Case Report :

An Atypical Nephrotic Syndrome

Shetty S.,* Popat I.,* Kadam NN.,** Viswanathan V.,# Nikhil B.,* Ragi R.***

*Residents, **Professors, ***Asstt. Professor, #Consultant Pediatric Rheumatologist; Department of Paediatrics, MGM Medical College & Hospital, Navi Mumbai, 410218, Maharashtra, India.
Coresponding author: Dr. Popat Ishani, Email-ishani.popat@yahoo.com
Received in December, 2015; Review completed in Feb, 2016

Abstract:

A 14 year old girl presented with peri-orbital puffiness of face, pedal oedema and decreased urine output for 2 weeks. She had similar history with hematuria 3 years back. On examination, she had generalized anasarca, pallor, faint malar rash, swollen and painful knees, hypertension and ascites. Earlier investigations had shown microalbuminuria, creatinine 1.7, urine albumin: creatinine ratio 560, ANA and dsDNA both positive, low C3 and high serum cholesterol. Ascitic fluid was sterile. The child had then received prednisolone but no resolution even after 6 weeks, followed by 7 cycles of IV cyclophosphamide. She was re-evaluated as an atypical nephrotic with SLE like features and a kidney biopsy taken. With the histopathological diagnosis of Lupus nephritis type V, she was put on appropriate therapy as per ACR, 2011 guidelines and showed good response. The current management guidelines of Lupus Nephritis discussed.

Key words:

lupus nephritis, atypical nephrotic syndrome, ACR guidelines

Case report:

A 14 year old female child presented with reduced urine output, puffiness around eyes, bilateral pedal edema and abdominal enlargement for last 15 days. Gave a similar history 3 years back when she also had hematuria along with the above complaints. However, there was no malar rash then. Investigations then had shown microalbuminuria (98), 24 hour urine protein -14 grams, creatinine 1.7, spot urine albumin: creatinine ratio 560, positive ANA and dsDNA, low C3 level (24) and high serum cholesterol (320). HIV, HBsAg and HCV were non-reactive. USG had shown gross ascites and mild pleural effusion. Therapeutic tapping was done twice. She was put on oral prednisolone in appropriate doses but no resolution of the symptoms even after 6 weeks. She continued to have high urine protein: creatinine ratio. Therefore was put on 7 cycles of IV cyclophosphamide as a nephritic type of nephortic syndrome. With this, she had improved. Swelling reduced for a couple of months but no complete recovery. The child however did not comply follow-up.

On examination:

The anthrometric measurements were as follows-Weight: 28 Kg, Height: 138 Cm, Weight for height -3rd percentile; US:LS:: 0.9, OFC: 48 Cm

Her general condition was poor. PR- 90 / min, RR- 22 / min, BP - 180/138 mmHg (> 99th percentile). Pallor, Malar rash including supra-orbittal region, generalized anasarca present. Swelling and restriction of movement in both knees, but no local rise of temperature. P/A: No engorged veins over abdomen. No flank veins. Ascites present. No organomegaly. R/S: Minimal pleural effusion both sides. All other systems were essentially normal.

Fig-1. Typical malar rash extending to supra-orbital region

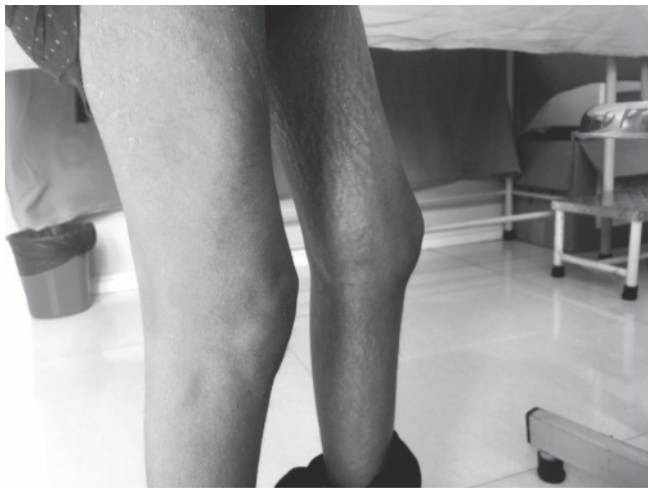

Fig-2. Rash, muscle wasting and arthrits both knees

Table-1. Investigations:

