DISSEMINATED CYTOMEGALOVIRUS DISEASE AND ESOPHAGEAL CANDIDIASIS IN INDUCTION TREATMENT OF CLASS IV + V LUPUS NEPHRITIS WITH MYCOPHENOLATE MOFETIL – A 60-MONTH FOLLOW-UP

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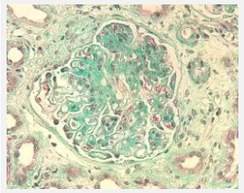
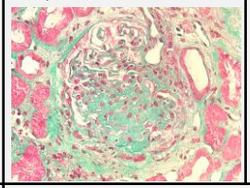
INTRODUCTION

Infections are the most frequent complication in patients with systemic lupus erythematosus (SLE).[1] Cytomegalovirus (CMV) infection is particularly challenging in SLE, as it may arise as a SLE flare trigger (or even mimicking a lupus flare) or as a complication of immunosuppression (IMS).[2] About 40% of SLE patients develop Lupus Nephritis (LN).[3] Mycophenolate Mofetil (MMF), previously reserved for transplant recipients, has been gaining importance in SLE, especially in the treatment of LN.[3] The 2020 EULAR/ERA–EDTA recommendations acknowledge that most LN flares seem to occur within the first 5–6 years of treatment (instead of the first 2 years), so IMS shouldn't be discontinued prior to that time.[3] CMV infection in LN patients has been an unexplored field for many years. Optimal antiviral strategy was yet to be defined. [4]

We present a case of a 59-year-old male, diagnosed with double opportunistic infection - disseminated CMV disease and esophageal candidiasis – in the context of induction treatment of a severe class IV (G/A) + V LN hemodialysis-dependent with massive proteinuria, using MMF-based therapy.

CASE PRESENTATION

- A 59-year-old caucasian male
- Past medical history: benign prostatic hyperplasia, renal lithiasis, hyperuricemia and contact with pigeons

Parameters / *Timeline*	Clinical presentation	Hb (g/dL)	WBC(x10^9/L)	Plat. (x10^9/L)	Creatinine (mg/dL)	Proteinuria (g/24h)	Autoimmunity	Kidney biopsy	Infectious complications	Therapeutics	Outcomes / observations / other data
0	2014: **nephritic-nephrotic syndrome.** Rapid decline of renal function and oliguria requiring HD	**6.6** / 9,3	5.8 / 10	295 / 324	**7.9** / 2.5	**11.7** / 2.1	Normal complement (C3 and C4) (+) anti-dsDNA Ab (+) ANA (+) anti-histone Ab (+) aCL (+) CICs	Light Microscopy (trichrome stain, x400): **LN class IV-G (A) + V**, with marked thickening of glomerular basement membrane, mesangial proliferation and endocapillary hypercellularity. 		**Induction treatment: MMF** (up to 2.5g/day) + **methylPDN** followed by oral **PDN + prophylactic** drugs.	**Stabilization of pCr (2.5mg/dL), normalization of autoimmunity markers, Pu improvement to 2.1g/d.** Stopped intermittent HD after 6 weeks.
2 M IMS	Asthenia, anorexia, gastric intolerance with weight loss, generalized edema, weakness of the lower limbs and occasional diarrhea, without fever	9.1 / 14	2.4 / 8.5	129 / 165	1.6 / 1.5 / 1.4	**5.9 / 9.2 / 7.9**	**Normalization of autoimmunity markers**	**KB was repeated in a stable condition:** LM (trichrome stain, x400): **LN class V-G (C)**, increased mesangial matrix, marked thickening of glomerular basement membrane and adhesion of a sclerotic segment to Bowman's capsule, also thickened. 	(+) IgM **CMV** and qPCR assay for CMV. **Upper endoscopy**: esophageal candidiasis, erosive gastritis and duodenitis. **Colonoscopy**: aphthous ulcers throughout the colon. **Immunohistochemistry** (+) for CMV Ag in duodenal cells. H&E stain (+) for fungal spores. ======== Disseminated CMV disease Esophageal candidiasis	**IV fluconazole + ganciclovir -»** valganciclovir (then reduced to prophylactic dose after (-) qPCR for CMV, and maintained for 6 months, as for transplant recipients). **MMF reduced** to 1g/day and PDN was rapidly tapered.	**Nephrotic range Pu relapse occurred** (9.2g/d) - it was assumed relapse of LN class V after reduction of IMS, with contribution of active infection and some degree of expected renal sclerosis. Supportive antiproteinuric drugs were optimized, and the patient evolved favorably (sCr, Hb, WBC, Pu).
7 M IMS	No reference to symptoms, under oral prophylactic nystatin	**6.1** / 10	6.6 / 7.5	164 / 343	1.81 / **1.38**	**6.5 / 5.3**	**Normalization of autoimmunity markers**	Routine endoscopic revaluation: recurrence of esophageal candidiasis, 2 months after increasing MMF until 1.75g/d due to sustained massive proteinuria, documented class V NL, along with the need of tapering PDN (to control glucocorticoid-induced diabetes).		IV fluconazole + IMS was reduced (MMF to 1g/d), with good results.	
1 Y	**Partial remission of LN was achieved at 1 year of follow up, with stable renal function and Pu 610mg/d, innocent urinary sediment, normal complement and autoimmunity.**										
3 Y	**At 3 years follow-up, under MMF 1g/d, complete remission was achieved was stable pCr 1.4mg/dL and Pu 420mg/d.**										
5 Y	**The patient reached complete remission, with MMF 500mg/d: pCr of 1.6mg/dL, sustained descent of proteinuria (355mg/d), innocent US, normal complement and autoimmunity.**										

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DISCUSSION AND CONCLUSIONS

Few studies demonstrate the clear association between LN, MMF and *herpesvirus* infection[4] , specifically in the induction phase.

Management between IMS and opportunistic infection control remains a challenge. Clinical suspicion, early diagnosis and appropriate treatment are essential for resolution without sequelae. Despite the histologically documented chronicity stigmas through KB, that predict permanent basal dysfunction, this reflects a successful case in controlling the underlying pathology, especially considering intercurrent infectious.

We highlight the probable need of screening these patients for CMV status as transplant recipients, especially if associated with other immunosuppressive states such as diabetes or massive proteinuria.

References

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