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Case report

Huntington's disease in a 31-year-old Ethiopian patient: A case report and a brief literature review

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Abstract

Background: *Huntington's disease is an inherited progressive neurodegenerative disorder characterized by choreiform movements, neuropsychiatric features, and cognitive impairment which leads to significant functional disability and caregiver burden. It is caused by a cytosine-adenine-guanine (CAG) trinucleotide repeat expansion in the huntingtin (HTT) gene on chromosome 4p and inherited in an autosomal-dominant pattern. We report the clinical and genetic characteristics of a patient with Huntington's disease with strong family history.*

Case report: *We report a case of a 31-year-old female with two years history of involuntary limb and trunk movements which were exacerbated by stress and disappeared during sleep. The symptoms gradually worsened with associated dysarthria, behavioral and mood abnormalities. She had a strong positive family history of similar illness with the involvement of both her siblings and three deceased family members. Her routine laboratory investigations were unremarkable. Brain magnetic resonance image (MRI) showed severe bilateral caudate and putaminal atrophy with ballooning of the adjacent lateral ventricle. Her genetic test identified a CAG repeat expansion of 48. The patient was started on Valproate and began follow-up at a Psychiatric unit as well, but she has only mild improvement in symptoms.*

Conclusion: *The present case highlights, the importance of genetics tests in the early diagnosis of Huntington's disease in resource-limited settings and multidisciplinary intervention to improve patient's quality of life.*

Keywords: *Huntington's disease; chorea; penetrance; family history; Ethiopia*
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Background

Huntington's disease (HD) is a rare neurodegenerative disease characterized by a range of symptoms that involve motor, cognitive, and psychiatric functions. It is an inherited disease that involves progressive degeneration of nerve cells in the brain, specifically within the basal ganglia. Typical onset occurs at the age of 30 to 40 years and the median survival time is 15 to 18 years after onset [1-3]. It occurs in all racial groups, and its prevalence varies widely with worldwide prevalence ranging from 0.4 -5.7 cases per 100,000 persons [4, 5]. There is no nationwide epidemiologic study on the disease in Ethiopia, but the one-year prevalence of chorea was reported to be 7.3% [6]. Huntington's disease is a "trinucleotide repeat" disorder, which is caused by an increase in the number of CAG repeats in the *HD* gene.

The number of triplet repeats determines penetrance with 40 or more repeats cause full penetrance and are associated with disease expression. It also exhibits genetic anticipation; earlier onset in successive generations within a pedigree. There is an inverse relationship between repeat length and age at onset [7,8]. At present, no treatment has been found to delay the onset of HD or to treat it effectively. As far as our knowledge is concerned, this is the first reported case of a family with Huntington's disease from Ethiopia.

Case report

Our patient is a 31-year-old female who came to the clinic with complaints of 2 years history of uncontrollable, dance-like involuntary limb and trunk movements. The movement was exacerbated by stress and disappeared during sleep.

The symptoms gradually worsened with difficulty of performing her daily tasks, like cleaning, cooking, and washing. She also had reduced voice, dysarthria, slow responses, and mild difficulty of swallowing. She confirmed mild depressive symptoms, but no history of psychotic symptoms. She had no significant problem remembering things, and no history of fits, visual impairment, body weakness, or sensory symptoms. No history of known chronic illnesses, drug use history, or substance use. She is currently divorced and has two children (10 and 5 years old) both didn't have any symptoms. She has a family history consistent with autosomal dominant inheritance. Her great-grandmother, grandmother, mother, and her two surviving siblings (her elder sister and younger brother) suffered from similar diseases, but her mother died at the age of around 50, and her grandmother died at the age of around 55 (Figure 1). The age of onset became earlier with each new generation. Her sister (now age 35) had severe psychiatric and choreiform symptoms making her bedridden and currently resides in a nursing home. Her younger brother had the rigid form of the illness with predominant dysarthria.

On physical examination, the patient was alert and oriented to person, place, and time. Her vital signs and systemic assessments were normal.

