

## Uncommon Clinical presentation of Auto Immune Encephalitis in an Adolescent Female

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### Abstract

In adolescents, anti NMDA-R encephalitis is the most common aetiology of autoimmune encephalitis presenting with various neuropsychiatric symptoms including catatonia [1]. NMDA receptors are responsible for synaptic plasticity and their disruption results in a host of neuropsychiatric symptoms including catatonia [2]. This disruption results from the generation of IgG autoantibodies against the NR1 subunit of the NMDA-R [3]. May lead to neurobehavioral, neurocognitive and neurological complications that may pose management challenges.

### Literature review

In adolescents, anti NMDA-r encephalitis is the most common aetiology of autoimmune encephalitis presenting with various neuropsychiatric symptoms including catatonia. NMDA receptors are responsible for synaptic plasticity and their disruption results in a host of neuropsychiatric symptoms including catatonia. This disruption results from the generation of IgG autoantibodies against the NR1 subunit of the NMDA-R [1-3].

In adolescents, catatonia is recognized as an uncommon yet severe psychiatric and motor dysregulation syndrome with a reported prevalence of 0.6 to 17.7% [4,5]. Approximately 20% of catatonias are due to an underlying medical condition, ranging from genetic, neurological, infectious and autoimmune disorders and are associated with high morbidity and mortality particularly in adolescents making early diagnosis and management imperative [6,7].

The presence of neurological, neurobehavioral, neurocognitive symptoms with an acute or subacute (less than 3 months) onset should initiate a detailed workup, including brain magnetic resonance imaging (MRI), electroencephalogram (EEG), and cerebrospinal fluid (CSF) analysis, to confirm autoimmune encephalitis and exclude other diagnoses [8]. This is further illustrated in the 2016 autoimmune encephalitis criteria by Graus et al. Catatonia, if present, can be diagnosed clinically using criteria of the Diagnostic and Statistical Manual of Mental Disorders 5<sup>th</sup> edition (DSM-5) and supported by the Bush Francis rating scale [9-11].

Definitive management for autoimmune encephalitis includes first-line immunotherapy (corticosteroids, intravenous immunoglobulins, or plasma exchange). If resistant to initial treatment, second line immunotherapy (rituximab, cyclophosphamide) should be considered. For refractory patients, third-line treatments such as tocilizumab or bortezomib have been suggested [3]. The management of psychiatric symptoms remains challenging. Antipsychotic use should be considered based on a risk-benefit analysis. Risks associated with neuroleptic use in the catatonic patient include an increased predisposition to neuroleptic malignant syndrome and worsening of the clinical symptoms associated with auto immune encephalitis [12-13].

### Case presentation

Miss. AY was a 16-year-old African female, grade 10 learner who was admitted at Edenvale district hospital in Johannesburg on the 15<sup>th</sup> of May 2021. The patient presented with a three-day history of psychotic

symptoms that included disorganised behaviour, verbal and physical aggression, and visual hallucinations. On collateral information, her uncle reported dysphoric mood, talkativeness, decreased need for sleep and increased energy levels. The presentation was thought to have been precipitated by a physical altercation with another learner at school. Her uncle reported that she appeared to have a “panic attack”, refused to calm down and displayed inappropriate behaviour. She required physical and chemical restraints at Edenvale hospital and risperidone (1mg) was commenced. During the admission, she was noted to deteriorate and fluctuate with emerging catatonic symptoms including selective mutism, negativism and posturing. Due to the deteriorating clinical picture, nutritional support via nasogastric feeding was initiated. There were concerns by the treating team regarding a possible seizure at Edenvale hospital, but the medical records were non-confirmatory and vague.

Due to limited psychiatric resources and complexity of the case she was subsequently referred to a specialised child psychiatry department at Chris Hani Baragwanath Academic Hospital (CHBAH) on the 5<sup>th</sup> June 2021. This was her index presentation to psychiatry. It was important to note that there was no history of illicit substance use or family psychiatric history. Her medical history included a diagnosis of allergic conjunctivitis since the age of eight years, keratoconus of both eyes (left more than right), HIV negative, with no other recent viral or flu like illnesses [5].

On admission to CHBAH, her mental state examination revealed a poorly kempt, dishevelled, awake, semi-cooperative, young female in four-point restraints. She was stuporous, staring, posturing and mute. She was euthymic with a restricted affect. It was difficult to assess her thought form and thought content. There were no perceptual disturbances and she displayed impaired insight and judgement. She

