Case Report

Hashimoto's encephalopathy misdiagnosed as pyogenic meningoencephalitis

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ABSTRACT

Hashimoto's encephalopathy is a controversial and under-recognized condition, associated with autoimmune thyroiditis. Presentation may be an insidious development of cognitive impairment or recurrent acute episodes of focal neurological deficit with confusion. Here, we present a case of middle-aged female that presented with headache, vomiting with alteration of sensorium and left side weakness and responded well to steroids. A negative microbiological screen of the cerebrospinal fluid (CSF) and serum along with raised CSF protein, elevated serum antithyroid antibodies, and characteristic electroencephalographic and neuroimaging findings yielded the diagnosis.

Key words: Cerebrospinal fluid, Hashimoto encephalopathy, nonvasculitic autoimmune meningoencephalitis, steroid-responsive encephalopathy

INTRODUCTION

Hashimoto encephalopathy (HE) also called as nonvasculitic autoimmune meningoencephalitis, nonvasculitic autoimmune inflammatory meningoencephalitis or steroid-responsive encephalopathy, steroid-responsive encephalopathy associated with autoimmune thyroiditis associated with autoimmune thyroiditis, has been described as a syndrome of encephalopathy/neuropsychiatric deficits, high serum antithyroid antibody concentrations, and the absence of evidence of cerebrospinal fluid (CSF) infection that is, responsive to glucocorticoid therapy.[1,2]

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Since the first description of neuropsychiatric disease associated with autoimmune thyroid dysfunction by Brain *et al*. in 1966,[3] the relationship between antithyroid antibodies and steroid responsive encephalopathy is subject to considerable debate.

The clinical features are varied, and some clinicians have proposed two subtypes of the disorder: (i) Vasculitic type, characterized by multiple strokelike episodes, and (ii) a diffuse progressive type, characterized by dementia, and psychiatric symptoms.[4]

Autoimmune cerebral vasculitis is likely because neuropathological examinations of biopsy and autopsy specimens have shown lymphocytic infiltration into the

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walls of arterioles and venules in brain parenchyma[5,6] and leptomeninges.[6]

Because a-enolase is expressed in vascular endothelial cells, autoantibodies against a-enolase may be associated with vasculitic processes, a useful diagnostic marker for HE.[7]

It is underrecognized by physicians, and the purpose of this report is to add to the literature and highlight the potential for the excellent clinical outcome with appropriate therapy.

CASE REPORT

A 50-year-old female presented with severe global headache followed by multiple episodes of projectile nonbilious vomiting for about 2 days. After that, the patient developed an alteration of sensorium in the form of decreased responsiveness and inability to recognize family members. This was associated with weakness of the left side of body. She had a past medical history of intermittent headache and vomiting for 4 years lasting for few days. She also had a history of hypertension for 8 years and primary hypothyroidism for 6 years. She had been receiving antihypertensive therapy and thyroxine 100 μg.

On admission, the patient was in Grade II encephalopathy, exhibited disorientation. Her concentration and memory were impaired. She had xanthelasmas over upper eyelids. Her cranial nerves were intact, and there was terminal neck stiffness. She had left side weakness (Grade III power) and extensor plantar response.

Apart from mild normocytic normochromic anemia with hemoglobulin of 10.70 g/L, her routine blood parameters including electrolytes, liver function tests, arterial blood gas analysis, blood, and urine culture were normal. Chest X-ray, electrocardiography, and abdominal ultrasonography were normal. CSF study showed 200 cells with predominant polymorphs (85%), protein-290 mg/dl, sugar-80 mg/dl with negative Gram's, and Ziehl-Neelsen stain. Noncontrast computed tomography head with choroid plexus hyperdensities as shown in Figure 1. She was diagnosed as probable pyogenic meningoencephalitis in view of terminal neck rigidity, high CSF polymorphic cells. She was initiated on antibiotic drugs (ceftriaxone and vancomycin).

After a week of antibiotics, the patient deteriorated clinically, and her sensorium worsened. She was reevaluated, electroencephalographic (EEG) showed generalized slowing (8-Hz). HIV and hepatitis virus screening were negative. CSF polymerase chain reaction for herpes simplex virus and tuberculosis were negative. India ink staining as well cryptococcal antigen was negative in CSF. The levels of serological markers for collagen disease, including antinuclear, anti-DNA, anti-SSA/SS-B, anti-neutrophil cytoplasmic and myeloperoxidase antineutrophil cytoplasmic antibodies, were within the normal ranges. Serologic tests for syphilis were also negative.

Magnetic resonance imaging (MRI) of brain with T2-weighted and fluid-attenuated inversion recovery sequences showed diffuse bilateral subcortical hyperintensities and left choroid plexus bleed as shown in Figures 2 and 3.

Thyroid profile showed high thyroid-stimulating hormone, 18.25 (normal 0.35–5.50 pg/ml), T3, 0.3 (normal 0.6–1.81pg/ml), and T4, 4.8 (5.01–12.45 pg/ml). Serum antithyroid peroxidase antibody (TPOAb) level was elevated, 343.50 IU/mL (normal <60 IU/mL), and antithyroglobulin antibody >500 U/ml (normal ≤60). Thyroid ultrasound showed heterogeneous echogenicity in both lobes. She was treated with high-dose intravenous glucocorticoid therapy followed by a slow taper. Thyroxine was augmented to 150 μg. Thereafter, he became more alert, conversant, and demonstrated marked improved in her weakness.