Her neurological examination revealed that she had severe dementia with MOCA-B of 18, delayed initiation of the saccade, difficulty with anti-saccadic tasks, and mild dysarthria.

The abnormal movement was characterized as fidgeting with the difficulty of sitting still, random choreiform movements involving the hands, legs, and face (involved forehead with grimacing, eyebrow wiggling, and perioral twitching), and some dystonic posturing of the right arm. She had motor impersistance with milkmaid grip and darting tongue. Blood work results were all normal. Brain MRI confirmed the presence of bilateral, severe atrophy of the caudate and putamen (Figures 2A and 2B). With the informed consent of the patient's family, genetic testing for HD was performed by polymerase chain reaction (PCR) analysis of the region encompassing the CAG repeat in exon 1 of the huntingtin gene (*HTT*) followed by fragment sizing through capillary electrophoresis. The results of diagnostic testing revealed a normal allele with 22 CAG repeats and expanded as well as an unstable polyglutamine-encoding allele with 45 CAG repeats. Due to financial reasons, we couldn't send genetic tests for her siblings. A neuropathological study wasn't done. It was not possible to get the first-line medications targeting her symptoms, due to financial and availability issues, so she was started on valproate and later Fluoxetine was added but, she had no significant symptom improvement.

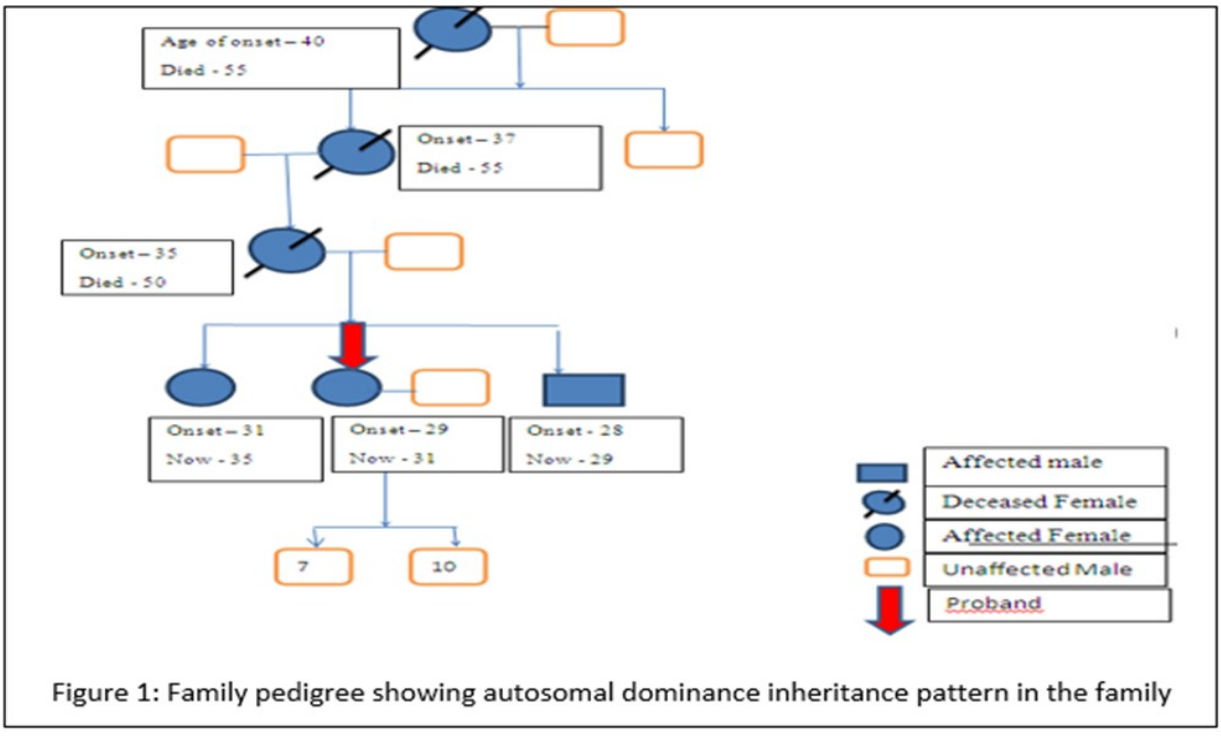

Figure 1: Family pedigree showing autosomal dominance inheritance pattern in the family

