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Gait Disturbance as the Presenting Symptom in Young Children With Anti-NMDA Receptor Encephalitis

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Pediatria d'Urgenza

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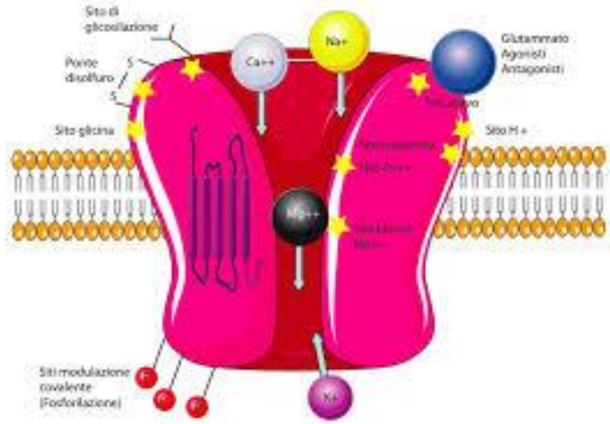
Encefalite anti – NMDAR



Paraneoplastic encephalitis, psychiatrics symptoms and hypoventilation in ovarian teratomas, Vitaliani R, 2005

Paraneoplastic anti N-methyl-d-aspartate receptor encephalitis associated with ovarian teratoma, Dalmau J, 2007

Anti N-methyl-d-aspartate receptor (NMDAR) encephalitis in children and adolescents, 2009

The frequency of autoimmune N-methyl-d-aspartate receptor encephalitis surpasses that of individual viral etiologies in young individuals enrolled in the California Enchephalitis Project, Gable MS, 2012

Caratteristiche cliniche dell'encefalite anti – NMDAR in età pediatrica

TABLE 1 Clinical Features of Anti-NMDAR Encephalitis

	Adults	Children
Initial presenting symptoms	Changes in mood, behavior, and personality; psychosis	Seizures, movement disorders, changes in speech, disrupted sleep patterns
Symptoms at illness peak	Seizures, decreased consciousness, memory deficits, movement disorders	Seizures, movement disorders, behavioral changes
Manifestation of autonomic instability	Cardiac arrhythmias, central hypoventilation	Hypertension, tachycardia, hyperthermia
Classic etiology	Ovarian teratoma, other tumor, postinfection	Suspected postinfection

Caratteristiche cliniche di 4 bambini con encefalite anti - NMDAR

TABLE 2 Cases: Clinical Characteristics

	Case 1	Case 2	Case 3	Case 4
Age at symptom onset, mo	39	25	36	17
Sex	Female	Male	Male	Female
Clinical symptoms at presentation				
Ataxia	Yes	No	No	No
Unilateral refusal to bear wt	No	Yes	Yes	Yes
Sleep disturbance	Yes	No	Yes	No
Behavior or personality change	Yes	No	Yes	Yes
Seizure	Yes	No	Yes	No
Chorea or orofacial dyskinesia	No	No	No	Yes
Speech disturbance or arrest	Yes	No	Yes	No
Recent preceding illness	Yes	Yes	No	No
Clinical symptoms subsequently developed				
Ataxia	Yes	No	No	No
Unilateral refusal to bear wt	No	Yes	Yes	Yes
Sleep disturbance	Yes	Yes	Yes	Yes
Behavior or personality change	Yes	Yes	Yes	Yes
Seizure	Yes	No	Yes	No
Chorea or orofacial dyskinesia	No	Yes	Yes	Yes
Speech disturbance or arrest	Yes	Yes	Yes	Yes

