Possible Steroid-responsive encephalopathy associated with autoimmune thyroiditis (SREAT) in a patient with impaired consciousness.

ABSTRACT

Steroid-responsive encephalopathy associated with autoimmune thyroiditis (SREAT), also known as Hashimoto's encephalopathy(HE) is a rare neurological disorder associated with thyroid autoimmunity. Clinical manifestationsinclude seizures, altered consciousness,transient aphasia,tremors,myoclonus, cognitive impairment, and psychiatric manifestations.Here, we report a case of a 55-year-old female presenting with altered sensorium for 4 days. The patient was a known case of Hypothyroidism, Hypertension and Diabetes.Serologic studies demonstrated elevated levels ofanti-thyroid peroxidase (anti-TPO) antibodies.The patient showed a remarkable response to steroid therapy. Hence, the diagnosis of SREAT should be suspected in cases of encephalopathy without an obvious cause, as a good response can be obtained withsteroid therapy; early diagnosis and treatment are very beneficial for such patients.

KEYWORDS

Steroid responsive, Hashimoto's encephalopathy; anti-TPO antibody; autoimmunity; steroids.

INTRODUCTION

Steroid-responsive encephalopathy associated with autoimmune thyroiditis (SREAT) is a rare syndrome associated with autoimmune thyroiditis [Hashimoto's thyroiditis (HT)], with high titres of anti-TPO antibody, as first reported by Brain et al in 1966[(1)].Hashimoto's thyroiditis (HT) is a common form of chronic autoimmune thyroid disease.[(2)]Thyroid hormone dysfunction ranging from hypothyroid to thyrotoxic stateis seen in SREAT, however, most of the reported cases were either euthyroid or hypothyroid.Peschen-Rosin et al[(3)] described the criteria for the diagnosis of Hashimoto's encephalopathy as unexplained episodes of various neurologic symptoms and at least 3 of the following:-

(i)Abnormal EEG

(ii)Positive anti-TPO Ab

(iii)Elevated CSF protein

(iv)Excellent response to steroids

(v)Normal MRI Brain findings.

The presence of high antithyroid antibody titres and the exclusion of other causes of encephalopathy viz. metabolic, infective or structural, support the diagnosis of SREAT.It is most often characterised by an acute to subacute onset of confusion with an altered level of consciousness, seizures, and myoclonus. In contrast to the cognitive dysfunction associated with hypothyroidism or hyperthyroidism, SREAT is believed to be an immune-mediated disorder rather than representing the direct effect of an altered thyroid state on the central nervous system. Such patients typically respond to steroids and show a remarkable response[4]; hence the name -steroid-responsive encephalopathy associated with autoimmune thyroiditis (SREAT).It is extremely important, though rarediagnosis which is most often misdiagnosed. It should be suspected in patients with encephalopathy due to unknown causes,after ruling out other metabolic, infective and structural neurological causes as the response to treatment are exemplary andit is a disease of the CNS having a good prognosis if diagnosed and treated early.

However, as per the new criteria proposed:

Diagnosis can be made when all six of the following criteria have been met[5]

- 1. Encephalopathy with seizures, myoclonus, hallucinations, or stroke-like episodes
- 2. Subclinical or mild overt thyroid disease (usually hypothyroidism)
- 3. Brain MRI normal or with non-specific abnormalities
- 4. Presence of serum thyroid (thyroid peroxidase, thyroglobulin) antibodies *
- 5. Absence of well-characterised neuronal antibodies in serum and CSF
- 6. Reasonable exclusion of alternative causes

According to these criteria, in the present case diagnostic criteria, 1 and 5 are not fulfilled, thepatient showed only a disturbance of consciousness and no antibodies weredetected inthepatient'sCSF.Hence, we can consider this case as a possible SREAT and not a confirmed one.

CASE REPORT

A 55year old female, with a known case of Hypothyroidism, Hypertension and Diabetes came to the Dhiraj Hospital emergency room with an altered state of sensorium for 4 days. There were no other associated symptoms. On examination, the patient was afebrile, pulse rate was 78 bpm and regular, blood pressure was 140/90 mmHg, her sensorium was altered, Glasgow Coma Scale [GCS] was E2M4V2, all deep tendon

reflexes were brisk, Babinski's sign was positive bilaterally. Meningeal signs were absent.Another general and systemic examination was unremarkable. MRI was done which showed no significant abnormality. Electroencephalogram(EEG) revealed characteristic diffuse slowing (without any focal epileptiform discharge) which was suggestive of encephalopathy(Figure 1,2).

