PSYCHOTIC DISORDERS GENERATED BY AUTOIMMUNE ENCEPHALITIS (CLINICAL CASE)

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PSYCHOTIC DISORDERS GENERATED BY AUTOIMMUNE ENCEPHALITIS (CLINICAL CASE) (Abstract): Encephalitis is a brain inflammation, which could involve also the meninges. The etiology of encephalitis could be: viral, bacterial, fungal or autoimmune. Anti-NMDAR encephalitis is an immune disorder, easy to diagnose and is a treatable condition. Most patients with anti-NMDAR encephalitis develop a multistage illness that progresses from psychosis, memory deficits, seizures, to catatonic state and breathing instability. We present a case report of a 20-year old woman, who presented: amnesia, visual hallucination, illusions, seizures after that occurred following autoimmune encephalitis. The exact incidence of anti-NMDAR encephalitis is unknown, but it seems to be more frequent than any other known paraneoplastic encephalitis. The present case is important considering that autoimmune encephalitis is a rare frequency disorder in Romania, with patients presenting resounding psychiatric and neurological manifestations. Keywords: AUTOIMUNE ENCEPHALITIS, PSYCHOSIS, NMDA ANTI-RECEPTORS.

Infectious psychoses represents specific psychiatric manifestations that may appear during infectious diseases. The occurrence of psychic disorders is related to the type of infectious agent, the patient’s constitution and the biological and psychological status of the affected organism. The infectious agent could be: a virus, bacteria, ricketts, protozoa etc (1, 2). Since its discovery in 2007, the encephalitis associated with antibodies against the N-methyl-D-aspartate receptor (NMDAR) has entered the mainstream of neurology and other disciplines. The exact incidence of anti-NMDAR encephalitis is unknown (3).

In 2005, studies described a syndrome manifested by: memory deficits, impairment in consciousness and other psychiatric manifestations in young women diagnosed with ovary teratoma. In these patients specific anti-NMDA antibodies were detected. Two years later, in 2007, this syndrome was called anti-NMDA antibodies encephalitis.

The disorder occurs with or without tumor association, and responds to treatment but can relapse. The presence of a tumor (usually an ovarian teratoma) is dependent
on age, sex, and ethnicity. The disorder predominantly affects children and young adults. About 80% of patients with anti-NMDAR encephalitis are women (3, 4, 5). About 70% of patients have prodromal symptoms consisting of fever, nausea, vomiting, or upper respiratory-tract symptoms. Within a few days, usually less than 2 weeks, patients develop psychiatric symptoms (visual hallucination, illusions) and many are seen initially by psychiatrists. Patients respond well to immunotherapy, but psychiatric symptoms can be challenging to manage. Anxiety, insomnia, fear, grandiose delusions, hyper-religiosity, mania, and paranoia are frequent manifestations (3, 6, 7). After diagnosis, treatment focuses on immunotherapy and appropriate treatment of a tumor if it exists. Corticosteroids and intravenous immunoglobulin (Ig) or plasma exchange are recommended in managing the immune response (4).

In this case report we present a young woman that suffered an aggressive autoimmune encephalitis which presents resounding psychiatric and neurological manifestations.

**CASE REPORT**
A 20-year-old woman, with no recorded medical history, presented in March 2015 with several medical complains, such as: headache, vertigo, tremor of the arms and balance deficits at the Infectious Diseases Hospital. Initially, the patient was hospitalized at the Infectious Diseases Hospital for 4 weeks. Further one, the patient was transferred to „Prof. Dr. Nicolae Oblu” Clinical Neurologic Hospital, for 2 weeks. During hospitalization at the Infectious Diseases Clinic (4 weeks) and at the Neurology Clinic (2 weeks), interdisciplinary examinations were made at the “Socola” Psychiatry Institute.

At this stage of the disease, the imaginistic evaluation such as tomography, cranial-cerebral MRI (nuclear magnetic resonance imaging), MRI angiography, CIV were normal.

The disease progresses with new symptoms and aggravation of the older one with rapidly progressive confusion syndrome, psychiatric phenomena, tremor and bilateral extra-pyramidal rigidity. The psychiatric status is progressively altered with hallucinatory episodes, psycho-motor agitation, and disturbances of orientation and memory.

