Hashimoto’s Encephalopathy Presenting with Chorea

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Abstract
Hashimoto’s encephalopathy (HE) is a steroid-responsive relapsing neuropsychiatric disorder associated with high titers of antithyroid antibody with or without thyroid dysfunction. We report a case of HE in a 78 year old female who developed sudden onset behavioral abnormalities associated with choreiform movement of extremities. All causes of vascular, infective, metabolic, autoimmune, paraneoplastic and toxic encephalopathy were excluded. Antithyroid peroxidase (anti-TPO) antibody was found to be raised with very high titre. A diagnosis of HE was made. Prompt treatment with high dose steroid led to dramatic improvement of symptoms including choreiform movement.

Introduction
Hashimoto’s encephalopathy (HE) is a rare neuropsychiatric syndrome, more common in women, associated with serologic evidence of antithyroid antibodies, when other causes of encephalopathy are excluded. Clinical presentation of this relapsing-remitting disease include seizures, stroke-like episodes, cognitive decline, neuropsychiatric symptoms and myoclonus. Association of choreiform movement with HE is rarely described.

Case Report
A 78 yrs old Hindu female, known hypertensive controlled on medication without any other co-morbidity was admitted in our hospital with sudden onset of behavioral disturbance for two weeks followed by abnormal movement of all four limbs for 10 days. The behavioral change was in the form of transient and recurrent episodes of disorientation, forgetfulness, inappropriate irritability, attention deficit, disinhibition, decrease in self care, insomnia and self-muttering which was suggestive of hallucination. Later an uncontrollable asymmetric abnormal movement developed which was confined to extremities and almost disappeared during sleep. There was no history of preceding fever, headache, any visual disturbance, convulsion and weakness of any limb or any subjective sensory symptom. Her relatives denied any history of recent drug intake or any substance abuse. There was no history of weight gain or loss, palpitations or tremor, heat or cold intolerance, skin rash, joint pain, abnormal vaginal bleeding or any palpable lump or mass. Her dietary habit was normal and she was non-vegetarian. Family history was non-contributory.

On clinical examination, general survey was unremarkable. There was no thyroid enlargement. She was not oriented to time, place and person. She was found to mutter with self which was suggestive of auditory hallucination along with episodic recurrence of inappropriate giggling, laughing, and crying. Mini-mental score was 16. Speech was normal. Neck rigidity was absent. There were no primitive reflexes or any release sign. All the cranial nerves were intact including normal fundoscopic finding. There was no motor weakness and all modalities of sensation were intact. Tone was reduced. Tendon jerks and superficial reflexes were preserved with bilateral flexor response of plantar. A choreiform movement was seen involving extremities, more prominent on left side. There was impersistence of tongue on protrusion. Milkman’s grip sign was present in upper limbs. There were no other extrapyramidal signs or symptoms. Other systemic examination was unremarkable.

Investigations: Hb-12gm%, WBC-9300/cmm, ESR- 34 mm. BUN- 12 mg/dl, creatinine- 1.1 mg/dl, serum bilirubin - 0.9 mg/dl, SGPT- 38 IU/L. Urine analysis was normal. Chest X-ray showed mild cardiomegaly. ECG showed inferior wall ischemia and 2D-echocardiography was suggestive of left ventricular hypertrophy. Ultrasonography of abdomen was normal. CECT scan of brain revealed diffuse brain atrophy and focal old left PCA territory infarct and MRI brain corroborated the CT finding. CSF study was normal including negative arboviral titer. Serology for HIV I and II, hepatitis B and C were found to be nonreactive. Vitamin B12 and serum folic acid level were 543 pg/ml (normal: 200-900 pg/ml) and 13.2 ng/ml (normal: 2.7-17 ng/ml): respectively. ANA (by Hep-2 method), ENA profile, APLA antibody (IgG and IgM), C-ANCA and P-ANCA were found to be negative. Tumor marker including AFP, CEA, CA-125, CA19.9 andNSE were found to be normal. Anti-VGKC and anti-NMDA receptor antibodies could not be done due to limitation of resources. 24 hours urinary copper was 24 µg/day (normal: 10-30 µg/day) and serum ceruloplasmin level was 23 mg/dl (normal: 15-60 mg/dl). Slit lamp examination for KF ring was negative. EEG was done with normal interpretation. Serum ammonia was 42 µg/dl (normal: 30-86 µgm/dl) and serum calcium was 8.9 mg/dl (normal 8.5–10.5 mg/dl). Arterial blood gas analysis revealed no hypoxia. Thyroid function test was also normal with TSH of 3.34 mU/L (normal: 0.5-5 µU/ml) and FT4 of 1.2 ng/dl (normal: 0.9-1.7 ng/dl). Anti thyroid-peroxidase (anti-TPO) antibody was found positive with high titer of 576 IU/ml, normal <34 IU/ml).

