

Recurrent Cerebellar Ataxia in a Young Lady with Hashimoto's Thyroiditis

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Abstract Hashimoto's thyroiditis (HT) is now considered as the most common autoimmune disease. Cerebellar ataxia can be a rare presentation of autoimmune (Hashimoto's) thyroiditis. We reported a 26 year old lady presented with recurrent episodes of bilateral cerebellar ataxia without any other neurological features. She was euthyroid but having very high circulating antibodies specially anti-thyroid peroxidase (TPOAb) antibodies suggestive of Hashimoto's thyroiditis.

Keywords: autoimmune thyroiditis, cerebellar ataxia, hashimoto's thyroiditis, hypothyroidism etc

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1. Introduction

Hashimoto's thyroiditis (HT) is a chronic inflammation of the thyroid gland initially described over a century ago but of still incompletely defined etiopathogenesis. It is now considered the most common autoimmune disease [1], the most common endocrine disorder [2] as well as the most common cause of hypothyroidism [3]. Hypothyroidism has been described as a cause of gait ataxia, presumably due to cerebellar dysfunction [4,5,6,7,8] although the exact mechanism(s) by which it might produce this syndrome is unclear. In most reported cases, the ataxia has been reversed by thyroid replacement therapy [11,12,13], suggesting that it was caused by the metabolic and physiological effects of the hormonal deficiency [10,11,13]. In some patients, however, despite thyroid replacement therapy the cerebellar syndrome has persisted and progressed [4,6,10]. In this paper we report on a patient seen at our institution presenting with recurrent cerebellar ataxia in a young lady and raised antithyroid antibody titres diagnostic of Hashimoto's autoimmune thyroiditis. She was treated with levothyroxine and corticosteroids, became symptom free and euthyroid with maintenance of adequate thyroid replacement therapy as needed. Infectious, demyelinating, vasculitic, metabolic, vascular, nutritional, paraneoplastic, and alcohol related causes of cerebellar ataxia were excluded.

2. Case Report

A 26-year-old normotensive, nondiabetic left handed lady presented with recurrent episodes of gait ataxia of about 2 months' duration. Firstly she presented with a two

days history of spontaneously resolving high grade fever followed by weakness and cramping pain in her both lower limbs for 15 days. She noted clumsiness of her hands with difficulty in writing, buttoning up of clothes, and pouring from a teapot. She also noticed difficulty in walking in the form of imbalance and tendency to fall more towards the left. She doesn't give any history of loss of consciousness, convulsion, headache, visual complaints and bulbar symptoms. She gives no history of sensory disturbances and her bowel & bladder function was normal. Her other medical history including menstrual history was unremarkable and she denied smoking and alcohol consumption. She is the second issue of parents with nonconsanguineous marriage. Her parents, one elder sister and one younger brother all possess good health without any neurological or endocrine disorders. General physical examination was normal including palpable thyroid gland. Neurologically, she was fully oriented. Language and memory were intact; she had scanning dysarthria. Horizontal nystagmus was present on lateral gaze bilaterally, slowing of rapid alternating movements in the upper limbs, and marked bilateral dysmetria on heel tapping. She had normal tone and muscle bulk with slight distal weakness (5-/5) in all limbs. Deep tendon reflexes were normal except diminished at the ankles. Plantar reflexes were flexor bilaterally. All primary sensory modalities including sense of position and vibration were intact. Her gait was broad based and staggering, tandem gait was unsteady. Romberg test was mildly impaired in open eyes. The remainder of the neurological examination and other systemic exams were normal. She was investigated thoroughly for young onset sub acute bilateral cerebellar ataxia. Interestingly Brain MRI disclosed nothing favouring any demyelinating, infectious or vascular lesion (Figure 1). TSH was mildly raised and FT4, FT3 were initially normal (Table 1). Her ESR was

12 mm/hour. LFTs, RFTs including serum electrolytes were normal. RBS was 5.4 mmol/L, viral serology for HSV and CMV IgM was negative. Syphilis serology (VDRL, TPHA) and vasculitic screening (ANA, cANCA, pANCA) were unremarkable. Analysis of CSF including CSF ADA, VDRL, Oligoclonal bands (OCB) & IgG Index was normal. NCS of crossed limbs revealed no

abnormality. She was then diagnosed as a case of Bilateral cerebellar ataxia due to Suspected first isolated attack of MRI negative MS and therapy with high dose Methylprednisolone (1g/day) for 3 days followed by oral prednisolone was given. There was rapid improvement of her symptoms and she was discharged with tapering dose of steroid for 14 days.

