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Case Report

IgAN Superimposed on MCD; A Case of Dual Glomerulopathy

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Abstract: Minimal Change Disease (MCD) is the most common cause of nephritic syndrome (NS) in children, while IgA nephropathy (IgAN) is the most common form of glomerulo nephritis (GN) worldwide, comprising 45% of all primary GN cases. Patients with IgA nephropathy typically present with hematuria and sub nephritic proteinuria. Nephritic syndrome is uncommon in IgA nephropathy. MCD is responsive to glucocorticoids, while the role of steroids in IgA nephropathy remains unclear. We are presenting this case report of a young patient having unusual clinical presentation & histomorphology of overlapping features of both the disease entities. Un common cases of MCD with nephritic range proteinuria & mesangial IgA deposits exhibit a clinical presentation, biopsy findings and outcome more typical of minimal change disease with superimposed IgA nephropathy .The observed syndrome can be considered a separate entity or subgroup belonging either to IgA nephropathy or MCD.
Keywords: IgA Nephropathy, MCD, NS

INTRODUCTION

Minimal change disease is the most common cause of nephritic syndrome in children. It accounts for 70– 90% of cases in children less than 10 years of age and 50% of cases in older children presenting with nephritic range proteinuria & have a very good prognosis being responsive to glucocorticoids [1]. IgA Nephropathy on the other hand is the most frequent form of glomerulo nephritis world wide. IgAN is typically an indolent disease with a slow progression to end stage kidney disease in approximately 30% of patients [1,2]. It has varied clinical presentations and usually presents with hematuria & sub nephritic range proteinuria. Nephritic syndrome is uncommon in IgAN. Histology of IgA Ndifferes as per stage of disease .Role of steroids as treatment modality in IgAN is unclear. Both the disease entities are distinctly separate in their clinical presentation, biological behavior & prognosis [3].

CASE REPORT

A 22 yr male presented with bilateral pedal edema for 1 month to nephrology department. He is a known case of MCD and has been on steroid therapy since childhood. His physical examination revealed his BP-140/78 mm of Hg with pitting edema in upper and lower extremities. There was puffiness in his face. Remainder of the physical examination was unremarkable. On further investigations after admission his serum total protein was 5.0 gm/dL ,serum albumin-2.2 mg/dL, BUN-42 mg/dL , serum creatinine-1.3 mg/dL, serum cholesterol-290mg/dL , serum triglyceride-137 mg/dL; Complete blood count findings:Hemoglobin-14.5 gm.dl, total leukocyte count-6700/cmm, total platelet count-3.4 lakh/ cmm, bleeding time-2.15 min, clotting time-3.4 min; HIV/HBsAg/HCV-Negative; Urine RE/ME analysis was significant for dark yellow urine, red blood cells-plenty/ hpf , pus cells-0-2/hpf,albumin-3+;24 hr urine protein-3.9 gm/day . His urine protein: creatinine ratio was 6.2, and his estimated glomerular filtration rate (eGFR) was 38mL/min/1.73m2. Serologic studies included negative anti ds DNA antibody and ANA and normal C3 (85.5) and C4 (28.6). The patient underwent Ultraso0snograpy guided percutaneous kidney biopsy for light microscopy & immune fluorescence study to assess the cause of heavy proteinuria. Grossly we ,in department of pathology received two grayish white linear tissue bits in formalin measuring 1.1 cm & 0.8 cm long for histopathological examination and another

tissue in PBS for direct immune fluorescence study. After histology processing and use of 4 special stains (H&E, PAS, JSM, MT) microscopic feature showed the renal core biopsies containing 9 glomeruli with associated tubules , interstitium & blood vessels. (Figure-1)

Fig-1:Renal biopsy under scanner view, Hematoxylin and eosin stain

All the glomeruli appeared morphologically normal without any membrane alteration or mesangial deposits. Tubules showed mild degenerative changes. Interstitium & blood vessels were unremarkable. FIGURE(2,3,4).

