Case Report

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A Case of Lupus Cerebritis

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ABSTRACT

Neuropsychiatric systemic lupus erythematosus (NPSLE) presents with a wide range of psychiatric and neurologic manifestations that can complicate diagnosis and management. We describe a 59-year-old woman with a history of bipolar disorder, tricuspid valve endocarditis, pulmonary fungal disease, and chronic total parenteral nutrition who was admitted for acute kidney injury and electrolyte abnormalities. During hospitalization, she developed progressive encephalopathy, hallucinations, paranoia and fluctuating orientation in the setting of biopsy-proven IgM dominant lupus nephritis. Distinguishing NPSE from psychiatric relapse was challenging, given overlapping symptoms. This case emphasizes the need for early recognition and treatment of NPSLE even without classic imaging or sclerosing findings, careful consideration of drug-drug interactions, and coordinated care specialty care to optimize outcomes in patients with overlapping autoimmune and psychiatric disease.

Abbreviations: NPSLE: Neuropsychiatric Systemic Lupus Erythematosus; TPN: Total Parenteral Nutrition; PRBC: Packed Red Blood Cells; PJP: Pneumocystis Jirovecii Pneumonia; SLE: Systemic Lupus Erythematosus; MRI: Magnetic Resonance Imaging; CSF: Cerebrospinal Fluid

Case Presentation

(2/06) Initial Visit

A 59-year-old Caucasian female with a past medical history significant for Staph epidermidis and Trichophyton tricuspid valve endocarditis status post vegetation removal, pulmonary fungal ball on chronic voriconazole therapy, deep vein thrombosis, primary biliary cirrhosis, gastroparesis status-post Roux-en-Y bypass and pyloric pyloromyotomy with a gastric pacemaker, severe protein-calorie malnutrition on chronic total parenteral nutrition (TPN), and bipolar disorder presents to the emergency department for electrolyte abnormalities. The patient was directed to the emergency department at the discretion of her primary care provider after her potassium and creatinine were elevated in outpatient labs. The patient was discharged from a neighboring hospital six days before where she was treated for AKI, dehydration, pneumonia, and encephalopathy. She reported that over the past week, she thought she was "losing it" and "delirious," as she was experiencing visual disturbances, weakness, and recurrent falls. Her laboratory evaluation was remarkable for the following: WBC 13.3 10x3 uL, Hemoglobin 8.9 g/dL, Hematocrit 26.9 %, Potassium 5.4 mmol/L, BUN 63 mg/dL, Creatinine 2.22 mg/dL, and Albumin 3.2 g/dL. EKG showed no acute findings. Chest x-ray showed improving interstitial pneumonitis compared to her previous imaging eleven days prior and adequate PICC line placement. Initial physical examination demonstrated the following:

Physical Exam in the Emergency Department

- **Vitals & Measurements:** T: 36.4°C (Oral) HR: 81(Peripheral) RR: 15 BP: 130/63 SpO2: 100% HT: 163 cm WT: 48 kg IBW: 55.1 BMI: 18.1
- **Constitutional:** Cooperative, conversant.
- **Head:** Normocephalic, atraumatic.
- **Eyes:** Pupils equal, round, reactive to light, sclerae anicteric.
- **ENT:** Dry mucous membranes, oropharynx clear, dentition normal.
- **Neck:** Supple, trachea midline
- **Respiratory:** Clear to auscultation bilaterally, unlabored breathing.
- **Cardiovascular:** Regular rate and rhythm, no murmurs, rubs, gallops, no JVD.
- **Gastrointestinal:** Soft, nontender, nondistended, normoac-

tive bowel sounds

- **Lymphatic:** No lymphadenopathy noted, no lymph node tenderness.
- **Musculoskeletal/Extremities:** No pedal edema
- **Skin:** Normal temperature, turgor and texture, no rash, intact.
- **Neurologic:** No focal neurologic deficits, moving all extremities.
- **Psychiatric:** Awake, alert, oriented x 3, cooperative, mood and affect flat.

