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Clinical Letter

Anti-*N*-Methyl-D-Aspartate Receptor Encephalitis Presenting as Isolated Psychosis in an Adolescent Female

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We describe an adolescent female presenting with first-episode isolated psychosis due to anti-*N*-methyl-D-aspartate receptor (NMDAR) encephalitis and ovarian teratoma. Rapid improvement in symptoms occurred after immunotherapy and tumor removal. This girl illustrates that anti-NMDAR encephalitis should be considered in the differential diagnosis of first presentation psychosis in children and adolescents, even in the absence of additional neurological symptoms or signs.

Patient Description

This previously well 14-year-old girl was admitted to the mental health unit of an Australian tertiary children's hospital with a two-week history of acute-onset, first-episode psychosis, involving thought disorder, paranoia, and auditory hallucinations. No infective or psychiatric prodrome occurred before symptom onset. No neurological symptoms developed, and examinations apart from mental state examination were normal. Investigations revealed strongly positive serum and cerebrospinal fluid (CSF) NMDAR antibodies. CSF was otherwise normal. Brain magnetic resonance imaging was normal, whereas electroencephalography showed a mildly encephalopathic background. An ovarian teratoma was detected on pelvic imaging and subsequently resected. Slight clinical improvement was seen with antipsychotic medication, but definitive treatment with intravenous steroids and intravenous immunoglobulin, commenced three weeks after onset, resulted in rapid recovery. No symptom recurrence has occurred over a 24-month follow-up period.

Discussion

Anti-NMDAR encephalitis first described in 2007[1] and in some studies is more prevalent than any single form of viral encephalitis.[2] Over half of individuals with anti-NMDAR encephalitis have prodromal symptoms,[1] followed by a highly characteristic constellation of clinical features, including psychiatric and behavioral disturbance, movement disorder, seizures, speech and language dysfunction, autonomic instability, and impaired

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consciousness. In the largest cohort study of anti-NMDAR encephalitis (366 adults and 211 children older than five years) almost 90% developed multiple neurological and psychiatric symptoms within the first month from presentation.[3] Only 1% of all patients were monosymptomatic at presentation and remained so throughout the disease course.[3]

Psychiatric disturbance is a prominent feature in adolescent (and adult) patients, although rarely seen in isolation.[4] Eighty percent of all adult patients with the disease are initially seen by a psychiatrist.[5] Standard organic evaluation for first-episode-psychosis is commonly unrevealing as brain magnetic resonance imaging[1] is often normal and it is not part of routine practice to perform a lumbar puncture, electroencephalography, or NMDAR antibodies. The most sensitive diagnostic test for anti-NMDAR encephalitis is CSF NMDAR antibodies, which are always positive.[1] In contrast, serum antibodies are negative in 15%.[1] Anti-NMDAR encephalitis is highly treatable with immunotherapy and tumor removal, and early treatment improves outcome.[3]

A high index of suspicion is therefore required for the diagnosis of anti-NMDAR encephalitis in isolated, first-episode psychosis to identify the rare but recognized monosymptomatic presentation of the disease. The short duration from symptom onset to definitive treatment in this patient may have halted the progression of disease and evolution of other typical symptoms, with some reports showing up to four months before a second symptom developed.[6] Early diagnosis in this case likely contributed to the rapid recovery and excellent outcome and reinforces the importance of prompt recognition of the condition.

Conclusion

This report demonstrates that isolated psychiatric symptoms without typical evolution of other characteristic manifestations can occur in anti-NMDAR encephalitis, particularly when identified and treated early. This disease should be considered in the differential diagnosis of first-episode psychosis, especially in young women with rapid onset of symptoms. Treatment with immunotherapy is effective with a full recovery in the majority. This patient is particularly informative for pediatricians and psychiatrists assessing adolescents with new-onset psychiatric symptoms.

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