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Infant onset systemic lupus erythematosus presenting as nephrotic syndrome

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ABSTRACT

Background: Membranous nephropathy (MGN) is one of the most common glomerular disease seen among adults. However, it is a rare histological presentation in pediatric population. In contrast to MGN in adults where primary form is known to be the leading subtype of the disease, secondary cause is more prevailing in children.

Case Presentation: We describe a case of an infant presenting with nephrotic syndrome (NS) and negative serology work-up. Kidney biopsy showed the picture of severe diffuse MGN confirmed by light, immunofluorescence and electron microscopy studies. "Full-house" pattern by immunofluorescence, numerous well-demarcated sub-epithelial deposits and tubuloreticular inclusions strongly suggested type V lupus nephritis.

Conclusions: NS due to MGN is rarely seen in infancy. Secondary causes such as autoimmune disease or systemic infection need to be considered for appropriate management.

Implication for health policy/practice/research/medical education:

Membranous glomerulonephritis is uncommon in children and in contrast to adults, is commonly due to secondary causes. Therefore, extensive investigations in children with membranous nephropathy (MGN) is necessary to rule out the underlying disorders, such as systemic lupus erythematosus or infections.

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1. Introduction

Membranous glomerulonephritis (MGN) is characterized by a progressive renal disease with nephrotic syndrome (NS). It rarely affects pediatric population, and is particularly uncommon in infants. MGN is known to be due to a secondary cause in this population. The clinical picture of MGN in children varies from sub-nephrotic proteinuria to classic NS that can occur with hematuria (1). Kidney biopsy is the golden standard for establishing the morphological diagnosis. Pathomorphological presentation is characterized by formation of epimembranous deposits along glomerular basement membranes. However, the histological features are shared between primary and secondary MGN. As illustrated

in the case presented here, we recommend full clinical assessment of infants presenting with MGN to rule out the secondary causes.

2. Case Presentation

A 2-month old girl presented to the emergency room with 2 day history of melena and bruises. Her physical examination was significant for edema and generalized petechiae and ecchymosis. The mother's obstetric and past medical history were unremarkable. Laboratory tests revealed a coombs-positive normochromic anemia, thrombocytopenia, low serum complement levels (C3/C4/CH50), normal renal function with nephrotic-range proteinuria and

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microscopic hematuria. She received intravenous immunoglobulin (IVIg) and IV methylprednisolone with partial response. Her urine protein/creatinine was 14076 mg/g, serum albumin and protein were 1.5 g/dL and 3.6 g/dL respectively. Serum creatinine and blood pressure were normal. All serological tests including ANA and anti-dsDNA were negative, in both the patient and her mother.

Renal biopsy showed diffuse proliferative glomerulonephritis (PGN) with marked mesangial and endocapillary hypercellularity. Glomerular basement membranes were thickened with silver-positive epimembranous spike-like extension (Figure 1a-d). Immunofluorescence showed “full-house” pattern. Electron microscopy revealed sub-epithelial deposits consistent with MGN. Many tubuloreticular inclusions were identified (Figure 2a-c). Accordingly, cyclosporine was added to oral prednisone resulting in complete remission of NS within few weeks.

3. Discussion

MGN is rare in young children (2). Unlike adults, MGN in children occurs most frequently secondary to systemic infections or autoimmunity (3). Our case presented with steroid resistant NS and her kidney biopsy unequivocally demonstrated characteristic immune-complex deposits of MGN in the context of a PGN with features of lupus nephritis. This morphologic picture strongly suggests the diagnosis of type V lupus nephritis (according to ISN/RPS 2004 lupus nephropathy classification). However, patient's age, clinical picture and persistently negative serology raises the differential diagnosis of a monogenic SLE or lupus-like phenotype caused by mutations in the genes involved in complement pathway (C1q), intracellular signaling (PKC- δ) and apoptosis regulation (Fas-L) (4). Further work-up and molecular testing is underway at this time.

4. Conclusions

Systemic lupus erythematosus (SLE) class V presenting as overt NS is rare in infants and it raises the concern for underlying etiologies. Complete clinical assessment and laboratory investigation for immune dysregulation syndromes such Juvenile SLE or type 1 interferonopathy need to be considered in such as cases.

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Authors' contribution

All authors passed all criteria for authorship contribution based on recommendations of the International Committee of Medical Journal Editors. PD and AR

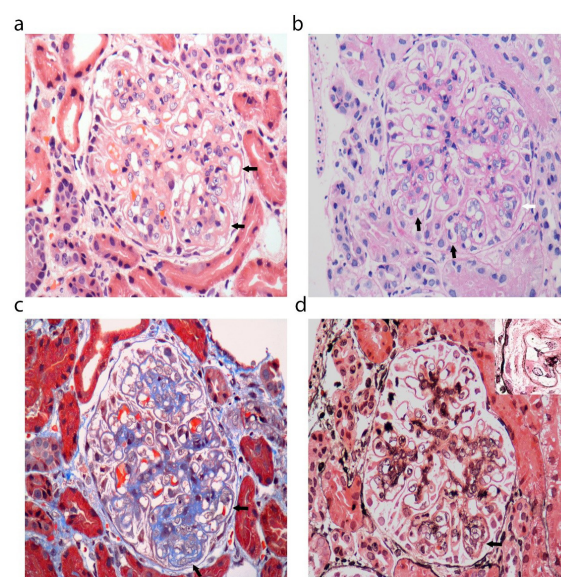


Figure 1. Light microscopy of a representative glomerulus ($\times 400$). (a) H&E stain; black arrows show rigid capillary loops with thickened glomerular basement membrane (GBM). (b) PAS stain; black arrows show diffuse endocapillary proliferation and white arrow shows PAS positive deposit along GBM. (c) Trichrome stain highlights fuchsinophilic deposits along GBM. (d) Silver stain; black arrow and the inset picture ($\times 600$) show argyrophilic GBM “spikes”.

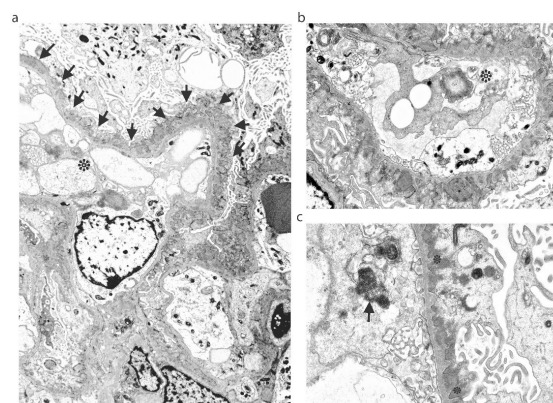


Figure 2. Representative electron micrographs of a glomerulus: (a) capillary loop (marked by arrows) with diffuse numerous sub-epithelial electron dense well demarcated immune-type deposits. (*) marks the lumen of the glomerular capillary ($\times 1500$). (b) Higher magnification of the capillary loop and the deposits ($\times 2000$). (c) Subepithelial deposits (*) and tubuloreticular inclusions inside the endothelial cell cytoplasm (\rightarrow) ($\times 2500$).

handled the case and prepared the manuscript. AA supervised the clinical workup. PD prepared the primary draft. Abdullah Abbas edited and finalized the manuscript. All authors read and signed the final paper.

Ethical considerations

Ethical issues (including plagiarism, data fabrication,

double publication) have been completely observed by the authors.

Conflicts of interests

The authors declared no potential conflicts of interest with respect to the case, authorship, and/or publication of this article.

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