HUNTING DOWN A CASE OF PROGRESSIVE MOVEMENT DISORDER, DEMENTIA, AND GENETIC ANTICIPATION – A CASE REPORT ON HUNTINGTON’S DISEASE

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Abstract
The Huntington Disease HD is a progressive, fatal, highly penetrant autosomal dominant disease considered by involuntary choreiform movements. A developing number of reformists generative conditions mirror the introduction of Huntington's ailment (HD). Separating between these HD-like conditions is vital once a patient by blend of development problems, psychological decrease, social irregularities and infection course demonstrates negative to the hereditary testing for HD causative transformations, that is, IT15 quality trinucleotide-rehash extension. The disparity finding of HD-like conditions is intricate and might prompt superfluous and exorbitant examinations. We suggest guidelines for this differential determination zeroing in on a predetermined number of clinical highlights ('warnings') that can be distinguished over precise clinical assessment, assortment of recorded information and a couple of routine auxiliary examinations. Present highlights incorporate the traditional foundation of the patient, the contribution of the facio-bucco-lingual and cervical region with development problem, the co-event of cerebellar highlights and seizures, the occurrence of exceptional stride examples and eye development irregularities, and an atypical movement of ailment. Extra assistance may get from the intellectual social introduction of the patient, just as by a limited amount of subordinate examinations, chiefly MRI and routine blood tests. These warnings ought to be continually refreshed as the phenotypic characterization and distinguishing proof of added dependable indicative indicators for HD-like disorder development completed the next years. HD is brought about by increment in the quantity of polyglutamine (CAG) rehashes (>40) in the coding arrangement of the good quality. Speeding up of this cycle with ensuing ages having bigger quantities of rehashes and prior period of malady beginning is called Anticipation. Here we account a circumstance of a 32 year old female with genetic anticipation and classical features of HD.

Keywords: Huntington Disease (HD), Huntington’s Chorea, Genetic Anticipation, Enlargement of Lateral Ventricle, Atrophy of Caudate nucleus, Putamen

ABBREVIATIONS:
HD-Huntington’s Disease, CAG-cytosine adenine guanine, ESR-Erythrocyte sedimentation rate, HTT-Huntingtin gene.

Introduction:
Huntington Disease (HD) is a progressive, fatal, highly penetrant autosomal dominant disease characterized by involuntary choreiform movements (formerly referred to as Huntington’s Chorea); Behavioural disturbance, cognitive impairment with Dementia, dysarthria, gait disturbance, oculomotor abnormalities are also common features. HD is brought about by increment in the quantity of polyglutamine (CAG) rehashes (>40) in the coding arrangement of the Huntingtin quality situated on the quick arm of chromosome [4][10]. Less than 26 repeats of CAG nucleotide is normal, 26-40 repeats is intermediate, 40 or more leads to symptoms. The bigger the quantity of rehashes, the previous the infection shows. Quickening of the cycle with ensuing ages having bigger quantities of rehashes and prior period of sickness beginning is called Anticipation [11][12]. We report a case of 32 year old female patient by non-patterned, abnormal, involuntary movements and other classical features of HD with genetic anticipation evident on proper history taking.

ETHNICITY:
Huntington disease (HD) affects both men and women of all ethnic groups. However, the frequency of the condition in different countries varies greatly.[15-20] In general, it affects about 3 to 7 per 100,000 people of western European descent. A few isolated populations of western European origin have an unusually high prevalence of HD that appears to have resulted from a founder effect. For example, the Lake Maracaibo region of Venezuela is believed to have the highest prevalence of HD in the world with about 700 per 100,000 affected. The condition occurs less frequently in Japan, China, and Finland, as well as among black people of African descent.[21-25]

The average age of onset for HD is 35 to 44 years. However, the range is large and varies from 2 years to older than 80 years. Onset in people younger than 10 years and in people older than 70 years is rare [26-30]

Case description
A 32 year old female patient was admitted to Mallareddy Institute of Medical Sciences, Hyderabad, with chief complaint of involuntary abnormal movements in limbs, trunk and neck since 18 months. Patient initially noticed abnormal movements in lower limbs, she also had gait abnormalities. She had difficulty in walking and standing for long, two months later noticed involuntary movements of upper limbs (swinging movements), trunk and neck. Over a year it progressed to rapid, non-patterned, involuntary movements all throughout the day which disturbed her daily routine and required her husband’s assistance to perform her routine activities but had no weakness in any of the limbs. Movements were less during sleep as told by patient’s attendee. Patient also complaints of stuttering speech since one and a half year. History of easy forgetfulness, behavioral changes like disturbances in mood, frequent outburst of anger, depressive mood since a year was told by her husband. No past of chest pain, breathlessness, or joint pain, loss of consciousness, seizures, sensory, bowel, bladder or any cranial nerve involvement. No history of drug intake/ similar complaints/ co-morbidities in past. Family history exposed that

