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REVIEW

Cerebellar Syndrome Associated with Thyroid Disorders

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Abstract

Thyroid disorders, including hypothyroidism, hyperthyroidism and Hashimoto encephalopathy, are considered the most common cause of cerebellar dysfunction due to hormonal imbalance. Typically, cerebellar impairment occurs in the course of hypothyroidism and Hashimoto encephalopathy. Information about demographic, clinical and laboratory features of cerebellar disease associated with thyroid disorders is poor. Our review of the literature (1965 to 2018) identified 28 cases associated with hypothyroidism and 37 cases associated with Hashimoto encephalitis. Both patients with hypothyroidism and Hashimoto encephalopathy presented with signs of ataxia that were similarly distributed in the two groups and were mostly predictive of vermis involvement and frequent impairment of cerebellar hemispheres. Additional neurological signs, like dystonia, psychiatric symptoms, ocular disturbances and myoclonus, could be found in the Hashimoto encephalopathy group alone. When present, atrophy of vermis and often of both cerebellar hemispheres was the main imaging abnormality in both hypothyroidism and Hashimoto encephalopathy. Anti-thyroid antibodies could be detected in three quarters of patients with hypothyroidism and in all patients with Hashimoto encephalopathy. In the patients with hypothyroidism, thyroid replacement therapy yielded complete or partial remission of ataxia. In the Hashimoto encephalopathy group, immunosuppressive treatment provided complete remission of ataxia in about 60% of patients, partial remission in the remaining cases. Owing to the treatable nature of the condition and the high prevalence of thyroid disease among general population, cerebellar syndrome associated with thyroid disorders should be considered an important clinical entity. Information from this review will hopefully stimulate and strengthen awareness of thyroid-associated ataxia among clinicians.

Keywords Ataxia · Cerebellum · Hypothyroidism · Hashimoto encephalopathy

Introduction

Cerebellum activity may be influenced by hormonal action in the context of several endocrine dysfunctions due to thyroid diseases, parathyroid disorders, diabetes mellitus, diabetes insipidus and hypogonadism [1, 2]. Thyroid disorders are considered the most common cause of cerebellar dysfunction due to hormonal imbalance [2]. Typically, cerebellar impairment occurs in the course of hypothyroidism [3–20] and Hashimoto encephalopathy (HE) [21–33]. The latter condition, also known as steroid-responsive encephalopathy, is associated with autoimmune thyroiditis and presents with encephalopathy and elevations in anti-thyroid antibodies without brain tumour, stroke or infection of the central nervous system. HE phenomenology is usually characterized by neurological features like seizures, psychosis and movement disorders but may also manifest as subacute or chronic ataxia without other neurological signs [2, 34].

Cerebellar diseases may be characterized by several signs and symptoms, including combinations of ataxia of limbs, gait and stance, oculomotor disturbances, dysarthria and other manifestations like cognitive impairment, dystonia, psychiatric symptoms, etc. [35]. Although it is usually not possible to precisely predict the site of cerebellar lesion/dysfunction with great accuracy from the clinical examination, clinic-anatomic correlations may reveal predominant patterns: ataxia of gait and stance may be mostly consistent with diffuse vermis involvement, while limb ataxia and vertigo/nystagmus may be more frequently associated with an impairment of cerebellar hemispheres and of flocculonodular lobe part, respectively

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[36]. Further features may also characterize the clinical spectrum of cerebellar diseases, according to the varying aetiology [37]. For instance, dystonia and slow saccades manifest in spinocerebellar ataxia type 2 (SCA2) [38–42], extrapyramidal signs in SCA3 [38, 42–44], delirium and ophthalmoplegia in Wernicke encephalopathy [45].

Information about demographic, clinical and laboratory features of cerebellar disease associated with thyroid disorders is poor. In this paper, we searched for all cases of cerebellar syndrome associated with thyroid disorders published in the worldwide literature in order to better define the phenomenology of the condition.

