

EXTRACORPOREAL NEPHROLOGY GROUP [ECNG]

NELL -1 MEMBRANOUS NEPHROPATHY

DR VILESH VALSALAN

CONSULTANT NEPHROLOGIST AND TRANSPLANT PHYSICIAN

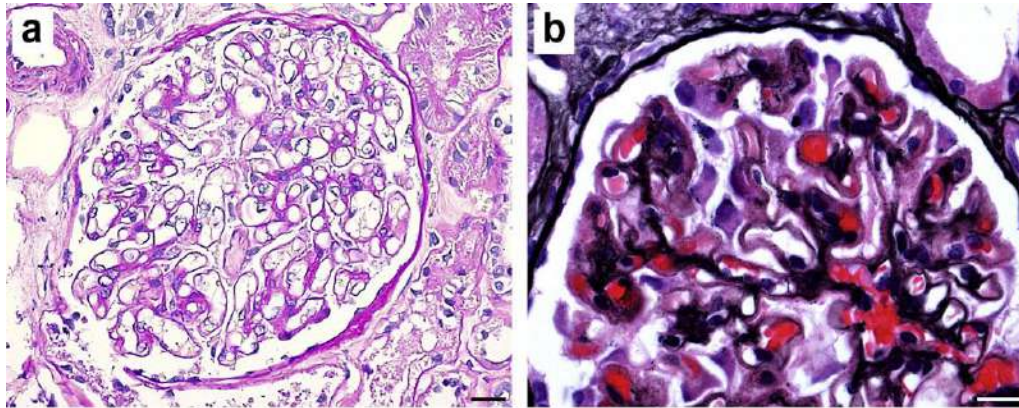
ACADEMIC CORDINATOR - ECNG

INTRODUCTION

- Neural epidermal growth factor-like protein 1 (NELL-1) is an autoantigen associated with both primary and secondary membranous nephropathy (MN) and is described **with malignancy, autoimmune diseases, lipoic acid, and traditional indigenous medicines**.
- NELL-1 is the **second most common** antigen after PLA2R in primary MN.
- NELL-1 encodes a protein kinase C-binding protein, which is expressed in the kidney tubules and rarely in the glomeruli.
- **Immunosuppression** is generally effective against NELL-1-associated MN.
- Anti-proteinuric treatment – **ACEI/ARB**. Treat the primary cause.

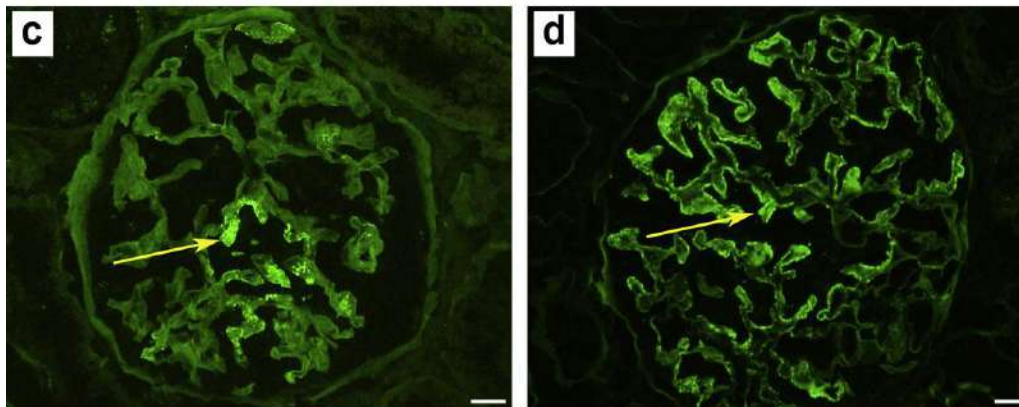
BIOPSY FINDINGS

Light microscopy:

