ORIGINAL ARTICLE

Head Tremor in Cervical Dystonia

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ABSTRACT: ***Objective:*** To compare the clinical characteristics, natural history, and therapeutic outcome of patients with cervical dystonia (CD) with head tremor (HT+) and without head tremor (HT-). ***Methods:*** We prospectively evaluated 114 consecutive patients of CD over a 9-month period with a detailed questionnaire. Chi-square and t-tests were employed for statistical analysis. ***Results:*** Seventy-eight (68.4%) patients had head tremor and 27 of them (34.6%) had tremor as one of the first symptoms. Age at onset of symptoms were similar in HT+ and HT– groups; however there was a higher prevalence in women in the former group (66.7% vs. 41.7%; p=0.01). HT+ patients had more frequent positive family history of essential-like hand/head tremor (21.8% vs. 5.5%; p<0.05), associated neck pain (92.3% vs. 77.8%; p<0.05), and essential-like hand tremor (40% vs. 8.3%; p<0.001). They also appeared to have more frequent history of preceding head/neck trauma (14.1% vs. 8.3%), frequent head rotation (88.5% vs. 69.4%) and antecollis (12.8% vs. 5.5%) but less often head tilt (37.2% vs. 47.2%) and gestes antagonistes (60.2% vs. 75%) than the HT– patients; however these differences were not statistically significant. The frequency of prior psychiatric illnesses, the incidence of dystonias in other parts of the body, frequency of retrocollis and shoulder elevation, and spontaneous remission were similar in the two groups. ***Conclusion:*** Head tremor is common in CD and is more commonly associated with hand tremor and family history of tremor or other movement disorders. This supports a possible genetic association between CD and essential tremor (ET). Linkage studies are required to evaluate the genetic association between CD and ET.

RÉSUMÉ: Le tremblement de la tête dans la dystonie cerviale. ***Objectif:*** Comparer les caractéristiques cliniques, l'histoire naturelle et la réponse thérapeutique de patients dystoniques avec tremblement de la tête (TT+) et sans tremblement de la tête (TT-). ***Méthodes:*** Il s'agit d'une étude prospective, effectuée sur une période de 9 mois, de 114 patients consécutifs présentant une dystonie cervicale (DC) évalués au moyen d'un questionnaire détaillé. L'analyse statistique a été faite au moyen du test du χ carré et du test de t. ***Résultats:*** Soixante-dix-huit patients (68.4%) avaient un tremblement de la tête et chez 27 d'entre eux (34.6%) ce tremblement était un des premiers symptômes. L'âge de début des symptômes était le même dans le groupe TT+ et TT-; cependant, il y avait plus de femmes dans le premier groupe que dans le second (66.7% contre 41.7%; p=0.01). Les patients du groupe TT+ avaient plus fréquemment une histoire familiale positive de tremblement de type essentiel de la tête/des mains (21.8% contre 5.5%; p<0.05), de la douleur cervicale associée (92.3% contre 77.8%; p<0.05) et un tremblement des mains de type essentiel (40% contre 8.3%; p<0.001). Ils semblaient également présenter plus fréquemment une histoire antérieure de traumatisme de la tête/du cou (14.1% contre 8.3%), une rotation de la tête (88.5% contre 69.4%) et une position de la tête en flexion (12.8% contre 5.5%), et moins fréquemment une position inclinée (37.2% contre 47.2%) et des gestes antagonistes (60.2% contre 75%) que les patients TT-; cependant, ces différences n'étaient pas significatives au point de vue statistique. La fréquence de maladies psychiatriques antérieures, l'incidence de dystonie au niveau d'autres parties du corps, la fréquence de rétrocollis et d'élévation des épaules ainsi que la rémission spontanée étaient similaires dans les deux groupes. ***Conclusion:*** Le tremblement de la tête est fréquent dans la DC et il est plus souvent associé au tremblement des mains et à une histoire familiale de tremblement ou d'autre désordre du mouvement, ce qui est en faveur d'une association génétique possible entre la DC et le tremblement essentiel (TE). Il faut recourir à des études de liaison pour évaluer l'association génétique entre la DC et le TE.