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her paternal grandmother has comparable complaints of involuntary movements and dementia when she was around 50 years and died at 60 years, father who was born out of a consanguineous marriage had similar complaints at the age of 42 years, succumbed to clinical course of the disease and depression, who died three years later. Her aunt also had history of dementia at 38 years but died in a car accident unrelated to the case. Patient is having two siblings, elder brother aged 34 years and younger sister elderly 30 ages

On broad physical assessment quiet had mellow paleness, she was afebrile, normotensive. Assessment of her cardiovascular framework, midsection and respiratory framework was ordinary. On focal sensory system assessment, her recent memory appears to be moderately impaired, oriented to time space and person, speech was dysarthric. Cranial nerve examination was normal. On motor examination she has usual control in all 4 members, deep tendon reflexes were normal, plantars were bilaterally flexor. Increased frequency of blinking, unable to fix gaze at a point hasin excess of 30 seconds. Protrusion of tongue was constantly interrupted. Rapid, involuntary, non-patterned, semi purposive movements are seen in both upper limbs and lower limbs (right limb more than left). Sensory, Cerebellar systems is usual. Bowel and bladder is complete. Skull and spine were normal.

Investigations showed haemoglobin of 9gm% , fringe blood smear was normocytic hypochromic with no anomalous cells. ESR is 18mm/first hr. Chest X-beam, echocardiography demonstrated no heart irregularity. Stomach Ultrasonography was ordinary. Rheumatoid factor and Antinuclear antibodies are negative and all biochemical boundaries were in ordinary reach. Ophthalmologic Slit light assessment was typical.MRI scan (Figure 2) showed enlargement of lateral ventricles, destruction of wall of forward horn due to wasting of caudated nucleus. Bicaudate nucleus remoteness among ventricles

Figure 1. pedigree chart

Figure 2. MRI showing Atrophy of caudate heads, Dilatation of lateral ventricles

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Was also increased. Axial flair image showed abnormal signal in the caudate and putamen. Genetic testing for HD revealed positive with 49 CAG repeats within the HTT gene.

Diagnosis of Huntington’s disease is completed and the patient is ongoing on Deuterated Tetrabenazine 12 mg/day, clinically improvement was seen in a day as the abnormal movements reduced slowly. Antianxiety drug Alprazolam 0.25mg once daily was started which helped the patient in anxiety caused by depression. Patient has been on regular follow-up and showed clinical improvement compared to her initial presentation.

DISCUSSION

Huntington’s disease (HD), also known as Huntington's chorea, is mostly an inherited neurodegenerative disease. The earliest symptoms are often subtle problems with mood or mental abilities[31-32]. A general lack of coordination and an unsteady gait often follow. As the disease advances, uncoordinated, jerky body movements known as chorea become more apparent. Physical abilities gradually worsen until coordinated movement becomes difficult and the person is unable to talk. Mental abilities generally decline into dementia. The specific symptoms vary somewhat between people. Symptoms usually begin between 30 and 50 years of age but can start at any age. The disease may develop earlier in life in each successive generation. About eight percent of cases start before the age of 20 years, and are known as juvenile HD, they typically present with parkinsonism symptoms rather than those of chorea [33-34].

HD is typically inherited, although up to 10% of cases are due to a new mutation. When inherited, the disease is caused by an autosomal dominant mutation in either of an individual's two copies of a gene called huntingtin (HTT). This means a child of an affected person typically has a 50% chance of inheriting the disease. The huntingtin gene provides the genetic information for huntingtin protein (htt). Expansion of CAG repeats of cytosine-adenine-guanine (known as a trinucleotide repeat expansion) in the gene coding for the huntingtin protein results in an abnormal mutant protein (mhtt), which gradually damages brain cells through a number of possible mechanisms. Diagnosis is by genetic testing, which can be carried out at any time, regardless of whether or not symptoms are present. This fact raises several ethical debates: the age at which an individual is considered mature enough to choose testing; whether parents have the right to have their children tested; and managing confidentiality and disclosure of test results[35-36].

There is no cure for HD, and full-time care is required in the later stages. Treatments can relieve some symptoms and, in some, improve quality of life. The best evidence for treatment of the movement problems is with tetrabenazine [3] HD affects about 4 to 15 in 100,000 people of European descent. It is rare among Japanese, while the occurrence rate in Africa is unknown. The disease affects men and women equally. Complications such as pneumonia, heart disease, and physical injury from falls reduce life expectancy. Suicide is the cause of death in about 9% of cases. Death typically occurs 15–20 years from when the disease was first detected.
Conclusion

It is very important for the clinicians and the medical students to understand the importance of detailed history taking in such neurological cases with ambiguity. Family history of the patient showing autosomal dominant inheritance pattern, clinical examination, investigations like Magnetic resonance imaging and CAG report helped to arrive at our diagnosis. Genetic testing is mainly useful for genetic counselling of the patient apart from confirming the diagnosis of HD. Therapy includes a multidisciplinary approach, with clinical, neuropsychiatric, social, and hereditary directing for the patients and their families. There is no Disease-Modifying therapy for this disorder, hence prompt diagnosis, symptomatic treatment and reassurance will be of great benefit to the patient.

References