Parameters	Value	Parameters	Value
Hb	8.2	ESR	80
TLC	17300	S.Protein	5.73
Plt	4.67	Alb/Glob	1.76/3.97
PCV	25.7	S.Creat	0.29
MCV	76.5	BUN	4.2
MCH	24.4	Urea	9
MCHC	31.9	Uric acid	4
N/E/L/M	76/0/22/2		
Sr.cholesterol :	126 mg/dl	Thyroid profile	WNL
Sr.triglycerides	180 mg/dl	PT	WNL
HDL	13 mg/dl	INR	WNL
LDL	76 mg/dl	APTT	WNL
VLDL	36.6 mg/dl	C3	14.3
ANA	Positive	dsDNA	3.4 (+ve)
ASO	Positive		
Urine RE/ME: Protein : 3+, EC: 2-3, PC: 5-10 RBC: Occasional Uriine culture: Sterile.		Urine micro albumin : creatinine ratio: 1264.5 Urine creatinine: 0.01818 gm/dl Urine micro albumin: 22.99 mg/dl Urine protein/creatinine ratio: 17616.6	

USG abdomen and chest: Bilateral pleural effusion with moderate ascites.

KIDNEY BIOPSY:

Diffuse global and membranous lupus nephritis, ISN/RPS, Class IV-C/V (Table-2)

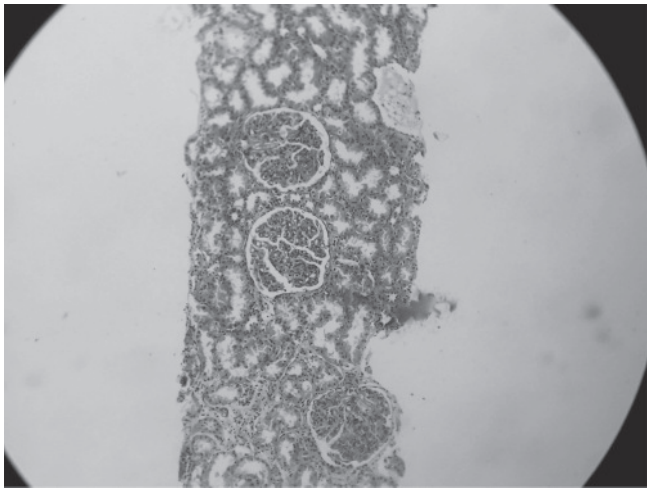

Fig-3. Histopathology showing mesangial hyper cellularity, few sclerosed glomeruli and matrix expansion. Diagnosis: Grade IV/V lupus nephritis[6]

Course in hospital:

For our indexed case, the treatment was instituted as per guideline followed in the ACR 2011 for Class III/IV induction therapy shown in the flow-diagram (Fig.1), besides appropriate diet, combination of ACE inhibitor and Nifedipine to control high blood pressure.

According to the SLICC classification, she satisfied[4] criteria (Both clinical and immunologic) for diagnosis of Lupus nephritis and was put on pulse therapy of methyl prednisolone initially; which continued daily for 3 cycles. As kidney biopsy showed diffuse global membranous lupus nephritis, she was started on IV cyclophosphamide, hydroxychloroquine (Immunomodulant) and anti-hypertensives. Ascites and pedal oedema subsided. Her blood pressure decreased and general condition greatly improved. She continues to be under remission on subsequent follow-up.

Discussion:

Goal of management:

1. To halt the disease process from getting worse
2. Reduce or abolish symptoms (Remission)
3. Avoid or delay need for dialysis or renal transplantation

The definitive management of Lupus nephritis such as - immunosuppressive therapy and the requirement to add biologicals (Monoclonal antibodies) has to be based on the stage of the disease as indicated in the renal histology (Table-2):

Table: 2. International Society of Nephrology Society 2003 Classification of LUPUS NEPHRITIS on Kidney Biopsy [1,2,4]

Class I Minimal mesangial LN
Class II Mesangial proliferative LN
Class III Focal LN (50% of glomeruli)
III (A): active lesions
III (A/C): active and chronic lesions
III (C): chronic lesions
Class IV Diffuse LN (> 50% glomeruli)
IV (S) Diffuse segmental
IV (G) LN : Global
IV (A): Active lesions
IV (A/C): Active and chronic lesions
IV (C): Chronic lesions
Class V Membranous LN+
Class VI Advanced sclerosing LN (>90% globally sclerosed glomeruli without residual activity)

Supportive measures:

1. Protein restriction in diet
2. ACE (Angiotensin converting enzyme) inhibitors to control hypertension and minimize leaking protein. Can be judiciously add any other AHD and adjust doses, depending on response.

