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Delayed immunological recovery in Hashimoto's encephalopathy

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Hashimoto's encephalopathy (HE) also known as Steroid Responsive Encephalopathy Associated with Autoimmune Thyroiditis (SREAT) is a rare autoimmune syndrome first described in 1966 (1). The estimated prevalence is approximately 2 per 100,000, with female predominance (1,2). Its clinical presentation ranges from an insidious onset to progressive cognitive decline and neuropsychiatric symptoms to acute encephalopathy with seizures or stroke-like episodes (3). Typical features include elevated serum/ cerebrospinal fluid (CSF) anti-thyroid peroxidase (anti-TPO) antibodies and anti-thyroglobulin antibodies, nonspecific CSF protein elevation, diffuse slow waves in EEG and normal or non-specific neuroimaging (2,3). Infective, metabolic, toxins, paraneoplastic and other autoimmune etiologies need to be excluded before concluding the definitive diagnosis (2,3). Patients' thyroid status can broadly vary from a thyrotoxic state to euthyroid or hypothyroid state (2,3).

Glucocorticoids remain the first-line therapy. Intravenous methyl prednisolone 500-1000mg/ day for 3 to 5 days, followed by oral prednisolone (1-2 mg/kg/day) with tapering, is recommended treatment (2,3). Most of the patients will show clinical improvement, often within weeks of steroid therapy. However, some patients need second-line agents such as therapeutic plasma exchange, intravenous immunoglobulin, azathioprine, methotrexate, cyclophosphamide or rituximab (2,3).

We report a case of a 48-year-old male patient who presented with progressive neuropsychiatric symptoms and who was subsequently diagnosed as having Hashimoto's encephalopathy (steroid-responsive encephalopathy associated with autoimmune thyroiditis).

Case presentation

A 48-year-old male with a 3-year history of type 2 diabetes mellitus with suboptimal control (recent HbA1c: 10%), presented with progressive abnormal behaviour over the past four months. These included prominent visual hallucinations of thieves and ghosts that led to persistent fearfulness and hypervigilance. There were no auditory hallucination or delusions.

He also developed marked apathy, emotional blunting, social withdrawal and significant neglect of personal hygiene. His interaction with family had diminished, and exhibited hypersomnolence, spending most of the day sleeping. His speech output was markedly reduced, and he showed minimal speech.

He had poor insight into his condition, significant disinterest in previously meaningful activities, and a progressive decline in memory and attention span. His oral intake substantially decreased due to disinterest in food, rather than dysphagia or nausea.

His psychomotor slowing was prominent, with delayed responses and reduced facial expressiveness, without signs of catatonia. Despite psychiatric treatment with pharmacotherapy and electroconvulsive therapy, his symptoms persisted with minimal improvement.

There was no history of fever or head trauma or weight loss. He denied any illicit drug use and had no past psychiatric history. He has had high-risk heterosexual contact.

On arrival to the ward, he was conscious but showed poor eye contact. His Glasgow Coma Scale (GCS) was 15/15. He was haemodynamically stable; blood pressure 120/70 Hgmm and pulse rate 72 / minute. There was no thyroid enlargement or lymph node enlargement. Cardiovascular, respiratory and abdominal examination was normal.

The neurological examination revealed no focal neurological deficits, rigidity, or gait abnormalities. Fundoscopic examination was normal.

Cognitive assessment showed marked impairment in the Mini-mental State Examination (MMSE), which was 18/30, and the Montréal Cognitive Assessment score was 13/30.

Basic investigations were largely unremarkable, but mildly elevated inflammatory markers of C-reactive protein 12 mg/l and erythrocyte sedimentation rate, 25 mm/hour. Serum vitamin B12 levels were mildly low, 196 pg./ml (248 -900 pg/ml).

The CSF analysis showed the presence of a low level of protein (66 mg/dl) without pleocytosis or microbiological growth. CSF for herps simplex virus antigen, HIV 1 and 2 antibodies, and VDRL tests were negative. EEG showed generalised slow waves suggestive of encephalopathy (Figure 1).

