IgA Nephropathy and Atypical Anti-GBM Disease: A Rare Dual Pathology in a Pediatric Rapidly Progressive Glomerulonephritis

Varun Bajaj\textsuperscript{a}    Shilpi Thakur\textsuperscript{a}    Adarsh Barwad\textsuperscript{a}    Aditi Sinha\textsuperscript{b}    Arvind Bagga\textsuperscript{b}    Geetika Singh\textsuperscript{a}

\textsuperscript{a}Department of Pathology, All India Institute of Medical Sciences, New Delhi, India; \textsuperscript{b}Division of Pediatric Nephrology, Department of Nephrology, All India Institute of Medical Sciences, New Delhi, India

Keywords
IgA nephropathy · Anti-GBM disease · Rapidly progressive glomerulonephritis · Rare disease · Crescentic glomerulonephritis

Abstract

Introduction: Anti-GBM nephritis in the pediatric age group is exceedingly rare with concurrent additional pathologies being even rarer. Tissue diagnosis requires a combination of crescentic histomorphology, immunofluorescence showing “paint brush stroke” pattern of linear IgG or rarely IgA, and serum anti-GBM antibodies subject to the disease course and treatment. The authors describe one such case with a dual pathology involving IgA nephropathy and atypical anti-GBM disease. Case Presentation: A 13-year-old girl presenting with features of rapidly progressive glomerulonephritis underwent a renal biopsy showing a mesangioproliferative histology with crescents and an immunofluorescence pattern indicating a dual pathology of IgA nephropathy and anti-GBM nephritis. Additional ancillary testing including staining for IgG subclasses and galactose-deficient IgA (KM55) helped to confirm the diagnosis. She responded to steroid pulses and plasma exchange therapy, was off dialysis after 8 weeks with a serum creatinine level of 1.5 mg/dL, and however remains proteinuric at last follow-up. Conclusion: Concurrent anti-GBM nephritis and IgA nephropathy is a rare occurrence and possibly arises from a complex interaction between the anti-GBM antibodies and the basement membrane unmasking the antigens for IgA antibodies. Additional newer techniques like immunofluorescence for KM55 are helpful in establishing the dual pathology.

Introduction

Pediatric anti-glomerular basement membrane (anti-GBM) disease is a rare occurrence accounting for 0.5% cases of end-stage renal disease in pediatric population [1]. Most cases in the pediatric age group tend to occur in teenagers with a male preponderance [2–6] with the youngest patient being 11 months of age [7]. It results from antibodies directed against NC1 domains of alpha 3 type IV collagen, and in its typical form presents with disruptive GBM necrotizing lesions/crescents in the kidney and pulmonary hemorrhage [8]. Tissue diagnosis re-
IgA Nephropathy and Atypical Anti-GBM Disease

Fig. 1. a Light microscopy showing glomeruli in various stages of sclerosis ranging from open with mesangial hypercellularity to sclerosed (*) with overlying crescent (arrow) (PAS stain, ×10). b Silver stain showing a cellular crescent with Bowman’s capsule disruption (arrow), adjacent glomeruli showing variable sclerosis (Jones Silver Methenamine stain, ×40). c Immunofluorescence for IgG shows “paint brush stroke” linear deposition of IgG (3+). d IgA shows mesangial deposits (2–3+) with capillary wall extension. e KM55 performed shows mesangial positivity with capillary wall extension (3+). f Similar linear capillary wall immunofluorescence observed in kappa (3+) (f) and lambda (3+) (g) (arrow) along with mesangial deposits more so in lambda compared to kappa. IgG subclasses show capillary wall linear deposition of IgG1 (3+) (h) and IgG4 (2+) (i).

Case Report

The patient is a 13-year-old girl who presented with generalized puffiness and cola-colored urine for 2 weeks associated with oliguria and headache for 1 week. There was no history of rash, arthralgia, oral ulcers, nasal discharge or stuffiness, cough, dyspnea, or hemoptysis; past history was not contributory. Physical examination did not reveal any abnormality except mild edema and hypertension stage 1 (130/90 mm Hg). Hematological and biochemical investigations indicated microcytic hypochromic anemia (hemoglobin 7.4 g/dL without schistocytes on peripheral smear), total leukocyte count 8,200/mm³, platelet count 400 × 10³/mm³, deranged renal function (urea 69 mg/dL, creatinine 3.4 mg/dL), and...
exchange, cyclophosphamide pulse (500 mg/m²) was also initiated (1 mg/kg/day). Once the child was shifted to alternate day plasma dose of 140 mg/kg (6 doses) and later switched to oral prednisolone formed with continued methylprednisolone pulses to a cumulative day) of double volume therapeutic plasma exchange were performed.

Immunofluorescence and ELISA, however was negative. Chest radiograph showed no evidence of pulmonary involvement except (patient being a minor) for publication of this case report and any accompanying images. Ethical clearance in this case was not sought as this was a single case, and all investigations performed were a part of the patient workup and diagnosis and were provided to the patient, and no additional diagnostic material was obtained for research purposes.

