

Filling the Gap: An Innovative Approach to Autoimmune Encephalitis Using an Index-of-Suspicion Model

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Background/Significance

- Autoimmune encephalitis (AE) poses a substantial diagnostic challenge, often masquerading as psychiatric disorders during initial evaluations^{1,2}
- Current literature primarily focuses on testing for AE only when overt neurological signs manifest or treating based on the assumption that labs and imaging have been obtained³
- There is a lack of guidance about when to pursue testing in cases with more psychopathologically compelling narratives

Objectives

- Develop an Index-of-Suspicion (IoS) model through an expert review of AE literature, weighting each factor based on its relative prevalence
- Conduct a retrospective analysis on three cases that presented to a general emergency room, all with subacute onset of symptoms and concern for AE
- Apply the IoS model and show how it can encourage testing and improve the timely and accurate diagnosis of AE, particularly in cases initially presenting with mainly psychiatric symptoms

IoS Model

	Case 1	Case 2	Case 3			
1 point	Decreased alertness or somnolence	X	X	X		
	Woman	X	X	X		
	Age 13-36	X	X	X		
	Speech dysfunction (pressured speech, verbal reduction, or mutism)	X		X		
	Onset 1-3 months					
3 points	Rapid onset (< 4 weeks)	X	X			
	Cognitive dysfunction (below baseline)	X	X	X		
5 points	Autonomic dysfunction					
	Catalepsy or rigidity					
	Seizure		X			
	Dyskinesia	X	X			
Total Points:				15	19	7
Final Diagnosis:				ANDMARE	ANDMARE	Schizophrenia

Table 1. Diagnostic Criteria and Weighting Factors for Possible Autoimmune Encephalitis. Case 1 scored 15 points (high suspicion—see Table 2) with a final diagnosis of ANDMARE (anti-NMDA receptor encephalitis). Case 2 scored 19 points (high suspicion—see Table 2) with a final diagnosis of ANDMARE. Case 3 scored 7 points (intermediate suspicion—see Table 2) with a final diagnosis of schizophrenia.

Low Suspicion (0-4 points)	<ul style="list-style-type: none"> Consider other diagnoses
Intermediate Suspicion (5-10 points)	<ul style="list-style-type: none"> Medication: Avoid first-generation antipsychotics; prefer SGAs such as olanzapine, or benzodiazepines Detainment: Psychiatric or “Medical Incapacity Hold” depending on hospital policy Tests: The patient may be able to consent <ul style="list-style-type: none"> Screening or spot EEG Lumbar puncture (oligoclonal bands, cell count, protein, autoimmune panel) MRI brain with contrast Tumor search: Abdominal or transvaginal U/S, especially in women Location: If CSF labs were obtained, the patient may be admitted to an inpatient psychiatric hospital and monitored for progression while awaiting test results
High Suspicion (10+ points)	<ul style="list-style-type: none"> Medications: Avoid first-generation antipsychotics; prefer benzodiazepines over antipsychotics Detainment: Utilize a “Medical Incapacity Hold” depending on hospital policy Tests: A surrogate may need to consent if the patient refuses. Consider general anesthesia. Consider ethicist involvement. <ul style="list-style-type: none"> Screening or spot EEG Lumbar puncture (oligoclonal bands, cell count, protein, autoimmune panel) Brain MRI with contrast Tumor search: Abdominal or transvaginal U/S, PET-FDG, and whole-body MRI with contrast Location: Admit to medical/neurological service for testing. <p>Note: Progression of symptoms or lab/imaging findings may raise the patient from low or intermediate suspicion to high suspicion</p>

Table 2. Stratification for the likelihood of autoimmune encephalitis based on total points from Table 1 and recommendations; SGA= second generation antipsychotic