Review of Systems in the Emergency Department

- **Constitutional:** Patient endorses chills and fever. Patient denies weight changes.
- **Neurologic:** Patient endorses weakness and dizziness. Patient denies numbness, paresthesia, and loss of consciousness.
- **HEENT:** Patient endorses vision changes, dry mouth, facial swelling, and denies hearing changes.
- **Pulmonary:** Patient endorses dyspnea. Patient denies cough and sputum production.
- **CV:** Patient denies chest pain and shortness of breath.
- **GI:** Patient denies nausea, vomiting, diarrhea, constipation, and, heartburn
- **Musculoskeletal/Extremities:** Patient denies any arthralgias, myalgias, joint swelling, joint stiffness, back pain, neck pain, or injury history.
- **Skin:** Patient denies skin lesions and rashes.
- **Heme/Lymph:** Patient denies bruising and bleeding.
- **Endocrine:** Patient denies polyuria, polydipsia, and temperature intolerance.
- **GU:** Patient denies dysuria, urinary frequency, hematuria, and urinary incontinence.
- **Psychiatric:** Patient denies any anxiety or depression.

Hospital Course

[will remove dates for publication]

- Day 2, (2/7) the patient is brought to the observation unit and is re-evaluated by the hospitalist. She is confused, more energetic, and speaking rapidly. Additionally, her Creatinine continued to increase to 2.3 mg/dL despite intravenous fluid resuscitation. Imaging from her prior hospitalization was reviewed, and CT of the abdomen and pelvis, as well as a renal ultrasound, showed no obstructive pathology. Nephrology is consulted for further evaluation of her acute kidney injury and a work-up for a wide differential, including the following: AKI in the setting of valacyclovir, lithium, or pantoprazole use, cardiorenal syndrome, diabetic nephropathy, autoimmune glomerulonephritis, and hepatitis.

- Day 3, (2/8) she has polyuria and frequent episodes of emesis. She has difficulty keeping up with her hydration with only TPN. The patient is weaned off lithium to rule out the possibility of a lithium-induced diabetes insipidus.

- Day 5, (2/10) The patient has an elevated WBC of 19.5 10x3/uL and procalcitonin of 3.68 ng/mL. Two out of three blood cultures are positive for Pseudomonas aeruginosa and Staphylococcus epidermidis. As the patient is on chronic TPN, her risk of bacteriemia is elevated. Infectious disease is consulted, who determines that the initial blood cultures were positive for Staphylococcus epidermidis as a contaminant. She is initiated on piperacillin-tazobactam and daptomycin for seven days and her PICC line is ordered to be removed. Additionally, the patient continues to have elevated creatinine with a result of 2.82 mg/dL and subnephrotic proteinuria, prompting the consideration of a kidney biopsy. The patient remains nauseous with nonspecific abdominal pain, and CT of the abdomen and pelvis showed some gas/fluid levels concerning diarrhea but no evidence of colitis. She also has some mild appendiceal dilation with the possibility of appendicitis; however, the patient is adamant she previously had an appendectomy.

- Day 6, (2/11) The patient's metabolic acidosis worsens, and she is initiated on a continuous bicarbonate infusion. Her serologic studies show positive antinuclear antibodies and low C4 complement. Nephrology further identifies the need for a kidney biopsy, but concerns are raised as the patient's platelets are descending, she is anticoagulated, and has positive blood cultures. At this time, the patient begins to become forgetful and unable to figure out how to open her phone and find her husband's phone number. She was transferred to the medical floor for closer nursing management.

