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CASE REPORT

Anti-NMDA Receptor Encephalitis - a case report

Wajeeha Qayyum, Zaland Yousafzai, Muhammad Fozan Khan, Sohail Khan, Muhammad Shahid Iqbal, Malghalara Afridi

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Author Information

Dr. Wajeeha Qayyum
Assistant Professor
General Medicine
Rehman Medical Institute,
Peshawar, Khyber
Pakhtunkhwa, Pakistan
(Corresponding Author)
Email:
wajeeha.qayyum@rmi.edu.pk

Dr. Zaland Yousafzai
Medical Officer
Rehman Medical Institute
Peshawar, Khyber
Pakhtunkhwa, Pakistan

Dr. Muhammad Fozan Khan
Consultant Medicine and
Stroke Medicine
Swat Institute of Medical
Sciences, Saidu Sharif, Swat,
Khyber Pakhtunkhwa,
Pakistan

Dr. Sohail Khan
Assistant Professor
Neurology
Rehman Medical Institute
Peshawar, Khyber
Pakhtunkhwa, Pakistan

Dr. Muhammad Shahid Iqbal
Assistant Professor
Neurology
Rehman Medical Institute
Peshawar, Khyber
Pakhtunkhwa, Pakistan

Dr. Malghalara Afridi
House Officer
Rehman Medical Institute,
Peshawar, Khyber
Pakhtunkhwa, Pakistan

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ABSTRACT

Autoimmune encephalitis presents with a variety of psychiatric and neurological symptoms, making the diagnosis difficult. It is strongly related to paraneoplastic syndromes and certain tumors like ovarian teratoma. A 17 years old female patient is reported in this case report diagnosed as a case of autoimmune encephalitis with a progressive course of deteriorating symptoms and initially treated as schizophrenia and neuroleptic malignant syndrome. Treatment with high dose steroids and plasma exchange followed by Rituximab completely resolved the symptoms. Autoimmune Encephalitis must be considered as a part of differential diagnosis of acute onset psychiatric features especially in young females.

Keywords: Encephalitis; Anti-N-Methyl-D-Aspartate Receptor Encephalitis; Neuropsychiatric; Autoimmune Diseases of the Nervous System.

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INTRODUCTION

Autoimmune encephalitis is defined as a group of autoimmune disorders causing inflammation of brain tissue. It presents with variable psychiatric and neurological symptoms making it challenging to diagnose on time. Over the past decade autoimmune encephalitis has become a major cause of encephalitis after viral etiologies with more cases reported each year, following the initial description of N-methyl-D-aspartate receptor (NMDAR) in 2007 by Dalmau et al.[1] Autoimmune encephalitis is found to have a strong correlation with paraneoplastic syndromes.[2] Autoimmune encephalitis is sub categorized by the location of the antibodies involved into neuronal surface and intracellular antibodies.[3] Anti-NMDA receptor encephalitis is the most common form of autoimmune encephalitis.[1] It is caused by the binding of IgG antibodies to the GluN1 subunit of the N-methyl-D-aspartate receptor in the brain tissue. The clinical findings in NMDAR encephalitis include a viral prodrome followed by psychiatric symptoms (delusions, hallucinations, psychosis) progressing to neurological symptoms like abnormal body movements, seizures and autonomic dysfunction (Dalmau psychosis).[4] The incidence is of NMDAR Encephalitis is estimated to be 1.2/100,000 per year.[4] The incidence is higher among African- American than Caucasians and it is four times more common in young females Anti-NMDAR encephalitis has been associated with certain tumors, most notably ovarian teratomas. It is also associated with preceding herpes simplex virus encephalitis.

Here we report a case of a young female who attended multiple psychiatric clinics for her psychiatric features, later on diagnosed with autoimmune Encephalitis. It is one of the few cases of Autoimmune encephalitis reported so far from Pakistan.

CASE REPORT

A 17-year-old unmarried female was brought to emergency department with four days history of abnormal body movements and one day history of depressed level of consciousness on July 25, 2019. Her history started three months back when her parents observed changes in her behavior. She became aggressive, developed mood swings, sleep disturbances, and abnormal eating behavior. She also started having visual and auditory hallucinations.

As the time progressed, her personality changes and behavioral issues became so marked that she had to be withdrawn from college. Gradually over this period she was not able to perform her daily activities independently and became fully dependent on her family. Her parents sought psychiatric opinion multiple times, but she was misdiagnosed and managed for acute psychosis with antipsychotic drugs along with 3 sessions of ECT. However, her symptoms worsened to the extent that she became fully bedridden and started having abnormal body movements specially of hands and face, along with deteriorating level of consciousness.

She was brought to RMI emergency department where her vitals were blood pressure 100/70 mmHg, heart rate 120/min, SPO_2 90%, temperature of 100^0F and with respiratory rate of 30/min.

She was an obese lady lying in bed completely disoriented from environment with GCS E3M5V1=9/15. She had generalized body rigidity with hyperreflexia, planter bilaterally down going, pupils were reactive and equal; there were no signs of meningeal irritation. On auscultation there were scattered crepitations bilaterally, heart

sounds were S1 and S2 the clinical examination were normal. with tachycardia. Rest of

She was admitted to Intensive care unit with provisional diagnosis of neuroleptic malignant syndrome based on her psychiatric illness, use of antipsychotic drugs and presentation with rigidity, dyskinesia, and fever. Complete blood count showed leukocytosis with slight neutrophilia. Other investigations including C Reactive Protein, Erythrocyte Sedimentation Rate, Liver Function Tests, Rental Function Tests, Serum Electrolytes, vitamin B12, folate and Thyroid Stimulating Hormone were within normal limits. Chest X-ray was normal, however electrocardiogram showed sinus tachycardia and 2-D echo showed right ventricular dysfunction.

