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Research Paper

Psychiatric Manifestation of NMDA Receptor Autoimmune Encephalitis

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ABSTRACT

Miss A, a 13-year-old female was admitted with complaints of sub-acute and continuous course of low mood and being lost in her own thoughts (on and off); odd behaviour in the form of seeing things not seen by others and two episodes of abnormal body movements, forgetfulness, decreased sleep and decreased food intake and restlessness for a period of 1 week. Initially her psychiatric symptoms led to a provisional diagnosis of a primary psychiatric disorder as stressor in the form of decreased academic decline was present. However, over the next few days, it was noticed that the patient's condition deteriorated as she kept lying on the bed staring blankly onto the roof. Even though the eyes were opened, she not aware of her surroundings and was very restless. She started producing low tone sounds as if humming which alternated with shouting incoherent sounds. Hand movements in the form of twisting and writhing which seemed that she was dancing as well as bizarre facial movements started manifesting. The patient also started having difficulty in breathing with sudden drop in SpO2 upto 86%. Two episodes of seizure also developed. Neurological consultation was sought and she was immediately shifted to Neuro ICU, where necessary investigations were performed. Even though brain MRI came out normal and CSF Analysis did not show other abnormalities, except for increased sugar level. AE panel report showed "strong positive" against NMDA receptor autoantibodies. She was treated with Inj. Methylprednisolone 750 mg in 500ml NS over 4 hours (for 5 days) which was followed by Inj. Prednisolone 50mg for 10 days, then 40mg for 10 days, and then 30 mg for another three months). Patient improved after about 15 days

Keywords: *Twisting and Writhing,Seizure,CSF Analysis,MRI,NMDA receptor autoantibodies*

Autoimmune encephalitis is a rare (1 in 1.5 million people affected each year) and newly described group of diseases involving autoantibodies directed against synaptic and neuronal cell surface antigens. Various types of autoimmune encephalitis are known of which NMDA receptor autoimmune encephalitis has affected around 900 people so far[1].

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After a prodromal phase with flu-like symptoms, behavioural abnormalities and acute polymorphic symptoms, often accompanied by catatonic symptoms, are typically observed. In addition, movement disorders, such as dyskinesia or rigidity, autonomous instability, or central hypoventilation, typically occur as the disease progresses, as do disturbances of consciousness. Epileptic seizures may also occur at any time. Thus, the typical clinical syndrome is neuropsychiatric in nature and thereby points to an organic cause, but there are occasional cases that present like primary idiopathic psychiatric disorders, typically with catatonia.[2].

Young women are most frequently affected[3].
It is increasingly being recognized as one of the common causes of encephalitis, but is frequently misdiagnosed especially in resource-constrained settings. With a simple test available to diagnose the disorder and prospects of good recovery following early immunotherapy, the disorder should be kept as a differential diagnosis in patients presenting with unexplained behavioural/psychiatric symptoms and progressive encephalopathy with movement disorders[4].

CASE REPORT

A 13 year old Christian female, VIIIth passed, from a middle socio-economic background, was admitted in Female Psychiatry Ward, RIMS, Imphal for the first time in January 2022. She had presented with complaints of sub-acute and continuous course of low mood and being lost in her own thoughts (on and off), odd behaviour, seeing things not seen by others and two episodes of abnormal body movements, forgetfulness, decreased sleep and decreased food intake and restlessness for a period of 1 week.

Patient was apparently all right till December, 2021 when after the declaration of her annual exam result wherein, she failed to secure her desired rank started being preoccupied with something on her mind (on and off). Over the next few days, the patient started keeping to herself more, stopped hanging out with her mother and started showing disinterest in everything which was not her premorbid self. The patient didn't respond sometimes when called and couldn't complete the task which was normally done with no difficulty, like washing utensils. She also started complaining of severe headache and became more irritable. She also started becoming more absent minded then before. An episode of hysterical laughing also happened while the family was sitting together and when the reason was asked, she replied that she saw a sheep and which looked very funny. There were periods of normal behavior too in between. One day prior to her first medical consultation, the mother noticed that the patient was having difficulty in walking as she was shaking as if she could not carry her weight.

She was taken to a doctor the next morning itself and a neurologist consultation was first sought as the mother felt instinctively that something might be wrong with her brain and while they were waiting for the doctor, she was not able to write her name properly and had an episode of abnormal movements suddenly while standing and was immediately supported by her mother. During the stay in the hospital, she had one episode of laughing out suddenly and started showing abnormal hand gestures which lasted for a minute or two. Brain Imaging and other routine investigations were done but no abnormality were detected.

