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

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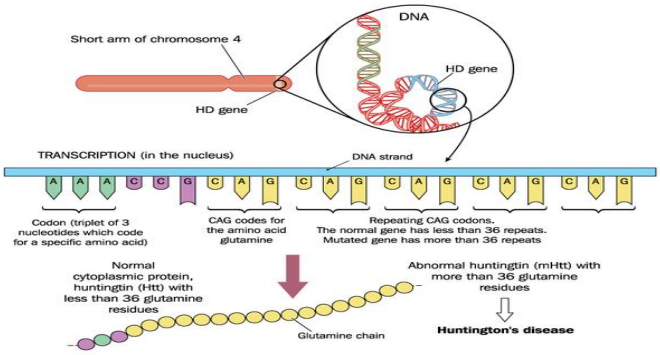
Abstract
Huntington's disease like syndrome are heredodegenerative disorder conditions which mimic the presentation of Huntington's disease. It is characterised by combination of movement disorders, cognitive decline, behavioural abnormalities and progressive disease course proves negative to genetic testing for hungtington's disease. Huntingtons disease is the most common hereditary neurodegenerative disorder with onset before mid-life and a distinct phenotype chararacterised by movement disorders like chorea, dystonia, in coordination, cognitive deteroiration, and behavioural changes. Here we present a 38year old male who presented to casuality with chief complaints of involuntary movements of both upper and lower limbs since 5 years, drooling of saliva and difficulty in eating sine 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 Hungtingtons 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

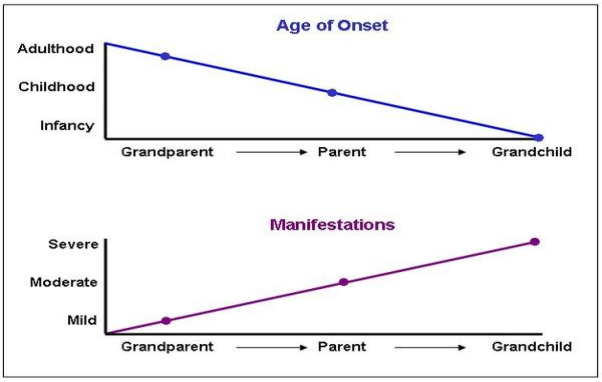
- Huntington's disease like syndrome are heredodegenerative disorder conditions which mimic the presentation of Huntington's disease.
- It is characterised by combination of movement disorders, cognitive decline, behavioural abnormalities and progressive disease course proves negative to genetic testing for hungtington's disease.
- Huntingtons disease is the most common hereditary neurodegenerative disorder with onset before mid-life and a distinct phenotype chararacterised by movement disorders like chorea, dystonia, in coordination, cognitive deteroiration, and behavioural changes.
- Progressive neural cell loss within cortico-straito tahlamic circuits, predominantly in neostriatum (caudate and putamen)[1]

- Huntingtons disease is trinucleotide repeat disorder with autosomal dominant mode of inheritance
- Causative mutation is prolongation (above 35 reapeats) of CAG stretch within IT15 gene, associated with full penetrance when this exceeds 40 and incomplete penetrance between 36 to 39

Pathophysiology



- Percentage of Huntingtons disease like syndrome which doesn't land up in huntingtons disease is between 1%-7% [2]
- 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 southen african origins which accounts for 0.7% of all Hungtions disease like presentation
- HDL2 should be suspected in every south african ancestry accounting for 24-50% of cases [3]

Clinical Manifestations

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

Physical Signs of HD	Mental and Emotional Signs of HD
Involuntary movements	Sadness
Trouble walking	Depression
Clumsiness	Lack of motivation
Unsteadiness, imbalance	Difficult to get along with
Trouble holding objects	Sexual problems
Speech difficulty	Memory loss
Weight loss	Intellectual decline
Difficulty with bladder control	Delusions or hallucinations
Difficulty with bowel control	Suspiciousness, paranoia
Changes in sleeping patterns	

**See "Participants and Methods" section for further explanation of the questionnaire.*

TABLE. Distinctions between juvenile and adult Huntington disease

Characteristics	Juvenile Huntington disease	Adult Huntington disease
Age at onset	≤ 20 years (childhood onset ≤ 10 years)	≥ 21 years
Genetics	Typically alleles with ≥ 60 CAG repeats	Typically alleles with ≥ 40 CAG repeats
Primary motor manifestations	Bradykinesia, dystonia, rigidity, oropharyngeal dysfunction[4,9,15]	Choreiform movements
Seizures	Common (generalized tonic-clonic are the most common[6]); seizures often difficult to manage[3,6]	Seizures less common
Cognitive changes	Deterioration in school performance; ADHD-like symptoms; language regression[15]; cognitive decline, which can include subcortical dementia[4]; behavioral changes and agitation	Cognitive decline, symptoms of subcortical dementia

Case Report

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

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

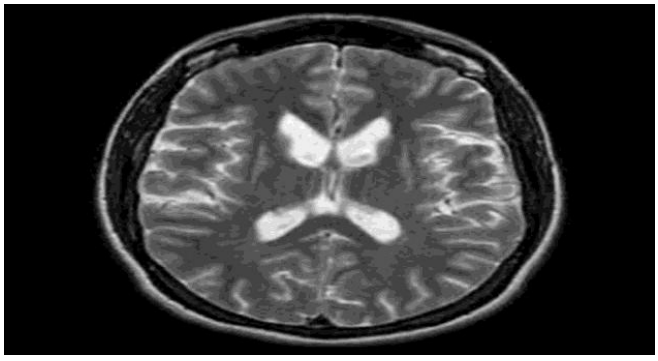
Investigations: HB-13.2, TLC-9400, Platelet count-1.87,

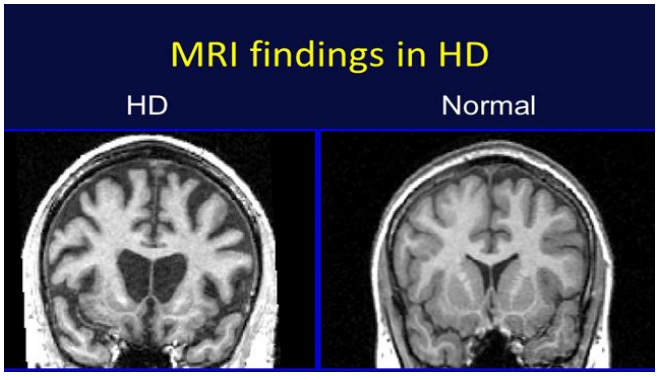
Liver and kidney function tests were within normal limits along with normal electrolytes levels

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

nucleotide CAG Repeats	
Number of repeats	clinical implication
10-26	normal
27-35	normal(rare expansion)
36-39	Huntington disease
39	Huntington disease

- 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, antiepileptics and haloperiidol

Differential Diagnosis

- Adult onset progressive chorea
- Huntingtons 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"

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