Graves Disease with Hashimoto's Encephalopathy

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ABSTRACT

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The authors report the case of an elderly diabetic lady who presented with generalized fatigability, loss of weight, memory disturbances, irrelevant talk and disorientation. She had goiter and proptosis. Her thyroid function tests revealed hyperthyroidism and markedly elevated anti TPO antibody levels. Imaging modalities and uptake study were suggestive of Graves' disease. The clinical findings, investigations of Graves' disease with Hashimoto's encephalopathy and treatment strategies are discussed here.

Keywords: Graves' disease, Hashimoto's encephalopathy, TSH receptor antibody

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INTRODUCTION

Hashimoto's encephalopathy is first described by Brain et al in 1966 and it is also known as Steroid -responsive encephalopathy associated with autoimmune thyroiditis (SREAT) and Nonvasculitic autoimmune meningoencephalitis (NAIM). Majority of patients are perimenopausal females with goiter and a family history of thyroid dysfunction. They can have two types of presentation; Acute stroke-like that accounts for 25% and diffuse progressive pattern of slow cognitive decline seen in75% of the patients.

Two clinical patterns may overlap over the course of the disease. Exact pathogenesis is unknown but considered to be an autoimmune encephalopathy where precise role of antithyroid antibodies is unclear. Till date, no shared antigen has been identified between thyroid gland and brain, except alpha enolase.

CASE REPORT

Sixty-five years old Khairunnissa, who is a diabetic on irregular treatment came with complaints of generalized weakness, irrelevant talk, memory loss, disorientation, decreased appetite and loss of weight for approximately 3 months duration.

On examination, she was drowsy, disoriented and afebrile. No evidence of pallor, icterus, cyanosis, clubbing, pedal edema or lymph node enlargement. No neck stiffness. Her pulse rate was 110/min, BP was 150/90 mm of Hg taken in right upper limb in supine position, and respiratory rate was 16/min. Diffuse goiter was detected along with proptosis. She was actively moving all her limbs. Respiratory, gastrointestinal, cardiovascular system examinations were with within normal limits.

Nervous system examination showed non-co-operative patient with irrelevant talks, impaired memory but no speech abnormality could be detected. Orientation to time, place and person was impaired. No cranial nerve involvement noted. Motor system examination revealed normal bulk of muscles, Grade 4 power all muscles. DTR were sluggish, Plantar – bilateral flexor. Signs of in-co-ordination couldn't be tested for. No sensory symptoms. No neck stiffness, spine tenderness.

Investigating her, we found, Hb - 11.4g/dL, Total count – 6500 cells/cmm, PLT – 275000/cmm, ESR - 75mm/1ST hr, Serum protein – 7.6 g/dL, Serum albumin – 4.5 g/dL, Serum globulin – 3.1 gdL, SGOT – 26 IU/L, SGPT – 32 IU/L, ALP – 108 IU/L, Serum bilirubin Total – 0.8mg/dL, Serum bilirubin Direct – 0.2mg/dL, Serum sodium – 136meq/L, Serum potassium - 3.7meq/L, RBS – 210mg/dL, Blood Urea – 41mg/dL, Serum creatinine– 0.8mg/dL. Urine analysis showed, Urine protein – negative, urine sugar – negative, urine acetone –negative, urine bile pigment, leukocytes, blood – negative, urine specific gravity – 1.02. Acid blood gas analysis showed, pH – 7.37, pO2 – 99mmHg, pCO2 – 41mmHg, HCO3 – 24mmHg. Serum cortisol was 12mcg/dL. Thyroid function test showed, T3 – 3.36ng/ml (0.8-2.0), T4 – 14.07ng/ml (5.1-14.1), TSH – 0.01microIU/L (0.27-4.2). Anti TpO was 749.50 IU/ml (<9) & TSH receptor antibody – 8.65 IU/L (<1.75).

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USG thyroid showed diffusely enlarged gland with increased vascularity without any focal lesions.USG abdomen revealed no significant intra-abdominal pathology. CT Brain was normal. Thyroid uptake study by technetium scan showed enlarged thyroid gland with increased perfusion and trapping s/o Graves' disease. MRI orbit report of this patient came as bilateral proptosis with oedematous extra-ocular muscles. Later she underwent FNAC of thyroid which revealed fireflare appearance of thyrocytes, dense cytoplasm, paravacuolar granules with thin colloid which are the features suggestive of Graves' disease.