Methods

Search Strategy

A computer-assisted review of the literature using PubMed as the search engine was performed to identify relevant articles. The search was run from 1965 to 2018. To select a preliminary list of articles, we used the terms cerebellar syndrome, thyroid dysfunction/disease and Hashimoto encephalopathy. To identify additional reports, we also joined cerebellar syndrome and ataxia with other terms including hypothyroidism, hyperthyroidism, Hashimoto thyroiditis and steroid-responsive encephalopathy associated with autoimmune thyroiditis. Finally, we reviewed the bibliographies of all identified articles. For the purpose of our review, we selected those studies reporting patients diagnosed with cerebellar syndrome or cerebellar ataxia who underwent specific examination to detect thyroid dysfunction or anti-thyroid antibodies. Overall, of 2434 hits, 47 papers were identified, including case reports and series, reviews, and letters to the editor. Sixteen papers did not satisfy inclusion criteria or did not provide sufficient information about relevant demographic variables including age, gender, thyroid status, clinical features, presence of anti-thyroid antibodies and responsiveness to treatment. By applying these criteria, the final list included 31 articles published in peer-reviewed journals [3–33].

Statistical Analysis

Data were presented as mean and standard deviation (SD) unless otherwise indicated. To compare groups, chi-square test, Fisher's test and Mann-Whitney *U* test were used as appropriate. Significance was set at the 0.05 level.

Results

We identified 65 patients with cerebellar syndrome and thyroid disturbances. Twenty-eight cases were associated with hypothyroidism [3–20]; 37 cases were associated with HE [21–33]. Demographic and clinical features of the two groups described below and summarized in Table 1.

Ataxia Associated with Hypothyroidism

This group included 24 patients (86%) with overt hypothyroidism (hypothyroidism associated with chronic autoimmune thyroiditis in ten cases [4, 6, 7, 9, 10, 15, 18, 20], iatrogenic hypothyroidism secondary to monoclonal antibody therapy in one case [12] and hypothyroidism with unknown aetiology in 13 cases [3, 5, 10, 13, 14, 16, 19]), and 4 patients (14%) with subclinical hypothyroidism [6, 8, 11, 17]. Since assay systems were not consistent among reports, we referred to relative value to the normal range to quantitatively assess the hormonal status. Information on this issue was only available for serum T3 and T4 from 6/24 patients with overt hypothyroidism [4, 7, 9, 15, 18, 20]. As compared to the normal range, mean lowering of serum T3 level was − 46% (range − 25 to − 88%), and mean lowering of serum T4 level was − 68% (range − 44 to 85%).

Most cases (20/28, 71%) came from Europe [3, 5–7, 9–14, 16], 6/28 (21%) from Asia [4, 8, 15, 17, 18] and 2/28 (8%) from America [19, 20]. Overall, there were 18 women (64%) and 10 men aged 55 years (SD, 12.6) at the onset of ataxia. Hypothyroidism was diagnosed 2.1 years (SD, 3.1) after clinical presentation of the cerebellar syndrome.

With regard to clinical manifestations, gait ataxia was present in all patients [3–21], limb ataxia was present in 17 patients (61%) [3–6, 8, 11, 13, 16–19], dysarthria was found in about half of patients [3–5, 7, 8, 11, 13, 14, 16–18], nystagmus in 6 patients (21%) [3, 4, 8, 14, 18] and vertigo in 1 patient (4%) [17].

Computed tomography (CT) or magnetic resonance imaging (MRI) of the brain was performed in 12/28 patients: imaging findings were normal in 9/12 patients [4, 6, 8, 9, 11, 12, 14, 18, 20] while cerebellar atrophy involving vermis and both hemispheres was observed in 3/12 patients (25%) [7, 15, 17]. Autopsy study performed in one additional patient showed degenerative changes in the cerebellum (anterosuperior part of the vermis), ventral pons, and middle and superior cerebellar peduncles [16]. We could not observe any correlation between imaging result and distribution of clinical features.

Anti-thyroid antibodies, namely anti-thyroid peroxidase (TPO) antibodies and anti-thyroglobulin (TG) antibodies, could be assessed in 13/28 patients because the assay was not available when the remaining patients were studied. Anti-TPO and/or anti-TG antibodies were detected in 10/13 cases (77%); in particular, anti-TPO antibodies alone were found in 8 cases [4, 8, 9, 11, 15, 17, 18, 20], anti-TG antibodies alone were found in one case [6] and both antibodies in one case [7]. According to the results of imaging studies, autoantibodies were reported in 3/3 patients (100%) who showed

Table 1 Demographic, clinical and laboratory features of 65 patients suffering from cerebellar syndrome associated with thyroid disorder, namely hypothyroidism and Hashimoto encephalopathy