Figure 1 : It shows characteristic diffuse slowing without any focal epileptiform discharge

Figure 2: Characteristic diffuse slowing in a compressed trace EEG

Routine blood investigations and thyroid-specific tests were done which are as follows:

INVESTIGATIONS

Haemoglobin	11.2 g/dL
Total counts[WBC]	4800/mm^3
Total platelet count	2,00,000/mcL
RBS	122 mg/dL
Serum Urea	37 mg/dL
Serum creatinine	1.0 mg/dL
Serum electrolytes [Na/K/Cl]	140/4.3/107 [mEq/L]
CRP	8 mg/L
HbA1c	6.2%
Liver function tests	WNL
Urine routine micro	NAD

THYROID SPECIFIC TESTS

Serum TSH	32.8 mIU/L [Normal = 0.1-4.5 mIU/L]
Free T3	0.2 pg/mL [Normal = 2.1-3.8 pg/ml]
Free T4	0.6 pg/mL [Normal = 0.8-2.0 pg/ml]
Anti-TPO antibody	**>1000 IU/mL** [Normal = <30 IU/ml]

CSF analysis was done which revealed the following findings –

Protein	60 mg/dL [Normal = <45 mg/dL]
Sugar	82 mg/dL [Normal = >50 mg/dL]
Total cells	2/mm^3

ADA	5 u/L [Normal = 0 – 30 u/L]
LDH	92 u/L [Normal = 50 – 285 u/L]
Culture	No growth

The patient was initially started on T. Thyroxine (75 mcg) along withother supportive treatments. All the investigations pertaining to metabolic, infectious and structural neurological causes were carried out, which were within normal limits. Serum TSH level was raised and anti-TPO antibody level was sent which was found to be remarkably high; and CSF revealed elevated protein levels, hence suspicion of Hashimoto's encephalopathy was raised. The patient was started on intravenous Methylprednisolone (1 gram) and there was a dramatic improvement in the sensorium of the patient with a single dose.The patient was given injectable MPS for 3 days and then switched to oral prednisolone. The patient completely recovered within 7 days and was discharged on oral prednisolone with a tapering dose and thyroxine.

DISCUSSION

Hashimoto's encephalopathy or SREAT is a rare disorder, with an estimated prevalence of 2.1/per 100,000[6]. Like other autoimmune disorders, itoccurs chiefly in females, with a male-to-female ratio of approximately 1:5, and the mean age of onset is between 45-55 years[7].The exact pathogenesis of SREAT is unknown. It is considered to be an autoimmune encephalopathy becauseof its higher female predominance, fluctuating course of illness, associationwith other autoimmune disorders and improvement withcorticosteroid therapy. Several mechanisms, such as autoimmune vasculitis, encephalomyelitis-associated demyelination, global cerebral hypoperfusion, intrathecal thyroid auto-antibodies, and neuronal dysfunction due to cerebral oedema have been proposed for Steroid-responsive encephalopathy associated with autoimmune thyroiditis (SREAT)[8]. Though there is no evidence that the anti-TPO antibodydirectly causes encephalopathy, other autoantibodies such as anti-parietal cell antibody or anti-intrinsic factor antibody, have also been reported in patients with SREATwhich mightinduce encephalopathy.Two types of clinical presentation are usually observed; the first type is an acute stroke-like presentation with transient focal neurological deficits such as transient aphasia, focal or generalized seizures and status epilepticus. The second form is of insidious onset, progressing to dementia, psychosis and coma over several weeks withoutany focal neurological deficits. Associated features include lack of concentration, sleep abnormalities, headache, tremors, myoclonus and ataxia. The thyroid function of patients with Steroid-responsive encephalopathy associated with autoimmune thyroiditis (SREAT)may manifest as subclinical hypothyroidism (35%),euthyroidism(30%), overt hypothyroidism (20%), orless frequently,hyperthyroidism (7%)[9].It is different from myxedema coma or thyroid storm because the change in consciousness that occurs in SREAT is unrelated to the thyroid hormone level.Though as per the study done by Graus et al(2016), all the criteria for SREAT are not met, our patient who presented with altered sensorium had overt

hypothyroidism, elevated levels of anti-TPO antibodies and abnormal EEG findings, to which a diagnosis of possible Steroid-responsive encephalopathy associated with autoimmune thyroiditiscould be considered. Also, the patient was given steroids, to which the patient showed great improvement.

CONCLUSION

Steroid-responsive encephalopathy associated with autoimmune thyroiditis (SREAT) is a rare clinical condition. However, it should be suspected in all the cases presenting with unexplained altered sensorium, especially in the patients with known hypothyroidism, after ruling out more common pathologies such as meningitis, hepatic encephalopathy, dyselectrolytemia, renal failure, sepsis, structural/vascular abnormality or any lesion in the brain, and neoplasm. Elevated anti-TPO antibodies, normal MRI findings and abnormal EEG can support the diagnosis of SREAT. Treatment with steroids shows a dramatic improvement, hence the possibility of SREAT should be considered in such patients, and early treatment leads to a better prognosis.

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