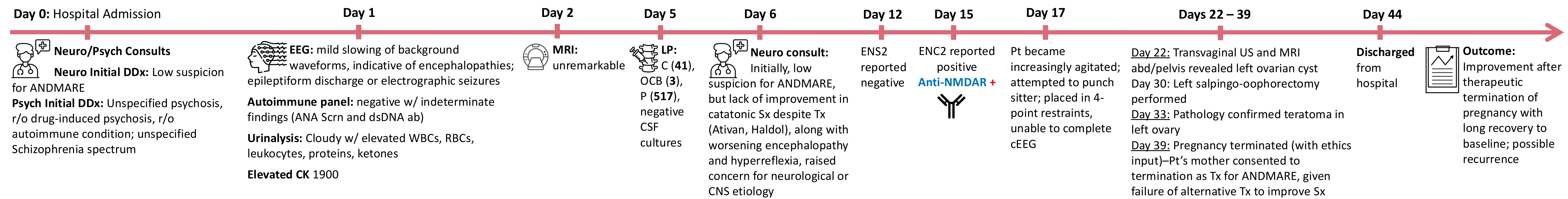
Conclusion/Discussion

- The IoS model combines objective and narrative assessments to address diagnostic challenges in AE, guiding decisions on psychiatric versus medical hospitalization, testing, and decision-making capacity
- This study shows that attributing symptoms to psychiatric causes too early can lead to premature closure and anchoring bias, underscoring the need for a nuanced clinical perspective
- The three cases demonstrate that a IoS model could prompt earlier and more targeted evaluation and ensure appropriate neurological or psychiatric care
- A consistent protocol like the IoS model is crucial for accurate and timely AE diagnosis, especially in cases presenting with psychiatric symptoms, to reduce missed diagnoses and support appropriate treatment
- Future research will evaluate and further develop the application of the IoS Model in clinical practice to improve patient outcomes

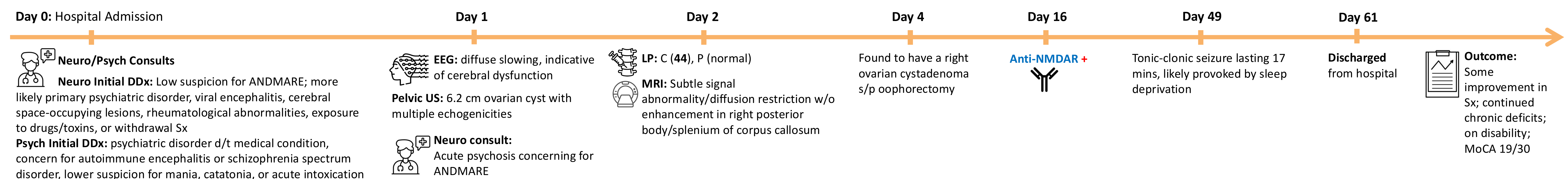
Case Presentations

Key: C = nucleated cells (norm = 0-5); OCB = oligoclonal bands (norm = 0); P = protein (norm = 15-60); Anti-NMDAR+/- = anti-N-methyl-D-aspartate receptor antibodies positive/negative; ANDMARE = anti-NMDA receptor encephalitis; ENS2 = Encephalopathy Autoimmune panel, Serum; ENC2 = Encephalopathy Autoimmune panel, CSF

Case 1: 18 y/o F G1P0 at 15w3d, no psychiatric hx, brought in by mother for 2-week hx of worsening, acute-onset psychosis with disorganized thinking, disorientation, and catatonia. Reports intermittent neck stiffness and poor sleep. Impulsive behavior on admission (attacked staff, sexually inappropriate), purposeless hand gestures, nonsensical speech; required physical restraints. Recent sexual assault, college student until month of admission.



Case 2: 19 y/o F, no psychiatric hx, brought in by mother for 5-day hx of abdominal pain and acute encephalopathy with Sx of feeling “weird” and that “something is not normal,” dyskinesia, disorganization, delusions of pregnancy, aggression, confusion, and poor sleep. Evaluated at outside hospital (abdominal cyst found). Aggressive on admission, required physical restraints. Nursing student, 4 months from graduation.



Case 3: 20 y/o F, unknown PMHx, brought in by police. Abdominal pain, guarded behavior, catatonia, flat affect, mutism, unable to engage or provide hx. Previous hospitalization 1-2 weeks ago for suspected 1st-break schizophrenia. Reported hx of childhood sexual abuse by male family member.

