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Anti-NMDAR Encephalitis

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Anti-NMDAR Encephalitis

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Introduction

- Anti-N-methyl-D-aspartate receptor (NMDAR) encephalitis is an autoimmune disorder that was only recently discovered through the identification of the anti-NMDAR autoantibody in 2007 (Brenton, Schwartz & Madoo, 2015, p. 14).
- With an increasing amount of new cases of this autoimmune disorder on the rise, it is important for healthcare providers to be aware of its pathophysiology, presentation, course of disease, and treatment modalities for the successful management of patient's with anti-NMDAR encephalitis.

Signs & Symptoms

- Various stages of the anti-NMDAR encephalitis disease course, with the initial stage being the prodromal phase, which typically lasts a few days to a few weeks. The prodromal symptoms typically include those involving the upper respiratory and GI tracts (nausea and vomiting), low grade fevers, and headaches.
- Several weeks later, new symptoms start to appear, such as behavioral changes that include irritability, various psychiatric symptoms, memory disturbances, speech disorders, seizures, dyskinesia, ↓ LOC, autonomic instability, and hypoventilation. The late stages of this disease almost always require ICU management (Brenton, 2015, pp. 15-16).
- In children, the initial symptoms tend to include more behavioral in nature, such as temper tantrums, hyperactivity, seizures, motor abnormalities, and irritability. Autonomic instability and hypoventilation tend to be more prevalent in adults than in children with anti-NMDAR encephalitis (Varma & Sapra, 2015, p. 574).
- Cardiac dysrhythmias have also been seen in anti-NMDAR patients (Park, Mittal, Lala & Patel, 2016, p. 35). Because of the diverse amount of symptoms in the initial stages of this disorder, missed diagnosis is not uncommon (Hong et al., 2015, p. 3).

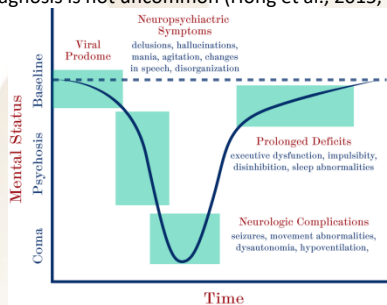


Figure 1. Anti-NMDAR disease course (Rare Disease Review, 2017)

Pathophysiology & its Significance

- NMDA receptors are neuronal ECF receptors in the brain that play a role in memory, behavior, and learning. Tumors (ovarian) appear to regulate the production of anti-NMDAR antibodies within the tumor tissue and the intrathecal areas of the brain. The IgG subclass, G1 autoantibodies, bind to the NR1 subunit of the NMDA receptors, causing significant (but reversible) loss of NMDA receptors in the brain (Brenton et al., 2015, p. 15).
- According to Hong, Klein-Gitelman & Wainwright (2015), a herpes simplex virus infection is emerging as another potential trigger for anti-NMDAR encephalitis (p.4).
- The hyperactivity of NMDA receptors can lead to neurotoxicity, and is possibly linked to the pathophysiology of acute brain injuries. When there is a sustained hypo-functioning of the NMDA receptors, it can lead to subsequent cognitive dysfunction, and is thought to be involved in the pathophysiology of psychosis, Alzheimer's disease, and autoimmune encephalitis (Varma & Sapra, 2015, p. 572).
- Once the IgG antibodies bind to the NMDARs, there is a reversible internalization of the receptors from both the synaptic and extra synaptic space. The number of synapses, dendritic structure, and cell survival are not affected. The loss of the NMDARs on the cellular surface then correlates with the antibody titers, which are discussed later. The NMDARs are affected on both excitatory and inhibitory neurons, and it is the internalization of these receptors that result in the behavioral and neurological changes seen within the course of this disease (Kayser & Dalmau, 2016, p. 37).
- The ↓ in the NMDARs on cellular surfaces results in ↓ functioning of the NMDA-receptor system, which in addition to causing anti-NMDAR encephalitis, is often associated with schizophrenia (van de Riet, Esseveld, Cuypers, & Schieveld, 2013, p. 319).
- Up to 80% of those afflicted by anti-NMDAR encephalitis are female, but it is becoming increasingly recognized in both genders across the entire lifespan, from one year old, to 90 year olds, with the median age being 21 years old (Varma & Sapra, 2015, p. 574).
- 40% of those diagnosed with anti-NMDAR are less than 18 years old (Brenton et al., 2015, p. 15).
- The presence of teratomas and other underlying tumors is dependent on the patient's age and sex. Children under 12 years old, and male patients, rarely have a tumor (Kayser & Dalmau, 2016, p. 36).
- Diagnosis involves a combination of MRI, which has shown abnormalities in 50% of the patients; EEG, which is abnormal in most cases, and CSF analysis, which is abnormal in most patients. Abnormalities in the CSF include a ↑ WBC count, and presence of CSF-specific oligoclonal bands in 60% of the patients (Marsland & Bray, 2012, p. 277).
- Gold standard for diagnosis is the identification of antibodies to the NR1 subunit of the NMDAR, with evaluation of the CSF being more sensitive than serum, but evaluation of both is recommended (Hong et al., 2015, p. 4).

