Case Report

An unusual case of altered mental status in a young woman

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Citation: Challapalli RMR, Chipinapi T, Bharadwaj S, Kissell K. An unusual case of altered mental status in a young woman. North Am J Med Sci 2011; 3: 518-519.

doi: 10.4297/najms.2011.3518

Abstract

Context: We describe a case of paraneoplastic neurologic syndrome, namely N-Methyl-D-Aspartic acid receptor antibody associated limbic encephalitis, a rare cause of altered mental status in the young. Case Report: A 28 year old Caucasian female nurse presented with acute onset difficulty with word finding and increasing confusion and agitation. She also had visual hallucinations, transient episodes of unresponsiveness, and lingual dyskinesias. Workup including blood, imaging and regular cerebrospinal fluid (CSF) studies was unremarkable. She subsequently developed complex partial seizures. Computerized Tomography scan of chest/abdomen/pelvis revealed a dermoid cyst of the left ovary and CSF N-Methyl-D-Aspartic acid receptor antibody returned positive confirming the diagnosis of paraneoplastic NMDA receptor antibody associated limbic encephalitis. She was treated with methylprednisolone therapy along with plasmapheresis and a left salpingo-ophrectomy was performed. The patient showed significant improvement with respect to her cognitive function and had no more seizures. Conclusion: N-Methyl-D-Aspartic acid receptor antibody associated limbic encephalitis is a rare paraneoplastic neurologic syndrome with symptoms including psychiatric manifestations, seizures, language disturbances and autonomic instability. It develops due to antibody induced decrease in N-Methyl-D-Aspartic acid receptors. There is a significant association with ovarian teratoma in >50% female cases. Treatment includes resection of tumor, glucocorticoids, plasmapheresis and Intravenous Immunoglobulin therapy.

Keywords: Paraneoplastic neurologic syndrome, N-Methyl-D-Aspartic acid (NMDA) receptor, limbic encephalitis, confusion, complex partial seizures, ovarian teratoma, plasmapheresis.

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Introduction

Paraneoplastic neurologic syndromes are a group of rare neurologic disorders associated with systemic cancers which affect any part of the nervous system. We describe one such rare case of paraneoplastic neurologic syndrome, namely N-Methyl-D-Aspartic acid (NMDA) receptor antibody associated limbic encephalitis.

Case Report

A 28 year old Caucasian female nurse, S. P., with past medical history significant for right ovarian teratoma status post removal 4 years prior to admission, presented to an outside facility with chief complaint of acute onset difficulty with word articulation. The patient, without any known past psychiatric history, was noted by observers to be increasingly confused and agitated with aggressive physical behavior for which she was admitted to a psychiatric unit with a diagnosis of acute psychosis. At the time of psychiatric admission, the patient displayed visual hallucinations, transient episodes of unresponsiveness, and lingual dyskinesias. Workup including complete blood count, comprehensive metabolic panel, thyroid studies, blood cultures, erythrocyte sedimentation rate, venereal disease research laboratory test (VDRL) screening test were within normal limits except for a creatinine phosphokinase (CPK) level of 19,000. Electroencephalography (EEG) showed nonspecific diffuse slowing. Magnetic resonance imaging and angiography (MRI/MRA) of brain was unremarkable.
Urine drug screen was negative except for benzodiazepines, which she received for agitation.

Upon transfer to our facility, the patient was noted to be mute except for occasional echolalia. Examination revealed Glasgow coma scale of 10 (E4, V2, M4), brisk reflexes, increased muscle tone with intermittent dystonic posturing of the extremities. Brainstem reflexes were intact. During hospital course, the patient developed complex partial seizures with secondary generalization. Cerebrospinal fluid analysis revealed glucose of 80, protein 28, red blood cell count 6, herpes simplex virus polymerase chain reaction negative, oligoclonal bands and myelin basic protein negative. Autoimmune etiologies, lupus cerebritis and porphyria were excluded. A CT scan of chest/abdomen/pelvis revealed a 2.1 x 2.27 x 2.43 cm dermoid cyst of the left ovary.

CSF NMDAR antibody returned positive confirming diagnosis of paraneoplastic NMDAR antibody associated limbic encephalitis. A left salpingo-oophorectomy was performed. Methylprednisolone therapy was initiated followed by plasmapheresis for total of seven treatments. Following plasmapheresis, the patient showed significant improvement with respect to language and cognitive function. Following therapy, she developed right wrist drop and left foot drop. On follow up, the patient continued to have short term memory impairment, however there was complete resolution of wrist drop and partial resolution of foot drop and no further seizure episodes were noted.

**Discussion**

NMDA receptor antibody associated limbic encephalitis is a rare paraneoplastic neurologic syndrome with symptoms including psychiatric manifestations (agitation, hallucinations and incongruous behavior), stupor with catatonic features, seizures, language disturbances such as mutism and echolalia, frequent dyskinesias, and autonomic instability [4].

Differential diagnosis includes primary psychiatric disorders, malignant catatonia, neuroleptic malignant syndrome, viral encephalitis [7], and encephalitis lethargica.

Evaluation includes CSF analysis which may be normal or show lymphocytic pleocytosis, EEG showing frequent slow disorganized activity, MRI brain which is often normal. Diagnosis of NMDAR encephalitis is confirmed by detection of antibodies to NR1/NR2 heteromers of the NMDAR in Serum or CSF [3, 4, 8, 9]. According to Dalmau et al, these antibodies cause a titer-dependent, reversible decrease of synaptic NMDAR by a mechanism of cross linking and internalization. On the basis of models of pharmacological or genetic disruption of NMDAR, these antibody effects reveal a probable pathogenic relation between the depletion of receptors and the clinical features of anti-NMDA receptor encephalitis. Approximately 50% of female patients >18 years also have uni/bilateral ovarian teratomas while in males, rarely a teratoma can be found in association.

Treatment includes resection of tumor, glucocorticoids, plasmapheresis and IVIG therapy [10]. Patients who do not improve with these first line therapies may improve with rituximab and cyclophosphamide. Relapse occurs in 15-20% cases and is often associated with occult or relapsing teratoma.

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