Huntington’s Chorea –
A Case Report with Typical Family Tree

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Abstract
A case of Huntington’s chorea with typical family tree is presented. The patient presented with classical triad of autosomal dominant inheritance, choreoathetosis, and dementia.

Introduction
In 1872, George Huntington (1850-1916), a medical practitioner of Pomeroy, Ohio, USA made the first complete description of this disorder among the population of Long Island in New York State. The disorder was then named after him as Huntington’s disease. This disease is distinguished by the triad of autosomal dominant inheritance, choreoathetosis, and dementia. Its cause has been linked to abnormal expansion in a length of a CAG triplet repeat sequence in a gene on chromosome 4p, now called the Huntington gene (HD). Huntington’s disease has a population frequency of about 7-10 per 100,000 population and usually starting in adult life-fourth or fifth decade. Huntington’s disease manifesting in early adulthood is rare. The patient who presented to us has classical family tree with rare early adulthood presentation, therefore this case is being presented.

Case report
A 28 years old female presented to the Medicine OPD with a history of abnormal movements of hands and face of one and a half year duration. These abnormal movements were of gradual onset with progressive course. She also had behavioural changes along with abnormal movements in the form of frequent outbursts of anger, loss of temper, depressive mood, and insomnia. These abnormal movements got aggravated during outbursts of anger, disturbances in mood, and were absent during sleep. There was no weakness in any of limbs, but she was unable to perform her regular household activities properly. There was no history of drug intake such as phenytoin, oral contraceptives, phenothiazines, haloperidol, L-dopa, lithium, isoniazid, amphetamines, tricyclic antidepressants etc. There was no history of chest pain, breathlessness, or joint pain or any other pointer towards Sydenham’s chorea.

Her family history revealed that her maternal grandmother and mother had similar kind of abnormal movements and had died at the age of 60 and 55 years respectively. The patient is having five siblings (two brothers and three sisters). Her elder brother committed suicide at the age of 25 years, and elder sister died at the age of 33 years. Both were having similar type of abnormal movements and abnormal behaviour. One of her younger sister aged 22 years is also having similar type of abnormal movements with depressive attitude. Her younger brother aged 17 years and the other younger sister aged 14 years are healthy and symptom free. Her two children – 8 year old son and 10 year old daughter – are symptom free.

Her general physical examination was non-contributory except mild pallor. She was normotensive. Her cardiovascular system, abdomen, and respiratory system were essentially normal. On central nervous system examination, her memory was intact and showed normal orientation in time, space, and person. She had normal power in all four limbs. The deep tendon reflexes in all four limbs were normal and plantars were bilaterally flexor. Sensory and cerebellar systems were normal and bladder, bowel were intact. However, she could not fix her gaze at one point for more than 30 seconds, with repetitive blinking movements, and was not able to protrude her tongue out for more than 30 seconds.

Investigations showed – Hb of 7.9 gm% and peripheral
blood smear showed normocytic hypochromic picture, without any abnormal cells. ESR was 15mm/1st hr. Chest X-ray and echocardiography showed no cardiac abnormality. Ultrasonography for abdomen was normal. Rheumatoid factor and LE cells were negative and all biochemical parameters were in normal range. Slit lamp examination for K.F. ring was also negative. Spiral CT head showed prominence of lateral ventricles and there was flattening of wall of frontal horn indicating atrophy of caudate nucleus. Bicaudate distance between ventricles was also increased. These findings were suggestive of early evidence of caudate lobe atrophy and are seen in Huntington's chorea.

Considering the history, clinical examination, investigations, spiral CT findings, and family history of the patient, there was no second thought in making a diagnosis of Huntington's chorea.

The patient has been on regular follow-up for the last six months and is being treated with haloperidol 0.2 mg/kg orally in divided doses. There was a partial response initially for two months, but thereafter she is maintaining status quo, as it is often difficult to treat these patients and the disease is progressive.

**Discussion**

The differential diagnosis of a case of hereditary chorea includes various causes (Table I).

