Education-Family Physician Corner

Huntington Disease with Psychiatric Presentation

Shahla A. Karim, MBBS, MD, ABOPSYCH (Arab Board of Psychiatry),
Fellowship of Liaison Psychiatry and Women Emotional Mental Health from Singapore General Hospital*
Feras Al Saif, MBBCh**

Huntington disease (HD) is a neurodegenerative disease. It is inherited as an autosomal-dominant disease characterized by a triad of progressive motor decline, deteriorating cognitive function, and a broad spectrum of psychiatric symptoms.

We report a case of a severe form of HD with significant cognitive impairment and psychosis that was fairly controlled with antipsychotics (Haloperidol and Olanzapine), anti-dementia medications (Memantine), and anti-chorea treatment (Tetrabenazine). The patient had three stages: pre-symptomatic, prodromal, and manifest. Early detection of HD will significantly improve the medical and mental condition; the current recommendation is not to screen those who are below 18 years of age.

Bahrain Med Bull 2020; 42 (1): 52 - 54

HD is characterized by a triad of progressive motor decline, deteriorating cognitive function, and psychiatric symptoms including depression that may be complicated with suicide, anxiety, apathy, obsessive-compulsive behavior, outburst, addiction, and rarely psychotic features[1]. The prevalence of this disease is rare. The European average prevalence was 9.71 per 100,000; in Japan, China, Korea, Finland, and South Africa, the prevalence was 0.1 to 2 per 100,000[2-5]. The mean age of onset is 45 years. Two-thirds of cases present with neurological symptoms; the remaining one-third present with abnormal behavior[6]. The natural course of illness runs into 3 stages: pre-symptomatic, prodromal, and manifest. The "pre-symptomatic stage" is where the individual is free from any symptoms or signs. The "prodromal stage" presents with a subtle form of the disease, mainly motor symptoms. In the "manifest stage", chorea is the most prominent feature followed by progressive cognitive and psychiatric impairments[7]. HD has been linked to CAG trinucleotide expansion in exon 1 of the huntingtin (htt) gene at the location 4p16.9[8].

HD could be due to neuronal aggregates, transcriptional dysregulation, excitotoxicity, mitochondrial dysfunction and altered energy metabolism, changes in axonal transport, and synaptic dysfunction that cause diffuse loss of neurons particularly involving the cortex and the striatum[9]. Assessment of patients with HD should include a primary care physician, neurologist, psychiatrist, geneticist, physical and occupational therapist, speech pathologist, nutritionist, social worker, and genetic counselor[1,6]. Little is known about the treatment of HD and clinicians are encouraged to publish these cases to improve the data on HD[10].

The aim of this report is to present a case of a severe form of HD with significant cognitive impairment and psychosis that was fairly controlled with antipsychotic, anti-dementia, and anti-chorea medications.

THE CASE

The patient is a fifty-five-year-old Bahraini female with four children. They all live together in one house. She did not finish secondary school and got married at the age of 25.

The patient first presented at the age of 47 with restlessness, irritability, insomnia, anxiety, depression, and apathy. After a couple of months, she started experiencing jerky, involuntarily, purposeless movements of both upper and lower limbs. The natural course of these motor symptoms was progressive. She was prescribed Haloperidol 5mg BD by a private neurologist. The patient developed rigidity and difficulty to swallow food. The medication was discontinued. The patient had ataxic gait and was unable to walk properly. Erythrocyte sedimentation rate (ESR) was 21 mm/hr, other investigations were within normal limits. MRI revealed diffuse mild cerebral atrophy with a significant decrease in the size of the caudate nuclei bilaterally and the basal ganglia with features of iron deposition in the lentiform nuclei, see figures 1 and 2.

