Case Report

Hashimoto's encephalopathy in association with retinitis pigmentosa – First reported case

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Abstract

Hashimoto's Encephalopathy (HE), also known as steroid responsive encephalopathy associated with autoimmune thyroiditis (SREAT), is a proteiform disorder known for its wide spectrum of presentations from subtle neuropsychiatric manifestations, movement disorders, seizures, stroke-like episodes to coma. Here, we report a case of HE which initially masqueraded as bipolar affective disorder (BPAD) and ultimately progressed to generalized tonic clonic seizures and coma. Although SREAT is characterized by exquisite responsive to steroid, in our case it was unresponsive to pulse methylprednisolone therapy. Rapid recovery was noted with intravenous immunoglobulin (IVIG) therapy. This case was also peculiar for its association with non-sydnromic retinitis pigmetosa (RP). To the best of our knowledge, this was the first reported case of HE which was associated with RP.

Keywords: Hashimoto's Encephalopathy, intravenous immunoglobulin, retinitis pigmentosa, thyroid

Introduction

Hashimoto's Encephalopathy (HE), also known as steroid responsive encephalopathy associated with autoimmune thyroiditis (SREAT), is a disorder known for its wide spectrum of presentations from subtle neuropsychiatric manifestations, movement disorders, seizures, stroke-like episodes to coma.[1] While some set of diagnostic criteria have been proposed, HE remains a diagnosis of exclusion after ruling out more common disorders by cerebrospinal fluid (CSF), magnetic resonance imaging (MRI) and electroencephalography (EEG) studies, presence of antibodies against thyroid antigens, and rapid response with steroids.[2] Although steroid responsiveness is a typical feature of HE, refractoriness to steroids have been documented in the literature.[3]

Retinitis pigmentosa (RP), a leading cause of progressive visual disability, is characterized by primary dystrophy of rod and cone photoreceptors. Although the majority of RP cases are non-syndromic, 20–30% of patients also have an associated non-ocular pathology.[4] Literature shows an increased occurrence of thyroid disease in patients with RP.[5]

Here, we report an index case of HE which initially masqueraded as bipolar affective disorder (BPAD), was unresponsive to steroid, resolved with intravenous immunoglobulin (IVIG), and associated with non-sydnromic RP.

Case Report

A 40-year-old presented to the emergency department (ED) with the first ever episode of seizure (semiology: Right-sided focal

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seizure with secondary generalization). At ED, she was stabilized with safe airway, uninhibited breathing, intravenous (IV) access, 4 mg IV lorazepam followed by levetiracetam 1 g/day.

History from family members revealed that for the last 8 months she was having subacute onset rapidly progressive mood turnabouts. She was often getting exceptionally agitated with emotional outbursts with occasional tearfulness, low affect, lack of interest and energy in activities, apathy indecisiveness, and feeling of being burnt out. This negative phase was interlude by intervals of exhilarated mood, unseemly laughter, inessential wordiness, increased psychomotor activities, exaggerated sexual urge, and decreased sleep. There was also a history of increasing forgetfulness of recent events, misplacement of objects, and executive dysfunction for 4 months (forget to add ingredients during cooking, clothing, cleaning, and marketing). There was no history suggestive of the involvement of other cognitive domains. Family members complained that for last 4 months she was complaining of dimness of vision especially in afternoon and evening hours. There was no history of substance abuse or family history of neuropsychiatric disorder. Previous treatment cards revealed she was on treatment for BPAD for last 6 months from the psychiatry outpatient department. She was on lamotrigine (200 mg/d), quetiapine (150 mg/d), lithium (1200 mg/d), sertraline (75 mg/d), clonazepam (1 mg/d), and cognitive behavior therapy (CBT) without any improvement.

Even after hemodynamic stabilization and control of seizures, sensorium did not improve completely (fluctuating GCS of E1V1M1 to E3V2M5). Thus, a detailed neurological examination could not be done in ED. She was afebrile, euglycemic, normotensive, and tachycardic. There was alternating hemiparesis (initially right hemiparesis which was thought to be due to Todd's paresis, improved within 72 h; later on prolonged hemiparesis involving the left side of body). All deep tendon reflexes (DTRs) were diminished with bilaterally extensor planter response. No signs of meningeal irritation could be elicited. Pupils were bilaterally small, equal, and reacting to light. Fundoscopy revealed typical RP [Figure 1].

MRI brain, comprehensive metabolic panel, and serum lithium level were normal. Workup for viral encephalitis, CSF cultures for bacteria and fungi, and CSF CBNAAT were negative. CSF IgG index was elevated (0.95, n. <0.7). Serum and CSF aquaporin-4 and anti-myelin oligodendrocyte glycoprotein (MOG) were negative along with normal visual evoked potential (VEP) test. CSF lactate-pyruvate ratio was normal. Connective tissue disorder profiles, autoimmune encephalitis profile, and vasculitis screen came out negative. Serologies for Hepatitis B, Hepatitis C, and HIV were non reactive. Mitochondrial genetics was negative for any mutation. However, thyroid panel revealed hyperthyroidism (free T4 – 6.89 ng/dl, n. 0.7–1.8, TSH – <0.01 microIU/ml, n. 0.3–5.5). Thyroid autoimmune screening showed high titer [anti-thyroid peroxidase (TPO) antibody- 969.7 IU/ml (n. <35.00), anti-thyroglobulin (ATG) antibody – 3523 IU/ml (n. <115.00) and TSH –Receptor antibody (TRAB) – 38.10 IU/ml (n. <1.75)]. The EEG demonstrated diffuse generalized slowing without any epileptiform potentials, suggestive of encephalopathy [Figure 2]. Ultrasonography of thyroid was suggestive of thyroiditis and fine needle aspiration cytology (FNAC) from thyroid swelling showed cytological features of adenomatoid goiter with the evidence of early autoimmune thyroiditis. Thus, a diagnosis of HE or SREAT was made.

