Epidemiology of Cerebellar Ataxia on the Etiological Basis: A Cross Sectional Study

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Abstract- Cerebellar ataxias are a heterogenous group of disorders, clinically and etiologically, that result in considerable health burden. Finding out about the various etiologies, and their relative prevalences in the population suffering from cerebellar ataxia helps the clinician to perform a better management, in treatment process. This is a cross sectional study designed to estimate the relative prevalence of each etiologic factor. One-hundred and thirty-five patients ,in the range of 6 to 73 years from march 1993 to march1999, were classified in different groups on the basis of etiological findings. Relative prevalence of each of the etiological factors , common accompanying disorders besides ataxia in the patients,CT and MRI changes,and CSF alterations are studied and recorded. A widely spread age group, and the extended number of the cases under study, are the advantages of the current study over the previously reported case series. Among the etiologic groups, multiple sclerosis, cerebrovascular accidents and hereditary cerebellar ataxia, were the most common etiologic factors associated with cerebellar ataxia respectively.

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Key words: Cerebellar ataxia; etiology; epidemiology

Introduction

Ataxia, regarded as the "cerebellar sign par excellence," refers to a disturbance in the smooth performance of voluntary motor acts (2). Cerebellar ataxias are clinically and etiologically a heterogenous group of disorders that result in considerable health burden (1). The clinicians task as referrral, medical treatment or conservative management is established upon the etiological findings. Knowing about the relative prevalence of various etiologies, and epidemiologic description of the disorder in relation to age, gender ,ethnicity and other variables, enables the clinician to put the accuracy of cause finding ,in a higher probability state.

In the literature review on cerebellar ataxia, etiological findings and epidemiological studies ,there was a study on the etiological basis in England declaring cerebrovascular accidents (CVA) as the leading cause of cerebellar ataxia (3). In another study on pediatric group in Nigeria, hydrocephalus was shown to be the most common cause at childhood(4). In a population based study of late onset cerebellar ataxias that excluded 55 cases of known acquired ataxia, the commonest causes of ataxia in the excluded population, in order of decreasing frequency were: multiple sclerosis, isolated and familial spastic paraparesis, cerebellar tumors and alcoholic cerebellar degeneration(5).

Recent advances in molecular genetics have indicated genetic basis for many forms of the disorder (2). There is a high endouver in finding genetic mutations responsible for various types of hereditary cerebellar ataxia; for instance, in a Japanese study, the most common form of hereditary cerebellar ataxias in Japan was declared to be Machado-Joseph disease (SCA 3) found with DNA replication techniques (6).

Patients and Methods

A retrospective cross-sectional study of 135 patients with cerebellar ataxia from March 1993 to March 1999 in Dr. Shariati Hospital, affilliated to the University of Tehran, was performed. Patients were spread in a wide range of age, from 6 to 73 years, and of both genders .This study group provided a more extended population compared to the previous studies. Patients with ataxia as a chief complaint were identified from the computerised

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search of hospital informatics center. Medical profiles were driven from the archieve center and reviewed to exclude patients with non-cerebellar ataxias. As a result, 135 patients were selected from 176 patients .

Our criteria for confirming the cerebellar origin of the ataxia was one or more of the followings: (i) cerebellar manifestations such as cerebellar nystagmus or cerebellar dysarthria (staccato in nature) (ii) positive findings in cerebellar tests on physical examination (iii) definitive findings of cerebellar radiologic studies (iv) confirmed diagnosis of a disease with definitive cerebellar involvement (7).

The 135 patients were classified in different groups, as traumatic, vascular, tumoral/paraneoplastic, hereditary, demyelinating, inflammatory/infectious, metabolic, drug related, nutritional and developmental causes of cerebellar ataxia, and the relative prevalence of each group was estimated.

The presence of accompanying manifestations, systemic disorders, cerebrospinal fluid (CSF) alterations and CT and MRI changes of the patients in each group, were studied and recorded.