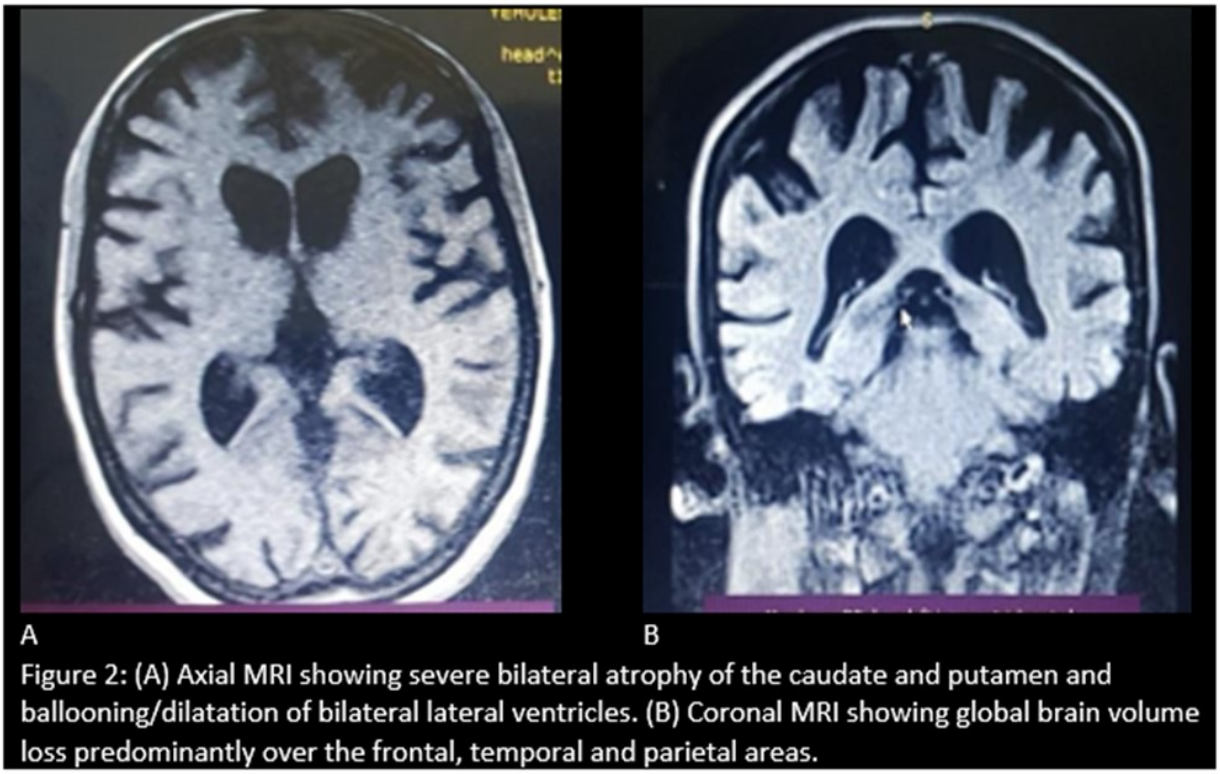

Figure 2: (A) Axial MRI showing severe bilateral atrophy of the caudate and putamen and ballooning/dilatation of bilateral lateral ventricles. (B) Coronal MRI showing global brain volume loss predominantly over the frontal, temporal and parietal areas.

Table 1: Summary of blood workups of the patient with Huntington's disease, on follow up at TASH, Addis Ababa, Ethiopia.