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Cervical dystonia (CD) is characterized by sustained or intermittent contractions of neck muscles, causing twisting and repetitive movements or abnormal posture of the head.[1] The frequency of hand, arm, and head tremor in CD patients has been reported to be 3-80%.[2-10] It is uncertain whether head tremor in CD is part of the dystonia or part of a coexisting essential tremor, which is a common movement disorder. Though there are many reports on the clinical characteristics, natural history and outcome of treatment in CD,[3,5,9-18] it is uncertain whether these differ between CD patients with and without head tremor.

In the present study we compared the clinical characteristics, natural history and therapeutic response between 78 CD patients with head tremor (HT+) and 36 without head tremor (HT–).

METHODS

Patients

The patients were all seen at the University of British Columbia Movement Disorders Clinic, and CD was diagnosed by neurologists in the field of movement disorders. All patients

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had a noncongenital, focal movement disorder of unknown etiology, characterized by intermittent or sustained head deviation as a result of involuntary contractions of neck muscles. All patients but one were returning for treatment with botulinum toxin-A (BT) injections.

Clinical assessment

Three neurologists experienced in movement disorders (PKP, AS, and JKCT) conducted an interview (using a detailed questionnaire), the neurological examination and chart review. All patients had had a complete neurological examination on at least one occasion before being enrolled in the study. At the time of interview a neurological assessment, which focused on the direction of head deviation, the presence of head and essential-like hand tremor, and dystonia in other parts of the body, was performed.

The items in the questionnaire included: age at onset of symptoms, precipitating factors if any, interval between symptom onset and the diagnosis of CD by a neurologist, the interval between symptom onset and first treatment (either oral medication or botulinum toxin (BT) injections), the range of medical and non-medical treatments tried before BT injection, mode of symptom progression, and spontaneous remission. Spontaneous remission was defined as at least three months of complete relief in the absence of treatment. We inquired about the family history of movement disorders, defined as the presence of any form of dystonia, tremor, or parkinsonism in first (parents, siblings, or children) or second degree (grandparents, grandchildren, siblings of parents) relatives. History of trauma related to CD was defined as the occurrence of head/neck injury up to one year preceding symptom onset. The severity of head/neck trauma was rated using a scale of 1-4 (1–minimal injury, not requiring immediate medical attention; 2–mild injury without loss of consciousness (LOC), but requiring medical attention; 3–moderate injury with brief (seconds to minutes) LOC, not requiring hospitalization; and 4–severe head injury with prolonged LOC and hospitalization).

Since the main symptoms were head deviation, head tremor and cervical pain, we recorded as best as possible the order in which these features occurred. Head tremor was defined as small-amplitude rhythmical oscillations of the head in coronal or saggital plane and was scored as present or absent. The presence of irregular, jerky movements of head (head jerks) was disregarded. For this, we also reviewed the past medical records. Cervical pain was rated using a scale of 1-4 (1–minimal, not requiring any analgesics; 2–mild, requiring non-narcotic analgesics; 3–moderate, requiring intermittent narcotics; and 4–severe, requiring chronic narcotics). Other specific questions were related to the presence of essential-like hand tremor, dystonias in other parts of body, gestes antagonistes and other relieving factors, aggravating factors, and presence of pre- and postmorbid psychiatric disorders.

The response to BT injections (lessened postural deviation of head and neck) was rated using a scale of 0-3 (0–no change; 1–fair; 2–good; and, 3–excellent). Since most patients had had multiple treatments, we took the average response to BT injections once the optimal dose and target muscles had been established (usually by the third injection). If the response fluctuated from treatment to treatment, the average response was taken for analysis.

Chi-square and t tests were applied for statistical analysis.

Results

Among the 114 patients with CD, 78 (68.4%) had associated head tremor. The demographics of these patients are summarized in Table 1. Head tremor was significantly more common in women (p=0.01). The mean age of presentation of the HT+ group was higher than the HT– group (p<0.05), though the age at onset of symptoms did not differ significantly.