Probable diagnosis of HE was suggested. Patient was started intravenous methylprednisolone (1 gm daily for 5 days). Her choreiform movement was dramatically reduced with complete resolution by 3 weeks. There was also gradual improvement of cognitive function and behavioral abnormalities. Patient was switched to oral prednisolone of 60 mg per day after 5 days. Her MMSE improved to 24 from previous score of 16 after 3 weeks of starting treatment. Anti TPO antibody was rechecked and it was reduced to
214 IU/ml after 3 weeks of starting therapy from the previous value of 576 IU/ml. Patient was discharged after 3 weeks of starting therapy with prednisolone 40 mg per day with gradual tapering of dose and advice for regular follow-up. Since last two months she is clinically normal without reappearance of symptom and she is now maintaining well on 10 mg/day of prednisolone.

Discussion

Since it was first described in 1966 by Brain et al., HE has gained prominence in the differential diagnosis of encephalopathy of unknown origin. It has characteristically dual mode of presentation, either in acute form which is characterized by sign of cerebral ischemia, seizure, and psychosis, or it may present as an indolent form with depression, cognitive decline, hallucination, myoclonus, tremors, and fluctuations in level of consciousness. In this case report, our patient’s clinical manifestations are more consistent with the second form of presentation, which is more common.

Other names for this disorder includes nonvasculitic autoimmune meningencephalitis (NAIM) and steroid responsive encephalopathy associated with autoimmune thyroiditis (SREAT). There is wide variation in age of onset with highest occurrence of the disease is found between the fifth and sixth decades of life with an average age of 47 years (range 14 to 78 years) and majority of patients are women.

The mechanism of HE does not appear to be related or correspond to thyroid status of the patient as in two recent reviews, 23% to 35% of patients had subclinical hypothyroidism, 17% to 20% had hypothyroidism, 7% had hyperthyroidism and 18% to 45% were found to be euthyroid. The pathogenesis of HE remains obscure. There are few proposed mechanism which include autoimmune cerebral vasculitis, toxic effect of thyroid stimulating hormone on the CNS or antibodies-induced neuronal reaction. Most likely, autoimmune mechanism plays a significant role behind its pathogenesis owing to the higher prevalence in women, fluctuating course and significant response with steroids. The vast majority of patients have positive serum anti-TPO antibodies (86%) where as fewer patient was found to have anti-Tg positivity (48%).

Although the CSF analysis results were normal in our patient, a lymphocytic pleocytosis has been found in 14% of reported patients, cell counts were found to be raised even more than 100/mm³ in few patients. Protein concentration was found to be elevated in 78% of patients and 20% of patients have concentration greater than 100mg/dl. Although the EEG finding in our patient was normal, nonspecific slow background activity are seen in 90 to 98% of patients. Focal spikes or sharp waves and transient epileptic activity are less frequent.

In most of the cases brain imaging are very non-specific and ranges from cerebral atrophy (most common abnormality) to ischemic changes. The MRI shows no changes in more than 50% of the cases and when it does, the most common finding is nonspecific hyperintense signal on T2 which occur usually in white matter, hippocampus, temporal lobe and splenium corporis callosi. These are suggestive of an edema or brain inflammation which may be reversible after treatment with corticosteroids. In our patient the brain scanning was suggestive of diffuse brain atrophy and old PCA territory infarct.

The differential diagnosis of HE can include toxic metabolic encephalopathies, paraneoplastic syndromes, Creutzfeldt-Jakob disease, drug withdrawal (serotonin syndrome, neuroleptic malignant syndrome) degenerative dementia, psychiatric diseases and recently described autoimmune encephalitis.

Patient with HE usually respond dramatically to steroid therapy. Initial dose of oral prednisolone varies from 50 to 150 mg daily and slowly tapered over weeks to months, depending on the clinical response of the therapy and course of the disease. High dose of intravenous methylprednisolone (1 gm/day) may also be given for initial three to seven days, followed by oral prednisolone therapy. Rapid clinical improvement can be observed within three days of therapy but significant clinical improvement may take an average of four to six weeks. Most patient stay in remission even after discontinuation of therapy but treatment may be required even for lifelong.

Conclusion

Although HE is a rare clinical condition, with a varying clinical course, it should be considered in any patient presenting with acute or subacute onset of encephalopathy of unknown etiology or in patients with diffuse cognitive decline with an intermittent or progressive course concomitant with choreiform movement. Suspected patients, with or without active thyroid disease, after excluding the main cause, should be tested for antithyroid antibodies in serum or CSF. As timely administration of steroid can salvage the patient, high index of suspicion and prompt diagnosis is needed.

References