- Day 8 (2/13), The patient has hematuria, and her CBC showed an RBC 1.82 10x6uL, Hgb 6.4 g/dL, and Hct 18.3%, requiring a transfusion of 2 units of packed red blood cells (PRBC). She underwent a kidney biopsy and became agitated, disoriented, and tried to climb off the operating table. The procedure was canceled, and psychiatry was consulted to further evaluate her mental status and co-morbid bipolar disorder. Upon examination by psychiatry, the patient endorses that she has been having difficulty "managing the perception of reality" as she has regular auditory and visual hallucinations of animals and people. She reports increasing paranoia throughout her hospitalization, with the

thought content of the hospital staff's work being conspiratorial. She endorsed one prior episode of suicidal ideation and multiple psychiatric hospitalizations for manic and depressive episodes. The psychiatrist identified that the patient may be in the midst of a mood episode and increased her lamotrigine and decreased her venlafaxine due to the increased risk of mania. It was also noted that the patient would benefit from antipsychotic therapy, but that it was contraindicated due to the CYP3A4 inhibition of the voriconazole she was on.

- Day 11, (2/16) The patient's kidney function continues to worsen as her creatinine reaches 4.6 mg/dL and BUN 55 mg/dL. Nephrology determined she is at high risk for needing dialysis and ordered the placement of a temporary dialysis catheter. Her WBC climbs to 22.6 10x3/uL, and nephrology highlights the difficulty of treating possible lupus nephritis with Solu-Medrol and mycophenolate mofetil. Immunosuppressive agents are held at this time. Additionally, her mentation continued to decline, and she is significantly more fatigued. A CT of the head showed mild global parenchymal volume loss, mild chronic white matter small vessel ischemic changes, and acute findings. She was transferred to the step-down unit for acute nursing management.

- Day 12 (2/17), A CT-guided kidney biopsy was performed, in which the pathology reported a focal proliferative immune complex glomerulonephritis, acute tubular injury, moderate to focally severe arteriosclerosis, interstitial fibrosis, and tubular atrophy. With the clinical picture, the results were consistent with IgM-dominant lupus nephritis, ISN/RPS class III. The plan to continue with dialysis was utilized as the patient's recent bacteremia and continued elevated white blood cell count were concerning for an occult infection. The patient continued to have paranoia and delusions regarding her hospital stay. The patient was initiated on olanzapine 2.5 mg twice daily.

- Day 13 (2/18), The patient's mentation improved, and she is tolerating olanzapine and lamotrigine without any adverse effects. Her WBC dropped to 7.5 10x3/uL, which raises the possibility that her elevated WBC count on hospital day 11 (2/16) was a false positive. As a result, there is a continued discussion between specialists regarding continuing forward with dialysis or initiating mycophenolate mofetil and methylprednisone. Her hemoglobin and hematocrit declined, and she was transfused with PRBC. The patient is evaluated at the bedside and is found to have a painful, firm, and semi-rigid abdomen. The patient underwent CT of the abdomen and pelvis, which showed a moderate-to-large amount of right perirenal hemorrhage with subcapsular blood, placing a mass effect upon the right kidney and blood in the perirenal and pararenal spaces. The findings were discussed with the interventional radiologist who administered a dose of desmopressin 0.3 mcg/kg over 30 minutes and conducted a right renal arteriogram embolization. It was determined that the patient had a large pseudoaneurysm off of the posterior inferior renal artery branch, likely secondary to renal biopsy.

- Day 16 (2/21), The patient receives one dose of 250mg intravenous methylprednisolone. The patient is evaluated by neurology for concerns of lupus cerebritis. During this consultation, the patient endorses a hospital course history of visual hallucinations of her deceased dog and intermittent confusion. The patient states that her sleep schedule has been "erratic." She also endorses binocular visual disturbances consisting of six images in multiple different gazes. Neurology highlighted the need for an MRI with and without contrast; however, the patient has a gastric pacemaker that would need to be investigated for MRI compatibility. An EEG is performed, which shows no seizure activity. Psychiatry considers a lumbar puncture for diagnostic precision of lupus cerebritis. They also note that following the initiation of steroids, her encephalopathy showed marked improvement.