Table 1: Clinical characteristics of patients of cervical dystonia

	HT+ (n=78)	HT– (n=36)	p
Men: women	1:2	3:2	0.01
Mean age	59.4±12.5 years	53.7±11.4 years	<0.05
Mean age at onset of CD	43.3±13.4 years*	41.2±13.3 years	NS
Pain associated with dystonia	72 (92.3%)	28 (77.8%)	<0.05
History of head/neck trauma	11 (14.1%)	3 (8.3%)	NS
Precipitating factors	21 (26.9%)	7 (19.4%)	NS
Presence of essential-like hand tremor	31 (40.0%)	3 (8.3%)	<0.001
Presence of extranuchal dystonia	20 (25.6%)	8 (22.2%)	NS
Prior psychiatric illness	18 (23.1%)	7 (19.4%)	NS
Specific alleviating factors	53 (67.9%)	27 (75.0%)	NS
Presence of gestes antagonistes	47 (60.2%)	27 (75.0%)	NS
Specific aggravating factors	70.0 (90%)	31 (86.1%)	NS

HT+: With head tremor, HT–: Without head tremor, CD Cervical dystonia, NS=Not significant

* Among the HT+ patients, the mean age of onset for those with and those without hand tremor was 43.9 years and 42.9 years respectively.

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Table 2: Family history of movement disorders in first and second degree relatives of patients with cervical dystonia

	HT+ (n=78)	HT– (n=36)
No. of patients	26 (33.3%)*	7 (19.4%)
Essential-like hand/head tremor†	17 (21.8%)	2 (5.5%)
1º relative	12	1
2º relative	5	1
Only head tremor	8	0
Only hand tremor	5	1
Head + hand tremor	4	1
Cervical dystonia	10	3
1º relative	8	2
2º relative	2	1
Parkinsonism	3	1
Blepharospasm	3	0
Jaw dystonia	0	1
Orofacial dyskinesia	1	0
Chorea	1	0

HT+: With head tremor, HT–: Without head tremor
*Some families had members with different abnormalities
†$p<0.05$

Family history of movement disorders

Family history of movement disorders was more common in HT+ patients. Family history of hand or head tremor was also significantly higher in HT+ patients ($p<0.05$) (Table 2). Patients with CD and hand tremor, with or without head tremor had a significantly higher ($p<0.05$) prevalence of family history of tremor than those CD patients with only head tremor, or those without tremor (isolated CD) (Table 3). However, the prevalence of family history of dystonia was not significantly different in these three groups (Table 3).

Nine of the 14 patients (64.3%) having only head tremor as the first symptom had a positive family history of tremor, while those who developed head tremor after the onset of head turning had lower prevalence of positive family history of tremor (8 of 51 or 15.7%).

Clinical characteristics (Table 1)

Prevalence of other movement disorders

Essential-like hand tremor was present in 29.8% of the CD patients. Its prevalence was significantly higher in the HT+ group than in the HT– group (40% versus 8.3%; $p<0.001$). Among the 31 patients with both head and hand tremor, 17 patients (54.8%) had head tremor before they developed hand tremor. Extranuchal dystonia in the form of blepharospasm, limb dystonia, vocal cord dystonia, and oro-mandibular dystonia, was seen in 25.6% and 22.2% of patients in HT+ and HT– groups respectively.

Precipitating factors, head/neck trauma, and neck pain

Though only 14.1% and 8.3% of the HT+ and HT– patients respectively had a history of head/neck trauma prior to the onset of symptoms, neck pain was a very frequent complaint: 92.3% in HT+ patients and 77.8% in HT– patients, the difference being significant ($p<0.05$). Among those with pain, in the HT+ group 70% had minimal (often described as soreness) to mild (often described as stiffness) pain relieved by rest, antispastic drugs or by non-narcotic analgesics, while 30% had moderate to severe pain requiring intermittent or chronic narcotic analgesics. In the HT– group, the corresponding figures were 60% and 40%. Apart from head and neck trauma, there were events such as severe stress, surgery, exposure to chemicals, drugs, etc., which were considered by some patients in both groups (HT+: 26.9%, HT–: 19.4%) to have been precipitating events prior to the onset of CD.