	Hypothyroidism (*n*. 28)	Hashimoto encephalopathy (*n*. 37)	*p* values
Number of women (%)	18 (64%)	24 (65%)	0.9
Age at ataxia onset (mean years ± SD)	55 ± 12.6	49 ± 13.8	0.01*
Time elapsing between ataxia presentation and diagnosis of thyroid disorder (mean years ± SD)	2.1 ± 3.1	2.3 ± 3.8	0.41
Thyroid status [*n*. patients (%)]			
Overt hypothyroidism	24 (86%)	3 (11%)	
Subclinical hypothyroidism	4 (14%)	2 (7%)	< 0.0001*
Euthyroidism	0	22 (82%)	
Not reported	0	10	
Clinical features [*n*. of patients (%)]			
Gait ataxia	28 (100%)	37 (100%)	1
Upper limb ataxia	17 (61%)	27 (74%)	0.29
Nystagmus	6 (21%)	7 (18%)	0.51
Dysarthria	14 (50%)	24 (65%)	0.29
Vertigo	1 (4%)	4 (11%)	0.38
Pyramidal signs	0	0	
Sensation loss	0	0	
Dysphagia	0	0	
Fasciculation	0	0	
Dystonia	0	2 (5%)	0.50
Psychiatric symptoms	0	4 (11%)	0.12
Ocular disturbance	0	5 (13%)	0.065
Myoclonus	0	3 (8%)	0.25
Brain MRI/CT scan [*n*. patients (%)]			
Not reported	16	15	0.014*
Cerebellar atrophy	3/12 (25%)	15/22 (68%)	
Normal findings	9/12 (75%)	6/22 (27%)	
Autoantibodies anti-TPO/anti-TG/NAE [*n*. patients (%)]			
Not reported	25	0	0.015*
Anti-TPO and/or anti-TG and/or NAE	10/13 (77%)	37/37 (100%)	
Anti-TPO	8	7	
Anti-TG	1	2	
Anti-TPO + anti-TG	1	16	
Anti-NAE	–	9	
Unknown type	–	12	
Clinical responsiveness to thyroid replacement therapy [*n*. patients (%)]			
Complete remission	20 (74%)	–	
Partial remission	7 (26%)	–	
Treatment not performed	1	–	
Clinical responsiveness to immune-modulatory treatment [*n*. patients (%)]			
Complete remission	–	17 (57%)	
Partial remission	–	13 (43%)	
Treatment not performed	–	7	

Anti-TPO, anti-thyroid peroxidase antibodies; *anti-TG*, anti-thyroglobulin antibodies; *anti-NAE*, anti-NH2-terminal of α-enolase antibodies

*$p < 0.05$

cerebellar atrophy and in 8/9 (89%) patients without cerebellar atrophy ($p = 1$).

Information on thyroid replacement therapy was available in 27/28 cases. This treatment yielded almost complete remission of ataxia in 20 (74%) patients [3–10, 12–14, 17–20] (3 with subclinical hypothyroidism [6, 8, 17]) and partial clinical remission in 7 (26%) patients [3, 11, 13, 15, 16] (one with subclinical hypothyroidism [11]). Patients with complete and partial remission did not significantly differ for duration of ataxia (1.8 ± 2.8 vs. 2.8 ± 4.1 years, $p = 0.24$) and frequency in the detection of anti-thyroid autoantibodies (8/10 vs. 2/3, $p = 1$). According to the results of imaging studies, complete remission of cerebellar symptoms was reported in two/three (66%) patients with cerebellar atrophy and in 8/9 (89%) patients without cerebellar atrophy ($p = 0.45$).

Ataxia Associated with Hashimoto Encephalopathy

This group included 3 patients (11%) with overt hypothyroidism [25, 27, 28], 2 patients (7%) with subclinical hypothyroidism [23, 33] and 22 euthyroid patients (82%) [21, 22, 24–26, 29, 32]. Information about thyroid status was not provided in 10 patients [25, 30, 31]. Most cases (26/37, 70%) came from Asia [24–26, 28, 29, 31], 7/37 (19%) from America [21, 30, 31], 3/37 (8%) from Europe [22, 27, 33] and 1/37 (3%) from Africa [23]. Overall, there were 24 women (65%) and 13 men aged 49 years (SD, 13.8) at the onset of ataxia. HE was diagnosed 2.3 years (SD, 3.8) after presentation of the cerebellar syndrome.

