IgA DOMINANT – INFECTION RELATED GLOMERULONEPHRITIS [IGA-IRGN]

DR VILESH VALSALAN

CONSULTANT NEPHROLOGIST AND TRANSPLANT PHYSICIAN

ACADEMIC CORDINATOR – EXTRA CORPOREAL NEPHROLOGY GROUP [ECNG]

INTRODUCTION

- Infection related - IgA dominant glomerulonephritis :- umbrella term for proliferative glomerulonephritis induced by *S. aureus* as well as pathogens in addition to *S. aureus*.

- Male-to-female ratio of 2:1 and age predominantly above 50 years.

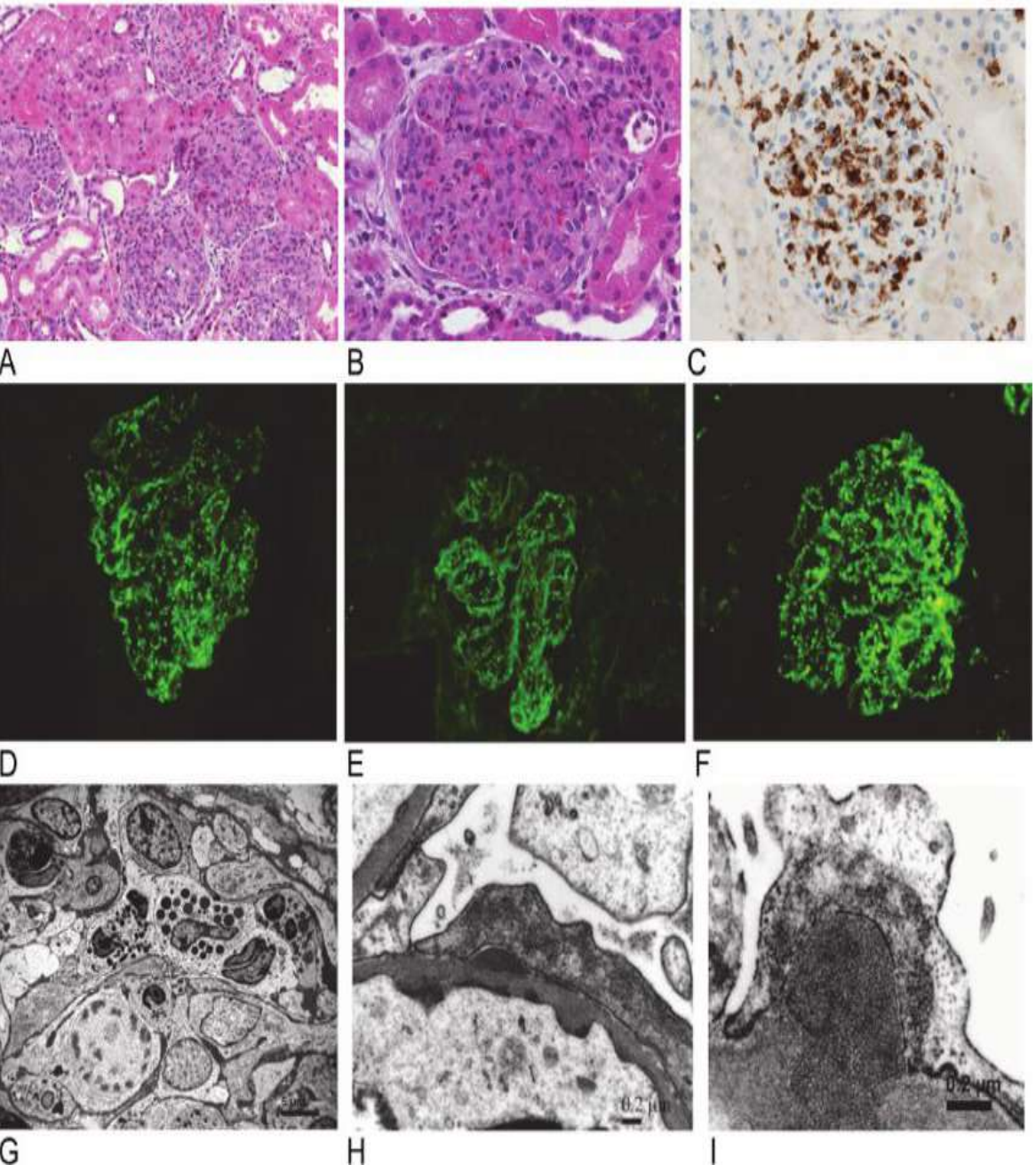
- Risk Factors : Diabetes, immunocompromised.
  Active infections : Skin infections , Osteomyelitis Endocarditis, Abscess.

- IgA dominant PIGN typically occurs shortly after an active infection and presents with acute kidney injury, hematuria and proteinuria.

- Pathogenesis : Infection → bacterial antigens → IgA immune response → IgA immune complexes → glomerular deposition → complement activation → glomerular inflammation → AKI.

Post Streptococcal GN	Staphylococcal Associated Infectious GN	IgA Nephropathy	C3 Nephropathy (MPGN)
Occurs 1-3 weeks post infection	Concurrent infection	Synpharyngitic: Concurrent infection	May flare with infection
Low C3: 90% Normalizes by 8-10 weeks post infection	Low C3: 80% Normalizes by 8-10 weeks post infection	Normal C3	Persistent Low C3
Diffuse endocapillary proliferative and exudative GN	Diffuse endocapillary proliferative and exudative GN	Mesangial Proliferative GN	MPGN
C3/ IgG Starry sky pattern	C3/ IgA or IgG Starry sky pattern	IgA dominant or codominant +/- C3	C3 dominant +/- IgG
Subepithelial Humps	Subepithelial Humps	Mesangial deposits	Variable: • Mesangial • Subendothelial • Intramembranous
Good renal prognosis	Poor renal prognosis	Good prognosis	Persistent/ recurrent GN

RENAL BIOPSY FINDINGS



(A) Five enlarged glomeruli in IgA-dominant acute PSGN showing diffuse global endocapillary hypercellularity.