Pattern of head deviation

There was no significant difference in the pattern of head deviation between the two groups, though head rotation (HT+: 88.5%, HT–: 69.4%) and antecollis (HT+:12.8%, HT–: 5.5%) were more frequent in HT+ patients, and lateral head tilt more common in HT– patients (HT+: 37.2%, HT–: 47.2%). The frequency of retrocollis (HT+: 23.1%, HT–: 22.2%) and shoulder elevation (HT+: 25.6%, HT–: 27.8%) was similar in the two groups.

Table 3: Family history of movement disorders in different subcategories of cervical dystonia according to the presence of hand/head tremor

	HT(-) HndT(-) (n=33)	HT(+) HndT(-) (n=47)	HT(±) HndT(+) (n=34)
Family history head tremor or essential-like hand tremor	2 (6.1%)	7 (14.9%)	10 (29.4%)*
Family history of dystonia	4 (12.1%)	6 (12.8%)	6 (17.6%)

HT: head tremor; HndT: essential-like hand tremor; (+):present; (-) absent; (±): present or absent.
In the HT(+) HndT(-) group, only 6 (12.8%) had isolated head tremor as their first symptom. In the HT(±) HndT(+) group, 31 (91.1%) had head tremor, and 8 of them (25.8%) had head tremor as the only initial symptom.
* $p < 0.05$ for family history of tremor. Rest of the p values were not significant.

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Table 4: Natural history and response to botulinum toxin-A injections

	HT+ (n=78)	HT–(n=36)
Onset to peak symptoms (years)*	7.3±8.0	3.9±6.9
Progressive disease	12 (15.4%)	5 (13.9%)
Time from onset to diagnosis (years)‡	7.9±9.4	3.5±5.6
History of a spontaneous remission	3 (3.8%)	1 (2.8%)
Botulinum toxin - A treatment:		
Time from onset to 1st treatment (years)†	10.8±9.6 (n=78)	6.7±11.2 (n=35)
Frequency of injection (months)	4.4±6.5 (n=77)	3.2±0.6 (n=35)
Duration of treatment (years)	5.9±3.5 (n=77)	5.8±3.7 (n=35)
Response to injection:		
Excellent	22 (28.2%)	5 (14.3%)
Good	39 (50.0%)	16 (45.7%)
Fair	14 (17.9%)	12 (34.3%)
No change	3 (3.8%)	2 (5.7%)

HT+: With head tremor, HT–: Without head tremor
* Analysis out of 47 HT+ and 21 HT– patients; 19 (24.4%) HT+ and 9 (25%) HT– patients were unable to specify the duration, as progression was insidious.
‡p<0.01, †p=0.05

Initial symptoms in patients with head tremor

Head turning was the initial symptom in nearly two-thirds (68%) of the patients. Other patients had only head tremor (15.4%), neck pain (14.1%), or both (2.6%) as the first symptoms. It is of note that nearly a third (34.6%) of the HT+ patients had head tremor as one of the initial symptoms and in 14 (17.9%) it was the only manifestation (together with neck pain in two) for some time. Of these, four patients were able to specify an approximate time span after which they developed head turning – six months, one, two, and five years; two patients had had tremor 'since childhood'; and the others were not able to specify as the onset of dystonia was insidious. Among the 51 patients who developed head tremor after head turning, only 14 patients were able to specify the time taken for such development, which ranged from 0.5-19 years (mean SD: 6.5 ± 5.4 years).

Alleviating and aggravating factors

HT– patients had more frequent gestes antagonistes and specific alleviating factors. In both groups support to the back of head or lying down on the back seemed to decrease the symptoms. In the HT+ patients, the gestes antagonistes most often relieved the head rotation rather than head tremor. Anxiety and stress were the most common aggravating factors in all patients.