With regard to clinical manifestations, gait and limb ataxia were detected in 37 (100%) [21–33] and 27 (74%) cases, respectively [21–23, 25–32]; 24 patients (65%) suffered from dysarthria [21, 22, 24–26, 29, 31, 32], whereas nystagmus was noticed in 7 cases (18%) [21, 23, 25, 30, 32], and other ocular disturbances in 5 (13%) [21, 22, 24]. Moreover, vertigo was observed in 4 patients (11%) [21, 23]. Finally, dystonia, psychiatric symptoms and myoclonus were detected in 2 [29, 32], 4 [25] and 3 patients [22, 24, 33], respectively.

Brain CT/MRI was performed in 22/37 patients. Imaging findings were normal in 7/22 patients [22–24, 26, 32] while cerebellar atrophy (involving vermis and both hemispheres) was observed in 15/22 patients (68%) [21, 25, 29–31]. T2-weighted sequences revealed a high-intensity signal in the left cerebellar hemisphere of one additional patient [27]. There was no correlation between imaging result and distribution of clinical features.

Anti-TPO and/or anti-TG antibodies were detected in all 37 cases. In particular, anti-TPO antibodies alone were found in 7 cases [21, 22, 25, 28, 30], anti-TG antibodies alone were found in 2 cases [23, 24] and both antibodies in 16 cases [21, 25, 26, 29]. Anti-NH2-terminal of α-enolase (NAE) antibodies could be assayed and detected in 9 patients [25, 26, 28]. No correlation was observed between clinical features and anti-NAE antibodies. Information about the type of anti-thyroid antibodies was not available in 12 cases [27, 31–33]. Since assay systems were not consistent among reports, we quantitatively compared the increased in anti-thyroid antibodies from HE patients with and without cerebellar involvement by calculating the relative increase to the upper normal value. Information on serum anti-TPO antibodies was available in 25 HE patients with cerebellar involvement and 53 HE patients without cerebellar involvement: mean increase ± SD, 153 ± 423 vs. 53 ± 123, $p = 0.11$. Information on serum anti-TG antibodies was available in 19 HE patients with cerebellar involvement and 27 HE patients without cerebellar involvement: mean increase ± SD, 92 ± 273 vs. 29 ± 91, $p = 0.13$ [21, 22, 24–26, 28, 29, 32, 33, 46–80].

Responsiveness to immunomodulatory treatment was the peculiarity of this group. Indeed, neurological symptoms completely disappeared after therapy in 17 cases (57%) [22–27, 30, 31], while ataxia partially persisted in 13 individuals (43%) [25, 29, 32, 33]. One further patient had an apparently spontaneous remission [28]. Information on immunomodulatory treatment was not provided in 6 cases [21]. Patients with complete and partial remission following immunomodulatory therapy did not significantly differ for duration of ataxia (1.8 ± 4.3 vs. 1.7 ± 2.9 years, $p = 0.47$) and detection of anti-thyroid autoantibodies (17/17 vs. 13/13, $p = 1$).

Information about both responsiveness to immunomodulatory treatment and imaging findings was available in 16 patients. In this group, complete remission of cerebellar symptoms was reported in 4/10 (40%) patients with cerebellar atrophy and in 4/6 (66%) patients without cerebellar atrophy ($p = 0.6$).

Comparison Between Patients with Hypothyroidism and HE

As reported in Table 1, the two groups did not differ for sex, time elapsing between ataxia presentation and thyroid disorder diagnosis, and distribution of clinical ataxic signs. However, the HE group showed lower mean age at ataxia onset and greater frequency of euthyroidism and of cerebellar atrophy on CT/MRI scan than the group with hypothyroidism. With regard to clinical features, it must be stressed that dystonia, psychiatric symptoms, ocular disturbances and myoclonus were exclusively present in a minority of patients from the HE group.

Discussion

This is the first attempt to systematically describe demographic, clinical and laboratory features of cerebellar syndrome associated with thyroid disorder. Our review identified 65 cases published from 1965 to 2018. Twenty-eight cases were

associated with hypothyroidism whereas HE was diagnosed in 37 patients. In the patients with hypothyroidism, thyroid status was characterized by overt hypothyroidism in most patients, by subclinical hypothyroidism in a minority of cases. Available data allowed us to check for the extent of T3 and T4 serum decrease only in a few hypothyroid patients [4, 7, 9, 15, 18, 20]. In addition, we could not find any data about the mean percent lowering of T3 and T4 serum levels in the general hypothyroid population. Therefore, we cannot know whether the 46% and the 68% decrease of T3 and T4 serum level would distinguish between patients with cerebellar involvement and general hypothyroid patients.