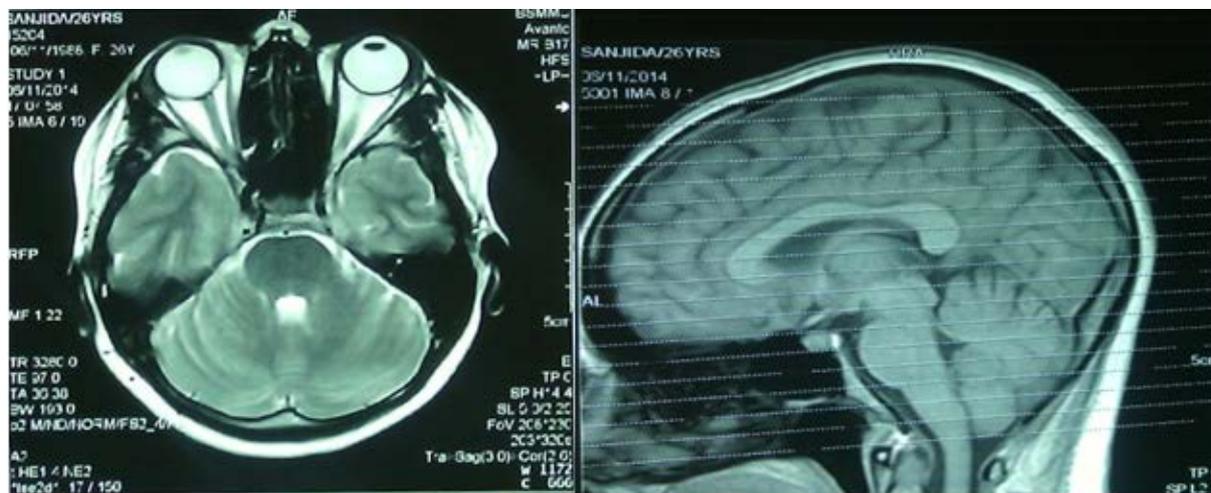


Figure 1. MRI of Brain Showing no cerebellar atrophy and normal brainstem

Four (4) days after completion of her oral steroid course, she again developed the similar type of difficulties as faced during first attack that is difficulty in walking with imbalance and scanning dysarthria. She again herself admitted in the department of Neurology, BSMMU for

further evaluation. This time, repeat MRI of brain with screening of whole spine with contrast with MRA & MRV were done. All were normal except incidental finding on MRA of absent Left PCom Artery (Figure 2).



Figure 2. MRI Screening of whole spine and MRA of cerebral vessels revealed no significant abnormality

CRP and ENA profile was normal. Thyroid profile was thoroughly investigated again and found FT3: 3.58 (Ref: 2.8-9.5 pmol/L), FT4: 20.59 (Ref: 9.5-25.5 pmol/L), TSH: 5.02 (Ref: 0.3-5.0mIU/L), normal anti-thyroglobulin antibody (TGAb): 6.62% (Ref:<30%), Very high anti-thyroid peroxidase antibody (TPOAb): 1262U/ml (Ref: <15U/ml). Ultrasonography of thyroid gland was normal and Radio iodine uptake test revealed normal uptake at 2 hours (8%) and 24 hours (11%). Auto antibodies were repeated in another centre and also showed very high Anti TPO Ab: 716 IU/ml (Ref: <35 IU/ml) and Anti TG Ab: 118 IU/ml (Ref: <40IU/ml) (Table 1).

Table 1. Thyroid Profile Before and 2 Months After Treatment:

Test Name	Before Rx	2 months after Rx	Reference range
FT3(pg/mL)	3.16	3.40	1.4-4.2
FT4(ng/dL)	1.13	1.39	0.8-1.8
TSH(μ IU/L)	5.02	2.20	0.35-5.5
TPOAb (IU/mL)	716.0	<10.0	<35
TGAb (IU/mL)	118.0	<20.0	< 40

After consultation with Endocrinology department, she was then finally diagnosed as a case of bilateral cerebellar ataxia due to autoimmune (Hashimoto's) Thyroiditis. Due

to her severe symptoms, again a 3 days course of high dose Methylprednisolone followed by oral prednisolone with levo thyroxine 25ug started. She recovered dramatically within a week and remain stable after 2 months of discharge with 25ug levo thyroxine and 10 mg prednisolone. Now her thyroid profile including thyroid auto-antibodies are within normal limit (Table 1).