Premorbid psychiatric illness

About one fifth of the patients had a well-defined psychiatric problem before the onset of symptoms. Depressive illness was the most common disorder.

Natural history of the illness and response to treatment (Table 4)

HT+ patients took twice as long as the HT– patients to receive a correct diagnosis (p<0.01). About one-fourth of the patients in each group were unable to say how long it took for them to develop maximally severe symptoms and in a small number of patients the symptoms were still progressing. A history of spontaneous remission in the past was present in 3.8% of HT+ patients and 2.8% in HT– patients.

Most of the patients (HT+: 67.9%; HT–: 63.9%) had tried oral medications (such as anxiolytics, analgesics, muscle relaxants, anticholinergics, betablockers, antidepressants, etc.) before trying BT injections and there had been either a partial improvement (short-term reduction in pain, muscle stiffness, tremor, anxiety) (HT+: 56.6%; HT–: 43.5%) or no improvement. A considerable proportion of patients (HT+: 70.5%; HT–: 77.8%) had also tried other treatment such as physiotherapy, acupuncture, meditation, chiropractic manipulation, electrical therapy, magnetotherapy, nerve block, rhizotomies, and other neck surgeries, etc. without any sustained improvement. BT injection was the first mode of treatment in 21 (26.7%) HT+ patients and 5 (13.9%) HT– patients. The HT+ patients on average took a longer time to start BT therapy, though this difference was not statistically significant. The frequency of treatment was usually determined by the duration of beneficial effects of BT injection and patients' subjective need for the injections. Though statistically insignificant, the HT+ patients had a longer time interval between injections and more frequent 'excellent'to 'good'responses to them than the HT– patients.

Discussion

We found 68.4% of patients with idiopathic CD had head tremor and of them 40% also had postural hand tremor that resembled essential tremor (essential-like hand tremor). Including the three patients among the HT– group, 29.8% of CD patients had hand tremor. This concurs with earlier observations that tremor distribution in patients with CD most commonly affects the head, followed by head and hands, followed by hands only.[19] Though there are abundant reports in the literature describing the association of tremor with CD, ranging from 3-80%,[2-10] most did not specify the prevalence of hand and head tremor separately. Duane et al[19] reported the prevalence of head and hand tremor in 50% and 32% of 231 CD patients while the corresponding figures were 28% and 23% in 266 CD patients studied by Chan et al.[3] The prevalence of hand tremor in our study was comparable to these reports, but that of head tremor was higher. The age of onset of symptoms in HT+ and HT– groups did not differ and was similar to that observed by Chan et al.[3] However unlike the latter study, we did not find an older age of onset in CD patients with hand tremor compared to those without.

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Though we observed a high incidence of neck pain in both the groups, it was more common in HT+ group. This difference may be partly explained by the higher association of head/neck trauma seen in the HT+ patients, though the difference was not statistically significant. The pattern of head deviation was almost similar in the two groups and their symptoms were markedly worsened by stress and anxiety. Gestes antagonistes were more frequently observed in the HT+ patients.

The natural history of CD, especially in those patients with associated head tremor, is unclear. We analyzed the temporal evolution of the three major symptoms in these patients – head turning, head tremor and neck pain. Though head turning was the initial symptom in nearly 68%, presentation with isolated neck pain (14.1%), head tremor (15.4%), or both (2.6%) were seen. Rivest and Marsden[20] described seven patients with head tremor, or arm and head tremor, who eventually developed obvious CD similar to the observations made in four of our 14 patients who had head tremor without head turning as the first symptom. However, the majority of the patients in this category were unable to specify how long it took for development of head turning, as it was insidious. On the other hand, 14 of the 21 patients who developed head tremor after head turning, were able to specify the time taken, which ranged from 0.5-19 years. This information is of epidemiological interest, especially in order to better characterize the natural history of these patients.