Results

Among 135 patients, 61 females and 74 males, 41 (30.4%) had multiple sclerosis, 40 (29.6%) had cerebrovascular accidents, 4 (3%) had tumoral/paraneoplastic disorder, 10 (7.4%) had inflammatory/infectious disorder, 15 (11.1%) had hereditary ataxia and 20 (14.8%) were grouped as cerebellar ataxia of unknown origin. There were no patient in nutritional, traumatic or drug-related groups of cerebellar ataxia.

Among these etiologic groups, multiple sclerosis, cerebrovascular accidents and hereditary cerebellar ataxia, were the most common etiologic factors associated with cerebellar ataxia respectively.

The mean age of the patients in the multiple sclerosis group was 30.8 (7.6)years. There were urethral sphincter dysfunction (41.5%) diplopia (36.6%), nystagmus (29.3%), dysarthria (29.3%) and optic neuritis (29.3) as the most common accompanying findings. There was only one patient that had nothing else but cerebellar ataxia.

The mean age of the patients with cerebrovascular accidents (CVA) was 59.3(15.3) years. The most common manifestations accompanying ataxia were nausea and vomiting (70%), true vertigo (65%), dysarthria (40%), hemiparesis (25%), headache (25%) and cranial nerve palsy (15%). The most common modifiable risk factors found in this group were hypertension (60%), diabetes mellitus(30%), ischemic heart disease (20%) and hyperlipidemia (10%).

There were 9 patients in the CVA group that had no major modifiable risk factor and 15 patients had more than one. The most common forms of CVA in our patients were cerebellar infarction, cerebellar hemorrhage and brainstem infarction (Figure 1).

The mean age of inflammatory/infectious group was 26.1 (20.0)years. The commonest form was post-infectious cerebellitis due to viral infections. The most common accompanying disorder in this group was dysarthria (40%), diplopia (30%) and fever (30%).

There were 4 patients with metabolic disorders. The mean age of the patients was 26 (16.4) years in this etiologic group, with the commonest accompanying manifestations of mental disorders (50%) and dysarthria (50%).

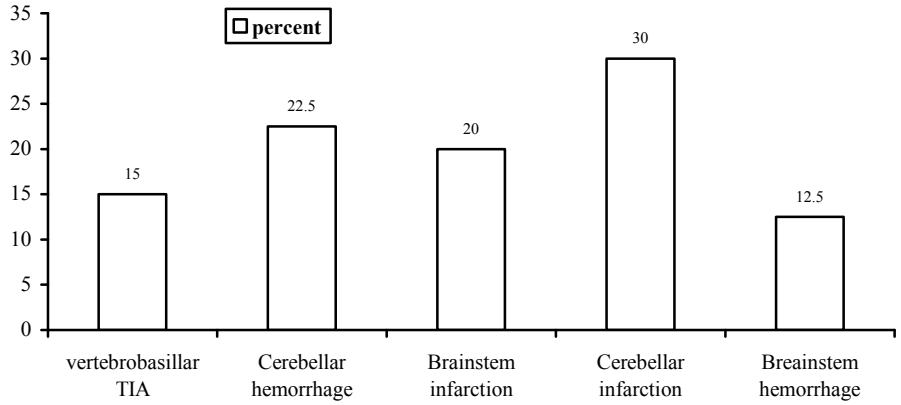

Figure 1. Subtypes of CVA presenting with cerebellar ataxia

Metabolic disorders associated with cerebellar ataxia were Wilson disease, Kearns-Sayer syndrome and ceroid lipofuscinosis.

In hereditary ataxia group (15 patients), the mean age of patients referred to our center, was 27.6 years, and the mean age of onset was 19.4 (14.8) years. Near 46.6% of the patients were in the range of 12 to 20 years. The most common manifestations accompanying hereditary ataxia were dysarthria (60%) and intention tremor (26.7%). Spinocerebellar ataxia and Friedreich ataxia were the most common disorders in this group.