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displayed a poor response to an increased dose of risperidone (2mg) and subsequently refused oral treatment. In view of this, a trial of haloperidol (2.5mg) injectable was initiated and titrated to haloperidol 2.5mg IMI mane and 5mg nocte. Her initial investigations, at CHBAH under the care of the child psychiatry team, included a full blood count, urea, electrolytes and creatinine, liver function tests, thyroid function tests, pregnancy test, SARS-CoV-2 PCR nasopharyngeal swab and syphilis serology. Of significance, blood investigations revealed elevated septic markers (C - reactive protein- 68mg/l), deranged kidney function (sodium-154mmol/l, chloride-115mmol/l, bicarbonate 15mmol/l, urea- 28.1mmol/l, creatinine 161mumol/l), with a normal biochemistry and microscopy, culture and sensitivity on cerebrospinal fluid analysis and a normal CT scan of the brain. She was then referred to the internal medicine department at CHBAH for further investigation and management. Supportive therapy such as fluid resuscitation, nutritional support and deep vein thrombosis prophylaxis was continued. On review, the internal medicine team referred her to neurology and neuropsychiatry on the 12<sup>th</sup> of July 2021 based on their preliminary examination and mental state examination in keeping with a delirium and possible encephalitis.

On the first neuropsychiatry consultation on the 12<sup>th</sup> of July 2021, catatonic symptoms including negativism, selective mutism, and posturing was noted to be present. The neuropsychiatry team noted the subacute nature of the symptoms, fluctuating presentation, and the presence of catatonia indicative of a possible diagnosis of autoimmune encephalitis. Her initial Bush Francis Scale severity score was 28. An intravenous lorazepam trial of 4mg three times daily was initiated with no clinical improvement of catatonic symptoms. The neuropsychiatry team opted to wean and stop haloperidol in view of concerns of superimposed extrapyramidal side effects and its role in precipitating neuroleptic malignant syndrome [6]. Concurrently, further investigations requested by the team included an autoimmune encephalitis workup panel consisting of NMDA, AMPA, LG1, CSPR, GABA-A, GABA-B autoantibodies on serum and cerebrospinal fluid (CSF), a viral panel on CSF, magnetic resonance imaging (MRI) brain and an electroencephalogram (EEG). MRI brain report was within normal limits and the EEG displayed slow wave activity in keeping with an encephalopathy. There was no indication of ictal activity, however this did not negate any seizure activity outside of EEG investigation. A positive serum NMDAR antibody was detected on the 23 July 2021. Further investigations for paraneoplastic sources associated with autoimmune encephalitis were negative.

The patient displayed ongoing disorganised behaviour which resulted in a trial of amisulpride (50mg titrated weekly up to 200mg nocte). The neurology team commenced intravenous steroids followed by an intravenous course of immunoglobulin therapy with minimal clinical response. This subsequently prompted the initiation of 5 cycles of plasma exchange on alternate days in early August 2021. The patient's clinical condition remained unchanged. Electroconvulsive therapy (ECT) was considered in conjunction with the immunotherapy to target the catatonic symptoms on the 19<sup>th</sup> August 2021. The protocol at CHBAH at the time included a repeat SARS-CoV-2 PCR nasopharyngeal swab prior to commencement of ECT, despite her initial negative COVID-19 swab on admission. She tested positive for COVID-19 warranting isolation and postponement of ECT. Following the isolation period, she was noted to display depressive features which warranted the initiation of citalopram 10mg which was titrated to 20mg after a two week trial.

Further delays in initiating ECT included obtaining consent from the family due to prolonged consultations amongst the family.

A rituximab trial was initiated post COVID isolation and ECT was commenced on the 8<sup>th</sup> of September 2021. Following six bitemporal ECT doses and the trial of rituximab, the patient displayed significant clinical response and was subsequently transferred to the psychiatric ward for further care on the 1<sup>st</sup> of October 2021. She received care from the multidisciplinary team and continued to improve until discharged on the 2<sup>nd</sup> of November 2021 on prednisone 20 mg per os daily, amisulpride 200mg per os nocte and, citalopram 20mg per os daily for ongoing outpatient, neuropsychiatric rehabilitation [7-9].

## Discussion

Evidence based research regarding psychiatric management in complex and critically ill patients as presented in this case report is limited. Medical literature focuses mainly on immunotherapy in autoimmune encephalitis patients [3]. NMDAR encephalitis frequently presents with psychiatric manifestations including catatonia which may persist and evolve throughout the course of the illness [3]. Although there is limited data on the use of ECT in the management of catatonia due to autoimmune encephalitis, this case report highlighted the possible benefits of ECT in adolescents with this presentation and contributes to a growing body of evidence supporting its possible incorporation in a treatment protocol [14]. It is imperative for a psychiatric multidisciplinary team to have a high index of suspicion for diagnosing autoimmune encephalitis. This is due to the potential for these patients to present to the psychiatry department on first presentation in view of neurobehavioural symptoms [15].

Considering an increase in case studies displaying the beneficial role of ECT in autoimmune encephalitis, it may be considered as an alternative or adjunct to immunomodulatory therapies, particularly in those with significant catatonia and other neuropsychiatric symptoms [14]. Further studies are needed to establish its role either alone or in combination with other treatments.

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