Definitive Therapeutic modalities: [4]

There are three modalities of treatment for lupus nephritis

- Immunosuppressive therapy
- Dialysis
- Renal transplant

Table. 3: Immunosuppresents modalities evolved over years as under [2,4]:

- 1949-adrenocorticotropic hormone, prednisone.
- 1950-cyclophosphamide.
- 1961-1974-Azathioprine
- 1978-cyclosporine
- 1984-Tacrolimus
- 1994-mycophenolate Mofetil
- 1997-Rituximab.

2011-Belimumab

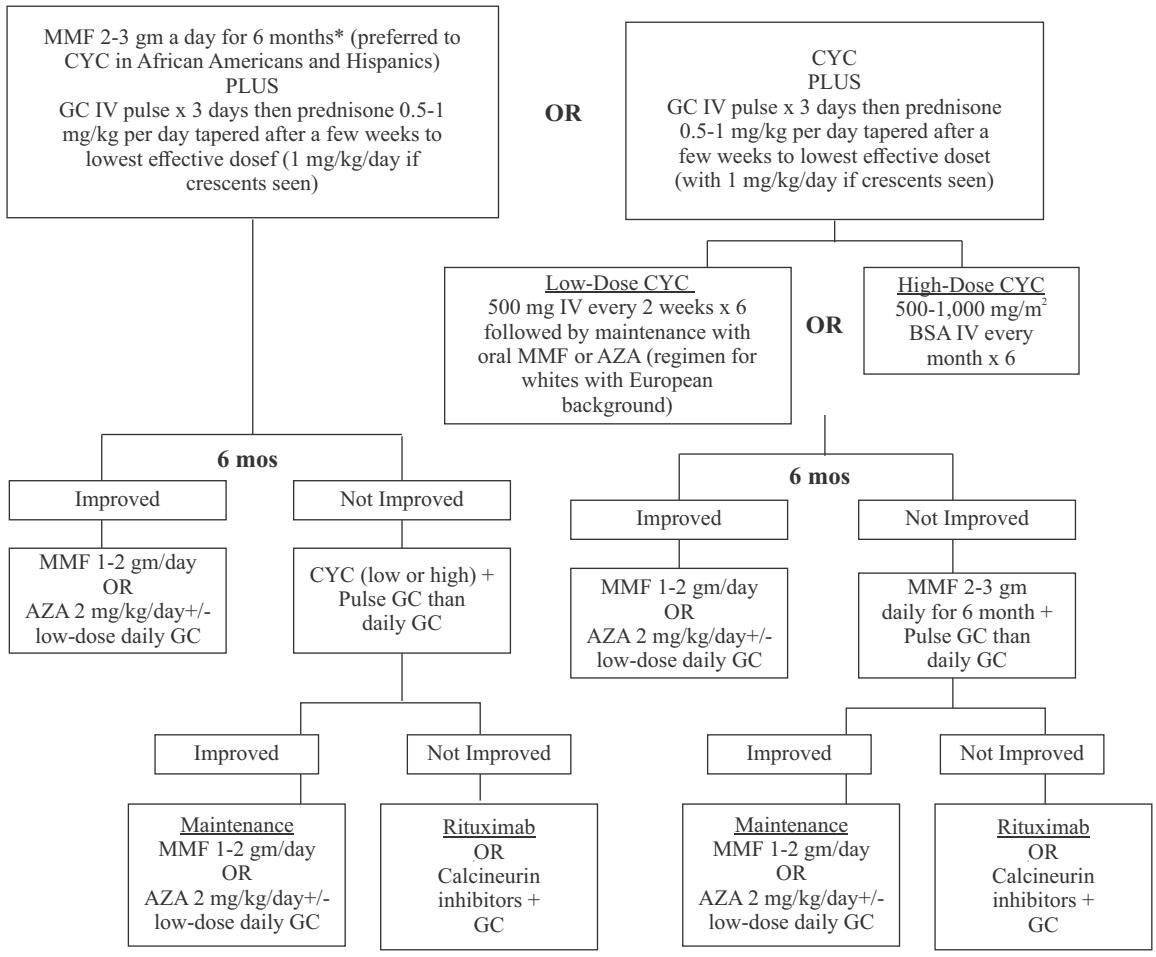

Fig. 4: Induction therapy Guideline for Lupus Nephritis, 2011[2,4]

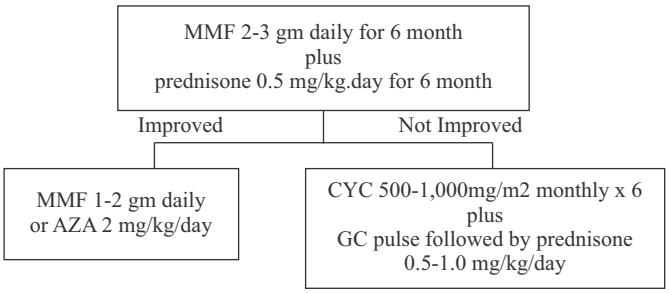

Fig. 5: Maintenance therapy for Lupus Nephritis, 2011[2,4]

Risk Factors Associated with Lupus Nephritis1:

- African American, Asian and Hispanic ethnicity
- Creatinine >140 µmol/L or >1.83mg/dl.
- Nephrotic range proteinuria.
- Delayed kidney biopsy.
- Younger age.
- Male gender
- Anti-Ro antibodies.
- Pathology : MPGN (WHO class IV) ,tubular atrophy
- Lack of access to medical care
- Poor response to immunosuppressive therapy.
- Co-morbidities: Hypertension, diabetes mellitus, higher body mass index.

Dialysis[4,6]: Analysis of the U.S. Renal Data System data from 1995 to 2006 indicated LN progression to end stage kidney disease (ESKD) in 11,317 patients. 85% of these patients were initiated on hemo-dialysis (HD), 12.2% on peritoneal dialysis (PD) and 2.8% underwent preemptive kidney transplantation at the onset of ESKD. Data regarding the modality that might be most advantageous for LN-associated ESKD indicated similar at 5-year and 10-year survival outcomes for HD and PD populations.