According to the literature on HE [34], euthyroid status predominated in this diagnostic group while overt/subclinical hypothyroidism was present in a few cases.

Owing to the lack of studies assessing cerebellar signs and symptoms in large cohorts of patients with thyroid disorders, estimates of prevalence/incidence of cerebellar syndrome associated with thyroid disorder could not be established. However, the small number of cases reported in the worldwide literature would suggest a rare occurrence of the association between cerebellar sings and thyroid disorder. With regard to the geographic origin of the reported cases, European patients predominated in the hypothyroidism group, Asiatic patients in the HE group. Possible publication bias makes it difficult to draw firm conclusions about geographical or ethnic variations in the prevalence of this condition.

Ataxia associated with thyroid disorders showed a clear predilection for women, as the general thyroid disorders did [34, 81]. Mean age at ataxia onset was in the 5th decade in the hypothyroidism group, in the 4th decade in the HE group, which was consistent with the typical age at onset of the general hypothyroid and HE patients [34, 81]. Because of the rarity of ataxia associated with thyroid disorder, we can assume that the demographic features of general hypothyroid and HE patients are representative of thyroid disorders without cerebellar disturbance. Since ataxia was the opening sign in most of our patients, the similar age at ataxia onset and age at onset of general thyroid dysfunction and HE would support a pathophysiological relationship between cerebellar syndrome and the correspondent thyroid disorder.

Both patients with hypothyroidism and HE presented with signs of ataxia that were similarly distributed in the two groups and were mostly predictive of vermis involvement and frequent impairment of cerebellar hemispheres. Signs/symptoms consistent with a dysfunction of the flocculonodular lobe (vertigo, nystagmus) were only evident in a minority of patients. Additional neurological signs, like dystonia [29, 32], psychiatric symptoms (personality changes and depression) [25], ocular disturbances [21, 22, 24] and myoclonus [22, 24, 33], could be found in the HE group alone.

When present, atrophy of vermis and often of both cerebellar hemispheres was the main imaging abnormality in both hypothyroidism and HE group. The frequency of cerebellar atrophy was greater in HE patients. Cerebellar atrophy might obviously have a pathophysiological role in ataxia associated with thyroid disorder even though we could not observe any correlation between imaging result and distribution of clinical features. The precise mechanisms linking thyroid disorders and cerebellar atrophy are not well understood.

Anti-thyroid antibodies could be detected in three quarters of patients with hypothyroidism and in all patients with HE. We could not find any difference in the frequency of autoantibodies between patients with and without cerebellar atrophy, but the finding might have been affected by the small size of the sample. Likewise, we could not find any correlation between clinical features and anti-NAE antibodies within the HE group. Indeed, the precise pathogenic role of these antibodies is not well understood, even in consideration of the high title prevalence in general population without any symptoms [82, 83]. Although we found a tendency for a greater increase of anti-TPO and anti-TG antibodies in HE patients with cerebellar involvement as compared with HE patients without cerebellar involvement, the difference did not reach the level of statistical significance. We do not know whether the finding was due to low statistical power or to lack of true differences between groups [21, 22, 24–26, 28, 29, 32, 33, 46–80].

In the patients with hypothyroidism, thyroid replacement therapy yielded complete or partial remission of ataxia, regardless of the presence of overt/subclinical hypothyroidism. Of note, the extent of ataxia improvement was not affected by duration of ataxia or detection of cerebellar atrophy and anti-thyroid autoantibodies.

In the HE group, immunosuppressive treatment provided complete remission of ataxia in about 60% of patients, partial remission in the remaining cases. Patients with complete and partial remission did not significantly differ for duration of ataxia or presence of cerebellar atrophy. When present, psychiatric symptoms usually resolve alongside HE with the immunosuppressive treatment without the need for psychotropic medication [34].