Then the patient was referred to a Psychiatrist the next morning, considering that the symptoms might be psychogenic in nature. The patient was brought to our department, wherein she was admitted in our inpatient psychiatric care.

On the 2nd day of stay, during rounds, it was informed to us by the mother that she was becoming more restless and that she did not sleep the previous night. When attempt to do a neurological examination was made it was noticed that the patient, though the eyes were opened was not aware of her surroundings. She was not responding to verbal commands and any attempt by the mother to talk to her was met with combativeness. She also started manifesting on and off involuntary twisting or jerky movements of her limbs. However neurological examination was unremarkable. The next day, she started producing low tone sounds as if humming which alternated with shouting incoherent words. Hand movements in the form of twisting and writhing which seemed that she was dancing as well as bizarre facial movements started manifesting. The patient also started having difficulty in breathing with sudden drop in SpO2 upto 86%. Two episodes of seizure also developed. Neurological consultation was sought and she was immediately shifted to Neuro ICU(Intensive Care Unit), where necessary investigations were performed. Routine investigations and brain MRI (Magnetic Resonance Imaging) came out normal. CSF(Cerebrospinal Fluid) Analysis did not show other abnormalities, except for increased sugar level. AE(Autoimmune Encephalitis) panel report showed *"strong positive"* against NMDA receptor autoantibodies. She was started on Inj. Methylprednisolone 750 mg in 500ml NS over 4 hours for a period of 4 days which was followed by Inj. Prednisolone 50mg for 10 days which was gradually tapered off.

Patient started responding with decrease in symtoms from the 3rd day of initiation of treatment and is currently maintaining well.

DISCUSSION

In NMDA receptor encephalitis the antibodies are directed against neuronal cell surface antigens which are highly expressed in the hippocampus and temporal lobe. There is a multi-staged presentation with behavioural, cognitive, psychiatric and neurological symptoms progressing to coma and death if untreated[5].

NMDA receptor encephalitis is a relatively newly identified and potentially treatable cause of psychiatric symptoms in both adults and children. Several hundred cases have been reported since its identification in 2007; however, clinicians may be unaware of developments in this field. It is vital for psychiatrists working across the age spectrum to be aware of this condition and to engage in timely liaison with our neurology colleagues, thus facilitating early screening and diagnosis[6].

The initial presentation is often psychiatric. Psychiatric symptoms occur generally early in the progress of the disease but may also appear during the course of the disease. This is a critical aspect as it is now clear that a rapid diagnosis is both necessary and limiting for good outcome of the patients. Neurological phase follows the psychiatric phase and is characterized by decreased responsiveness that may alternate with periods of agitation and catatonia. Abnormal movements and autonomic instability predominate in this phase. Orofacial dyskinesias are particularly striking. Other abnormal movements include choreoathetosis, complex and stereotypic movements, dystonic posturing, episodic opisthotonus, oculogyric crisis. Autonomic manifestations include hyperthermia, tachycardia, hypersalivation, bradycardia, hypotension, and hypoventilation. Compared to adults, autonomic manifestations are less severe in children.Seizures are common. Recovery occurs in reverse order of symptom presentation and usually there is complete amnesia for the entire event[4].

Psychiatrists have a key role in the diagnosis process and orientation of the patients since they encounter many of them in their daily practice and often establish the first clinical diagnosis. This task is difficult as studies giving the specific symptomatology that would allow psychiatrists to establish their diagnosis and appropriate care are lacking[1].

CONCLUSION

AE is a treatable disease, and timely diagnosis is imperative to improve outcomes and decrease mortality. Early treatment can reduce long-term complications, rapid rehabilitation, and less likelihood of AE relapses. It is important to differentiate organic possibilities first in each patient where clinical presentation and response to treatment are variable[7].

The presence of pronounced psychiatric symptoms drives patients to psychiatric institutions, which can hinder the diagnosis, physicians need to be aware of AE and propose the detection of autoantibodies as early as possible to provide optimal medical care to such patients[8].

This case is significant as timely diagnosis and intervention had given a second chance at life and we psychiatrists need to beware of it because the outcome could have been otherwise too.

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Conflict of Interest
The author(s) declared no conflict of interest.

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