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Journal

Proceedings of UCLA Health, 22(1)

Authors

Hanna, Ramy M
Kaldas, Marian

Publication Date

2018-12-27

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CLINICAL VIGNETTE

Systemic Lupus Erythematosus Causing ISN-RPS Class III Focal Proliferative Glomerulonephritis and Cerebritis with Resulting Cerebrovascular Accident

Ramy M. Hanna, MD and Marian Kaldas, MD

Introduction

Systemic Lupus erythematosus (SLE) is a multisystem autoimmune disease[1] resulting from various antibodies against nuclear antigens and deoxyribonucleic acids.[2] There are diverse manifestations of this disease such as autoimmune antibody markers, oral ulcers, rashes and hematologic abnormalities, but the most feared ones are cerebritis and nephritis.[3-5] SLE nephritis is widely associated with worse outcomes, and many patients require renal replacement therapy despite aggressive cytotoxic treatment.[3] SLE cerebritis can result in seizures, and cerebrovascular accidents and its presentations can be varied from neuropsychiatric symptoms to hemiparesis.[4]

We present a case of a 33-year-old Hispanic female who presented with biopsy proven class III Focal proliferative glomerulonephritis (FPGN), according to the International society of nephrology-royal pathology society (ISN-RPS) classification system. We report the initial response of the SLE nephritis to mycopheonlate mofetil, and the subsequent need to change her therapy to cyclophosphamide post cerebrovascular accident. Systemic remission and proteinuria were then achieved and maintained.

Case Report

A 33-year-old Hispanic female presented to an outside hospital with arthralgias, which she had been medicating with non-steroidal anti-inflammatory agents (NSAIDs). She was noted to have proteinuria and hematuria with initial concern for renal injury or glomerular disease secondary to NSAID use. A renal biopsy showed focal proliferative glomerulonephritis (class III SLE nephritis). Biopsy findings included focal fibro-cellular crescents, wire loop deposits, full house immunoflouresence staining. Electron microscopy demonstrated sub-endothelial, sub-epithelial, and mesangial deposits. Tubuloreticular deposits classic for lupus nephritis were also seen under electron microscopy (see Figure 1). The patient was started on mycophenolate mofetil and a high dose steroid taper (1gram/kilogram).

Two months after her initial presentation she presented to the emergency department with right hemiparesis and aphasia and transferred care at UCLA-Health. Imaging findings showed diffuse luminal irregularity and narrowing throughout much of the anterior and posterior intracranial arterial circulation. MRI also demonstrated, mild to moderate stenosis involving the right supraclinoid ICA as well as focal segments of at least moderate narrowing involving the bilateral M1 segments and bilateral distal middle cerebral artery (MCA) branch. MRI initially confirmed an infarct in lenticulostriate territory in addition to the narrowing in cerebral arteries consistent with vasculitis and cerebritis.

Figure 1

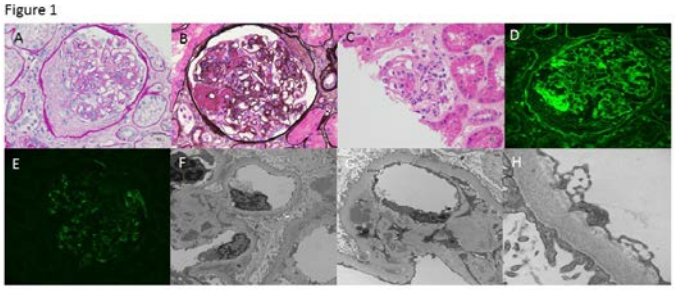

Figure 1: Renal biopsy pathology slides demonstrating ISN RPS [international Society of Nephrology- Renal Pathology Society] grade III lupus nephritis.
A) Light microscopy, 40x, hematoxylin and eosin stain fibrocellular crescent
B) Light microscopy, 40x, methenamine silver stain, wire loop deposits
C) Light microscopy, 40x, hematoxylin and eosin stain segmental necrosis
D) Immunofluorescence, Glomerular and extra glomerular IgG deposits, ANA binding
E) Immunofluorescence, glomerular C1q binding
F) Electron microscopy, sub epithelial and sub endothelial deposits
G) Electron microscopy, mesangial deposits
H) Electron microscopy, Tubuloreticular inclusion

The patient was started on cyclophosphamide (0.7 gram BSA/m^2) after a long discussion about risks, and benefits, as well as offering her oocyte preservation and contraception. She improved neurologically with continual improvement of her gait and strength with near resolution of neurological deficits. Proteinuria also continued to improve to a complete remission (0.3-0.5 grams protein/gram creatinine on urine spot protein to creatinine ratio). After completing four cycles of her induction regimen with cyclophosphamide she transitioned to mycopheonlate mofetil maintenance. Please see Figure 2 for graph of the patient's creatinine, urine protein to creatinine ratio, anti-nuclear antibody (ANA) titer, C3/C4 complement levels, and titer of anti-double stranded DNA (ant ds DNA) titer.

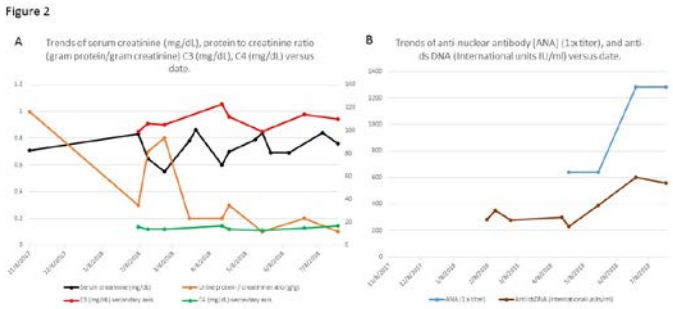

Figure 2: A) Trends of serum creatinine (mg/dL), protein to creatinine ratio (gram protein/gram creatinine) C3 (mg/dL), C4 (mg/dL) versus date. B) Trends of anti-nuclear antibody [ANA] (1:x titer), and anti-ds DNA (International units IU/ml) versus date.

Discussion

This 33-year-old patient with SLE nephritis who had to be taken off mycophenolate mofetil and transitioned to cyclophosphamide induction after developing a cerebrovascular accident due to lupus cerebritis. The patient's nephritis remained in remission after cyclophosphamide despite the data that Hispanic patients with SLE nephritis usually respond better to mycophenolate mofetil.[6,7] After resolution of her SLE cerebritis symptoms and concurrent complete remission of proteinuria, she was transitioned back to mycophenolate mofetil maintenance with continued clinical response.

Acknowledgement

We would like to thank Dr. Jean Hou from Cedars Sinai pathology for renal biopsy images.

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Submitted November 1, 2018