Nursing Implications

- The prompt diagnosis and treatment of anti-NMDAR encephalitis has been shown to significantly ↓ the morbidity and mortality, and ↓ the risk of irreversible neuronal damage
- Treatment includes various modalities, with the primary emphasis being on the surgical removal of the associated tumor/malignancy, along with immunosuppression therapy, such as with the use of corticosteroids, IVIg, plasmapheresis, rituximab, cyclophosphamide, and azathioprine (Gulyayeva, Massie & Duhamel, 2014, pp. 162-163).
- Specialized psychiatric care is needed to treat & manage the severe neuropsychiatric symptoms associated with this disease (van de Riet, 2012, p. 322).
- Nursing care of the anti-NMDAR encephalitis patient can be very challenging due to the acute confusion/encephalitis..
- Nursing care can be divided into 3 stages: the acute phase, the rehabilitation phase, and the discharge phase. During the acute phase, nursing responsibilities include: frequent observations to monitor for clinical deterioration and seizures, frequent neuro assessments, assisting with LPs, clustering of care, monitoring fluid balance, and administering meds frequently and promptly. During the rehab phase, nurses should ensure patient understands discharge plan, consider a referral to psychological services for familial support, and participate in the multidisciplinary meetings with patient and family. During the discharge phase, it is important for the nurse to: provide support to patient and their family, provide information on encephalitis to patient, including various support groups, start the discharge planning as soon as possible, consider referral to mental health services if depression is suspected, and ensure patient has appropriate follow up visits scheduled (Matata et al., 2015, pp. 52-53).

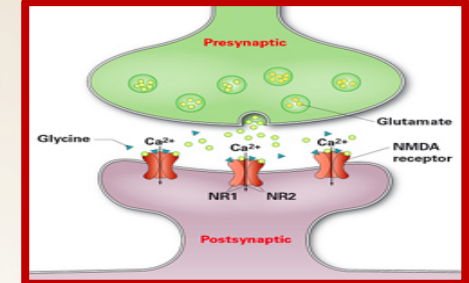


Figure 2. Anti-NMDA receptor (Euroimmun US, 2017).

Conclusion

Anti-NMDAR encephalitis is going to be seen more often in the years to come, and therefore it is imperative that the APN is familiar with its pathophysiology, signs and symptoms, disease course, and treatment options available. The patient outcomes with anti-NMDAR encephalitis improve exponentially when quick identification of the disease leads to prompt initiation of the various treatment modalities. The APN, in the many various areas of healthcare, can assist in the successful outcomes for patients with anti-NMDAR encephalitis through their knowledge on this complicated disease.

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