With the above features, we made a diagnosis of Graves' disease with Hashimotos encephalopathy since there was clinical evidence of Graves' disease with encephalopathy and raised anti-thyroid antibody levels excluding other causes of metabolic encephalopathy. The patient was treated with Carbimazole 40 mg/day, Propronolol 40 mg/day and parenteral corticosteroid initially and then continued with tapering oral dose. Patient showed steady improvement, became conscious. Prompt response with steroid also favors the diagnosis of Hashimotos Encephalopathy.

DISCUSSION

Hashimotos Encephalopathy is an unusual neurologic disorder whose etiology, pathogenesis and histologic characteristics are unclear. A systematic review published in 2003[1] reported only 85 well-documented cases in the literature; however, this syndrome may be under-recognized. A hospital-based epidemiologic study of neurologic symptoms consistent with Hashimotos encephalopathy estimated its prevalence to be about 2.1 per 100,000[4]. The disorder occurs more frequently in females with a female-to-male ratio of four to one[1,5].The clinical manifestations usually include acute to subacute onset of confusion with alteration of consciousness. Two major patterns of presentation were described:

25% of patients follow a stroke-like pattern of multiple recurrent episodes of focal neurologic deficits with a variable degree of cognitive dysfunction and consciousness impairment[1,2]. 75% present with a diffuse progressive pattern of slow cognitive decline with dementia, confusion and hallucinations[1,2]. These two clinical patterns may overlap over the course of the disease. In this case report, our patient's clinical manifestations are more consistent with the second form of presentation, which is more common.

Two-thirds of patients may experience focal or generalized tonic-clonic seizures, and 12% may present with status epilepticus. Also, myoclonus or tremor is seen in up to 38% of patients[1,2&5].The mechanism of Hashimotos encephalopathy does not appear to be related to the thyroid status, which can vary greatly from hypothyroid to hyperthyroid states. The presence of elevated antithyroid antibodies is an essential part of Hashimotos encephalopathy diagnosis, and suggests the presence of thyroid autoimmunity[1,5].

The pathogenic role of thyroid antibodies remains unknown, there is no evidence that they react with brain tissue or affects nerve function, and also no clear correlation between the severity of the neurologic symptoms and the concentration of these antibodies[1,4]. Infrequently, the titers of antithyroid antibodies (TPOAb and TgAb) are measured in the CSF. A systematic review found that 13% of published cases of HE reported antithyroid antibodies in the CSF [5]. However, the titers of antithyroid antibodies in the CSF do not correlate with the clinical stage of the disease, and the sensitivity and specificity of this finding remain unclear[4,5].

An autoantibody against the amino terminal end of the enzyme α-enolase, an antigen of the thyroid and the brain, has been identified as a potential biomarker of Hashimotos encephalopathy[5,8]. A study found serum autoantibody reactivity in five of six patients with Hashimotos encephalopathy compared with two of 17 patients with Hashimoto's thyroiditis but no Hashimotos encephalopathy and in none of 25 healthy control subjects[8]. This antigen is also found in endothelial cells, suggesting an autoimmune vasculitic mechanism; however, this has not been confirmed by neuroimaging techniques[5].An elevated protein concentration in CSF can be seen in 78% of patients, and in 20% of patients, it may be greater than 100 mg/dL.

The differential diagnoses of Hashimotos encephalopathy include stroke or TIA, cerebral vasculitis, carcinomatous meningitis, toxic metabolic encephalopathies, paraneoplastic syndromes, CJD, degenerative dementia and psychiatric diseases[1,5].

The long-term prognosis is variable, although a high percentage of patients respond to treatment; others could have a progressive or a relapsing course[1,5]. The symptoms usually improve with glucocorticoid therapy; however, it is not necessary because of treatment. A systematic review of 85 cases published of Hashimotos encephalopathy found clinical response in 98% of patients treated with glucocorticoids, 92% of patients treated with glucocorticoids and levothyroxine

and 67% of patients treated with levothyroxine only[1]. Other measures include plasmapheresis, intravenous Immunoglobulin and steroid sparing drugs.

Although Hashimotos encephalopathy is usually associated with Hashimoto thyroiditis which predominantly present as hypothyroidism, this patient had features of Graves' disease with raised anti-TPO antibodies which is found to be rare. Our patient had a dramatic improvement with steroid, beta blocker and carbimazole.

Clinical clues for diagnosis include presence of metabolic encephalopathy, goitre with variable thyroid function, significant elevation of anti-thyroid antibody and no other cause for encephalopathy.

END NOTE

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