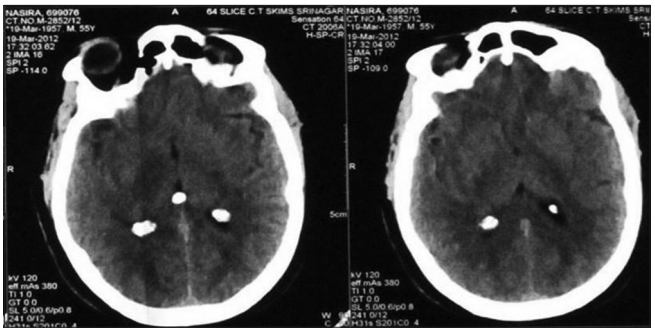

Figure 1: Non contrast CT head with choroid plexus hyperdensities

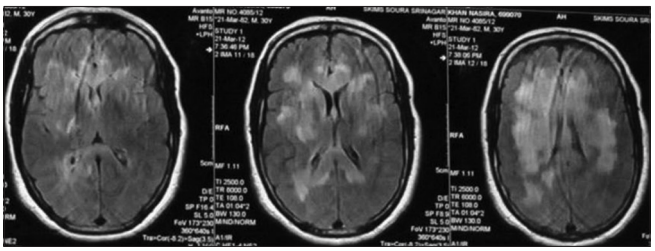

Figure 2: MRI brain with T2-weighted images

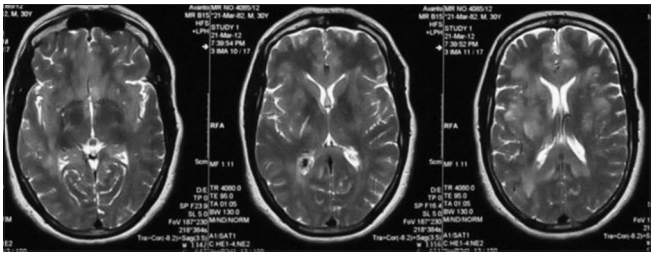

Figure 3: MRI brain with FLAIR sequences

DISCUSSION

HE is a controversial disorder with an estimated prevalence of 2.1/100,000 and the mean age of onset of 42 years.[8] Females are more often affected than males (3.6:1).[9]

Primary demyelination, vasculitis, immune complex deposition, and direct antibody-mediated neuronal injury have all been proposed as mechanisms of disease. It is characterized by confusion with or without myoclonus, seizures, hyperreflexia, and psychosis.

The presentation may be an insidious development of cognitive impairment or recurrent acute episodes of the focal neurological deficit with confusion.[10]

Peschen-Rosin *et al*. outlined the first diagnostic criteria for HE that included patients with neurocognitive deficits and at least three of the following conditions: An abnormal EEG, elevated thyroid antibodies, elevated CSF protein and/or oligoclonal bands, an excellent response to steroids, and a nonspecific but abnormal cerebral MRI.[11] Chong *et al*. criteria include the exclusion of other diseases such as infection, stroke, metabolic, and toxic causes as well as other factors leading to encephalopathy, normal thyroid status or thyroid dysfunction not able to justify the symptoms, elevated plasma anti-TPOAb level, and a good response to corticosteroid therapy.[12]

We present the case of a middle-aged female with headache, progressive impaired cognitive function, and left side weakness. She was treated as probable pyogenic meningoencephalitis in view of terminal neck rigidity, high CSF polymorphic cells, and received antibiotic drugs. She failed to achieve improvement, and rather deteriorated. The extensive evaluation in our hospital found elevated serum antithyroid antibodies, EEG showed generalized slowing, with pleomorphic leukocytosis in CSF, and high protein. The patient responded to high dose steroid therapy.

Antithyroid antibodies – anti-TPOAb and or antithyroglobulin antibody (TgAb) – are the hallmark of this disease. Sensitivity ranges from 73% to 100% for these antithyroid antibodies.[8]

Patients have thyroid dysfunction. Overt hypothyroidism is seen in 17–20% of patients, 7% are hyperthyroid, and 38–47% are euthyroid.[8] Our patient was hypothyroid. CSF protein elevation is seen in 75%, and lymphocytic pleocytosis is present in 10–25%.[8] Our patient demonstrated elevated protein, peaking at 290 mg/dL, and polymorphic pleocytosis.

EEG abnormalities when present are usually nonspecific with background slowing is observed in 94% of patients. Sharp waves and transient epileptic activity are less commonly seen.[8,13,14] Our patient demonstrated background slowing on EEG.

MRI may be normal or demonstrate nonspecific T2 signal abnormalities in the subcortical white matter that do not enhance with gadolinium. In rare cases, diffuse white matter changes or meningeal enhancement have been described.[10] Initial treatment is with high-dose steroids titrated according to clinical response.[4] Thyroid dysfunction should also be appropriately treated if present. Response to steroid therapy is usually excellent and is followed by slow steroid tapering and eventual discontinuation. Steroid intolerant patients may respond to cyclosporine or azathioprine. There are also several case reports describing good clinical outcomes following plasma exchange[15] and intravenous immunoglobulin.[9]

CONCLUSION

HE should be considered in patients with unexplained encephalopathy or rapidly progressing dementia. Elevated serum levels of anti-TPOAb and TgAb's coupled with a marked response to corticosteroids is diagnostic. HE often has a favorable prognosis.

Before consideration of HE, we should rule out any probable causes of encephalopathy, such as infections, electrolyte imbalance, toxins, and neoplasms.

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Conflicts of interest
There are no conflicts of interest.

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