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NMDA RECEPTOR ENCEPHALITIS IN A PREGNANT WOMAN: AN UNUSUAL ENTITY

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ABSTRACT

A 28 year old woman at 24 weeks pregnancy, with no history of neuro –psychiatric disorder in the family or past; presented with short history of frank psychosis, abnormal movements and signs of autonomic instability presented to the obstetrics outpatient clinic .There was no history of fever and joint pain. Her neurology consultation was done and a strong possibility of autoimmune encephalitis was kept and serum NMDA receptor antibodies were assessed. She was diagnosed of having NMDA receptor encephalitis. No ovarian tumour was diagnosed along with that. She responded well to second line immune suppression therapy.

INTRODUCTION

Pregnancy and postpartum period are known for new occurrence of severe mental illness and worsening of prior psychiatric disorders (1). When we come across acute psychosis during pregnancy then we must rule out other organic causes also like encephalitis, space occupying lesion in brain, rabies, hypoglycaemia, thyroid disorder, toxic agents etc. before labelling it as psychotic disorder. Anti NMDA receptor encephalitis is an autoimmune encephalitis which occur when antibodies produced by the body´s own immune system; attack NDMA receptors in the brain. Function of these receptors is critical for judgement, perception of reality, human interaction, the formation and retrieval of memory, and the control of unconscious activities such as breathing.

NDMA receptor encephalitis is a rare entity and even rarer during pregnancy. It is a potentially life threatening condition but early diagnosis and prompt treatment can save the life and prevents disabling morbidity. High index of suspicion is necessary to make the diagnosis.

CASE SUMMERY

A 28 year old woman gravida 2 parity 1 presented at 24 weeks of pregnancy with change of behaviour for past 30 days. She had been under regular ante natal visits prior to the change in her behaviour. Initially she developed irrelevant talks and bizarre behaviour along with decreased personal care and hygiene. She was not taking care of her child also. Then she developed sleep disturbances. After five days of onset of illness she started having speech disturbances like stammering and stopping in the middle of sentences and hence had difficulty in communication. After few more days she developed visual hallucinations and her condition deteriorated rapidly and she became violent. One week prior to admission in to our hospital she developed involuntary jerky movements of right side of the body with facial twitching and oral automatism which occur several times in a day and not responded to medications. Patient developed altered sensorium with periodical fluctuation of consciousness and altered sleep – wake cycle. There was no history of fever, headache, joint pain or rashes. There was no past history or family history of neuro- psychiatric disorder. Patient was admitted under the care of obstetrician and a medicine review was taken.

On examination her pulse rate was 98 bpm and BP was 100/60 mmHg. She was in altered sensorium and having irrelevant talk with vocalization and involuntary movements of right upper limb with oral automatism. Pupils were bilaterally symmetrical and normally reactive. Meningeal signs were absent. Bilateral muscle tone, bulk and power were normal. Co-ordination and sensations could not be assessed. Bilateral deep tendon reflexes, corneal reflexes and planter reflexes were normal. As she was a young female with no features of infectious disease with presenting features of psychiatric disorder with seizures, a strong possibility of auto-immune encephalitis was kept other than the differential diagnosis of trauma, tumour, infection, thyroid dysfunction, hypoglycaemia, intoxication, hepatic encephalopathy, electrolyte imbalance, rabies, idiopathic encephalitis with psychiatric manifestations and patient was investigated further. CBC, LFT, KFT, toxicology screen, blood cultures and arterial blood gas analysis were within normal limits. Her anti TPO and ANA were raised and CSF examination showed lymphocytic pleocytosis. Ultrasound whole abdomen showed single live intrauterine foetus of 24 weeks gestation with no evidence of adnexal mass or teratoma. MRI brain was normal and MRI abdomen was not done. Continuous EEG monitoring showed no seizure correlate. Her serum and CSF anti NDMA receptor antibody were positive.

Patient was put on IV methyl prednisolone (MPS) and antiepileptic drugs for five days and then planned for IVIg in view of no improvement with MPS. With IVIg patient had relief in focal seizures but continued to have neurobehavioral abnormalities and oral dyskinesia. Patient gradually improved and almost reached her baseline status after 3 months of therapy with steroids. Patient had full term normal vaginal delivery of a 3.2 kg healthy baby at the hospital.