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Neuroimaging, EEG e liquor

TABLE 3 Cases: Diagnostic Findings

	Case 1	Case 2	Case 3	Case 4
MRI brain (region of abnormalities)	Cingulate, dentate, parahippocampal	Right frontal, cingulate	Normal	Normal
Magnetic resonance spectroscopy brain	Not done	Normal	Normal	Not done
MRI spine	Not done	Normal	Not done	Normal (cervical)
Malignancy evaluation	Abdominal ultrasound and computed tomography of the chest, abdomen, pelvis normal	Abdominal and scrotal ultrasound normal	Not done	Abdominal ultrasound and MRI pelvis normal
EEG	Focal slowing	Normal	Focal slowing and focal seizures	Bilateral slowing
CSF studies				
White blood cells/mm^3	10	1	21	4
Glucose, mg/dL	51	73	53	56
Protein, mg/dL	18	13	16	21
IgG index[a]	Not done	0.9	1.2	0.5
Oligoclonal bands[b]	Pattern 2	Pattern 2	Pattern 2	Pattern 1
Bacterial or viral testing	Negative	Negative	Negative	Negative
Paraneoplastic panel	Negative	Not done	Negative	Negative
NMDAR Antibody	Positive	Not done	Positive	Positive
Serum studies				
Paraneoplastic panel	Negative	Negative	Negative	Negative
NMDAR Antibody	Not done	Positive	Positive	Positive

[a] Normal immunoglobulin G (IgG) index ≤0.8.

[b] Oligoclonal bands pattern 1: No oligoclonal IgG bands present in CSF or serum. Oligoclonal bands pattern 2: Two or more oligoclonal IgG bands identified in CSF on intrathecal synthesis of IgG).

Christian, 5 anni

Agosto 2012
“Sensazione di scossa all’AS sn, seguita da parestesie, pdc di pochi minuti e in seguito ipertono dello stesso arto”.
EON : ipostenia AI sn con impaccio motorio, fini movimenti atetoidi mano sn
EEG : nella norma
TC encefalo e RMN encefalo : nella norma
Remissione della sintomatologia

Settembre 2012
“Parestesie del piede dx, seguite da clonie, ipertono e difficoltà a deambulare, seguite da caduta a terra per cedimento degli arti inferiori”. In PS clonie del piede sn e successiva crisi convulsiva tonico-clonica generalizzata con pdc.
EEG : modesto rallentamento F-C-P dx anche di possibile natura post-critica
Terapia anticomiziale

Dicembre 2012
Afasia e stato di agitazione, aprassie buccali e linguali con difficoltà di alimentazione, atassia, dismetria
NMDAR Ab su liquor : positivi

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Trattamento e prognosi

TABLE 4 Cases: Treatments and Outcomes

	Case 1	Case 2	Case 3	Case 4
Seizure treatment	Levetiracetam → valproic acid	None	Levetiracetam → oxcarbazepine	None
Insomnia treatment	Clonidine	Clonidine	None	Clonidine
Attention treatment	None	None	Methylphenidate	None
Chorea treatment	None	Carbamazepine	None	None
Immune therapy				
IVIg	Not administered	2 g/kg divided over 5 days	2 g/kg divided over 5 days	2 g/kg divided over 3 days, then monthly for 6 months
IV methylprednisolone	Not administered	30 mg/kg per day for 5 days	30 mg/kg per day for 5 days	30 mg/kg per days for 5 days
Rituximab	Not administered	Not administered	Not administered	375 mg/m^2 weekly for 4 weeks
Posthospitalization disposition	Home	Inpatient rehabilitation	Inpatient rehabilitation	Inpatient rehabilitation
Follow-up				
1 mo	Seizure-free, mild behavior and sleep problems	Able to stand independently, residual gait disturbance	Baseline mobility, mild language and attention problems	Poor oral intake, mobility symmetric, unable to sit, lack of verbalization
3 mo	Not available	Improved insomnia and chorea, clonidine and carbamazepine weaned off	Baseline mobility and attention, mild language delay	Able to sit but unable to bear weight, insomnia, lack of verbalization
6 mo	At baseline	At baseline	Not available	Stands unassisted, chorea resolved, full oral diet, minimal verbalization
8 mo	Not available	Not available	Not available	Walks unassisted, clonidine weaned off, minimal verbalization