Renal transplantation therapy[2, 3, 5]: Despite improvements in overall prognosis in lupus nephritis, 10-30% of patients with proliferative renal involvement progress to end stage renal disease, depending on severity of disease and associated socioeconomic factors. Kidney transplantation has been recognized as the most appropriate treatment for such patients, but several issues remain after renal function restoration in a lupus recipient. Among these is the fear of lupus nephritis recurrence in the graft, choice of immunosuppressive therapy in cases of recurrent lupus for a patient who has already received a toxic and prolonged immunosuppressive course, and finally, the management of comorbidities to reduce associated morbidities in the long term.

References:

1. Progression of lupus nephritis to ESKD—risk factors and associations.ESKD, end-stage kidney disease MPGN, membranoproliferative glomerulonephritis; WHO, World Health Organization.
2. Delvin A, Waikar S, Solomon D, et al. Variation in initial kidney replacement therapy for end-stage renal disease due to lupus nephritis in the United States. Arthritis Care Res 2011;63:1642–53.
3. Kang SH, Chung BH, Choi SR, et al. Comparison of clinical outcomes by different renal replacement therapy in patients with end-stage renal disease secondary to lupus nephritis. Korean J Intern Med 2011; 26:607.
4. The American Journal of the Medical Sciences October 2013; 4:346.
5. World Journal of Transplant. 2014 Sep 24; 4(3): 176–182.
6. Howard A. Austin III, Larry R. Muenz, Kathleen M. Joyce, Tatiana A. Antonovych, Margarita E. Kullick, John H. Klippel, John L. Decker, James E. Prognostic factors in lupus nephritis: Contribution of renal histologic data.The Am Jl of Medicine Sept 1983; 75.3: 382-391