Keeping in mind the bed ridden status of the patient, sinus tachycardia, right ventricular dysfunction on echo, we had a suspicion of pulmonary embolism which was confirmed on computed tomography pulmonary arteriogram (CTPA) and we started her on anticoagulation. Pulmonary embolism was not the primary diagnosis as it did not explain all her symptoms, it was rather one of the complications of the primary disease.

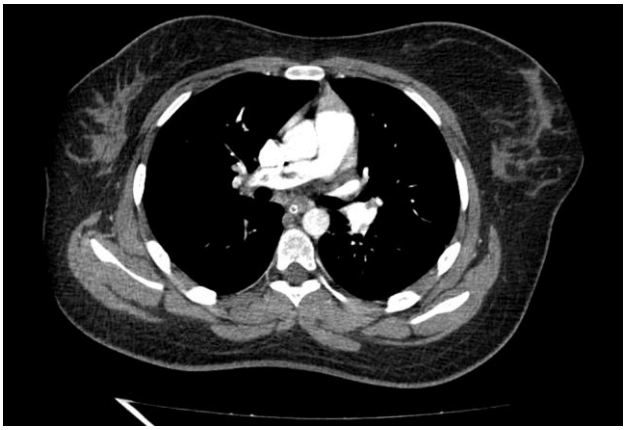

Figure 1: CTPA Arrow points towards filling defect in pulmonary trunk indicative of pulmonary embolism

To reach the primary diagnosis we further imaging and investigations including Magnetic resonance imaging of brain with contrast and cerebrospinal routine examination which were normal. Keeping in view her gender, age and neuropsychiatric symptoms, we wanted to rule out systemic autoimmune disease; did quantitative Antinuclear antibody profile and antiphospholipid antibody; which both came out negative.

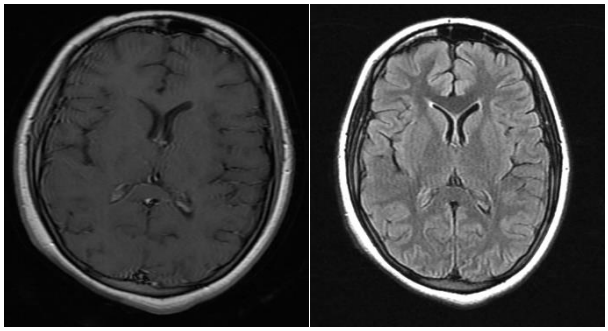

Figure 2: MRI brain Flare and contrast enhanced sequence showing no abnormality

After ruling out systemic illness, we wanted to look for some rare disease entity causing predominantly neuropsychiatric symptoms in young females, so we sent autoimmune encephalitis profile in serum and cerebrospinal fluid, which turned out to be positive of anti-NMDA antibodies and solved the diagnostic dilemma.

Next challenging was to devise treatment plan for her disease. She was administered with pulse therapy in the form of intravenous one-gram Methylprednisolone once daily for five days. Failure to achieve an optimal response, she was offered five sessions of plasma exchange on alternate days.

Outcome

With this treatment the patient's clinical condition improved markedly, her Glasgow's coma scale increased to 13/15 from 9/15 after one week. She became mobile with minimal assistance and was discharged on August 10, 2019, on oral steroids. However, her psychiatric symptoms although improved but remained significantly enough to impair her daily life activities. For this reason, 2nd line treatment was opted.

She was readmitted for the second time on October 01, 2019, for Rituximab infusion followed by second dose 15 days apart on October 15, 2019. On a follow-up visit 2 months later steroids were tapered to 5mg once daily. She was totally symptom free with an mRS score of 1 and was ready to rejoin her studies.

DISCUSSION

Anti NMDAR encephalitis is the most common Autoimmune encephalitis. Symptoms starts as prodromal phase consisting of flu like illness, last for a week followed by an illness phase in which patient develops neuropsychiatric symptoms that can last for 1-3 weeks. After 2nd phase patient can recover completely or land in the phase of prolong deficit. 25% recovered patients can relapse months or years after the 1st attack. In a case series of 100 patients diagnosed with Anti NMDA receptor Encephalitis, 77 initially presented to psychiatric services.[5] Later, Stainer and Colleagues (2015) screened 121 patients diagnosed with schizophrenia and found that 10 percent were suffering from Autoimmune Encephalitis.[6] Likewise, our patient also presented in second phase of illness after she has been treated by psychiatrist.

Consistent with other published case series, our patient was also a young female. However, we didn't find any evidence of ovarian teratoma or any other malignancy in our patient in her acute phase as well as on a 2-year follow-up till this report. In most of the cases reported in young females showed presence of ovarian teratoma.[7,8]

Our case had normal MRI, EEG and CSF parameter. MRI of 53 diagnosed cases of Anti NMDAR encephalitis showed that 28 patients had normal MRI and majority were females so normal MRI does not rule out the possibility of autoimmune encephalitis. CSF in autoimmune encephalitis show variable pleocytosis but it can be normal initially.[9] Our patient presented

in relatively advance stage and still had normal CSF. EEG findings are abnormal in 90% of patients with anti-NMDAR encephalitis, normal EEG was unique to our patient.[10]

Our patient responded well to treatment with complete recovery in 9 months. Initially her psychiatric symptoms were not controlled by 1st line treatment so we offered her second line treatment. As patients without underlying malignancy have shown a higher rate of relapse.[10] Our patient is under surveillance for the last 2years and till now she is cancer and relapse free.

CONCLUSION

One should keep the suspicion of autoimmune encephalitis high in acute onset psychiatric features especially in young females. The timely diagnosis and management carry good prognosis.

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