USAGE OF CYCLOSPORINE IN LUPUS NEPHRITIS CLASS III, IV AND V – ONE CENTRE EXPERIENCE

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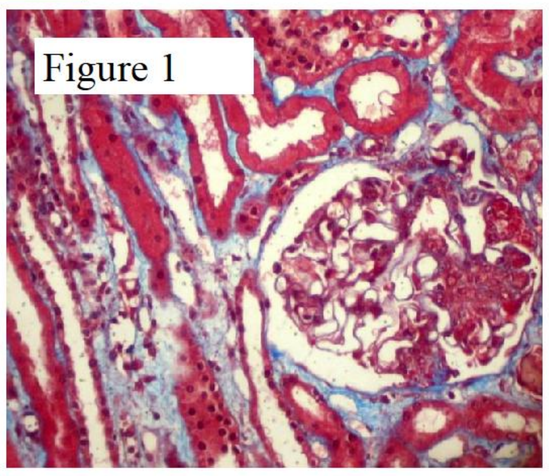
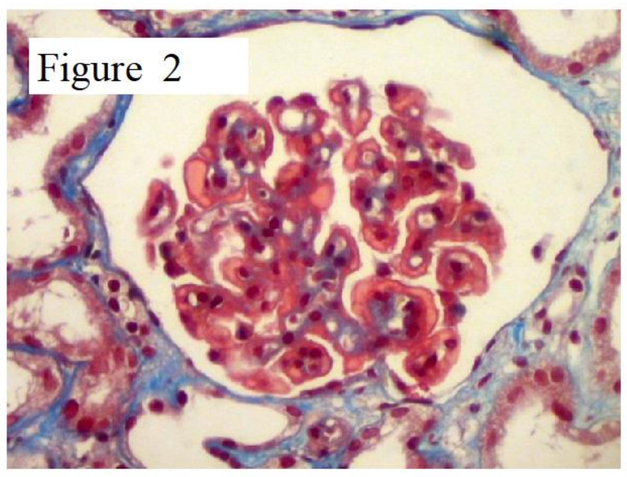
OBJECTIVES

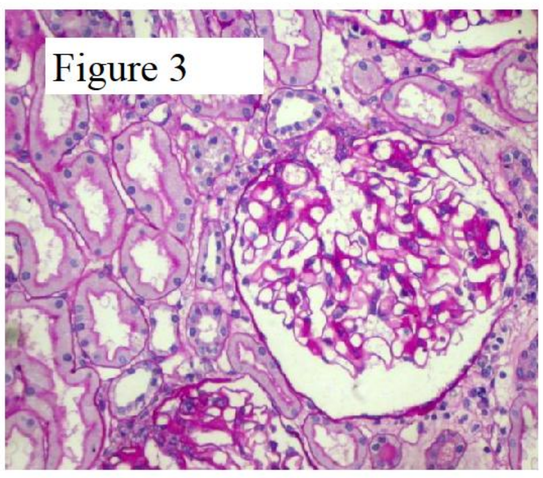
Current KDIGO Guidelines for Glomerulonephritis and EULAR/ERA-EDTA Recommendations for Management of Lupus Nephritis suggest Cyclosporine (CYC) as alternative option for initial treatment of lupus nephritis (LN) class V with persistent nephrotic proteinuria, resistant disease not responding to more than one of the recommended initial regimens, and subsequent treatment in patients with pure class V or class III/IV intolerant of mycophenolate mofetil and azathioprine (AZA). CYC is also acceptable during pregnancy. We aimed to evaluate retrospectively efficacy of CYC in our cohort of patients with LN

METHODS

Using electronic clinical and pathology database we searched 106 LN patients, treated in our unit since 2002, when we introduced CYC for LN, to 2012. Patients with class I, II and VI, and those never received CYC were excluded from analysis. Study group included 14 patients, 12 female and 2 male, median age 27.5 [17;39] years. 2 patients had class III, 6 – class IV and 6 – class V LN (Figure 1-3).
Disease duration prior to switching to CYC was 60 [5;168] months, previous treatment included prednisone in all cases, cyclophosphamide (CP) "pulses" in 12, mycophenolate mofetil/micophenolic acid (MMF/MPA) in 5, and AZA in 4 cases. Indications for CYC were non-responsiveness or intolerance of CP and MMF/MPA in 6, renal flare after CP and/or MMF/MPA initial and re-induction regimens in 4, and subsequent treatment in 4 patients intolerant of MMF/MPA and AZA. Initial dose of CYC was 200 mg/day [150;250], with dose adjustment to plasma concentration. Duration of therapy constituted 14.5 [1;84] month, duration of follow-up – 18 [1;84] months







Figures 1-3:
Figure 1. LN class III, Masson x 250
Figure 2. LN class IV, Masson x 250
Figure 3. LN class V, PAS x 250

Table 1. Influence of CYC on proteinuria and kidney function

	Before CYC	At last evaluation	P value
Median proteinuria (g/day)	2.6 [0.15;15.0]	0.3 [0.0;9.5]	<0.05
Median creatinine (µmol/l)	102 [68;300]	100 [74;441]	NS

Table 2. Results of CYC treatment in different LN classes

	Complete response achieved/sustained	Partial response achieved/sustained	No response
Class III	0/1	1/0	0
Class IV	1/0	2/1	2
Class V	2/2	2/0	0
Total	3/3	5/1	2

RESULTS

6 patients (42.8%) achieved and/or sustained complete remission, 6 patients (42.8%) – partial remission, and only in 2 (14.3%) cases CYC treatment was non-effective. Changes in proteinuria and kidney function and distribution of efficacy in different LN classes are shown in tables 1 and 2.
In one case of LN class V after 5 years of treatment with sustained partial remission 2-nd kidney biopsy did not show any signs of CYC-toxicity. 3 patients had 4 normal pregnancies and delivered healthy babies, only in 1 case after delivery developed renal flare, successfully treated with MMF. There was no other flares in patients treated with CYC

CONCLUSIONS

In our cohort of 106 LN patients 13% were treated with CYC. In 85.6% of cases complete or partial remissions were achieved/sustained with lowering of median proteinuria from 2.6 to 0.3 g/day and nicely preserved kidney function. The best results were seen in LN class V (100% of remissions, mostly complete), the worst - in class IV (only 66.6% of remissions, mostly partial)

REFERENCES:

1.KDIGO Practice Guidline for Glomerulonaphritis . *Kidney inter., Suppl.* 2012; 2:139-274
2.Joint European League Against Rheumatism and European Renal Association–European Dialysis and Transplant Association (EULAR/ERA-EDTA) recommendations for the management of adult and paediatric lupus nephritis. *Ann Rheum Dis* 2012; 71:1771-1782