Lowenstein and Aminoff[5] reported a wide variation in the speed of onset to maximum severity of CD, ranging from one month to 18 years. Our findings concurred with their results. Compared to the HT– group, the HT+ group had taken a longer time from onset to maximum severity, for a correct diagnosis, and for the initiation of BT therapy, though these differences were not statistically significant. The isolated symptoms of head tremor delayed the diagnosis in some patients until they developed head rotation and some patients with head tremor (especially those with hand tremor) tried medical treatment for the tremor before they decided on treatment with BT. The response to BT was as effective in patients with head tremor as in those without, implying that the presence of head tremor itself was not a predictor of poor outcome.

Patients with CD often have other family members suffering from CD as well as a variety of other extrapyramidal disorders.[3,9,10,19] In agreement with an earlier report,[19] we also observed a higher prevalence of family history of movement disorders, especially that of head/hand tremor in the HT+ patients compared to the HT– patients. This supports the evidence that CD patients with tremor have an increased probability of family history of tremor. It is interesting to note that among the HT+ patients, positive family history of tremor was present in 64.3% of those with only head tremor as the first symptom, but in only 15.7% of those who developed head tremor after the onset of head turning.

From our observations, we classified the patients with CD into three subgroups depending on the occurrence of head tremor, hand tremor, and family history of tremor:

(a) CD patients without head or hand tremor (pure CD). In them a family history of tremor is infrequent.

(b) CD patients with only head tremor and no hand tremor. These patients more often have a family history of tremor than those in group A, but less than that observed in group C. In them, isolated head tremor as an initial symptom is uncommon. This may suggest that this head tremor may be a part of CD, and is not related to essential tremor.

(c) CD patients with hand tremor with or without head tremor. The majority (>90%) of them have head tremor, and in a quarter it is the only symptom for a while. A family history of tremor is present in nearly a third, suggesting that the tremor shares more similarity with essential tremor. Though it is possible that head tremor in these CD patients may be a part of the manifestations of dystonia, those CD patients with predominantly essential-like hand tremor probably have an association between dystonia and essential tremor. It is uncertain whether this association is purely coincidental, given the high prevalence of essential tremor in the population or whether the phenotypic manifestations of head tremor and CD in these patients are a result of the genetic defects in the same or two very closely situated loci. Clinical observation made in patients with essential tremor support a genetic linkage between CD and head tremor.[21] Of the 350 patients with essential tremor, 47.1% patients had coexisting dystonia (26.8% had CD), 62.5% had at least one first degree relative with tremor, and 3.4% had a family history of dystonia.[21] However, the genetic markers for essential tremor and sporadic CD have yet to be identified. A gene (DYT7) causing one form of autosomal dominant late-onset focal dystonia with reduced penetrance has recently been localized on chromosome 18p in a family from northern Germany.[22] The incidence of tremor in this family is unknown. An alternative way of explaining the close association between CD and tremor is that in both these disorders the striato-pallido-thalamo-cortical loop is implicated.

There are certain limitations of our study which need to be addressed. We have not examined the family members and therefore the family history may not be accurate. Moreover, since accurate history from patients depend on the memories of the patients, the temporal evolution of certain symptoms may not be accurate as these are very insidious. However, in our study, the nature and pattern of initial symptom was meticulously documented at the first visit of the patient in our clinic, and during this questionnaire survey, we further confirmed the information. Since CD is an insidious disease, and the patient usually takes time to consult a neurologist, these problems of inaccuracy are bound to occur in any study on natural history of CD. Further follow-up studies will be needed on these patients to see whether the patients without tremor develop hand or head tremor in the future. Our study probably had a selection bias, as a large number of patients had severe, chronic, and treatment resistant CD (though some patients attended our clinic as soon as they were diagnosed as having CD by their family physician). Therefore, some of the conclusions regarding the natural history and spontaneous remission in our study need to be taken with caution.

Whatever the mechanism of association between CD and head tremor, our observations suggest that the clinical characteristics are not different in CD patients with or without head tremor and the presence of head tremor itself is not a poor predictor of therapeutic outcome. If head tremor is a manifestation of essential tremor in a subset of CD patients, the medical treatment used to treat essential tremor may also be

useful in treating head tremor in this group. Further clinical and genetic studies are needed on larger cohorts for a final conclusion.

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