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A CLINICAL STUDY OF 39 FAMILIES OF HUNTINGTON'S DISEASE IN EASTERN INDIA

General Medicine

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ABSTRACT

Huntington's disease is an inherited disease which occurs due to increased number of CAG trinucleotide repeats within the Huntingtin gene on chromosome 4. Usually, its symptoms like uncontrolled movements, emotional disturbances and cognitive dysfunction start to appear when a patient is in his/her thirties. Although there are no epidemiological studies in India, a prevalence rate of 1.75 per 100000 has been shown in Indian migrants of UK.1This study puts in an effort to look at the varied presentation of Huntington's disease in Eastern India.

KEYWORDS

INTRODUCTION:

Huntington's disease is a hereditary, progressive neurodegenerative disorder transmitted in autosomal dominant pattern. The disease is prevalent in Europe, North America, South America and Australia but is rare in African blacks and Asians.[2]

The disease manifests due to an excessively long repeat of the trinucleotide CAG (normally, there are 11 to 34 consecutive repeats) within the Huntingtin or HTT gene (Chromosome location 4p16.3). It is the length of CAG triplets within this gene which determines the age of onset and clinical severity of the disease. CAG repeats of more than 28 shows instability on replication. This instability is greater in spermatogenesis than oogenesis. These findings also account for the phenomenon of anticipation in Huntington's disease. Rarely, alternative mutation termed HDL2 (Huntington disease-like-2) which is associated with CATCG repeat expansion of the juntophilin-3 gene (chromosome location 16q24.2) may have clinical features similar to Huntington's disease.[3]

Huntington's disease may have varied manifestations. It is characterized by involuntary choreiform movements, dysarthria, gait disturbances, oculomotor abnormalities, behavioral disturbances, cognitive impairment with dementia and depression with suicidal ideation. In the pre-diagnostic phase, individuals might become irritable or disinhibited and unreliable at work.[4] Cognitive dysfunction in Huntington's disease, often spares long term memory but impairs executive functions like organizing and planning. Deterioration in speech is faster than deterioration in comprehension.[5]Patients who have an early onset of the disease (below 20 years) deteriorate rapidly whereas the ones with late onset (above 20 years) have a relatively slower progression of disease.[6-7]

Genetic studies is done to confirm the diagnosis in a symptomatic patient and to screen at-risk individuals. The treatment involves a multi-disciplinary approach with medical, neuropsychiatric, social and genetic counseling for patients and their families.[2]

AIMS AND OBJECTIVES:

To study the clinical features of Huntington's disease in Eastern India

MATERIALS AND METHODS:

A cross-sectional study of 45 patients of Huntington's disease from 39 families in Eastern India. This study was done in the Department of General Medicine, Rajendra Institute of Medical Sciences, Ranchi in collaboration with Advanced Diagnostic Centre, Ranchi.

INCLUSION CRITERIA:

Patients with family history, clinical features and genetic studies suggestive of Huntington's disease were included in the study.

EXCLUSION CRITERIA:

Patients having chorea due to other acquired known causes like stroke, drugs, chorea gravidarum, Syndenham's chorea etc were excluded from this study.

RESULTS:

Forty five patients from thirty nine unrelated families were studied. Forty one (91%) patients had a positive family history with pedigree study suggestive of autosomal dominant inheritance. Majority of the patients in this study were male (M:F=29:16). Mean age of onset of illness was 29.75 years (range 9 to 55 years). Six patients (13.3%) developed featured of Huntington's disease before 20 years of age. Of these six patients, two patients (4.4%) presented with a characteristic rigid-hypokinetic syndrome. Five patients (83%) out of these six patients had rapid deterioration in comparison to twenty one patients (53%) above 20 years. The mean delay between the onset of symptoms and diagnosis of illness was 6.25 years (range 1 to 12 years).

Initial symptoms to appear, in decreasing order of frequency, is tabulated below (Table 1):

Table 1: Initial symptoms

Initial symptoms	n (%)
Choreiform movement	29 (65%)
Behavioural changes	14(31%)
Gait disturbances	6(13%)
Poor scholastic performances	3(6%)

Seven patients (16%) had more than 2 initial symptoms.

Clinical features at the time of first evaluation are tabulated below (Table 2):

Table 2: Symptoms at the time of first evaluation

Symptoms	n (%)
Chorea	43(95.5%)
Dementia	34(75.5%)
Psychiatric manifestation	33(73.3%)
Impaired saccadic movement	24(53.3%)
Pyramidal signs	18(40%)
Ataxia	2(4.4%)
Tremor	2(4.4%)

Nineteen patients had paternal transmission with mean age of onset of 29.2 years whereas twelve patients had maternal transmission with mean age of onset of 31.4 years.

On radiological evaluation (CT scan in 36 and MRI in 9 patients), caudate atrophy was seen in 41 patients (91%) while 4 patients (9%) had normal caudate nucleus at the time of diagnosis.

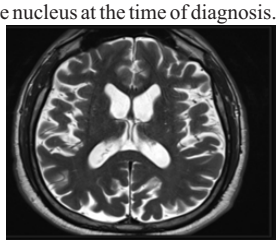

Figure: MRI T2W showing atrophy of caudate nucleus in a patient of Huntington's disease

Exact expanded CAG repeat length was reported in all the patients under study and the trinucleotide repeat length varied from 44 to 52.

DISCUSSION:

Huntington's disease is a genetic disorder with a high penetrance. More that ninety percent of the patients under study had a family history with pattern suggestive of autosomal dominant inheritance. Mean age of onset of disease in Eastern India, if the number of CAG trinucleotide repeats ranged between44 to 52, was around thirty years. Majority of patients in whom the disease sets in before 20 years of age deteriorate rapidly when compared to the group of patients who develop Huntington's disease after 20 years.

A few patients belonging to the group of early onset Huntington's disease had a rigid-hypokinetic syndrome. These patients are said to have Westphal variant of Huntington's disease.

In Huntington's disease, choreiform movement was the most common initial symptom followed by behavioural changes. At the time of evaluation, patients usually had chorea, dementia, other psychiatric manifestations and impaired saccadic movements in decreasing order of frequency.

Patients who had disease due to paternal transmission developed symptoms at an earlier age when compared to the group who had Huntington's disease due to maternal transmission.

Both CT and MRI scan showed caudate nucleus atrophy in a majority of the patients at the time of diagnosis.

CONCLUSION:

Huntington's disease is an autosomal dominant neurodegenerative disorder with multiple clinical manifestations. Typically, it is a disease which starts manifesting in the third and fourth decade of life. Age of onset of the disease is related to the number of CAG repeats, which in turn is related to the severity and progression of the disease process. In Eastern India, chorea and dementia are the two most common presenting complaints of Huntington's disease. Genetic tests are done to confirm the diagnosis. It has also become an important tool for screening of asymptomatic cases in the affected family. Radiological studies show caudate atrophy in most of the patients. Treatment of the disease is mainly symptomatic and overall prognosis of the disease is not good.

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