** (66 %). At presentation, **proteinuria** is the most common finding, followed by **hematuria** (approx. 50 – 80 %), **renal insufficiency** (70 %) and **hypertension** (65 %). The medical conditions associated with this disease are Diabetes mellitus, Autoimmune conditions (Crohn's disease, lupus, Grave's disease, ITP), Malignancies, lymphoproliferative disease, Dysproteinemia, Hepatitis C etc.

On light microscopy, the **most common pattern** is **mesangial proliferative** (approx. 70 %). Other patterns described are **MPGN**, **diffuse proliferative** and exudative, **segmental necrotizing and crescentic**, **membranous** and **diffuse sclerosing**. The deposits are usually **PAS reactive, silver negative, stains** blue (with aniline blue) with **Masson trichrome** and is negative with **Congo red / Thioflavin T**.

Immunofluorescence shows **"smudgy" mesangial and linear peripheral capillary wall staining for IgG** along with C3, Kappa and Lambda light chains. **IgG subtyping** shows positivity for **IgG4 and IgG1** (IgG4 intensity more than IgG1), but absence of IgG2 and IgG3. The staining is c**onfined to glomeruli, but rarely arterioles are also stained.**

Electron Microscopy shows **organized, randomly oriented, non-branching fibrils with a mean diameter of 20 nm** (range 15–25 nm). In comparison, Amyloid deposits are 7 to 15 nm while Immunotactoid are 10 to 90 nm (frequently 25 to 35 nm).

Recently, in **2018**, 2 independent groups, identified **DNAJB9**. Staining for **DNAJB9** has been found to have a **sensitivity of 98%** and **specificity of 99%** for the diagnosis of FGN and has made it possible to **diagnose FGN in absence of electron microscopy. DNAJB9** has been shown to **co-localize with IgG** and components of the **classic complement pathway** in **glomeruli**. This suggests a **possible autoimmune pathogenesis.**

FGN has a **poor prognosis**, treatment options are currently limited, and transplant recurrence is not uncommon

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References

1. Rosenmann E, Eliakim M. Nephrotic syndrome associated with amyloid-like glomerular deposits. Nephron. 1977;18:301–308.
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