Huntington’s Disease Like Syndrome: A Rare Genetic Dilemma For Clinicians

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Abstract
Huntington’s disease like syndrome are heredodegenerative disorder conditions which mimic the presentation of Huntington’s disease. It is characterised by combination of movement disorders, cognitive decline, behavioural abnormalities and progressive disease course proves negative to genetic testing for huntington’s disease. Huntingtons disease is the most common hereditary neurodegenerative disorder with onset before mid-life and a distinct phenotype characterised by movement disorders like chorea, dystonia, in coordination, cognitive deterioration, and behavioural changes. Here we present a 38 year old male who presented to casualty with chief complaints of involuntary movements of both upper and lower limbs since 5 years, drooling of saliva and difficulty in eating since 2 years. Patient was already on antipsychotic medication (details not available) along with tetrabenazine at dose 25 mg (p/o) tds. Patient had an episode of GTCS on 3rd day of admission associated with uprolling of eyeballs and frothing from mouth. On MRI Brain Caudate head atrophy on either side associated with enlargement of frontal horns of lateral ventricle-box like configuration (possibly represents Huntington’s disease). Patient started tetrabenazine, haloperidol and added antiepileptic on 3rd day. The patient improved over a period of 7 days and choreiform movements decreased. Patient was discharged on Tetrabenazine, Antiepileptics and Haloperidol.

Introduction and Background
- Huntington’s disease like syndrome are heredodegenerative disorder conditions which mimic the presentation of Huntington's disease.
- It is characterised by combination of movement disorders, cognitive decline, behavioural abnormalities and progressive disease course proves negative to genetic testing for huntington’s disease.
- Huntington’s disease is the most common hereditary neurodegenerative disorder with onset before mid-life and a distinct phenotype characterised by movement disorders like chorea, dystonia, in coordination, cognitive deterioration, and behavioural changes.
- Progressive neural cell loss within cortico-straito thalamic circuits, predominantly in neostriatum (caudate and putamen)¹
Huntington's disease is a trinucleotide repeat disorder with autosomal dominant mode of inheritance. Causative mutation is prolongation (above 35 repeats) of CAG stretch within IT15 gene, associated with full penetrance when this exceeds 40 and incomplete penetrance between 36 to 39.

**Pathophysiology**

- Percentage of Huntington's disease-like syndrome which doesn't land up in Huntington's disease is between 1%-7%
- Juvenile onset of Huntington's disease is characterised by hypokinetic-rigid syndrome (West-Pal variant) and adult onset there is choreatic syndrome and less severe progression of motor and non-motor features.

**Ethnicity**

- HDL2 is autosomal dominant disorder described is an autosomal disorder seen in families of Southern African origins which accounts for 0.7% of all Huntington's disease-like presentation.
- HDL2 should be suspected in every South African ancestry accounting for 24-50% of cases.

**Clinical Manifestations**

<table>
<thead>
<tr>
<th>Physical Signs of HD</th>
<th>Mental and Emotional Signs of HD</th>
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<tbody>
<tr>
<td>Involuntary movements</td>
<td>Sadness</td>
</tr>
<tr>
<td>Trouble walking</td>
<td>Depression</td>
</tr>
<tr>
<td>Clumsiness</td>
<td>Lack of motivation</td>
</tr>
<tr>
<td>Unsteadiness, imbalance</td>
<td>Difficult to get along with</td>
</tr>
<tr>
<td>Trouble holding objects</td>
<td>Sexual problems</td>
</tr>
<tr>
<td>Speech difficulty</td>
<td>Memory loss</td>
</tr>
<tr>
<td>Weight loss</td>
<td>Intellectual decline</td>
</tr>
<tr>
<td>Difficulty with bladder control</td>
<td>Delusions or hallucinations</td>
</tr>
<tr>
<td>Difficulty with bowel control</td>
<td>Suspiciousness, paranoia</td>
</tr>
</tbody>
</table>

Changes in sleeping patterns

**Table 1. Signs of Huntington Disease (HD) as Indicated on Affected Individual Questionnaire**

<table>
<thead>
<tr>
<th>TABLE. Distinctions between Juvenile and Adult Huntington Disease</th>
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<tbody>
<tr>
<td>Characteristics</td>
</tr>
<tr>
<td>Age at onset</td>
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<tr>
<td>Genetics</td>
</tr>
<tr>
<td>Primary motor manifestations</td>
</tr>
<tr>
<td>Seizures</td>
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<tr>
<td>Cognitive changes</td>
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</tbody>
</table>

**Case Report**

A 38-year-old male/presented to casualty with chief complaints of:

1) Involuntary movements of both upper and lower limbs since 5 years
2) Drooling of saliva and difficulty in eating since 2 years

Patient was already on antipsychotic medication (details not available) along with tetrabenazine at dose 25 mg (p/o) tds

Patient had an episode of GTCS on 3rd day of admission associated with uprolling of eyeballs and frothing from mouth

Neurology reference was taken and patient was further investigated.
On Examination: General condition was moderate, patient was vitally stable. Neurological examination: patient was conscious oriented to time, place and person, choreiform movements present with eating dystonia and truncal dystonia.

Investigations: HB-13.2, TLC-9400, Platelet count-1.87,
Liver and kidney function tests were within normal limits along with normal electrolytes levels
Fundus examination was done to see for KF ring which was within the normal limits

Special Investigations: serum ceruloplasmin levels-23.10(20-60)
- Urine copper level-25.6(<40)
- Ds dna-negative
- Apla-negative
- Aso titre-200
- Ps for cell type-no acanthocytes were seen
- Thyroid function test-within normal limits
- 2d echo-within normal limits
- MRI(BRAIN): Caudate head atrophy on either side associated with enlargement of frontal horns of lateral ventricle-box like configuration (possibly represents Hungtingtons disease)

Genetic Workup
- Blood investigation-DNA PCR was done to see for the repeat expansion 25 CAGs

<table>
<thead>
<tr>
<th>nucleotide CAG Repeats</th>
<th>clinical implication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of repeats</td>
<td></td>
</tr>
<tr>
<td>10-26</td>
<td>normal</td>
</tr>
<tr>
<td>27-35</td>
<td>normal(rare expansion)</td>
</tr>
<tr>
<td>36-39</td>
<td>Huntington disease</td>
</tr>
<tr>
<td>39</td>
<td>Huntington disease</td>
</tr>
</tbody>
</table>

- With 36-39 have reduced penetrance
- >39 have full penetrance

Genetic CAG triplet repition test was normal for the patient (25)

Course and Treatment In Hospital
- Patient started tetrabenazine, haloperidol and added antiepileptic on 3rd day. The patient improved over a period of 7 days and choreiform movements decreased. Patient was discharged on tetrabenazine, antiepiletics and haloperiidoil

Differential Diagnosis
- Adult onset progressive chorea
- Hungtonts disease
- Wilsons disease
- Spinocerebellar ataxia

Discussion and Conclusion
- As the patient presented with symptoms suggestive of huntingtons like disease and imaging is supporting for the same. But the genetic workup that is DNA PCR for blood was normal. So the condition can be labelled as “HUNTINGTONS LIKE SYNDROME”

References