

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

Case 1: 18 y/o F G1PO at 15w3d, no psychiatric hx, brought in by mother for 2-week hx of worsening, acuteonset 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.

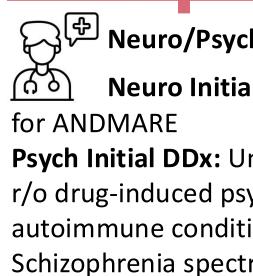
Case 3: 20 y/o F, unknown PMHx, brought in by police. Abdominal pain, guarded behavior, catatonia, flat affect, mutism, unable to engage or provide hx. Previous hospitalization 1-2 weeks ago for **suspected 1st-break** schizophrenia. Reported hx of childhood sexual abuse by male family member.

1 point points 5 points

Table 1. Di schizophrenia

Key: C = nucleated cells (

Day 0: Hospital Ad



Day 0: Hospital A

유^伊 Neuro/Psyc (63) Neuro Initia likely primary psych space-occupying le to drugs/toxins, or Psych Initial DDx: concern for autoim disorder, lower sus

Day 0: Hospital A

다. 아이 Neuro/Psyc 63 Neuro Init abuse/trauma, cat **Psych Initial DDx:** catatonia, r/o acute encephalitis

References: (1) Endres, Dominique, et al. "Autoimmune encephalitis as a differential diagnosis of schizophreniform psychosis: clinical symptomatology, pathophysiology, diagnosis of schizophreniform psychosis: clinical symptomatology, diagnosis of schizophreniform psychosis: clinical symptomatology, diagnosis of schizophreniform psychosis: clinical symptomatology, and therapeutic considerations. "European archives of psychiatry and clinical symptomatology, diagnosis of schizophreniform psychosis: clinical sympt phenotypic analysis of individual patient data." The Lancet Psychiatry 6.3 (2019): 235-246. (3) Abboud, Hesham, et al. "Autoimmune encephalitis: proposed best practice recommendations for diagnosis and acute management. " Journal of Neurology, Neurosurgery & Psychiatry 92.7 (2021): 757-768.

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

Jeanie Kim, BA¹; Mark Ard, MD, MA^{2,3}; Matthew Allen, MD³; My Phuong Tong, MD³ ¹Loma Linda University School of Medicine, ²Loma Linda Veterans Affair Hospital, ³Loma Linda University Health

IoS Model

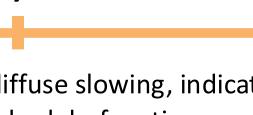
	Case 1	Case 2	Case 3	Low Suspicion
Decreased alertness or somnolence	X	X	X	(0-4 points) Intermediate
Woman	X	X	X	Suspicion
Age 13-36	X	X	X	(5-10 points)
Speech dysfunction (pressured speech, verbal reduction, or mutism)	X		X	
Onset 1-3 months				
Rapid onset (< 4 weeks)	X	X		
Cognitive dysfunction (below baseline)	X	X	X	High Suspicio
Autonomic dysfunction				(10+ points)
Catalepsy or rigidity				
Seizure		X		
Dyskinesia	X	X		
Total Points:	15	19	7	
Final Diagnosis:	ANDMARE	ANDMARE	Schizo- phrenia	

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

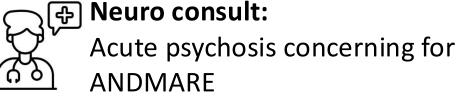
Table 2. Stratification for the likelihood of autoimmune encephalitis based on total points from Table 1 and recommendations; SGA= second ge antipsychotic

