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Hunting down a case of Progressive Movement disorder, Dementia and Genetic Anticipation – a case report on Huntington's Disease

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ABSTRACT: Huntington Disease (HD) is a progressive, fatal, highly penetrant autosomal dominant disease characterized by involuntary choreiform movements. HD is caused by increase in the number of polyglutamine (CAG) repeats (>40) in the coding sequence of the Huntingtin gene. Acceleration of this process with subsequent generations having larger numbers of repeats and earlier age of disease onset is called Anticipation. Here we report a case of a 32 year old female with genetic anticipation and classical features of HD.

Key words: Huntington Disease(HD), Huntington's Chorea, Genetic Anticipation, Enlargement of Lateral Ventricle, Atrophy of Caudate nucleus and Putamen.

Abbrevations

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

I. INTRODUCTION

Huntington Disease (HD) is a progressive, fatal, highly penetrant autosomal dominant disease [1] characterized by involuntary choreiform movements (formerly referred to as Huntington's Chorea) ; Behavioural disturbance, cognitive impairment [2] with Dementia, dysarthria, gait disturbance, occulomotor abnormalities are also common features. HD is caused by increase in the number of polyglutamine (CAG) repeats (>40) in the coding sequence of the Huntingtin gene located on the short arm of chromosome 4 [2,4]. Less than 26 repeats of CAG nucleotide is normal, 26-40 repeats is intermediate, 40 or more leads to symptoms. The larger the number of repeats, the earlier the disease manifests. Acceleration of the process with subsequent generations having larger numbers of repeats and earlier age of disease onset [3] is called Anticipation. We report a case of 32 year old female patient with non-patterned, abnormal, involuntary movements and other classical features of HD with genetic anticipation evident on proper history taking.

Case description

A 32 year old female patient resident of Jeedimetla village 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 attender. Patient also complaints of stuttering speech since one and a half year. History of easy forgetfulness, behavioural changes like disturbances in mood, frequent outburst of anger, depressive mood since a year was told by her husband. No history 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.

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Her Family history revealed that her paternal grandmother had similar 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 an car accident unrelated to the case. Patient is having two siblings, elder brother aged 34 years and younger sister aged 30 years are healthy currently and symptom free. Patient is born out of a Consanguineous marriage (Figure 1) , she has two children, 6 year old son and 4 year old daughter who are symptom free.

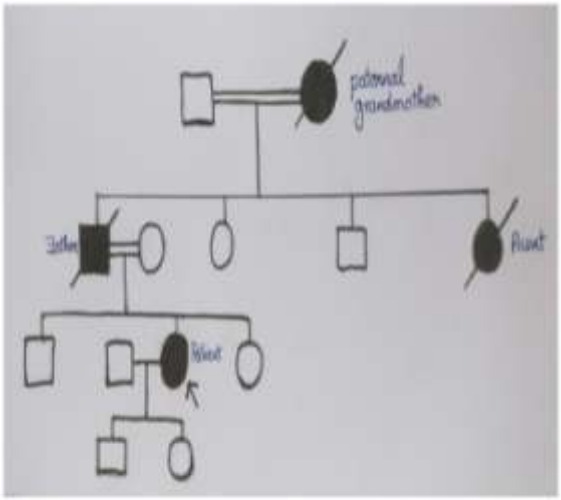

Figure 1: Pedigree Chart

On general physical examination patient had mild pallor, she was afebrile, normotensive. Examination of her cardiovascular system, abdomen and respiratory system was normal. On central nervous system examination, 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 had normal power in all four limbs, deep tendon reflexes were normal, plantars were bilaterally flexor. Increased frequency of blinking, unable to fix gaze at a point for more than 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 were normal. Bowel and bladder were intact. Skull and spine were normal.

Investigations showed haemoglobin of 9gm% , peripheral blood smear was normocytic hypochromic without any abnormal cells. ESR was 18mm/1st hr. Chest X-ray, echocardiography showed no cardiac abnormality. Abdominal Ultrasonography was normal. Rheumatoid factor and Antinuclear antibodies were negative and all biochemical parameters were in normal range. Opthalmologic Slit lamp examination was normal. MRI scan (Figure 2) showed enlargement of lateral ventricles, flattening of wall of frontal horn due to atrophy of caudate nucleus. Bicaudate nucleus distance between ventricles 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.

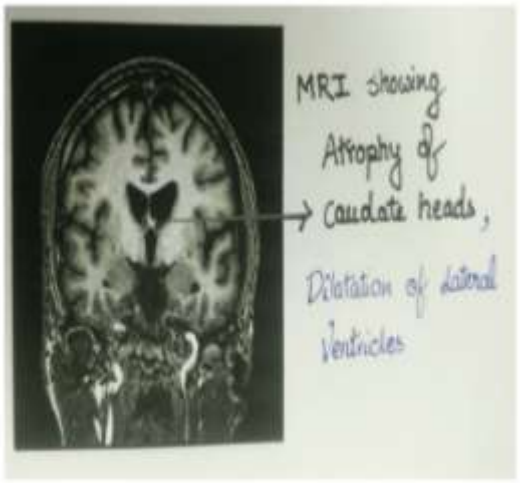

Figure 2: Magnetic Resonance Imaging

Diagnosis of Huntington's disease was made and the patient was started 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 followup and showed clinical improvement compared to her initial presentation.

II. DISCUSSION

Huntington's disease onset is typically between the ages of 25 to 45 years (range: 3-70 years), with a prevalence of 2-8 cases per 100,000 and average age of death of 60 years. Our patient,

presented in the typical age group, There was no history of chest pain, breathlessness, or joint pain, ruling out Sydenham's chorea. After proper history taking, differential diagnosis (Table1) of hereditary chorea were clinically excluded before arriving at the diagnosis of HD [5,6]. Neuroacanthocytosis is autosomal recessive and patients present with features of early onset of chorea, mild-to-moderate mental deterioration along with acanthocytosis. Benign Hereditary chorea is usually seen in childhood and there is absence of mental deterioration. Patients of Wilson's disease having neuropsychiatric disturbances are accompanied by Kayser-Fleischer's ring and have autosomal recessive pattern [7,8]. Patients with ataxia telangiectasia present in the first decade of life with progressive telangiectatic lesions associated with deficits in cerebellar function and nystagmus. Early onset of disease in the patient when compared to her father and her father also had early onset of disease and death when compared to his mother (patient's paternal grandmother) is one of the clenching points to arrive at our diagnosis.

Table 1: CAUSES OF HEREDITARY CHOREA

Common Causes	Rare Causes
Huntington's Disease	Wilson's Disease
Neurocanthosis	Dentatorubral-Pallidoluysian Atrophy
Benign Hereditary Chorea	Paroxysmal choreoathetosis
	Lesch Nyhan syndrome
	Ataxia Telangiectasia

On examination of our patient with chorea, Darting Tongue sign (flapping of tongue), constant random movements of individual fingers when hands are outstretched (piano-playing movements) [9], inability to hold the hands above head with palms extended as the hands turn into a position of hyperpronation, Milkmaid grip [9] (characterized by the inability to hold examiner's finger in her fist, there are constant twitches of individual fingers) was seen. However classical hung-up reflexes due to chorea interfering in the reflex contraction were not seen in our patient. [10]

III. 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. Treatment involves a multidisciplinary approach, with medical, neuropsychiatric, social, and genetic counselling for the patients and their families. There is no Disease-Modifying therapy for this disorder [11], hence prompt diagnosis, symptomatic treatment and reassurance will be of great benefit to the patient.

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