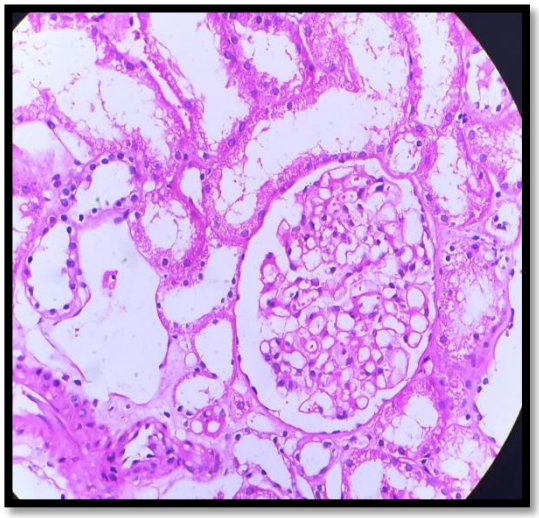

Fig-2: A glomerulus with normal histology, H&E stain 100X

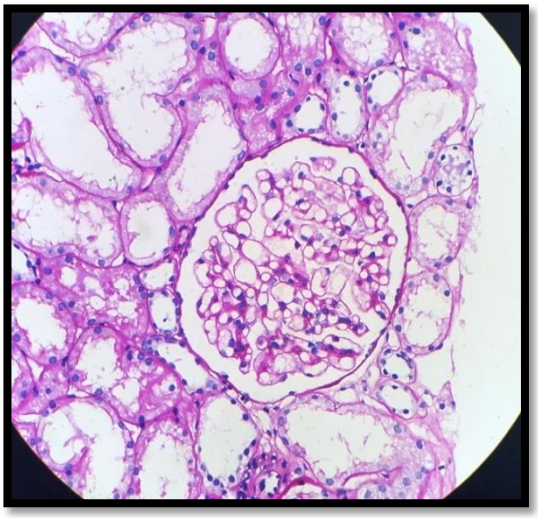

Fig-3:A glomerulus with normal histology PAS stain 100X

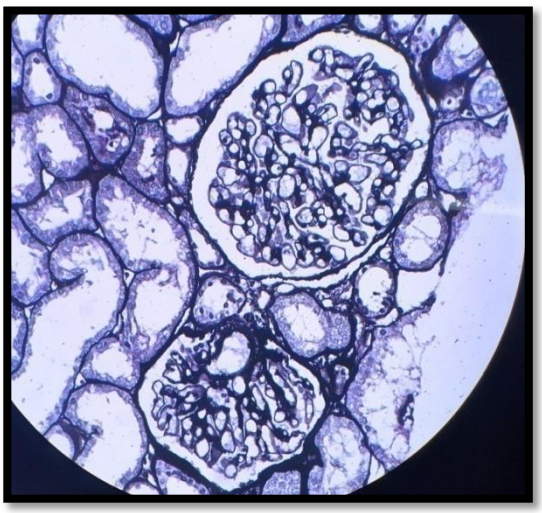

Fig-4: A glomerulus with normal histology, June's silver methenamine stain 100X

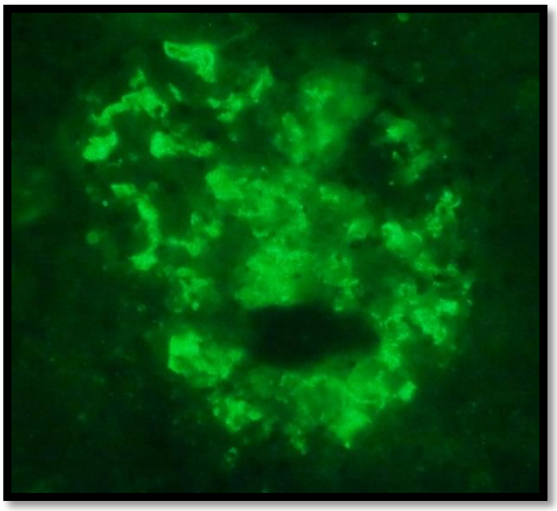

Fig- 5: Immunofluorescence reveals 3+ intensity staining for IgA restricted to mesangial areas,400x

Immunofluorescence examination revealed renal tissue with 5 glomeruli. Immunofluorescence against IgA antihuman antisera was 3+ positive in intensity & confined to a dominant mesangial deposition(90-95%)Figure-(5)],IgMantihuman antis era showed 1+positivity mostly in mesangial region (40-60%). IgG,C3,Fibrinogen antihuman antisera showed no immunofluorescence. So a final impression of IgA Nephropathy superimposed on minimal change disease was given due to striking change in immunofluorescence pattern associated normal glomerular histologic appearance& nephritic range proteinuria.

