Graves’ encephalopathy – A case of steroid-responsive organic psychosis

Nitisha Goyal¹, Pankaj Satyanarayan Rathi¹, Rahul Jain², Dinesh Chouksey³

From ¹DM-Senior Resident, ²Assistant Professor, ³Associate Professor, Department of Neurology, Sri Aurobindo Institute of Medical Sciences, Indore, Madhya Pradesh, India

Correspondence to: Dr Nitisha Goyal, Department of Neurology, 4th Floor, Sri Aurobindo Institute of Medical Sciences, Indore, Madhya Pradesh - 453 111, India. E-mail: nitishagoyal@gmail.com

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ABSTRACT

Thyroid disorders are frequently associated with neurological manifestations affecting either the central or peripheral nervous system. We present the case of a 35-year-old female patient presenting with acute onset neuropsychiatric manifestations in the form of abusiveness, aggressiveness, hallucinations, and disorientation. Further, imaging of the brain was normal and cerebrospinal fluid examination showed normal cellularity, protein, and glucose composition and an absence of common autoimmune and paraneoplastic antibodies. Additional testing in this young, thin female revealed showed a marked imbalance in thyroid function test with thyroid-stimulating hormone level <0.005 mU/L, free T3 of 680 pg/dl, and free T4 of 3.2 ng/dl and colossal level of >1300 U/ml of thyroid peroxidase antibody (Anti-TPO). A diagnosis of Encephalopathy Associated with Autoimmune Thyroid Disease (EAATD) was considered, with newly diagnosed Graves’ disease (GD). She was promptly started on high dose steroid therapy and recovered dramatically. Classically, EAATD is thought to be associated with Hashimoto’s thyroiditis, but patients with GD can also present with it, with almost similar clinical, immunological, radiological, electrophysiological, and therapeutic manifestations. Our case and subsequent discussion highlight this rare neurological presentation in a patient with previously undiagnosed GD.

Key words: Autoimmune, Encephalopathy, Graves’ disease, Hashimoto’s encephalopathy, Psychosis, Steroid responsive psychosis

Case Report

thyroid disorders are frequently associated with neurological manifestations affecting either the central or peripheral nervous system. Sometimes, a neurological problem may be the chief complaint or only complaint on presentation with an undiagnosed thyroid disorder [1]. Encephalopathy Associated with Autoimmune Thyroid Disease (EAATD) is an uncommon neurological manifestation associated with autoimmune thyroid disorders with an estimated prevalence of 2.1/1 lakh population [2]. As a common understanding, EAATD is considered to be associated with Hashimoto’s autoimmune thyroiditis (HT) and hence, also named eponymously in the literature as Hashimoto’s encephalopathy. However, there are a few case reports describing the occurrence of EAATD with Graves’ disease (GD) [2,3]. Our case explores a patient presenting with acute neuropsychiatric symptoms, who was diagnosed as a case of EAATD associated with newly diagnosed GD.

CASE REPORT

A 35-year-old female patient was referred to the emergency of our hospital from a peripheral center with a provisional diagnosis of inorganic psychosis, unresponsive to high doses of antipsychotics, and tranquilizers. She had a history of progressively increasing aberrant behavior, disorientation to time, place, and person, insomnia, bed-wetting, poor oral intake, and hallucinations for around 8–10 days before presentation with a background history of intermittent high-grade fever for over a month. She was seen constantly either talking to non-existent people around her or muttering to self. She made no eye contact with anyone. On attempting to talk to her or go near her for examination or medication, she became uncontrollably aggressive and abusive. There was no history of seizures or vomiting. As per the patient’s family, who had brought her to the hospital, there was no history of headache, visual, or auditory complaints during the illness. There was no prior history of psychiatric disorders in the patient or any psychiatric or hereditary familial medical conditions. The family members gave a history of significant weight loss over the course of the past 2 years, for which no treatment had been sought.

Initial physical examination of this lean lady, after giving mild tranquilizers (because of extreme aggression), showed a blood pressure of 110/60 mmHg, pulse rate of 120 beats/min, respiratory rate of 16 breaths/min, temperature of 100°F, and oxygen saturation of 100% on room air. There was no abnormality of eyes, skin, or nails. A thorough workup for causes leading to such a clinical presentation was initiated.

Treating neurologists quickly investigated and discarded any structural alterations in the brain with the help of magnetic resonance image (MRI); central nervous system (CNS) infections (Cerebrospinal fluid [CSF] examination) or autoantibody associated encephalopathy (NMDA, AMPA –GluR1, AMPA-GluR2, GABA-B receptor antibody, LGI-1 [VGKC type], and
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CASPR2 antibody [(VGKC type)]. Electroencephalograph (EEG) showed diffuse background slowing without any focal changes. Furthermore, serum electrolyte imbalance, kidney or liver dysfunction, sepsis, malignancies, hyperparathyroidism, and toxic manifestations of any drugs were ruled out. Chest roentgenogram and sonography of the abdomen and pelvis also revealed no abnormality. Keeping in mind the young age, female sex, tachycardia, and a history of weight loss, thyroid profile of the patient was ordered which showed marked imbalance with thyroid-stimulating hormone level <0.005 mU/L, free T3 of 680 pg/dl, and free T4 of 3.2 ng/dl. Further workup revealed a colloidal level of >1300 U/ml of thyroid peroxidase antibody (Anti-TPO). A color flow Doppler ultrasoundography of the neck was ordered which revealed that the thyroid gland was markedly enlarged and hypoechoic with heterogeneous echotexture with diffuse hypervascularity, demonstrating a thyroid inferno on Doppler with the markedly increased peak systolic velocity, end-diastolic velocity, and mean velocities of inferior thyroid artery were markedly raised, as reported by the sonologist, thus, confirming the diagnosis of GD. EAATD, in this case, GD was diagnosed.