All patients underwent brain imaging of whom 100 had abnormal findings in their images, that 55% of them had abnormalities in the cerebellum, 22 females and 33 males. Hemorrhage (16.3%), infarction (20.0%) in CT scan, cerebellar atrophy (14.5%) and T2-hyperintense plaques (21.7%) in MRI, were the commonest radiological findings in the population under study .

From patients that underwent lumbar puncture, 7 patients had cerebrospinal fluid changes, 4 had oligoclonal bands, 1 had high protein, decreased glucose and pleocytosis, and 2 had changes compatible with viral meningoencephalitis (mild protein elevation and lymphocytosis).

In 135 patients, 4 patients were in paraneoplastic/tumoral group that were previously under the diagnosis of hereditary cerebellar degeneration. Patients with paraneoplastic cerebellar ataxia had hepatocellular carcinoma and bronchogenic carcinoma, The other 2 patients had cerebellar astrocytoma and brainstem glioma with cerebellar peduncle involvement.

thirteen of 115 patients with definite diagnosis had diagnostic delay, defined as not having definitive diagnosis in first hospitalization and further work ups, 8 of whom had hereditary cerebellar ataxia.

No one in our study group, was alcoholic and 12 patients were cigarette smoker who were all in CVA group.

Using the Instat 2.02 software and T-test for analyzing the relationship between cigarette smoking and the age of onset of cerebellar ataxia, no significant relation was found (t=0.28 (df=38°) and P=0.781).

The relationship between ethnicity and cerebellar ataxia was analyzed by means of the Instat 2.02 software and Fisher test; there was significant relation between the belonging to the Turkish ethnical group and the prevalence of cerebellar ataxia (P=0.0018). The ethnic groups were defined as Fars, Arab, Turkish, Kurdish, Baluchi, Armenian and Jewish.

In the acquired forms of the cerebellar ataxia, considering all causes, there were no significant difference between genders (50 males compared to 49 females). Comparatively, there was significant difference between the genders in MS and CVA groups (female to male ratio was 2.73:1 in MS group and 1:2.08 in CVA group). In the hereditary group, female to male ratio was 1:2.

Discussion

In this retrospective cross sectional study, that was designed to evaluate relative prevalence of various etiologies of cerebellar ataxia, the acquired causes of the disorder were found to be the leading causes and hereditary causes were less prevalent in comparison (74.0% compared to 11.1%).

Considering all causes, the highest prevalence of cerebellar ataxia was between 30 to 40 years.

It would be worthy of attention to have a look at the literature in similar studies. In a study in 1992 in England (3) on 45 patients over 60 years, cerebrovascular accidents were found to be the commonest cause of the cerebellar ataxia.33.3% of their study population (15 of 45) had CVA, and hereditary cerebellar ataxia was the second common etiology. The prevalence of cerebellar ataxia due to CVA in the England study (33.3%) was near to ours (29.6%), the little difference could be for the advanced age of their study group (over 60).

There was a significant difference in the prevalence of hereditary ataxias, 20% compared to 11.1% in our study, that could be due to different prevalence of genetic alterations responsible for these conditions and their different mode of expression in different populations and additionally because of underdiagnosis of hereditary cerebellar ataxia in our study because of lesser availability of familial histories.

In an other study in Nigeria in 1992 (4), Enugu reviewed 30 patients of pediatric age group with cerebellar ataxia. The commonest etiologic factor was reported as to be hydrocephalus and perinatal complications with the prevalence of 23.3% and 20% respectively. All of the study population were under 10 years.

There were no case of hydrocephalus in our study and there was only a patient with the history of perinatal complications of hypoxia that was a case of ataxic cerebral palsy. This significant difference in the results would be due to age difference in study groups. However, we had only 8 patients under 10 years and the commonest cause, was acquired cerebellar ataxia due to post-infectious cerebellitis in this group.

Undoubtedly practical advantage of this study is to facilitate the diagnostic process and identifying the pa-

tients that could be helped with prophylactic managements.