The patient was put on intravenous methylprednisolone (1 g/day for fve consecutive days), without clinical recovery. So, IVIG (2 gm/kg/day for five days) was instituted. Sensorium was completely recovered within five days of IVIG therapy. Left hemiparesis improved but persisted for another two weeks before complete resolution. A repeat MRI brain was again non-conclusive. She was discharged with prednisolone (40 mg/d), carbimazole (60 mg/day), lamotrigine (100 mg/day), quetiapine (50 mg/day), and sertraline (25 mg/day).

At follow up after one month, she only had visual symptoms due to RP. She was seizure free with no mood, cognitive, and

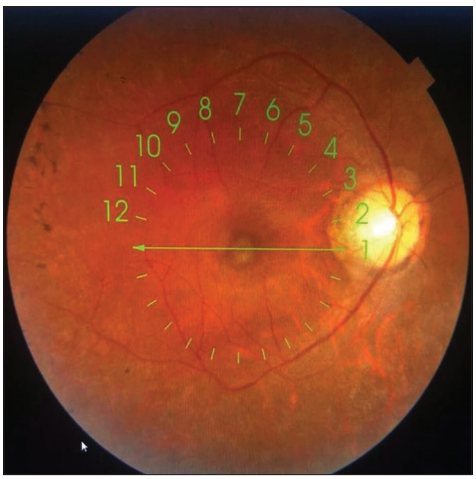

Figure 1: Fundoscopy showing "bony spicules"-like peripheral pigmentation, disc pallor, choroidal sclerosis, and arteriolar attenuation, typical of RP

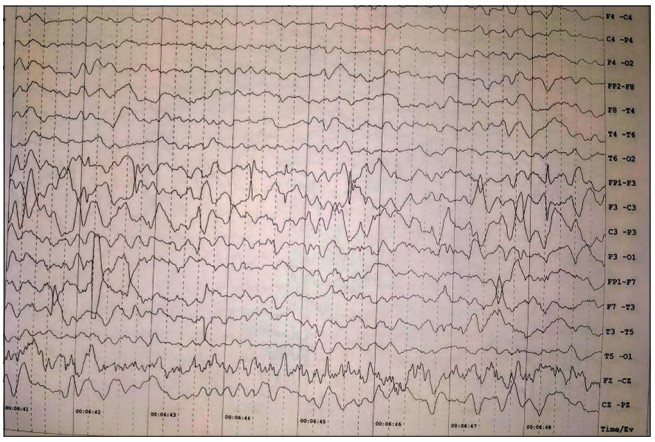

Figure 2: EEG showing diffuse generalized slowing without any epileptiform potentials, suggestive of encephalopathy

behavioral problems. Lamotrigine, quetiapine, sertraline, and prednisolone were tapered rapidly and put off within the next three months. At 12 months follow up, she remained seizure free without any anti-epileptics, and free from any psychiatric illness without psychotropic drugs.

Discussion

Although thyroid hormones have long-been known for its pivotal role in the development of nervous system and cognitive functioning, the clinical presentations, pathogenesis and diagnosis of autoimmune thyroid disorders (AITD), and HE still remain an enigma.[6] This was a case where spectrum of illness started almost one year back with BPAD which then progressed to involve multiple cognitive domains and further got complicated with visual diminution, seizures, encephalopathy, and paresis. SREAT or HE pretending as psychotropic-refractory major depressive disorder, schizophreniform disorder, and BPAD are increasingly being acknowledged.[7-12] In this context, we recommend for routine screening of thyroid autoantibodies even in the setting of euthyroid state for early diagnosis of a reversible catastrophe.

Our case was diagnosed as SREAT applying Castillo's criteria.[2] Although classically SREAT is exquisitely responsive to pulse methylprednisolone therapy, unresponsiveness to steroid should not deter the physicians from considering this diagnosis. Rather IVIG, plasmapheresis, rituximab, and other immunosuppressive therapies should be zealously tried as evident in the existing literature.[6,10,13]

Thyroid disorders have been found to be more prevalent among RP patients than control.[5] Scanelli *et al.* showed statistically significantly higher prevalence of AITD in the patients with RP and in their relatives, compared with the control population.[14] Similar conclusion was drawn from the study by Proto *et al.*[15] Our case was peculiar in the aspect that HE in association with RP was never previously reported.

Conclusion

This case underscored the importance of screening of thyroid autoantibodies among psychotropic-refractory patients in psychiatric or cognitive clinic. To the best of our knowledge, this was the first reported case of HE in association with non-syndromic RP.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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