DISCUSSION

Mood disorders are twice more prevalent in women as compared to men. Neuro-hormonal changes associated with pregnancy could be responsible for this difference although not well established (1). Pregnancy and childbirth are the two important events in life of a female when she is more likely to have relapses or develop these mental disorders (2). Various neurological disorders may also present with psychiatric features during pregnancy. Anti NMDA Receptor encephalitis should be strongly suspected in a woman, who is in reproductive age group and shows rapid development of psychosis, decreased level of consciousness, accompanied by abnormal postures or movements (mostly orofacial and limbic dyskinesia),intractable focal and clonic seizures and variable signs of autonomic instability, hypoventilation , cerebellar ataxia ,hemiparesis ,loss of consciousness or catatonia ,impaired cognition ,memory deficits and speech problems including aphasia ,preservation or mutism or echolalia (3)(4) (5). Initial symptoms are usually psychiatric in nature, which may make it difficult to have a differential diagnosis of NMDAr encephalitis in early stage. Because most of the patients are initially seen by psychiatrists, it is critical that all psychiatrists must be familiar with and consider this entity as a possible cause of

acute psychosis in young patients with no past neuro-psychiatric history; high level of clinical suspicion is necessary. NMDAr encephalitis is associated with antibodies against NR1-NR2 heteromers and the peculiar movement disorder is believed to be an interruption of forebrain corticostraital inputs by anti NMDA receptor antibodies that remove tonic inhibition of brainstem pattern generators which in turn releases primitive patterns of bulbar and limb movements(6)(7). Supportive findings include abnormal CSF findings showing lymphocytic pleocytosis, mildly raised protein concentration (30% cases) ,and CSF specific oligoclonal bands (60% cases) (8)(9); electro encephalogram (EEG) with infrequent spikes ,but frequent, slow, disorganised, sometimes rhythmic activity that does not correlate with most abnormal movements (3); slow ,continuous , rhythmic activity in the delta theta wave predominates in the catatonic like stage (10). This activity is not associated with abnormal movements and does not respond to antiepileptic drugs (11). A pattern referred to as extreme delta brush is pathognomonic EEG abnormality (12) (13) .

Patient may have abnormal MRI findings (50%cases) that are transient FLAIR or contrast –enhancing abnormalities most commonly (9). In a series of 577 patients, 81% patients were female and the median age was 21 years, mostly belonged to 20-40 year age group. Forty six per cent of all women had an underlying neoplasm. . 94% of the tumours were ovarian teratomas (4). A study in UK showed anti NMDA encephalitis as second most common immune mediated cause after acute disseminated encephalomyelitis(5). Number of new cases a year is unknown. . According to the California encephalitis project, the disease has a higher incidence than its individual viral counterpart in patients younger than 30 years (14). Autoantibodies that target NDMA receptors in brain can be produced by cross reactivity with NDMA receptors in teratomas. Most patients have intrathecal synthesis of NMDAr antibodies. Serum NDMA receptor antibodies are consistently found at higher concentration than cerebro-spinal fluid (15). This strongly suggests antibody production is systemic rather than in brain or CSF. Prodromal symptoms may precede the onset of symptom complex specific to anti- NMDA receptor encephalitis. During acute phase, most patients require intensive care unit admission to stabilize breathing, heart rate and blood pressure. If tumour is detected, its removal is necessary with first line immunotherapy that involves steroids, IVIg and plasmapheresis. Because tumour removal result in fast recovery when associated with first line immunotherapy (9) (10). A study showed that, about half the patients improved after receiving first-line immunotherapy for 4 weeks. However those who have no tumour or diagnosed late usually require additional treatment with second-line immunotherapy (10)(16)(17). Cyclophosphamide and rituximab, (drugs used to eliminate dysfunctional immune cells) ,have been shown to be successful second-line treatments in patients where first-line immunotherapy has failed. These destroy excess antibody-producing cells in the thecal sac. Other medications, such as alemtuzumab remain experimental. The recovery seemed to accelerate after delivery and about 79% of patients with NMDAr antibodies recover or have mild sequel by 2 years; rest all died or remain severely disabled.(9).Although final outcome was same in patients with or without tumour but recovery was fast in those who have tumour removal. Spontaneous recovery is reported but it is very slow. About 25% cases show relapses and these can be separated by months .Relapses usually occur in those cases where tumour found. Such patients require continued immunosuppression for at least one year.

CONCLUSION

The disease responds well to the treatment in most of the cases if diagnosed on time and properly treated and is potentially fatal if left uncared for. High index of suspicion is required to make the diagnosis

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