DISCUSSION

Minimal change disease (syn-nil disease/lipoid nephrosis) presents with nephrotic syndrome (heavy proteinuria ≥ 3.5 gm/day, hypoalbuminemia, generalized edema, hyperlipidemia &lipiduria).It is characterized by younger age group affection, nephrotic range proteinuria, normalin histomorphology, no or minimal immune deposits &diffuse effacement of foot processes of podocytes seen in electron microscopy. IgAN(Berger disease) usually affects adult population, presents with subnephroticlevel of protein excretion in urine, hematuria and hypertension ; varied apperance in histology as per the stage of disease and pathognomomicdominant IgA immune deposits in mesangiumin immunofluorescence study along with electron dense deposits in mesangiumon ultra structural evaluation [2,3]. According to Haas classification IgAN has five classes. Class I exibits minimal or no mesangial hypercellularity, class II shows focal and segmental glomerulosclerosis without cellular prolifertion, class III characterized by focal proliferative glomerulonephritis, class IV shows diffuse proliferative glomerulonephritis, class V shows ≥ 40% globally sclerotic glomeruli with tubular atrophy. Among these class I is mildest form and class V is the most severe form of IgA nephropathy. Disease progression depends on these clinic pathological classes [4].

NS is an unusual presentation in IgAN, seen only in 5% cases. Heavy proteinuria and/or NS in patients with IgAN are often accompanied by biopsy findings of more aggressive disease state like endocapillary proliferation, segmental glomerular sclerosis, crescent formation and tubulointerstitial scarring as there is reasonable degree of correlation between clinical and pathologic findings. In our case peculiarly we had minimal histologic alteration associated with nephritic range proteinuria. Though IgA nephropathy has class I (minimal mesangial hypercellularity) which is indistinguishable from light microscopic feature of MCD, it is not associated with heavy proteinuria. < 5% of MCD cases may show immune deposits, but they are usually IgM in nature, are faint or of less intensity and confined tomesangium. IgA immune deposits can be seen in MCD cases ,may be due to nonspecific trapping in mesangium; but the intensity is usually ≤ 1+ ,unlike our case[5].So this case appears to be developing features of IgAN .Rare cases of MCD with nephritic range heavy proteinuria &prominent mesangial IgA deposits have been reported which exhibit clinical features, biopsy findings and outcome more typical of minimal change disease with superimposed IgA nephropathy. Our case seems to fit in this category. The observed syndrome can be

categorized as a separate entity or a subgroup belonging either to IgA nephropathy or to MCD having dual features. The prognosis & clinical behavior of such cases is debatable asit is difficult to predict whether they will have the often benign long-term course of mild IgAN or the frequently relapse-ridden course of MCD. With administration of steroids MCD have an overwhelming improvement in clinical symptoms and fewer than 10% of IgA nephropathy have resolution of urinary manifestations with the administration of steroids. In recent years, first-line treatment of MCD (i.e., corticosteroids)[8] also has been established as a standard therapy for patients with IgAN with significant proteinuria, generally considered to be >1 g/d despite effective use of rennin angiotensin system-blocking drugs[6,10].Thus, the patient who presents with NS and is found to have findings suggestive of both MCD and mild IgAN should be a straightforward treatment decision.

CONCLUSION

Unusual cases of MCD with nephritic range proteinuria &intense mesangial IgA deposits can be considered a separate disease category or a subgroup belonging either to IgA nephropathy or to MCD. Renal biopsy is particularly important to distinguish these two groups, because patients with mild IgAN and MCD should receive treatment directed to MCD and have a more favorable prognosis, albeit one that may be associated with a relapsing course and the need for prolonged therapy.

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