Written informed consent was obtained from the patient’s parent (patient being a minor) for publication of this case report and any accompanying images. Ethical clearance in this case was not sought as this was a single case, and all investigations performed were a part of the patient workup and diagnosis and were provided to the patient, and no additional diagnostic material was obtained for research purposes.

The authors declare no conflicts of interest.
IgA Nephropathy and Atypical Anti-GBM Disease

Funding Sources

The authors have not received any external funding for this report.

Author Contributions

Conception and design of the work: Geetika Singh and Varun Bajaj. Data collection and imaging: Varun Bajaj and Shilpi Thakur. Data analysis and interpretation: Geetika Singh, Adarsh Barwad, and Varun Bajaj. Drafting the article: Geetika Singh and Varun Bajaj. Critical revision of the article: Geetika Singh and Aditi Sinha. Final approval of the version to be published: Geetika Singh, Aditi Sinha, and Arvind Bagga.

Data Availability Statement

All data pertaining to the case have been included in the manuscript and are part of the case report.

References

1. 2014 USRDS Annual Data Report, vol. 2. Chapter 7: pediatric ESRD. Am J Kidney Dis. 2015. https://doi.org/10.1053/j.ajkd.2015.04.032.
2. Master Sankar Raj V, Warnecke D, Roberts J, Elhadi S. Antiglomerular basement membrane disease in a pediatric patient: a case report and review of the literature. Case Rep Nephrol. 2017;2017:1.
3. Levin M, Rigden SPA, Pincott JR, Lockwood CM, Barratt TM, Dillon MJ. Goodpasture’s syndrome: treatment with plasmapheresis, immunosuppression, and anticoagulation. Arch Dis Child. 1983;58(9):697–702.
4. Boven K, Miljoen HPJ, Van Hoeck KJ, Van Marck EA, Van Acker KJ. Anti-glomerular basement membrane glomerulopathy in a young child. Pediatr Nephrol. 1996;10(6):745–7.
5. Williamson SR, Phillips CL, Andreoli SP, Nai- lescu C. A 25-year experience with pediatric anti-glomerular basement membrane disease. Pediatr Nephrol. 2011;26(1):85–91.
6. Bakkaloglu SA, Kasapkara CS, Soylemezoglu O, Peru H, Fidan K, Hasanoglu E, et al. Successful management of anti-GBM disease in a 5 1/2-year-old girl. Nephrol Dial Transplant. 2006;21(10):2979–81.
7. Bigler SA, Parry WM, Fitzwater DS, Baliga R. An 11-month-old with anti-glomerular basement membrane disease. Am J Kidney Dis. 1997;30(5):710–2.
8. McDaid SP, Pusey CD. Anti-glomerular basement membrane disease. Clin J Am Soc Nephrol. 2017;12(7):1162–72.
9. Lee M, Suzuki H, Kato R, Fukao Y, Nakayama M, Kano T, et al. Renal pathological analysis using galactose-deficient IgA1-specific monoclonal antibody is a strong tool for differentiation of primary IgA nephropathy from secondary IgA nephropathy. CEN Case Rep. 2021;10(1):17–22.
10. Suh KS, Choi SY, Bae GE, Choi DE, Yeo MK. Concurrent anti-glomerular basement membrane nephritis and IgA nephropathy. J Pathol Transl Med. 2019;53(6):399–402.
11. Ge YT, Liao JL, Liang W, Xiong ZY. Anti-glomerular basement membrane disease combined with IgA nephropathy complicated with reversible posterior leukoencephalopathy syndrome: an unusual case. Am J Case Rep. 2015;16:849–53.
12. Gupta Y, Swain M, Gowrishankar S. Antiglomerular basement membrane disease combined with IgA nephropathy. Indian J Nephrol. 2019;29(5):375–7.
13. Trpkov K, Abdulkareem F, Jim K, Slez K. Recurrence of anti-GEM antibody disease twelve years after transplantation associated with de novo IgA nephropathy. Clin Nephrol. 1998;49(2):124–8.
14. Kamimura H, Honda K, Nitta K, Horita S, Kobayashi H, Uchida K, et al. Glomerular expression of α2(IV) and α5(IV) chains of type IV collagen in patients with IgA nephropathy. Nephron. 2002;91(1):43–50.
15. Wang A, Wang Y, Wang G, Zhou Z, Xun Z, Tan X. Mesangial IgA deposits indicate pathogenesis of anti-glomerular basement membrane disease. Mol Med Rep. 2012;5(5):1212–4.
16. Yasutake J, Suzuki Y, Suzuki H, Hiura N, Yanagawa H, Makita Y, et al. Novel lectin-independent approach to detect galactose-deficient IgA1 in IgA nephropathy. Nephrol Dial Transplant. 2015;30(8):1315–21.
17. Noël LH, Aucouturier P, Monteiro RC, Preud’homme JL, Lesavre P. Glomerular and serum immunoglobulin G subclasses in membranous nephropathy and anti-glomerular basement membrane nephritis. Clin Immunol Immunopathol. 1988;46(2):186–94.