- Day 20, (2/25) The patient shows clinical improvement with hemodialysis and steroid therapy. She receives her second day of mycophenolate mofetil treatment and underwent an interventional radiology placement of a central venous catheter for TPN and a hemodialysis catheter. Upon examination by psychiatry, the patient endorses anxiety and a mildly depressed mood secondary to her prolonged hospital stay. She continues to endorse visual as well as auditory hallucinations.

- Day 22, (2/27) The patient is seen by psychiatry, and she endorses an increased severity of anxiety and depression; however, she denies having any hallucinations in the past two days. Fluoxetine is added to her psychiatric medication regimen to treat bipolar depression. She has orange-maroon colored stools, and her hemoglobin drops to 5.7 g/dL. She is transfused and seen by the gastroenterology service. The patient undergoes an esophagogastroduodenoscopy, which diagnoses a bleeding marginal ulcer at her Roux-en-Y anastomosis. Resolution of bleeding is achieved with a Hemoclip and electrocauterization. The patient was restarted on proton pump inhibitors, which were previously held by nephrology due to the concern of acute interstitial nephritis. By day 22, she has received three doses of intravenous methylprednisolone and oral prednisone, and her creatinine is down to 2.4 mg/dL. Notably, her confusion and diplopia have improved following this glucocorticoid administration.

- Day 24 (3/1), The patient transfers out of the step-down unit as she has become more medically stable. She endorses that she believes her hallucinations have been worsened by steroid therapy. As a result, it was planned to taper her steroids. Creatinine has decreased to 2.13 mg/dL, and she is adequately making urine. She has not required dialysis since hospital day 21, and her hemodialysis catheter is ordered to be removed. Nephrology plans to continue prednisone 60 mg every other day to help limit

side effects, as well as mycophenolate mofetil 500 mg twice daily. They also plan to increase mycophenolate mofetil to 1000 mg twice daily late next week. Her potassium is stable at 4.8 mmol/L despite being on daily sulfamethoxazole-trimethoprim for Pneumocystis jirovecii pneumonia (PJP) prophylaxis.

- Day 25 (3/2), Her potassium is elevated at 5.5 mmol/L, and her potassium supplement is stopped. She is treated with regular insulin and dextrose, and it is noted that she may not be able to tolerate daily sulfamethoxazole-trimethoprim due to the risk of hyperkalemia, warranting restarting dialysis. Repeat potassium after treatment is 5.0 mmol/L. The patient has an episode of urinary incontinence as well as increased frequency of urination, which the hospitalist team reports is likely a side effect of her steroid treatment. In addition, the patient requests to be taken off olanzapine as she thought it was causing the recurrence of hallucinations and initiation of nightmares. Otherwise, her mood, energy, sleep, and appetite are intact with no increase in anxiety or depression.

- Day 29 (3/6), The patient's gastric pacemaker was investigated and deemed compatible with MRI. Brain MRI with and without contrast reveals mild atrophy with chronic white matter changes, and no acute stroke of hemorrhage was detected. The patient's tunneled hemodialysis catheter is removed from the right femoral vein by interventional radiology. Additionally, to prevent further possibility of hyperkalemia, her TPN was changed to a formula with a lower potassium content given the need to remain on sulfamethoxazole-trimethoprim for PJP prophylaxis. She is deemed stable for discharge and will follow up closely with nephrology and rheumatology for continued management of steroid and immunosuppressive therapy, as well as psychiatry for bipolar disorder.

