Thymoma and Anti-GAD65 Antibody Positivity in Schizoaffective Disorder

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Glutamic acid decarboxylase (GAD) enzyme catalyzes the conversion of glutamate to γ-aminobutyric acid, the main inhibitory neurotransmitter within the central nervous system.[1] Autoimmunity targeting the GAD65 isoform represents a cluster of autoimmune disorders, which are most commonly non-neurologic conditions such as type 1 diabetes mellitus but can involve neurologic disorders like stiff person syndrome, ataxia, and limbic encephalitis, as well as psychiatric manifestations such as psychosis and depression.[2] Thymoma is also associated with GAD65 autoimmunity and sometimes with limbic encephalitis or psychosis in the paraneoplastic context. Hence, in neuropsychiatric presentations, the possibility of occult cancer needs to be considered.[3–5] This report describes a case of concurrent occurrence of thymoma, anti-GAD65 antibody positivity, and psychiatric manifestations of schizoaffective disorder.

CASE REPORT

A 32-year-old man presented with a continuous illness of 7 years, characterized by psychotic symptoms overlapped with affective episodes. The psychotic symptoms included disorganized behavior, persecutory delusions, and poor self-care. He had a depressive episode in 2014 and a manic episode in 2017. The current episode was of 1.5 years duration, precipitated by drug default and exacerbated for the last 4 months. The episode was characterized by irritability, self-muttering, setting belongings on fire, wandering behavior, persecutory delusions, over talkativeness, over religiosity, grandiosity, poor self-care, and poor oral intake in the absence of neurologic symptoms. There was no past or family history of psychiatric illness. The patient had a history of excessive beedi smoking suggestive of nicotine dependence. There was a history of significant extrapyramidal symptoms (EPS) of tremors, rigidity, and sedation with low doses of antipsychotics. His body mass index (BMI) was 18 kg/m^2 (low normal), and his vitals were stable with no neurologic signs. The patient had increased psychomotor activity, increased speech, and derailment, with grandiose delusions and expansive ideas.

Investigations and Treatment

Routine blood investigations were performed along with computed tomography scan of the brain, chest x-ray, ultrasonography of the abdomen, and a sexually transmitted disease profile (HIV, hepatitis B surface antigen, hepatitis C antibodies, and VDRL [venereal disease research laboratory test]) in view of weight loss and appetite decline, which were within normal limits. Thyroid function test revealed subclinical hypothyroidism (thyroid-stimulating hormone: 0.74 μIU/mL, T4: 4.04 μg/dL, T3: 61.65 ng/dL). He had low folate levels and received supplementation. He received a high protein diet for low BMI and nicotine replacement therapy for craving management.

He was started on tablet risperidone up to 2 mg and valproate up to 1,000 mg; however, these medications were withdrawn in view of significant EPS. Tablet quetiapine was started up to 550 mg per day with regular electrocardiogram monitoring. He had mild EPS, but over 1 month his symptoms subsided. A serum autoimmune panel was done in view of his high neuroleptic sensitivity, and anti-GAD65 antibodies were found to be positive, with negative results for autoimmune encephalitis mosaic antibodies, paraneoplastic neuronal antibodies, antititin antibodies, and antineutrophil cytoplasmic antibodies. He was referred to the neurology team for evaluation. The cerebrospinal fluid autoimmune profile and other parameters were within normal limits. The positron emission tomography magnetic resonance whole body scan revealed a hypermetabolic soft tissue lesion in the perivascular region of the anterior mediastinum without invasion of neighboring structures, suggestive of thymoma.

The patient underwent a repeat nerve stimulation test, anti–muscle-specific kinase antibody, and anti-acetylcholine receptor antibody assessment to rule out myasthenia gravis, as advised by the neurology team. These tests were negative. He was referred to oncology and was advised to receive regular monitoring and laparoscopic thymectomy. After improvement of his psychiatric symptoms, he was discharged. The patient had a relapse

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of psychotic symptoms after 6 months due to nonadherence in the prior 2 months. Quetiapine was restarted up to 900 mg, and his symptoms decreased. The patient continued monitoring with his oncologists.

DISCUSSION

This case describes the importance of assessing autoimmunity in patients with neuropsychiatric symptoms, especially if sensitive to developing side effects to psychotropic medications. Psychiatric disturbances might constitute the presentation of a milder form of autoimmune encephalopathy. A meta-analysis[6] reported prevalence of GAD65 autoantibodies among people with psychosis to be 5.8% and double that of the general population, whereas a recent study[7] noted that GAD antibodies are very rare and do not seem to be increased in patients with psychotic disorders. As noted earlier, paraneoplastic syndrome associated with thymoma can sometimes present with GAD65 autoimmunity and neuropsychiatric symptoms. The surgical resection of thymomas can resolve paraneoplastic syndrome in a majority of patients.[5] Thus, for any patient with suspected paraneoplastic cause of GAD65 autoimmunity, early comprehensive assessment for cancer detection is important for the overall health outcome.

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