Case Presentations

s (norm = 0-5); OCB = oligocle	onal bands (norm = 0); P = p	protein (norm = 15-60); Anti-NM	DAR+/– = anti-N-methy	/l-D-aspartate re	eceptor antibodies positive/nega	ative; ANDM	ARE = anti-NMDA re	eceptor encephalitis; ENS2	2 = Encepl
Admission	Day	1	Day 2	Day 5	Day 6	Day 12	Day 15	Day 17	
Eych Consults tial DDx: Low suspicion Unspecified psychosis, psychosis, r/o dition; unspecified ectrum	epileptiform discharge of	icative of encephalopathies; or electrographic seizures gative w/ indeterminate dsDNA ab) levated WBCs, RBCs,	MRI: unremarkable	LP: C (41), OCB (3), P (517), negative CSF cultures	Neuro consult: Initially, low Suspicion for ANDMARE, but lack of improvement in catatonic Sx despite Tx (Ativan, Haldol), along with worsening encephalopathy and hyperreflexia, raised concern for neurological or CNS etiology	ENS2 reported negative	ENC2 reported positive Anti-NMDAR +	Pt became increasingly agitated; attempted to punch sitter; placed in 4- point restraints, unable to complete cEEG	Day 22: abd/pel Day 30: perform Day 33: left ova Day 39: input)–l termina failure o
Admission		Day 1		Da	y 2	Day	4	Day 16	
sych Consults itial DDx: Low suspicion for chiatric disorder, viral enc lesions, rheumatological a or withdrawal Sx : psychiatric disorder d/t n immune encephalitis or sc uspicion for mania, catator	ephalitis, cerebral bnormalities, exposure nedical condition, hizophrenia spectrum	EEG: diffuse slow of cerebral dysfu Pelvic US: 6.2 cm ovariar multiple echogenicities Neuro consult: Acute psychosis ANDMARE	n cyst with	enhanceme		Found to h ovarian cys s/p oophor	stadenoma	Anti-NMDAR +	Tonic-cl mins, lil depriva
l Admission		Day 2	Day	7	Day 16: 2	2 nd Admissi	on	Day 20	
esych Consults Initial DDx: Psychiatric comp atatonia, low suspicion for atatonia , low suspicion for atatonia , low suspicion for utatonia, low suspicion for atatonia, low suspicion for atato	plaint, victim of Serun encephalitis CSF V disorder,	US : 4.2 cm left ovarian cyst n RPR: Reactive (1.2) DRL: unremarkable	LP: studies wer MRI: Single, no in right frontal matter w/o en	onspecific T2 ir subcortical wh	Admitted for continued no nite LP: pleoc encephal	nverbal, cat	atonic state	EEG: a genera consistent wit encephalopath	h mild









Consider other diagnoses

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

• 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 psych hospital and monitored for progression while awaiting test results

Medications: Avoid first-generation antipsychotics; prefer benzodiazepines over antips **Detainment:** Utilize a "Medical Incapacity Hold" depending on hospital policy Tests: A surrogate may need to consent if the patient refuses. Consider general anesthe Consider ethicist involvement.

• 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 **Location:** Admit to medical/neurological service for testing.

Note: Progression of symptoms or lab/imaging findings may raise the patient from low or intermediate suspicion to high suspicion

ephalopathy Autoimmune panel, Serum; **ENC2** = Encephalopathy Autoimmune panel, CSF Days 22 – 39 Day 44 **Outcome**: Discharged 22: Transvaginal US and MRI || Improvement after pelvis revealed left ovarian cyst from hospital 30: Left salpingo-oophorectomy | therapeutic termination of rmed pregnancy with <u>33:</u> Pathology confirmed teratoma in long recovery to baseline; possible <u>39:</u> Pregnancy terminated (with ethics))–Pt's mother consented to recurrence ination as Tx for ANDMARE, given re of alternative Tx to improve Sx Day 49 Day 61 Outcome: Discharged c-clonic seizure lasting 17 Some from hospital , likely provoked by sleep improvement in ivation Sx; continued chronic deficits; on disability; MoCA 19/30 **Day 23 Outcome:** nal with Anti-NMDAR -Limited response to slowing, antipsychotics; (No concerns for ovarian stabilized at lower teratoma as a cause of level of function on ANDMARE) clozapine



	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
hiatric	 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
sychotics nesia.	 The three cases demonstrate that a IoS model could prompt earlier and more targeted evaluation and ensure appropriate neurological or psychiatric care
n contrast	 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
generation	 Future research will evaluate and further develop the application of the IoS Model in clinical practice to improve patient outcomes