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9-month course of refractory anti-NMDA receptor encephalitis with initial negative markers: diagnostic and therapeutic challenges

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9-Month Course of Refractory Anti-NMDA Receptor Encephalitis with Initial Negative Markers: Diagnostic & Therapeutic Challenges

Background:
Anti-NMDA receptor encephalitis is a progressively debilitating, clinically heterogeneous, frequently fatal disease caused by autoantibodies directed against the N-methyl-D-aspartate receptor that affects 1 in 1.5 million people each year. Risk of misdiagnosis or delayed treatment is high due to variable presentations and potential false negative results.

Case report:
A 28-year-old female without significant medical history or substance abuse presented with suicidal ideation and amnesia, one week after experiencing flu-like symptoms. Within days she developed auditory hallucinations, nonsensical speech, became withdrawn, delusional, impulsive, catatonic, and then selectively mute leading to psychiatric placement. On day 4, she developed status epilepticus leading to respiratory failure requiring intubation, mechanical ventilation and eventual tracheostomy. Constant dyskinesia- and myorhythmia-like movements were observed in the face and extremities. Elevated temperature, fluctuating blood pressures and heart rate demonstrated dysautonomia. Cerebrospinal fluid (CSF) and serum anti-NMDA receptor antibodies were negative. Magnetic resonance imaging was inconclusive, however electroencephalogram demonstrated extreme delta brush, concerning for anti-NMDA receptor encephalitis. Pelvic computerized tomography revealed a right adnexal teratoma. High clinical suspicion led to treatment with high-dose steroids and intravenous immune globulin with no improvement. On day 22, after one plasmapheresis session, repeat CSF serology revealed markedly elevated NMDA antibodies. Rituximab was added onto her regimen and the teratoma was laparoscopically resected, with pathology confirming neuronal components. On day 80, after no improvement, cyclophosphamide was initiated, however intermittent infections repeatedly delayed treatment. On day 147, after three cycles of cyclophosphamide her neurological status began to improve. She participated in intense rehabilitation and was eventually discharged home on day 269.

Conclusion:
Recognizing the variable presentation of anti-NMDA receptor encephalitis is important in avoiding misdiagnosis and delayed treatment. If clinical suspicion remains high despite negative results, repeat testing should be pursued. Clinical response should guide treatment decisions in refractory cases, such as this, where prolonged cyclophosphamide therapy reversed disease progression.