The MRI scan of the brain and contrast-enhanced CT scan of the chest, abdomen and pelvis were normal.

Thyroid autoantibodies were significantly elevated (anti-thyroglobulin 73.2 IU/mL (Ref. 0-36 IU/ml) anti-TPO 42.1 IU/mL *(*Ref. 0-32 IU/ml), despite normal thyroid hormone levels, anti-nuclear antibodies (ANA) were weakly positive with a cytoplasmic pattern (1:80).

Its subacute presentation and the presence of thyroid antibodies, strongly support the diagnosis of Hashimoto's encephalopathy with coexisting mild vitamin B12 deficiency.

The patient was started on intravenous methyl--prednisolone pulse therapy at a dose of 1g daily for five days, followed by oral prednisolone at 1 mg/kg/day (60 mg). Intramuscular vitamin B12 at 1000 µg was started on alternate days for six doses, followed by monthly injections.

At the time of the discharge (Day 7 of hospital stay), his GCS was 15/15, and MMSE score was 16/30.

He poorly responded to corticosteroid therapy. Upon follow-up at the neurology clinic, his GCS remained 15/15, but he had poor eye contact and limited responsiveness. Electroencephalogram continued to show generalised slow wave-activity, suggestive of persistent encephalopathy Figure 2 illustrates EEG taken after 3 months of treatment which shows resolution.

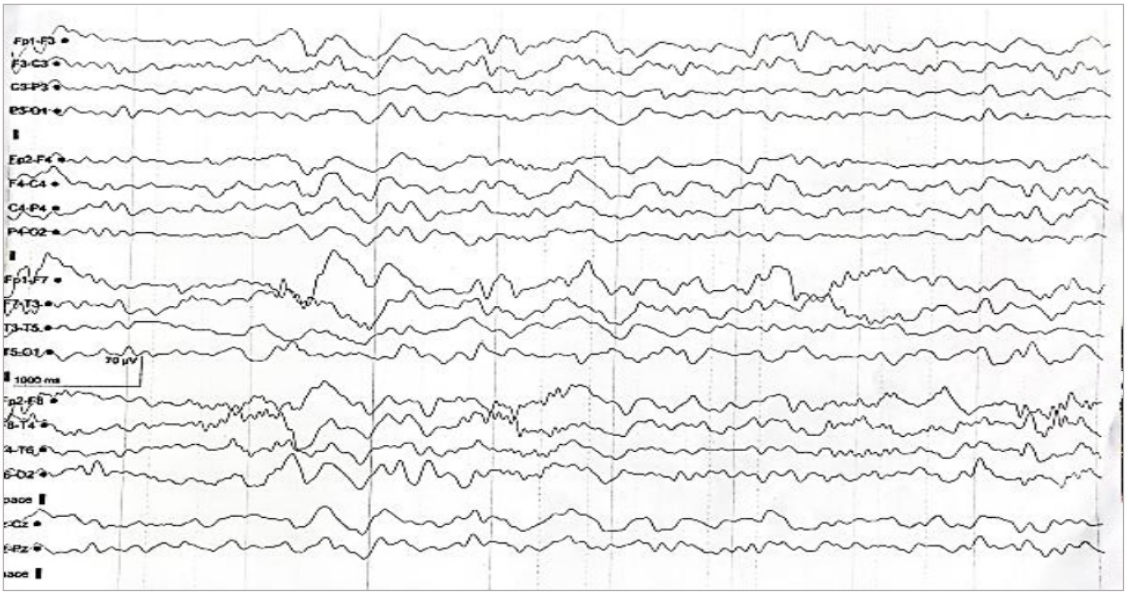

Figure 1: Pre-treatment EEG showing diffuse slow waves suggestive of encephalopathy