The patient was promptly started on therapy with intravenous methylprednisolone (1 g/day), anti-thyroid drugs, and beta-blockers. Within 1 day, the patient’s sensorium markedly improved. Her abusiveness and aggressiveness also waxed down. Over the course of treatment, the patient showed drastic improvement and by the end of the 5th day, she became totally oriented to time, place, and person. She started feeding herself without assistance and could maintain her personal hygiene adequately with minimal assistance. She became afebrile and tachycardia also settled down. EEG repeated after 5 days was also normal. Subsequently, the patient was shifted to oral medications and was discharged in good health.

DISCUSSION

EAATD, also known as Steroid-Responsive Encephalopathy associated with Autoimmune Thyroid disease (SREAT), is an uncommon disease with an estimated prevalence of 2.1/1 lakh population. However, anti-thyroid antibodies may be detected in up to 10% of the healthy population. EAATD predominantly affects females (4:1 ratio) with a mean age of onset in the fourth decade [2,4].

The clinical presentation of EAATD is heterogeneous, frequently being insidious (75%), with the cognitive and behavioral disturbance that may be associated with tremor, myoclonus, or ataxia. Less often, clinical onset may be acute (25%) as stroke-like episodes, epilepsy, or psychosis [4,5].

Laboratory investigations are non-specific and there is no direct correlation between thyroid hormone levels or anti-thyroid antibody titers and the clinical presentation or course of the disease [2,6]. The majority of patients of EAATD are euthyroid (18–45%) or hypothyroid (clinical in 25–35% and subclinical in 17–20%) and less commonly present with hyperthyroidism (7%) [2,6]. Anti-TPOs are found in around 85%–100% of the patients; however, around 50% of the patients may have anti-thyroglobulin antibodies present [4,7]. CSF analysis is mostly non-specific and may show mild inflammation with mononuclear pleocytosis or slightly increased proteins. These changes revert with treatment [2,7]. In 62–75% patients, abnormal elevation of CSF thyroid antibodies may also found and this persists even after clinical recovery [7,8].

EEG abnormalities are non-specific and present in around 90% patients with diffuse backgrounds slowing being the most common finding. Other EEG findings that may be seen include frontal intermittent rhythmic delta activity, periodic lateralized epileptiform discharges, and temporal epileptiform activity. Interestingly, there is usually a correlation between the slowing severity and the encephalopathy severity, and an EEG normalization occurs with successful treatment [9,10]. MRI brain is usually normal and is important primarily to exclude other diagnoses [2,9].

EAATD is a diagnosis of exclusion and its diagnostic criteria include the association of neurological or psychiatric manifestations, high titers of anti-thyroid antibodies, exclusion of other possible causes, and a good response to immunosuppressive therapy [3,5]. The general accepted diagnostic criteria for EAATD are listed in Table 1.

A prompt response to steroids occurs in most patients with good clinical response if timely treatment is initiated [11,12]. However, the absence of response to steroids should not be used to exclude the diagnosis as other immunosuppressive therapies (methotrexate, cyclophosphamide, azathioprine, intravenous immunoglobulin, and perhaps, and plasmapheresis) must be tried before labeling the patient as non-responsive to immunosuppressive therapy [2,13,14].

Classically, EAATD is associated with HT; however, the hugely variable neuro-psychiatric manifestations occurring in GD mirror those occurring in HT. In both conditions, EAATD clinical manifestations can be fluctuating and relapsing [3,4,15]. There are not many cases reporting EAATD with GD hence, rigorous comparison cannot be done; however, Tamagno et al. have found that the clinical, immunological, radiological,
electrophysiological, and therapeutic features of EAATD associated with HT and GD do not differ [3].

Our patient presented with acute, progressive neuropsychiatric manifestations that were unspecific and could have been the result of several different conditions such as metabolic abnormalities, toxins, CNS infections, cerebrovascular accident, autoimmune encephalitis, or paraneoplastic syndromes. However, all other possible etiologies were ruled out with appropriate testing. Further, the patient responded dramatically to immunosuppression with steroids with excellent clinical recovery and also, correction of EEG abnormalities, thus, favoring our diagnosis.

CONCLUSION

EAATD is a rare neurological disorder with varied manifestations and presentations and should be kept in mind when diagnosing any patient of chronic, sub-acute, or even acute onset neurological or psychiatric complaints, particularly in females in third to fourth decade of life with personal or familial history of auto-immune disorders, independent of thyroid functional status. Another learning point is to remember that EAATD is not synonymous with Hashimoto’s Encephalopathy and that patients with GD can also present with EAATD and have identical clinical, immunological, radiological, electrophysiological, and therapeutic manifestations. Immunosuppressive therapy must be given early on for complete remission and favorable prognosis.

REFERENCES