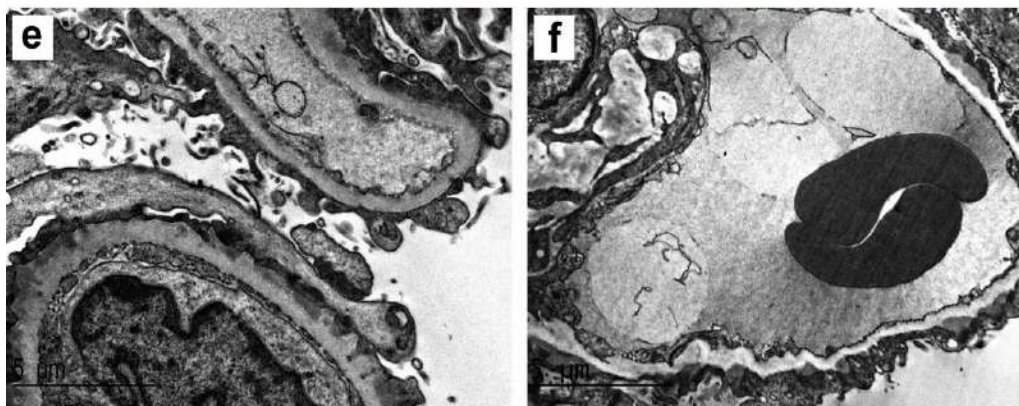


(a) Periodic acid-Schiff showing non-proliferative pattern and prominent capillary loops.

(b) Jones methenamine silver stain showing “spikes” along the glomerular basement membrane spikes and holes.

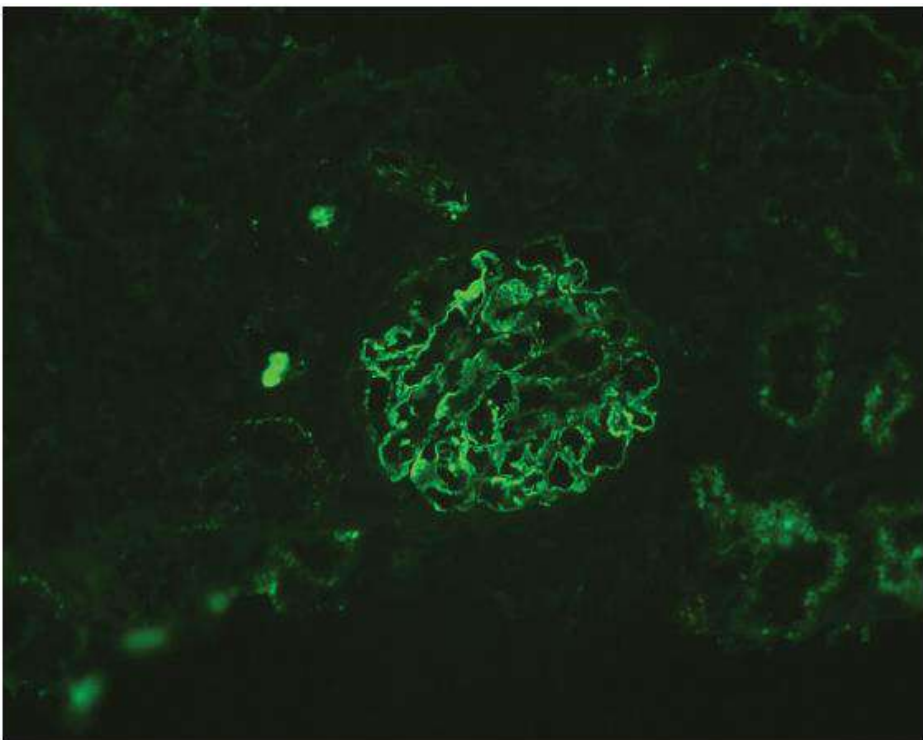


(c & d) Immunofluorescence microscopy demonstrating segmental and incomplete global IgG staining in glomeruli.