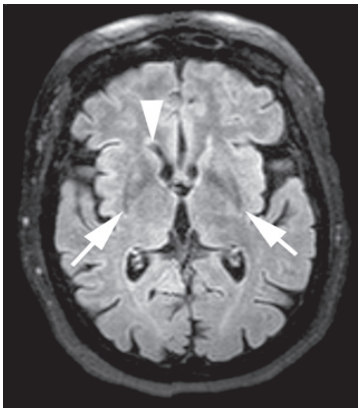

Figure 1: The White Arrows Point toward the Caudate Head Atrophy Bilaterally with Low Signal Intensity Suggestive of Iron Deposition. White Arrowhead Points toward the Enlargement of the Frontal Horns

* Consultant Liaison Psychiatry
** Training Psychiatry Resident
Psychiatric Hospital
Ministry of Health
P.O. Box 5128 Manama
Kingdom of Bahrain
E-mail: dr.feras.alsaif@gmail.com, drshahla007@gmail.com

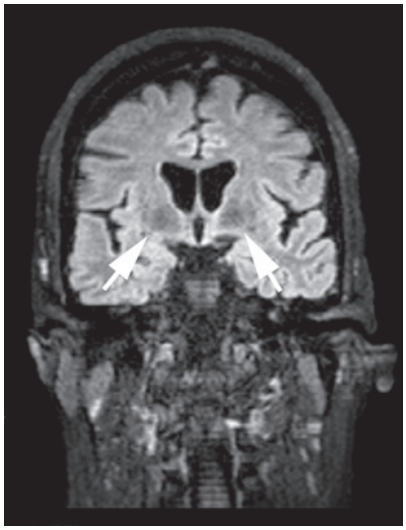

Figure 2: The White Arrows Point toward the Caudate Head Atrophy Bilaterally. Diffused Mild Cerebral Atrophy Reported

Genetic testing revealed that one of the alleles showed pathogenic expansion of 45 +- 1 CAG-repeats which is known to cause HD. The other allele showed a normal expansion of 18 +- 1 CAG-repeats. The patient was advised to start on Tetrabenazine 25mg TDS (was not available in Bahrain at that time) and physiotherapy.

The patient developed significant deterioration, more frequent chorea movements, trouble with balance and walking, delay in response to questions, apathy most of the time, poor concentration, delay in recalling recent events and speech difficulties. She was unable to talk properly or maintain a conversation and had poor pronunciation. While she was cooking, she had several incidental burns. Her husband eventually prevented her from any house activities.

The patient had significant improvement after receiving Tetrabenazine 25mg TDS. The patient showed a progressive decline in function from 2014-2018. She was admitted to the hospital after being dispensed the wrong medication of "Terbinafine 250mg TDS for a month" instead of "Tetrabenazine 25mg TDS tablets". She was discharged with Haloperidol 1.5mg bd as Tetrabenazine was out of stock.

The patient was admitted again for intermittent explosiveness, agitation, aggressive behavior toward relatives associated with persecutory and grandeur delusions with visual and auditory hallucinations. She believed that she was blessed by the prophet to fight the Jews in holy Palestine and that she can see dead relatives, the angels, and the prophet talking to her. There was an alteration of her sleep cycle and a decrease in her appetite. She was prescribed Olanzapine VT 5mg bd and later increased into 5mg TDS with Tetrabenazine 25mg TDS which controlled HD movement and behavioral disturbance. The patient's Montreal Cognitive Assessment (MoCA) score was 6/30 which suggested significant cognitive impairment; this was an indication to add Memantine 20mg od to her treatment plan[11]. The Behavior Observation Scale Huntington (BOSH) was used on the patient and revealed significant deterioration of ADLs, marked deterioration of social and cognitive abilities, and mental rigidity and aggressive behavior[12].

HD runs in her mother and mother's family. Accurate data for the age of onset of HD was not possible for some members of the family, see figure 3.

