ORIGINAL RESEARCH PAPER
Volume - 11 | Issue - 11 | November - 2022 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

A RARE CASE OF NELL 1 POSITIVE (NEURAL EPIDERMAL GROWTH FACTOR LIKE 1 PROTEIN) MEMBRANEOUS GLOMERULOPATHY

Internal Medicine

Dr Parth Gandhi 3rd year resident, Department of General Medicine, Medical College Baroda , Baroda

Dr.Gunjan Dholariya 3rd year Resident, Department of General Medicine, Medical College Baroda , Baroda

Dr Mahendra Parmar Professor, Department of General Medicine, Medical College Baroda , Baroda

Dr Ajay Dabhi Associate Professor, Department of General Medicine, Medical College Baroda , Baroda

KEYWORDS

INTRODUCTION

Membraneous nephropathy(MGN) is among the most common causes of the nephrotic syndrome in non diabetic population adults, accounting for upto one third of biopsied cases of nephrotic syndrome. The term MGN reflects the primary histologic change noted on light microscopy: Glomerular Basement Membrane(GBM) thickening with little or no cellular proliferation. MGN is the most often primary(idiopathic), although it has been associated with hepatitis B antigenemia, hepatitis C, syphilis, autoimmune diseases like SLE, thyroiditis, malignancies(particularly carcinoma of prostate, lung, breast, bladder or GIT malignancies) and use of certain drugs such as NSAIDs, gold, penicillamine, captopril. Certain antigens like PLA2(Phospholipase A2); Thrombospondin type 1 domain containing 7A; NELL 1(Neural Epidermal Growth Factor like 1); Semaphorin 3B, Protocadherin 7 and Neutral Endopeptidase are implicated in pathophysiology of MGN.

CASE DESCRIPTION

33 years old female patient not a known case of any major medical illness came to SSG hospital with complaints of bilateral pedal edema since 15 days which is pitting type, upto knee joint, insidious in onset and gradually progressive from below upwards; facial puffiness since 10 days which was more in morning hours; frothy urine since 10 days .

There was no complaint of nausea/vomiting, decreased urinary output, Gross hematuria, burning micturition, recent history of fever, rash, abdominal pain, breathlessness, chest pain, orthopnea or paroxysmal nocturnal dyspnea.

Patient's vitals were: blood pressure 110/80 mmhg; pulse rate 92/min; respiratory rate 14/min; SpO2 98% on RA and rest systemic examination being normal.

INVESTIGATIONS

On further investigating the patient, CBC, RFT, LFT were normal; Urine routine micro suggestive of +4 proteinuria and occasional RBC/hpf; UACR suggestive of Nephrotic range proteinuria of 8809.8 mg/gm of creatinine ; lipid profile suggestive of hypercholesterolemia(Total Cholesterol 352 mg/dl, LDL cholesterol 254.4 mg/dl); hiv, hbsag, hcv were negative, S. albumin was 2.7g/dl; ESR 5/min; CRP negative; ASO negative; Thyroid Profile was normal; C3 C4 levels normal ANA profile was negative USG abdo+kub s/o bilaterally normal sized kidney with CMD preserved; HRCT Thorax and CECT Abdomen+Pelvis showed no malignancy.Considering Adult onset nephrotic syndrome Renal Biopsy was done. Renal biopsy report was suggestive of NELL 1 Ab positive MGN.

TREATMENT

Considering Adult onset Nephrotic Syndrome, patient was started on Injectable Methylprednisolone for 3 days followed by Tablet Prednisolone 1mg/kg. After biopsy report came, considering low risk of progression of MGN, patient was discharged on tapering dose of prednisolone, enalapril, atorvastatin.

RESULT

Patient improved and pedal edema and facial puffiness were resolved on routine followup. Patient's kidney function is normal; CBC is normal and UACR decreased significantly(from 8809.2 mg/g to 3606 mg/g of creatinine) on follow up.