(B) An enlarged glomerulus with global closure of the capillary lumina caused by endogeneous predominantly mesangial cell proliferation and infiltrating blood-borne monocytes and polymorphonuclear leukocytes.

(C) Numerous brown stained CD68-positive monocytes infiltrating the enlarged hypercellular glomerular tuft.

D-F) Immunofluorescence microscopy showing granular mesangial and glomerular capillary wall immune deposits with a “starry-sky” pattern of IgA dominance.

(G)Glomerular lobule showing a pronounced endocapillary hypercellularity caused by proliferating predominant mesangial cells.

(H) Discrete electron dense subendothelial and sub epithelial deposits.

(I) A solitary hump-shaped electron dense deposit on the outer aspect of the glomerular basement membrane

Feature	IgA-IRGN	IgA nephropathy
Age	Older adults	Younger patients
Infection	**Active infection present**	Often mucosal infection trigger but not active
Complement	**Low C3 common**	Usually normal
Histology	Endocapillary proliferation, neutrophils	Mesangial proliferation
Deposits	IgA + strong C3	IgA dominant
EM	Subepithelial humps	Mesangial deposits

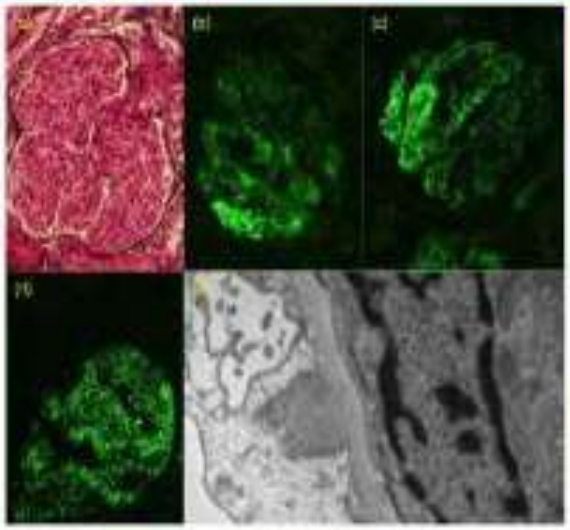
IgA-dominant infection-associated glomerulonephritis in the pediatric population

Graphical Abstract

HYPOTHESIS: IgA dominant infection-associated glomerulonephritis (GN) in children has better prognosis than in adults.

DESIGN & OUTCOMES:

Cohort study:
Review of 1,117 pediatric native kidney biopsies from 2005-2015.
Biopsies with IgA-dominant GN with features related to infection identified.



Features of IgA-dominant infection-associated GN: exudative, IgA, C3, hump-type deposits

9 patients identified (0.8%)

7 recovered

2 kidney failure

1 progression of CKD

2^0 FSGS without deposits

CONCLUSIONS: Pediatric IgA-dominant infection-associated glomerulonephritis is rare and shows a generally favorable prognosis, in contrast to poor outcomes in adults with severe comorbidities.

Grosser et al. 2021

Pediatric Nephrology
Journal of the International Pediatric Nephrology Association
IPNA

Pediatric population has favorable prognosis compared to adults [worse prognosis]

MANAGEMENT

- Search aggressively for infection.
- Start appropriate antibiotics immediately [Gram positive cover]
- Provide supportive renal care (BP, diuretics, dialysis if needed).
- Avoid steroids during active infection.
- Consider steroids only if GN persists after infection resolution.

- Risk factors for CKD progression: Older age , diabetes , delayed infection treatment , crescents on biopsy and severe AKI.

- About 30–50% may progress to CKD or ESKD.

The Diagnostic Conundrum of Glomerular Crescents With IgA deposits

ISN INTERNATIONAL SOCIETY OF NEPHROLOGY

Methods & cohort

Ohio State Wexner Medical Center

Native kidney biopsies
- ✓ Glomerular IgA deposits
- ✓ Crescents
- ✓ LN excluded

Identified from biopsy archives

Clinical follow-up in a subset at 1yr

Results

Clinicopathologic cases
N = 285
IgA vasculitis (n = 7) not included

- IgAN n = 108
- SAGN/IRGN n = 43
- ANCA-GN n = 26
- Group X (unclassifiable) n = 101

Atypical combination of clinicopathologic features and lack of definitive active infection resulted in high Group X count

Follow-up (n = 72/101)

	IgAN	SAGN/IRGN	ANCA-GN	Other
Clinician's working diagnosis	43%	22%	28%	7%

Variable treatment approaches were identified; supportive/antibiotics vs immunosuppression

Renal loss higher in the no-immunosuppression group *(but not statistically significant)*

C3-dominant staining & possibility of recent infection was unique to no-immunosuppression group

LN: lupus nephritis; SAGN/IRGN: staphylococcus or other infection-associated-GN; ANCA-GN: anti-neutrophil cytoplasmic antibody associated-GN

KI REPORTS
Kidney International Reports

Kitamura M et al. 2023

Visual abstract by:
Sophia Ambruso, DO
@Sophia_kidney

Conclusion Diagnostic overlap may remain unresolved in a substantial number of kidney biopsies with glomerular crescents and IgA deposits. A case-by-case approach, appropriate antibiotics if infection is ongoing, and consideration for cautious immunosuppressive treatment for progressive renal dysfunction may be needed for best chance of renal recovery.