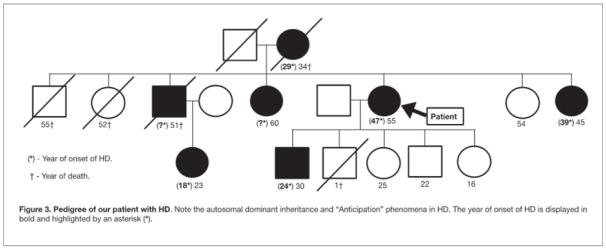

Figure 3. Pedigree of our patient with HD. Note the autosomal dominant inheritance and "Anticipation" phenomena in HD. The year of onset of HD is displayed in bold and highlighted by an asterisk (*).

Figure 3: Pedigree of the Patient. Note the Autosomal Dominant Inheritance and "Anticipation" Phenomena in HD. The Year of Onset of HD is Displayed in Bold and Highlighted by an Asterisk (*)

In 2019, she was in a wheelchair with fixed posture and normal reflexes in all limbs. The patient was vitally stable, but had rigidity in both upper and lower limbs. Pupils were rounded and reactive toward lights and no other neurological findings elicited.

The patient was quiet but communicated with the examiner with the help of her husband; she had minimal speech sounds. These sounds were low in volume, comprehended with difficulty. She looked happy, reactive with the examiner and her husband. She was able to recognize her husband, current location and time. Poor cognitive ability was noticed.

DISCUSSION

The management of HD is a challenging task for clinicians. There is no cure or treatment that delays the onset or the progression of the illness[1,2]. The treatment of HD could be pharmacotherapy and non-pharmacotherapies[1,9].

Chorea should be reduced to a tolerable level to the patient rather than eliminated[9]. The only drug approved by the FDA to control Chorea is Tetrabenazine. It should be titrated weekly in 12.5 mg increments to a maximum of 100 mg/day or the development of intolerable adverse effects. It works by inhibiting the vesicular monoamine transporter type 2 binding and monoamine depletion which is reversible within a few hours. It has the potential risk of suicide and clinicians should be cautious to prescribe it to patients with depression[1,9]. Antipsychotics such as Haloperidol (1.5–10.0 mg/day), Olanzapine, Risperidone, Quetiapine, Clozapine (150 mg/day) or Aripiprazole had limited benefits in the treatment Chorea[1,9]. The NMDA antagonist such as Amantadine (400mg/day) or Riluzole (200mg/day) reported some improvement in the treatment of Chorea[9]. A benzodiazepine such as clonazepam (up to 5.5 mg/day) may be helpful to suppress Chorea[9]. HD needs frequent assessments and changes in doses every couple of months. HD with akinetic form (Westphal variant) should be prescribed anti-parkinsonism medications such as levodopa, dopamine agonist, or Amantadine[13]. Cannabinoids or Olanzapine can aid in weight loss, while antipsychotics should be prescribed to control the psychosis, irritability or aggression[9]. SSRI, SNRI, or TCA are used to manage depression, obsessive-compulsive behavior or apathy, but the evidence to prescribe them is still not convincing[9].

Other non-psychopharmacological therapies include physical and occupational therapy, gait support and home safety measures (e.g., hazard removal, grab-bars, shower chairs) are important. Speech therapists could help with dysarthria and dysphagia. A dietician could be consulted for food modifications and high-calorie supplements for weight loss and minimal distraction should be advised while eating and swallowing[1]. Other forms of treatment include music therapy, exercise, dance, or playing video games[9].

There are currently 172 registered clinical trials on Huntington Disease in the world[14]. There is a potential use of RNA interference to reduce the expression of mHTT[9].

There is a notable inverse relation that exists between the number of CAG-repeats and the onset of HD[6]. Two phenomena of HD exist; the first is called "Penetrance" which measures alleles and CAG repeats. More than 36 CAG-repeats are considered at high risk of developing HD. Those who contain more than 40 CAG-repeats are called completely penetrant and will results eventually with HD development. The second is called "Anticipation", the phenomenon in which HD increases in severity with decreasing onset of illness in the next generations with HD.

