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Case Report

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Autoimmune encephalitis presenting as a psychiatric disorder: A diagnostic challenge.

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Abstract

Introduction: Autoimmune encephalitis (AE) manifests with various neurologic and psychiatric symptoms.
Case presentation: We present a case of a 39-year-old female, postpartum seven months, who presented with altered behaviour, visual hallucinations, and headache without any focal neurological signs. The electroencephalogram showed a focal seizure. However, the possibility of a primary psychiatric condition was considered as there was inadequate response to initial immunosuppressant therapy. Nevertheless, after referring the patient to the psychiatry team, her condition worsened with electroconvulsive therapy. Then the repeat electroencephalogram showed a secondary generalized seizure of temporal lobe origin supporting the diagnosis as AE. She improved after treatment with immune suppressants, intravenous immunoglobulin and plasmapheresis. This case emphasizes the diagnostic difficulty of autoimmune encephalitis, especially when it only presents with psychiatric symptoms.

Keywords: Autoimmune encephalitis, Psychiatric symptoms, Therapeutic plasma exchange

INTRODUCTION

Autoimmune encephalitis (AE) refers to a group of conditions that occur when the immune system of the body mistakenly attacks healthy brain cells, leading to inflammation of the brain. People with AE may have various neurologic and psychiatric symptoms. Neurologic symptoms may include impaired memory and cognition, abnormal movements, seizures, and balance, speech, or visual problems. Psychiatric symptoms may include psychosis, aggression, inappropriate sexual behaviours, panic attacks, compulsive behaviours, euphoria or fear. Symptoms may fluctuate but often progress over days to a few weeks. Symptoms can progress to loss of consciousness or even coma 1. This is a case of AE of a patient who presented with psychotic symptoms where the diagnosis and management were challenging.

CASE PRESENTATION

Mrs S, a 39-year-old female, postpartum seven months, presented with four-days history of altered behaviour, aggressiveness towards family members, sleep disturbance and reduced oral intake. The symptoms were of acute onset and progressive. Before the onset of the symptoms, she had episodic mild to moderate headache for

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the past one month duration. On further inquiry, she was having visual hallucinations but no auditory hallucinations. She was muttering to herself as well as talking to some unseen persons. She did not have fever, convulsions, photophobia, phonophobia, episodes of loss of consciousness or any limb weaknesses.

On examination, the vital parameters were stable with a 110/80 mmHg blood pressure, pulse rate of 88 beats per minute, and peripheral oxygen saturation (SpO2) of 98%. There were lip lacerations, probably due to lip bites, and she was not oriented in time, place and person. The patient also had catatonia. However, she had a Glasgow Coma Scale (GCS) score of 15/15. There was no neck stiffness, and bilateral pupils were equal and reactive. No focal neurological signs were detected.

On admission to the outpatient department, the working diagnosis was made as an acute psychotic episode and the patient was admitted to the psychiatry ward, where they transferred the patient to the medical ward to find out any organic pathology behind these symptoms. The psychiatry team had prescribed haloperidol, midazolam, olanzapine and clonazepam, which were continued. Non-contrast and contrast-enhanced CT scan of the brain was done, which showed no abnormalities. Cerebrospinal fluid (CSF) analysis was normal. However, her C-reactive protein (CRP) level was 53.2 mg/L, and her erythrocyte sedimentation rate (ESR) was 30 mm in the 1st hour. Then she was treated with acyclovir with the suspicion of encephalitis to cover the herpes viruses. However, her ESR was continuously rising to 90 mm in the first hour within few days, although her CRP level came down to 11.91 mg/L. Therefore, investigations were done to exclude any other infections, and the urine culture became positive with *E.coli*, where she was treated with ceftriaxone. All the other haematological parameters were normal. With this management for one week, the patient showed no improvement. Then serum antinuclear antibody (ANA) level was done which came as positive (1:80). Anti-ds-DNA was negative. Complement 3 level was 87.3 mg/dL (90-180) and complement 4 level was 32.2 mg/dL (10-40). The direct antiglobulin test was negative. Electroencephalogram (EEG) showed focal frontoparietal slow-wave run with the suggestion of a focal seizure. With these findings, she was decided to be having a possible AE and started on methylprednisolone. After five days of methylprednisolone, the patient did not improve and was having persistent psychotic symptoms. Therefore, after discussing with the neurology team it was decided that her symptoms are more likely to be due to an acute psychotic episode. Hence, the psychiatry team took over the patient and started electroconvulsive therapy (ECT). However, during the first ECT, the patient developed a generalized tonic-clonic convulsion, which lasted for about one minute, and the patient did not gain full consciousness for several hours. Repeat EEG was performed, which suggested secondary generalized seizure of temporal lobe origin. However, the next EEG showed generalised slowing with spike and wave complexes suggesting a seizure tendency. After that the psychiatry team referred the patient back for further evaluation for an organic pathology while she was on antipsychotics with dose adjustments.