**Table I : Causes of hereditary chorea.**

<table>
<thead>
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<th>Common causes:</th>
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<tbody>
<tr>
<td>1. Huntington’s disease</td>
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<tr>
<td>2. Neuroacanthocytosis</td>
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<td>3. Benign hereditary chorea</td>
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<tr>
<th>Rare causes:</th>
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<tbody>
<tr>
<td>1. Wilson’s disease</td>
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<td>2. Dentatoubro Pallido Luysian atrophy (DRPLA)</td>
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<td>3. Paroxysmal choreoathetosis</td>
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<td>4. Lesch - Nyhan syndrome</td>
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<td>5. Ataxia telangiectasia</td>
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<td>6. Haller vorden - Spatz disease</td>
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<td>7. Pelizaeus - Merzbacher disease</td>
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Patients of neuroacanthocytosis have autosomal recessive pattern of inheritance and present with features of early onset of chorea, mild-to-moderate mental deterioration alongwith acanthocytosis (thorny or spiky appearance of erythrocytes). Benign hereditary chorea is characterised by onset in childhood and there is absence of mental deterioration. Patients of Wilson’s disease having neurological or psychiatric disturbances are accompanied by Kayser-Fleischer’s ring and also having autosomal recessive pattern. Patients with ataxia telangiectasia present in the first decade of life with progressive telangiectatic lesions associated with deficits in cerebellar function and nystagmus3,4.

In the present case, the patient presented with all the features suggestive of Huntington’s disease which was further substantiated by the family history (Fig. 1) and CT scan finding (Fig. 2). Huntington’s disease is a genetic, autosomal dominant, degenerative brain disorder. This is one of the most common hereditary nervous system disease. Exhaustive geneologic documentation has established the cause to be an autosomal dominant gene with complete penetrance. To quote Huntington, the rule has been that “when either or both of the parents have shown manifestation of the disease, one or more of the offspring invariably suffer from the disease, if they live to adult life. But if by any chance these children go through life without...
it, the thread is broken and the grand children and great grand children of the original shakers may rest assured that they are free from disease3.

Huntington disease was mapped to the tip of the short arm of chromosome in 1983. Huntington gene contains a CAG repeat sequence which varies in size. In Huntington’s disease there is an excessively long repeat of trinucleotides (CAG)5. In normal population, there is mean of around 19 CAG repeats with a range from 9 - 37. The patients with HD, the repeat sequence is expanded with average repeat length 46 and range of 36-86. The length of repeat sequence determines not only the presence of the disease but also the age of onset6. Disease exhibits the phenomenon of anticipation. Recent generations are affected at an earlier age and more severely than older generations within same family, with a progressive increase in length of repeat sequences.

Neuropathologically, the brain in HD may show cerebral atrophy ranging from mild-to-marked, with a corresponding reduction in total brain weight of about 30%. On cut surfaces, the main abnormality is atrophy of caudate nucleus (57%), putamen (64%), and globus pallidus. Neurotransmitters such as GABA, substance P, acetylcholine, enkephalins, cholecystokinin are decreased while there is an increase in levels of somatostatin, neurotensin, and thyrotropin releasing hormone3,4.

Huntington’s disease usually manifests in middle adult life, with development of abnormal movements which are first and most evident in hands and face. Person feels difficulty in performing a sequence of hand movements. Movement disorder is usually slowly progressive and eventually may become a disability. Attention, judgement, awareness, and executive functions may be seriously deficient at an early stage, but memory is frequently not impaired until late in the disease. These abnormal movements accompanied by disturbance of mood, particularly depression are common. Noteworthy is the high suicide rate in Huntingtonians7.

The diagnosis is made clinically, but this is supported by the finding of atrophy of the caudate nucleus on CT or MRI. DNA analysis and determination of the length of the CAG expansion has a sensitivity of 98.8% as a diagnostic test and appears highly specific. Huntington’s disease pursues a steadily progressive course and death occurs, on an average 15-20 years after onset. The psychologic and social consequences of the disease require supportive therapy, and genetic counselling is essential.

The dopamine antagonist haloperidol, in a daily dose of 2-10 mg is probably the most effective agent in suppressing the movement disorder. Although an uncommon neurological disorder, but considering the adult age of onset and the associated debilities, if this disease is diagnosed at the early stage, at the least the patient can be given the benefit of psychological and other supportive treatment. Genetic counselling, of course, would go a long way in the eradication of this debilitating disease.

References
3. Maurice V, Allan HR. Degenerative diseases of the nervous..