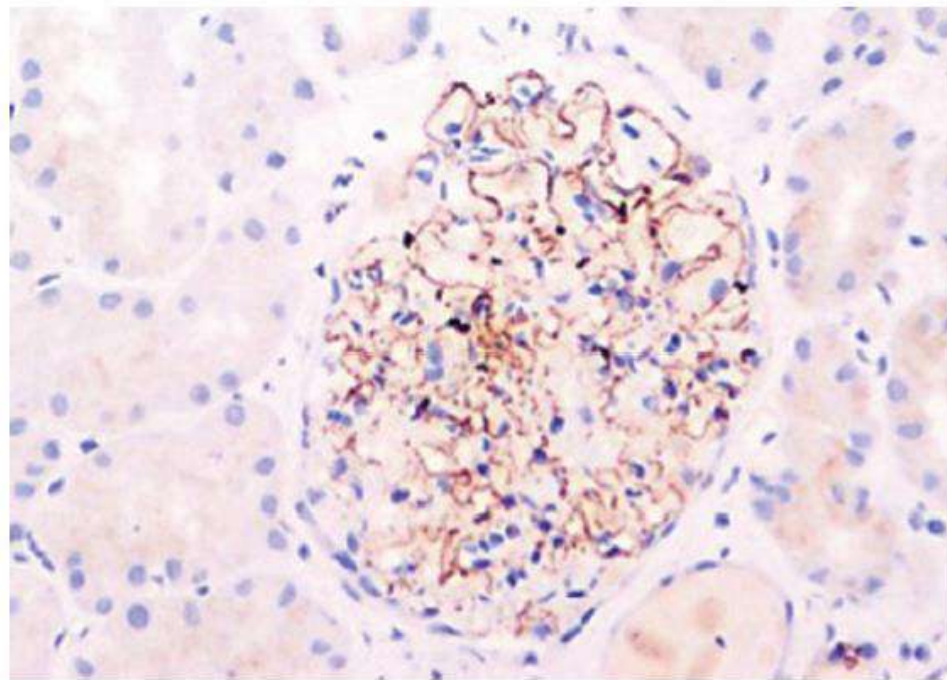


(e) Electron microscopy showing capillary loop sparing of electron-dense immune-type deposits.

(f) Immunohistochemical staining for neural epidermal growth factor-like 1 protein (NELL-1) showing segmental positivity.



NELL-1 staining on immunofluorescence (Original magnification x200). NELL-1: Neural epidermal growth factor-like 1.



NELL-1 antigen demonstration by immunohistochemistry (Original magnification x200). NELL-1: Neural epidermal growth factor-like 1.

NELL-1-associated membranous nephropathy linked to skin fairness cream use: Insights from an Indian case series



Cohort	Methods		Outcomes	
 Single Centre	 All biopsy proven PLA2R negative NELL1 positive MN	 Heavy metal screening in blood &/or urine	 13/15 NELL1MN used fairness creams	 Mercury > 10 ⁴ times acceptable limits on cream analysis
 Ambispective analysis	 Autoimmune, infection, basic malignancy workup	 Chemical analysis of creams	 Median age 30y (14-44 y) 6 ♂ & 7 ♀	 High levels of mercury in blood &/or urine in 9/11 patients
 Jul 2021-Sep 2023	 Fairness cream use	 Clinical features and outcomes	 Subtle symptoms Fatigue, frothuria	 Partial or complete remission in all with cessation of usage of cream & RAAS inhibition
 Biopsy proven NELL1 MN			 Mean proteinuria 13.3g (6.5-22.1 g) GFR preserved	 Mean time to partial remission 4.8 months and complete remission 10.3 months

Narayanan R et al, 2024
Visual abstract by Sajeesh Sivadas. X @drsajeesh1

CONCLUSION
Increasing incidence of NELL1 MN linked to use of fairness creams with high mercury content
Cessation of cream usage without immunosuppression has favourable clinical outcomes
Enhancing public awareness, physician sensitization and regulatory authority alertness is crucial

Characteristics and Outcomes of NELL1 Membranous Nephropathy (MN) in Lipoic Acid Users and Non-users



Methods and cohort



Retrospective cohort



Clinicopathologic features of NELL1 MN



70 patients



Median age 66 years



Median proteinuria 5.9 g/day



Median follow-up 11 months

NELL1 MN clinical association



Lipoic acid 36%



Heavy NSAIDs use 27%



Autoimmune diseases 23%



Malignancy 17%



Mercury 1%



No association 11%

Outcomes



All NELL1 cases

72%

Complete or partial remission in NELL1 MN



In lipoic acid users

91%

vs 62%

Remission, for > 6 months follow-up, in NELL1 MN associated with lipoic acid

4%

vs 41%

Lower immunosuppression rate in NELL1 MN associated with lipoic acid

NELL1 MN= Neural epidermal growth factor like 1 membranous nephropathy