At this point in the course of her illness she was in the hospital for almost 5 weeks, but the symptomatic improvement was minimal. Therefore, considering all the evidence the diagnosis of autoimmune encephalitis was considered. Magnetic resonance imaging with angiogram was planned, but could not be performed due to limited resources. She was prescribed mycophenolate mofetil (MMF) and planned to start intravenous immunoglobulin (IVIg) therapy. She showed a considerable improvement within few days after IVIg therapy. Therapeutic plasma exchange was carried out one week after IVIg treatment, following which she showed a dramatic improvement. She was clinically improved with mild abnormality in the behaviour after few cycles of therapeutic plasma exchange. She was responsive and communicated with her family members.

DISCUSSION

Autoimmune encephalitis involves several types of diseases with different pathophysiology. Understanding the pathophysiology of these

diseases helps to use diagnostic testing and choose appropriate therapies. The first group includes the classic paraneoplastic disorders associated with antibodies to intracellular antigens, such as anti-Hu. These disorders are strongly cancer-associated and involve T-cell responses targeting neurons. The prognosis tends to be unsatisfactory due to irreversible neuronal killing by these mechanisms, the severity of associated cancers, and the difficulty controlling these sorts of immune responses. The second group involves autoantibodies to extracellular epitopes of ion channels, receptors and other associated proteins, such as the NMDA receptor. The cancer associations are variable, and the prognosis tends to be much better. Occupying an intermediate position are diseases with autoantibodies to intracellular synaptic proteins such as GAD65. It is unclear whether this group involves T-cell responses and functional effects of antibodies. A final group includes other forms of AE in which specific antigens are less clearly established, such as lupus cerebritis or acute disseminated encephalomyelitis (ADEM). Some diseases in this group have systemic manifestations outside the nervous system 2.

Diagnosis of possible AE can be made when all three of the following criteria have been met. The first is subacute onset (rapid progression of fewer than three months) of working memory deficits (short-term memory loss), altered mental status or psychiatric symptoms. The second criterion includes the presence of at least one of the following: new focal neurological signs, seizures not explained by a previously known seizure disorder, CSF pleocytosis (white blood cell count of more than five cells per mm3), and MRI features suggestive of encephalitis. The third criterion is the reasonable exclusion of alternative causes such as central nervous system infections, septic encephalopathy, metabolic encephalopathy, drug toxicity, cerebrovascular disease, neoplastic disorders, Creutzfeldt-Jakob disease, epileptic disorders, rheumatologic disorders (e.g., lupus, sarcoidosis), Kleine-Levin, Reye syndrome (children), mitochondrial diseases and inborn errors of metabolism (children) 3. In this patient, she had a subacute onset of altered mental status and psychotic symptoms. Her EEG findings were compatible with a focal seizure. Based on the clinical features and other investigations, an alternative diagnosis was also unlikely. Therefore, she fulfils these criteria for diagnosing AE.

However, a diagnostic pitfall occurred when considering the inadequate response to treatment with methylprednisolone, where she was suspected of having a psychotic illness without any organic pathology. Treatment options for AE range from corticosteroids to targeted immunotherapy. As in most other inflammatory disorders, corticosteroids are used as the initial therapy to treat AE, acting to inhibit the inflammatory process broadly. However, corticosteroids possess less specificity for the antibody-mediated immune process, and their efficacy is limited in cases of AE, and they are associated with several systemic side effects 4. Therefore, the response to methylprednisolone is not reliable to exclude the diagnosis of autoimmune encephalitis.

Other lines of treatment of AE are based on various specific steps in AE's pathogenesis. Therapeutic targets for these treatments include autoantibodies and other immune mediators (IVIg), B cells and short-lived plasma cells (rituximab) and specific cytokines associated with the autoimmune and inflammatory process (tocilizumab and low-dose interleukin (IL)-2). In addition, antiproliferative agents targeting lymphocyte proliferation (cyclophosphamide, azathioprine, and MMF) are also used in refractory cases or to maintain remission 4. Standard treatment protocols for AE include tumour removal (when present) and first-line immunotherapy, such as steroids, intravenous immunoglobulin (IVIG), and therapeutic plasma exchange (TPE). TPE is a therapeutic apheresis procedure used to remove pathogenic antibodies. It is used in combination with immunotherapy to suppress antibody production 5. In our patient, she responded well to MMF, IVIg and therapeutic plasma exchange and her symptoms improved dramatically.

CONCLUSION

Diagnosis of autoimmune encephalitis can be challenging, especially when it only presents with psychiatric symptoms., Different treatment

options are available and the therapeutic response to them can vary. Therefore, the response to treatments should not be used as the sole factor to exclude the diagnosis of autoimmune encephalitis.

Author declaration
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We express our gratitude to the patient who kindly gave consent for this case to be presented in this paper.

Author Contribution
All authors involved in the management of the patient and generating the concept. All authors made an intellectual contribution and wrote the paper. All authors read and approved the final manuscript.

Conflict of Interest
The authors declare that there is no conflict of interest regarding the publication of this article.

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Data Availability
The authors confirm that the data supporting the findings of this study are available within the article.

Consent for publication
Informed written consent was obtained from the relatives of the patient for publication of this case report.

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