However because the most common cause of the cerebellar ataxia is multiple sclerosis in this study and the most common age of the disorder due to all causes is 30 to 40 years, it is recommended that all of the patients with cerebellar ataxia that come for the first time, undergo MRI studies. There was suggestive MRI findings in most of the MS cases and near one third of the MS patients had T2-hyperintense plaques in their cerebellum.

As the most common systemic disorders accompanying CVA, are hypertension, diabetes mellitus and hyperlipidemia in this study, entities that are previously known as risk factors for CVA, and its complications such as cerebellar ataxia, better control of Hypertension, diabetes mellitus and hyperlipidemia in this group of patients is recommended strongly.

We found that cerebellar ataxia due to paraneoplastic/tumoral cause and degenerative disorders are highly mistaken for each other, that would be important considering that, mostly, neurological symptoms may appear before the discovery of the malignancy itself. Finding out about the exact cause of cerebellar ataxia would help us to manage the tumor in earlier stages and improve patient survival. As the commonest tumors, that have cerebellar ataxia as their paraneoplastic manifestation,are bronchogenic carcinoma, ovarian tumors, breast cancer and lymphoma, it is recommended to do tumor work up in cases of cerebellar degenerative disorder with a negative family history.

As there was a close relativity in 2 of 4 patients of hereditary cerebellar ataxia, genetic consults is highly recommended for their first degree relatives .Genetic basis of cerebellar ataxia is unique in that the diagnosis automatically invokes the issue of recurrent risk to relatives and prenatal diagnosis.Identification of a genetic basis may require referral for medical genetics evaluation and counceling.

As a high percentage of our patients (14.8%) had ataxia of unknown origin and because most of the patients with diagnostic delay (8 of 13) were of the hereditary cause, it would be useful to pay more attention on the genetic studies.

As declared, cerebellar ataxia was found to have high prevalence in Iranian Turkish ethnicity; it is proposed to researchers to design extended studies to estimate the exact prevalence of the disorder and find out about many factors influencing the epidemiologic features, such as genetic basis or environmental factors. Prioritization in DNA testing, based on ethnic origin and geographical location, is recommended in a study, and suggested that analogous approach may be applied to other countries as well (8).

References

1. Harding AE. The Hereditary Ataxias and Related Disorders; Clinical Neurology and Neurosurgery Monographs, Vol 6. New York: Churchill-Livingstone; 1984.
2. Brazis PW, Masdeu JC, Biller J. Localization in Clinical Neurology. 4th ed. Philadelphia, Lippincott Williams & Wilkins; 2001. p. 376-7.
3. Safe AF, Cooper S, Windsor AC. Cerebellar ataxia in the elderly. J R Soc Med 1992;85(8):449-51.
4. Iloeje SO; College of Medicine, University of Nigeria, Enugu. Cerebellar ataxia in childhood: a review of clinical features, investigative findings and aetiology in 30 cases. East Afr Med J 1992;69(2):58-63.
5. Muzaimi MB, Thomas J, Palmer-Smith S, Rosser L, Harper PS, Wiles CM, et al. Population based study of late onset cerebellar ataxia in south east Wales. J Neurol Neurosurg Psychiatry 2004;75(8):1129-34.
6. Dürr A, Stevanin G, Cancel G, Duyckaerts C, Abbas N, Didierjean O, et al. Spinocerebellar ataxia 3 and Machado-Joseph disease: clinical, molecular, and neuropathological features. Ann Neurol 1996;39(4):490-9.
7. Cano SJ, Hobart JC, Hart PE, Korlipara LV, Schapira AH, Cooper JM. International Cooperative Ataxia Rating Scale (ICARS): appropriate for studies of Friedreich's ataxia? Mov Disord 2005;20(12):1585-91.
8. Juvonen V, Hietala M, Kairisto V, Savontaus ML. The occurrence of dominant spinocerebellar ataxias among 251 Finnish ataxia patients and the role of predisposing large normal alleles in a genetically isolated population. Acta Neurol Scand 2005;111(3):154-62.