3. Discussion

Hypothyroidism has previously been recognized as a cause of gait ataxia as well as other symptoms of cerebellar dysfunction [6-13]. The onset and progression of this syndrome has mostly been described in relation to laboratory evidence supportive of decreased thyroid function. This is by contrast with the patient reported here, who was euthyroid at the onset of her neurological disorders. The pathogenesis of cerebellar dysfunction in patients with decreased thyroid function is uncertain. Restoring a euthyroid state with L-thyroxine has reversed the cerebellar symptoms in most patients [6-11], suggesting that their symptoms were due to endocrine mediated dysfunction of the cerebellum [6,11]. Our patient got Levothyroxine and she was completely asymptomatic within a week. Physiological reduction of cardiac output, cerebral blood flow, and reduced oxygen and glucose consumption by cerebellar neurons has been suggested [6,10,16]. Adams et al [15] favoured slowed muscle relaxation (pseudomyotonia) over cerebellar dysfunction as the cause of ataxia in hypothyroidism. Hashimoto's, or chronic lymphocytic thyroiditis is often a subclinical condition. It is characterized by lymphocytic infiltration of the thyroid gland and circulating antithyroid antibodies to thyroglobulin or thyroid peroxidase, which are present in 70%-95% of patients [14,17]. An encephalopathy has been reported in association with subclinical Hashimoto's thyroiditis [18,19,20] and is steroid responsive in some patients [18,19] indicating a likely autoimmune pathogenesis and possibly an underlying cerebral vasculitis [20]. The reason for the occurrence of cerebellar dysfunction in some, but not all, hypothyroid patients is not clear; additional metabolic and infectious factors or surgical stress may contribute. There are several mechanisms by which autoimmunity associated with Hashimoto's thyroiditis might induce cerebellar degeneration. As widespread autoimmune reactivity can be seen in patients with Hashimoto's disease [14], cerebellar degeneration may be mediated by another unidentified circulating anti Purkinje cell antibody. In this case, the autoimmune thyroiditis would be serving as a "marker," identifying the presence of a more generalized autoimmune disorder involving the cerebellum. Alternatively, if immunological cross reactivity exists between shared thyroid and cerebellar antigens, antithyroid antibodies could specifically affect the cerebellum. McGeer PL et al described that they were not aware of any substantial evidence implicating the presence of antibodies against cerebellar neurons in patients with Hashimoto's thyroiditis. They described the relation of cerebellar degeneration with antibodies to glutamic acid decarboxylase (GAD-Ab) [21]. Indirect evidence from studies of thyrotoxic periodic paralysis, a calcium channel disease, and spinocerebellar ataxia points to a possible

link between autoimmune thyroid disease and Purkinje cell-type calcium channelopathy [15]. The present report highlights the association of subacute non-familial adult onset cerebellar ataxia with Hashimoto's/ autoimmune thyroiditis, signalled by increased TPO-Ab. The therapy of the primary and permanent hypothyroidism seen in many forms of HT consists in the daily, lifelong, oral administration of synthetic levo-thyroxine (L-T4) [22,23], which is given at doses of 1.6–1.8 µg per kg of body weight. It is therefore a symptomatic treatment, which addresses the symptoms rather than the pathogenesis of HT. A short-course of glucocorticoids should be tried in patients with the IgG4-related variant of HT, since this treatment can actually cure the disease avoiding the development of permanent hypothyroidism and thus the need of life-long monitoring and thyroxine replacement [24]. In this case, though we could not perform test for IgG4 variant, we still treated the lady with Methyl Prednisolone followed by low dose oral steroid in addition to levothyroxine to combat autoimmunity.

4. Conclusion

We present a case of cerebellar ataxia in a patient with subclinical hypothyroidism due to Hashimoto's thyroiditis. Although no definitive conclusions may be derived from a single case, it may be prudent to be vigilant of factors that predispose to cerebellar ataxia. Classical signs of hypothyroidism may not be obvious in patients with ataxia. We recommend testing for thyroid functions and antithyroid antibodies as appropriate and other evidence of autoimmunity in patients who present with subacute or recurrent cerebellar ataxia.

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Competing Interests

None.

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