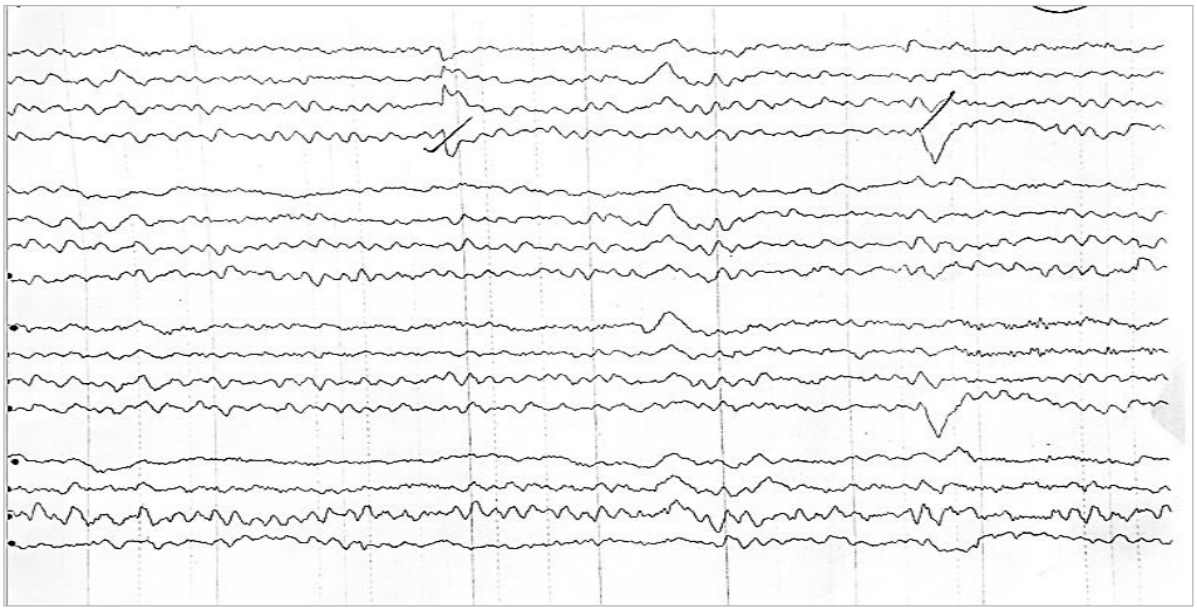

Figure 2: Three weeks after treatment EEG showing resolution

Discussion

This patient fulfilled the clinical and laboratory criteria for Hashimoto's encephalopathy / SREAT, presenting with a subacute progression of neuropsychiatric symptoms. These features are characteristic of autoimmune encephalopathy. The severity and rapid progression, along with prominent EEG abnormality with diffuse slowing, strongly support SREAT as the primary diagnosis.

Although only a mild vitamin B12 deficiency was identified, it is unlikely to be the principal cause of the clinical picture. Vitamin B12 deficiency generally manifests with an insidious onset cognitive decline, peripheral neuropathy or myelopathy rather than acute psychosis or marked encephalopathy. In this patient, it was a contributory factor for slow recovery rather than the main cause for his symptoms (4, 5).

There was poor response to corticosteroids in this patient, although it is uncommon in SREAT (6) Many factors could have contributed to the poor response.

Firstly, the delayed diagnosis is likely to have allowed irreversible neuroinflammatory damage, synaptic dysfunction or gliosis to develop, reducing therapeutic recovery. Secondly, poorly controlled diabetes mellitus may have contributed to limited steroid efficacy through chronic inflammation and microvascular injury (7). Thirdly, the presence of a weakly positive antinuclear antibody raises the possibility of an overlapping autoimmune process. Specific neuronal antibody testing is not freely available in resource-limited settings; therefore, excluding such conditions will be a challenge. Finally, the prolonged use of psychotropic medication and electroconvulsive therapy may further complicate recovery.

Escalation to second line immunotherapies such as therapeutic plasma exchange or intravenous immunoglobulin should be considered to achieve clinical recovery (8).

Conclusions

This case highlights the diagnostic challenges of Hashimoto's encephalopathy and importance of early recognition and prompt intervention. Clinicians should maintain high index of suspicion for autoimmune encephalopathies when patient presenting with unexplained neuropsychiatric symptoms.

Informed written consent has ben obtained from the patient to publish this case report.

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