RENAL PATHOLOGY REPORT @ **

SPECIMEN : Kidney biopsy panel 1

CLINICAL HISTORY : Proteinuria, Spot UPCR- 4087.37, S. creatinine 0.63mg%, S. albumin 2.7 g/dl

GROSS : 1. Received 1 linear tissue core measuring 1.3 cm in formalin.
2. Received 1 linear tissue core measuring 1.3 cm for DIF studies.
[Entire tissue : 5940 /22]

MICROSCOPY : Multiple sections stained with H&E, PAS, MT, silver methenamine and Congo red include renal medulla and cortical parenchymal area including upto 18 glomeruli, none globally sclerosed. The glomeruli reveal diffuse thickening of capillaries, which reveal intramembranous matting in silver methenamine stained sections. There is no evidence of segmental sclerosis, tuft necrosis, subendothelial/ Congophilic deposits, endocapillary cellularity, intracapillary thrombi or crescent formation in the visualized glomeruli.

Tubular atrophy & interstitial fibrosis involve less than 10% of sampled cortex. Tubules show focally prominent cytoplasmic vacuolar change. Few hyaline & granular casts in tubular lumina and focal mild chronic interstitial inflammation are observed.

Arteries show mild medial thickening & subintimal sclerosis, while arterioles reveal focal vacuolization in smooth muscle cells of media.

DIF : Tissue for DIF shows renal cortical parenchyma including up to 13 glomeruli. Following immunostaining pattern is observed:

Page 1 of 3

CONCLUSIONS

NELL 1 may be the antigen responsible in approximately 16 percent of cases of PLA2R negative Primary MGN. Both mass spectrometry data and limited characterization of circulating NELL 1 Ab suggested that the predominant IgG subclass in this disease may be IgG1 rather than IgG4. One study revealed that upto one third of patients with NELL 1 associated MGN have a higher risk of malignancy. Cases of NELL 1 associated MGN following LIpoic acid supplementation has also been described. In such individuals, discontinuation of lipoic acid lead to remission of disease with no requirement of immunosuppressioin.

General supportive measures in all patients with MGN include dietary sodium restriction, BP control, minimization of proteinuria with RAAS inhibition, treatment of dyslipidemia, in selected patients anticoagulation.

In Primary MGN, regardless of PLA2 AB status, consider the patients at high risk of progression if any 2 of following features present: S. Cr >1.5 mg/dl; progressive decline in renal function; severe disabling life threatening nephrotic syndrome(S albumin <2.5 g/dl and refractory edema and thromboembolic event). In such patients initial therapy with immunosuppressive therapy is recommended. In other patients, only general mesures recommended and monitoring for signs of progression of disease is recommended. After 3 to 6 months of observation period, again stratification of patients based on temporal trends of clinical parameters and serological parameters done:

Risk stratification of patients with primary membranous nephropathy*

	Risk of progression			
	Low	Moderate	High	Very high
	Over an observation period of 3 to 6 months¶, at least 2 of 3 criteria must be present:			2 or more of the following **at the time of diagnosis**:

Kidney function	• Normal or stable (<25% decrease) eGFR over the observation period	• Normal or stable (<25% decrease) eGFR over the observation period	• Decrease in eGFR ≥25%, not explained by other causes, **at any time** during the observation period	• Serum creatinine ≥1.5 mg/dL (≥133 micromol/L), considered due to active MN • Decrease in eGFR ≥25% from baseline over the prior 2 years, considered due to active MN • Severe, disabling, or life-threatening nephrotic syndrome[Φ]
Proteinuria	• <4 g/day at the end of the observation period	• Between 4 and 8 g/day at the end of the observation period	• >8 g/day at the end of the observation period **or** Persistent nephrotic syndrome[Δ]	
Serum anti-PLA2R antibody levels (only in patients with anti-PLA2R antibody-positive MN)	• Serial titers are persistently low (arbitrarily defined as <50 RU/mL by ELISA) or are decreasing ≥25% by over the observation period	• Serial titers are <150 RU/mL and stable or increasing by <25%	• Serial titers are high (arbitrarily defined as ≥150 RU/mL by ELISA) and not declining **or** are increasing to ≥150 RU/mL	

eGFR: estimated glomerular filtration rate; MN: membranous nephropathy; PLA2R: phospholipase A2 receptor; ELISA: enzyme-linked immunosorbent assay.

In patients with low risk of progression only general measures are required and in those with moderate/high risk of progression immunosuppression is required.

REFERENCES

1. Harrison Textbook of Internal Medicine, 20th Edition.
2. Brenner's and Rector's The Kidney.
3. Kidney Int. 2021;99(4):967. Epub 2020 Aug 20.
4. KDIGO 2021 Clinical Practice Guideline for the Management of Glomerular Disease.