Discussion

Neuropsychiatric systemic lupus erythematosus (NPSLE) represents a diverse range of psychiatric and neurological complications which arise from immune-mediated injury to the central nervous system. Pathogenesis is multifactorial, involving cytokine-driven inflammation, antibody-mediated neuronal damage, and disruption of the blood-brain barrier. [1,2] This may manifest as a spectrum of clinical features, including altered consciousness, hallucinations, mood disturbances, cognitive decline, and cerebrovascular disease, typically exhibiting a variable course. Women are disproportionately affected, and while NPSLE may occur at any stage of systemic lupus erythematosus (SLE), it most frequently arises during periods of heightened systemic disease activity. [3] Our patient exhibited a rapidly progressive neuropsychiatric syndrome, manifesting as paranoia, visual and auditory hallucinations, and disorientation, occurring in the setting of biopsy-confirmed lupus nephritis. Her pre-existing bipolar disorder complicated symptom attribution, as both psychiatric relapse and inflammatory CNS involvement remained plausible explanations. However, the presence of active systemic lupus, serologic abnormalities such as ANA positivity and hypocomplementemia, and immune-complex-mediated renal disease supported an inflammatory etiology. The intermittent course of delirium and perceptual disturbances aligned with patterns typically observed in NPSLE.

Distinguishing NPSLE from primary psychiatric disorders presents a significant diagnostic challenge. The overlap of presentations between NPSLE and mood disorders, psychosis and delirium contributes to misdiagnosis and delayed diagnosis [4]. Yet, despite continued clinical investigation, no laboratory or imagining modality has been held as the gold standard for a comprehensive diagnosis of NPSLE. [5] Neuroimaging utilizing magnetic resonance imaging (MRI) has long been utilized to assess patients with SLE. Pathology is identified via brain lesions reflected as hyper or hypotense areas and gross morphological changes such as global atrophy [6]. However, approximately 50% of patients with NPSLE have no detectable abnormalities on MRI. 7. As advancements are made in MRI software, there may be increased sensitivity to distinguish changes in NPSLE patient's brains, thus pleading the need for further research into neuroimaging and characterization of lesions. [6,7] Additionally, elevated levels of IL-6 in cerebrospinal fluid (CSF) is a notable biomarker for patients diagnosed with NPSLE [6]. While IL-6 is not specific, it has been suggested as a useful marker to monitor disease progression and treatment response [6]. In our patient, brain MRI showed only chronic small vessel changes, and CSF analysis was deferred due to procedural risks, which is not uncommon in clinical practice.

Thus, it is imperative that clinical discussion among the healthcare team weigh the risk and benefit of patients undergoing additional tests that may not lead to diagnosis. This case illustrates that the absence of classic MRI or CSF abnormalities should not delay treatment, especially when clinical suspicion for inflammatory CNS involvement is substantial. Corticosteroids are the primary treatment for lupus cerebritis, with medications such as cyclophosphamide and mycophenolate mofetil used in moderate to severe or refractory cases [8]. As the pathogenesis of NPSLE is becoming more advanced, there is promising development of immunomodulating drugs that target B cells, T cells, and cytokines [8]. In this patient, antipsychotic management was further complicated due to potential drug-drug interactions. Olanzapine, which is primarily metabolized by CYP1A2 was chosen to avoid pharmacokinetic interference from voriconazole therapy, which is a potent CYP3A4 and CYP2C9 inhibitor. While the patient's neuropsychiatric symptoms improved, her hospital course was complicated by infection, acute kidney injury, and post-renal biopsy hemorrhaging stressing the need for coordinated care across neurology, psychiatry, rheumatology, infectious disease, and nephrology.

In patient cases such as this, interdisciplinary speciality management was crucial to navigating the complexity of overlapping medical and psychiatric conditions. Continued follow-up care remains crucial

to detect relapse, tailor immunosuppressive therapy and manage any psychiatric sequelae. This case highlights the diagnostic and management challenges of NPSLE in the absence of standard markers, particularly when psychiatric comorbidities further obscure the clinical picture. The patient's robust response to corticosteroid therapy emphasizes the need for early recognition and immunosuppression in neuropsychiatric manifestations of lupus. Multidisciplinary, individualized management is essential for optimizing outcomes in these cases.

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