It is not recommended to test asymptomatic at-risk individuals below the age of 18 years out of respect for the autonomy of the child[6].

CONCLUSION

HD is a rare disease and the treatment is limited to pharmacotherapy. The non-pharmacotherapy options are adjunctive but widely available. There is ongoing research today to identify disease-modifying agents that would help individuals with HD. We recommend a randomized controlled trial of HD patients.

Author Contribution: All authors share equal effort contribution towards (1) substantial contributions to conception and design, acquisition, analysis and interpretation of data; (2) drafting the article and revising it critically for important intellectual content; and (3) final approval of the manuscript version to be published. Yes.

Potential Conflicts of Interest: None.

Competing Interest: None.

Sponsorship: None.

Acceptance Date: 5 January 2020.

Ethical Approval: Approved by the Ethical Committee, Psychiatric Hospital, Ministry of Health, Bahrain.

REFERENCES

1. Dayalu P, Albin RL. Huntington Disease Pathogenesis and Treatment. Neurol Clin 2015; 33(1):101-14.
2. Rawlins MD, Wexler NS, Wexler AR, et al. The Prevalence of Huntington's Disease. Neuroepidemiology 2016; 46:144–53.
3. Pringsheim T, Wiltshire K, Day L, et al. The Incidence and Prevalence of Huntington's Disease: A Systematic Review and Meta-Analysis. Mov Disord 2012; 27:1083–91.
4. Sipilä JO, Hietala M, Siitonen A, et al. Epidemiology of Huntington's Disease in Finland. Parkinsonism Relat Disord 2015; 21:46–9.
5. Xu M, Wu ZY. Huntington Disease in Asia. Chin Med J (Engl) 2015; 128:1815–9.
6. Caron NS, Wright GEB, Hayden MR. Huntington Disease. In: Adam MP, Ardinger HH, Pagon RA, et al, eds. GeneReviews. Seattle (WA): University of Washington, Seattle; 1993-2019. Available from: https://www.ncbi.nlm.nih.gov/books/NBK1305/
7. Ross CA, Aylward EH, Wild EJ, et al. Huntington Disease: Natural History, Biomarkers and Prospects for Therapeutics. Nat Rev Neurol 2014; 10:204–16.
8. The Huntington's Disease Collaborative Research Group. A Novel Gene Containing a Trinucleotide Repeat That is Expanded and Unstable on Huntington's Disease Chromosomes. Cell 1993; 72:971–983.
9. Frank S. Treatment of Huntington's Disease. Neurotherapeutics 2014; 11(1),153–160.
10. Taylor D, Paton C, Kapur S. The Maudsley Prescribing Guidelines in Psychiatry. 12th edition. NJ, United States: Wiley Blackwell: 2015.
11. Nasreddine ZS, Phillips NA, Bédirian V, et al. The Montreal Cognitive Assessment, MoCA: A Brief Screening Tool for Mild Cognitive Impairment. J Am Geriatr Soc 2005; 53 (4): 695–9.
12. Timman R, Claus H, Slingerland H, et al. Nature and Development of Huntington Disease in a Nursing Home Population: The Behavior Observation Scale Huntington (BOSH). Cogn Behav Neurol 2005; 18(4):215-22.
13. Low PA, Allsop JL, Halmagyi GM. Huntington's Chorea: The Rigid Form (Westphal Variant) Treated with Levodopa. Med J Aust 1974; 1: 393–394.
14. ClinicalTrials.gov. U.S. National Library of Medicine. https://www.clinicaltrials.gov Accessed on 7 December 2019.
15. Nahhas FA, Garbern J, Krajewski KM, et al. Juvenile Onset Huntington Disease Resulting From a Very Large Maternal Expansion. Am J Med Genet A 2005; 137A:328–31.
16. Semaka A, Kay C, Doty C, et al. CAG Size-Specific Risk Estimates for Intermediate Allele Repeat Instability in Huntington Disease. J Med Genet 2013; 50:696–703.