The neurological examination raises the suspicion of anti R NMDA autoimmune encephalitis and the patient is transferred at the Neurology Clinic for treatment. The examination revealed: confusion state, diminishing attention, speech and memory deficits, seizures, amnesia. Mini-Mental State Examination (MMSE) was initially 15 points. Also, during her hospital stay at the Neurology Clinic, the patient benefited from psychological consults, in which an increase of MMSE from 15 points to 18 points was observed. The patient was examined by a gynecologist and neither ovary teratoma, nor other forms of tumors were found.

Further one, the patient developed generalized tonic seizures, and oral and tracheal intubations were performed and ICU (Intensive Care Unit) stabilization was mandatory for 41 hours.

Our patient, cerebrospinal fluid (CSF) was examined and the results indicated anti-NMDAR encephalitis. Patient electroencephalograms (EEG) presented increased incidence of theta rhythm on bilateral hemispheres with rare sharp, asynchronous left TPO (temporal-parietal-occipital) waves.

Without any psychiatric history, the pa-
patient presented into the ambulatory of the “Socola” Psychiatry Institute in March 2015, with confusion, visual hallucinations, unsteady gait and extra-pyramidal syndrome. At her second psychiatric exam, in April 2015 the patient was confused, partially oriented to space and time, and presented generalized tremor of the extremities. A month later, in May 2015, the patient had the next psychiatric consultation in ambulatory setting. Following the psychological exam a MMSE (Mini Mental State Examination) of 23 points is noted. The patient is treated with a combination of antipsychotic and benzodiazepines.

During Infectious Diseases Clinic and Neurological Clinic hospitalization, the patient received treatment with corticosteroids, cerebral anti-edematous medication, liver-protective medication, hydroelectrolytic support. The evolution is slowly favorable under a high dosage corticoid treatment.

DISCUSSION

We also discuss several confounding factors that often delay the recognition of this disorder, and propose an algorithmic strategy to guide treatment. Many symptoms that a patient presents (bizarre or stereotypical behaviors, insomnia, and memory deficits) cannot be classified as cortical (3).

The current knowledge about autoimmune encephalitis is that the disorder evolves progressively, with psychotic symptoms, convulsions, memory impairment, and speech disturbances up to a comatose state. In majority of cases, this disorder could be associated with tumors, such as ovary teratoma in approximately 90% of the total cases. In only 2% of the cases may include other types of tumors such as: Hodgkin’s lymphoma, or mammary tumors. At our patient, neither ovary teratoma, nor other forms of tumors were found. The autoimmune encephalitis responds well to adequate treatment, but the risk of future relapses is also present (1, 5). About 70% of patients have prodromal symptoms consisting of headache, fever, nausea, vomiting, diarrhea, or upper respiratory-tract symptoms. Within a few days, usually less than 2 weeks, patients develop psychiatric symptoms and many are treated initially by psychiatrists. Short-term memory loss is common but underestimated (3).

Electroencephalograms (EEG) are abnormal in most patients, usually showing disorganized activity, sometimes with electrographic seizures. Slow, continuous, rhythmic activity in the delta-theta range predominates in the catatonic stage (3). Electroencephalograms (EEG) are abnormal at our patient, with predominant theta waves. The cerebrospinal fluid (CSF) is initially normal in 80% of patients and becomes abnormal later. At our patient, the results indicated anti-NMDAR encephalitis.

In our case we did not find teratomas, but the clinical evolution with: seizures, impaired memory, speech and comatose state and the laboratory exams sustain the diagnostic mentioned above. Almost 75% of the patients with severe anti-NMDAR encephalitis are fully recovered or remain with mild sequels (2, 3, 7). The present case received high-dose immunosuppressive therapy, anticonvulsants and antipsychotic to reduce symptoms. The patient remains under close medical supervision with mild sequels (amnesia) (4, 5, 6).

In patients without a tumor (in whom relapse is more common), continued im-
munosuppressive therapy is recommended for at least 1 year and periodic screening for an ovarian teratoma over 2 years (4).

**CONCLUSIONS**

In the present clinical case, the patient diagnosed with autoimmune encephalitis remains with mild symptoms such as a persistence of amnesia 2 months after the illness occurred. Also, high risk of relapse is considered in case of this patient.

This complex disorder requires sustained management and coordination of care between multiple medical specialties. Future clinical work will need to examine, in depth, the psychiatric manifestations of the disorder and how to provide optimal care, not only during acute faze hospitalization but also in the prolonged recovery process. Future studies should clarify the best treatment approach, and clinical strategies to accelerate the process of recovery.

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**REFERENCES**