The treatability of ataxia associated with thyroid disorders highlights the relevance of an accurate diagnosis. Although there may be sometimes lack of clarity about the time elapsing between presentation of ataxia and the diagnosis of thyroid disorder, it was apparent that thyroid disorder far more frequently was diagnosed several months or years after ataxia presentation, even in the most recent case reports. This was because diagnosis could easily have been mistaken for heredodegenerative ataxias [38–44], sporadic adult-onset ataxia [84] and other forms of ataxia secondary to systemic conditions [37]. Table 2 provides a demographic and clinical comparison among ataxia associated with thyroid disorder, SCA3 or Machado-Joseph disease (the most frequent form of SCA worldwide) [38, 42–44], SCA2 (the most frequent form of heredodegenerative ataxia in Southern Italy) [38–42], sporadic adult-onset ataxia (a form of

Table 2 Demographic and clinical comparison among cerebellar syndrome associated with hypothyroidism, Hashimoto encephalopathy, spinocerebellar ataxia type 3, spinocerebellar ataxia type 2, sporadic adult-onset ataxia and alcoholic cerebellar degeneration. Age at ataxia onset was expressed as mean years ± SD and/or age range. Data are from the present study and from references 37–44, 84

	Hypothyroidism	Hashimoto encephalopathy	Spinocerebellar ataxia 3	Spinocerebellar ataxia 2	Sporadic adult-onset ataxia	Alcoholic cerebellar degeneration
Women frequency (%)	64%	65%	50%	50%	30%	30%
Age at ataxia onset (mean years ± SD and/or range)	55 ± 12.6 (26–75)	49 ± 13.8 (17–78)	32.1 ± 11.9	30.5 ± 13	41–56	45–55
Clinical features (frequency)						
Gait ataxia	+ + +	+ + +	+ + +	+ + +	+ + +	+ + +
Upper limb ataxia	+ +	+ + +	+ + +	+ + +	+ + +	+ + +
Nystagmus	+	+	+ + +	+	+	+
Dysarthria	+ +	+ +	+ +	–	+ +	+ +
Vertigo	+	+	–	–	+ +	–
Pyramidal signs	–	–	+ + +	+	+ +	–
Sensation loss	–	–	+ +	–	+ +	–
Dysphagia	–	–	+ +	+ +	+ +	–
Fasciculation	–	–	+ +	+	–	–
Dystonia	–	+	+	+ +	+	–
Psychiatric symptoms	–	+	+ +	–	–	+
Ocular disturbance	–	+	+ +	+ +	+ +	+ +
Myoclonus	–	+	–	–	+	–

+ + +, usually reported; + +, often reported; +, rarely reported; −, not reported

idiopathic cerebellar syndrome not associated to gene mutation, acquired cause or neurodegenerative disease) [84] and alcoholic cerebellar degeneration (one of the most common type of acquired cerebellar ataxia) [37]. Although there may be demographic differences in sex distribution and age at ataxia onset among the various types of ataxia, gait and limb ataxia were present in the vast majority of patients affected by heredodegenerative, sporadic and acquired ataxia, as we observed in ataxia associated with thyroid dysfunction. Among extracerebellar signs, pyramidal signs, sensation loss, dysphagia and fasciculation were mostly observed in heredodegenerative ataxias and never reported in thyroid associated ataxia; whereas, dystonia, ocular disturbances and psychiatric symptoms could be observed in genetic, idiopathic and acquired ataxia as well as in thyroid associated ataxia, though to a lesser extent. This comparison suggests that the possibility of misdiagnosis is probably greater when ataxia is pure or with fewer prominent additional features.

Conclusion

Owing to the treatable nature of the condition and the high prevalence of thyroid disease among general population, cerebellar syndrome associated with thyroid disorders should be considered an important clinical entity.

The responsiveness of cerebellar symptoms to thyroid replacement therapy in ataxia associated with hypothyroidism and the efficacy of immunosuppressive treatment in HE ataxia support a cause-and-effect relationship between cerebellar syndrome and the correspondent thyroid disorder. Nevertheless, information from this review indicates that our knowledge upon the pathophysiology of cerebellar syndrome associated with thyroid disorder is still incomplete and more rigorous case documentation alongside experimental studies on the relationships between thyroid gland and cerebellum are required. Gaps that remain to be filled include the frequency and possible ethnic variations of the condition in the population of patients with thyroid disorders, the significance of cerebellar atrophy and its relationships with hypothyroidism and HE, and the pathophysiological role of anti-thyroid autoantibodies.

Information from this review will hopefully stimulate and strengthen awareness of thyroid-associated ataxia among clinicians. Assessment of thyroid status and identification of HE by anti-TPO and anti-TG antibodies testing (which may not be included in conventional "autoimmune panels") should be considered as part of the workup of subacute and chronic progressive cerebellar ataxia in order to avoid delay in diagnosis and treatment.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

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