Investigation	Results
CBC	Normal
OFT	Normal
ELE	Normal
TFT	Normal

Abbreviations: CBC: complete blood count, OFT: organ function test, ELE: electrolytes, TFT: Thyroid function test, TASH: Tikur Anbessa Specialized Hospital

Discussion and conclusion

In this report, we describe a case of a patient diagnosed with Huntington's disease, a neurodegenerative condition caused by a dominantly inherited CAG trinucleotide repeat expansion in the huntingtin gene on chromosome 4.

The clinical information as well as the genetic results of our patient matched the typical HD presentation [2,9,12,14]. Our patient has expanded allele with 45 CAG repeats that cause full penetrance and is associated with disease expression.

Her presentation, the choreiform movements involving the hands, legs, especially the forehead with grimacing and eyebrow wiggling can be explained by the involvement of caudate and putamen. In addition, the presence of severe cognitive impairment and though mild, psychiatric symptoms are typical of adult-onset HD [7,8,13]. There was history of varying degrees of dementia and abnormal body movements in their mother, grandmother and great grandmother [figure 1]. Her surviving two siblings had also developed the symptoms. Her elder sister started to have symptoms at the age of 31, she was experiencing more severe psychiatric symptoms. She is now 35-year-old, overtime developed worsening of symptoms, became bed ridden and lives in nursing home. Apathy, irritability and depression are the most common and problematic neuropsychiatric symptoms in HD. An increased risk of suicide has been recognized since Huntington's seminal description of the condition. Non-motor features have greatest effect on functional independence and quality of life, so require recognition and management [3,9,15]. The younger sibling on the other hand had onset at the age of 26. His sister reported difficulties understanding his speech, and frequent throat clearing.

Motor symptoms such as rigidity and tremor were more prominent. In addition, examination revealed reduced voice, severe dysarthria, and mild choreiform movements. He also had mild depressive symptoms. Brain MRI revealed bilateral caudate atrophy. Due to financial reasons, a genetic test was not done for him. These types of HD are labeled as Westphal variants as rigidity is the dominant feature. However, based on previous studies, parkinsonian features are reported in juvenile cases, in which the father is the affected parent three to four times more frequently than is the mother and there is female preponderance and the age of onset is before 20 years of age [1,7,16].

Several other cases of HD have been reported but it is very rare to find cases of all siblings affected, similar to our presented cases. An earlier report from Oman had described three siblings (two girls and one boy) and their father who developed Huntington's disease. All the children developed the symptoms before the age of 12. Dystonia and severe & refractory seizures were the features in the children. the father had choreiform movements and emotional changes, but his symptoms occur after the symptoms appeared in his children [10, 11].

Though it has been suggested that the frequency of HD is probably low among people of African origin, documentation remains poor and evidence is inconclusive. A study in the South African population showed that the mean CAG-tract size in black South Africans was significantly lower than that in the Caucasian and mixed-race subpopulations, with most sizes falling in the range of 40 and 44 [4, 5,17]. HD is known to occur in most African countries, but short of confirmatory genetic tests, the epidemiological data is incomplete. Another study described that A new genetic variant- Huntington's disease-like 2 (HDL2)-occurring more frequently in blacks, and showed a tendency towards a later age of onset [18]. This serves as an important confirmation that HD can present in different forms, indicating the need to have a high index of suspicion in atypical presentations as well. Moreover, not many reports of three affected siblings and a parent are there in the literature[8, 11].

Because the disease inevitably affects the patient's closest ones, it is crucial to also provide adequate psychological and social support to all the family members.

When adequate multidisciplinary support is available, the diagnosis provides a possibility to ensure better elaborate support of quality of life for patients and their families

Ethics approval and consent to participate:

The authors' institution does not require ethical approval for the publication of a single case report.

Consent to publication:

The patient's family provided written informed consent for the publication of this report and any applicable materials and a copy of the consent form is accessible for review by the Editor-in-Chief of this journal.

Availability of data and materials:

All data sets on which the conclusions of the case report are based, are to be available as a medical record document and available from the corresponding author on reasonable request from the editors.

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Competing interests: The authors declare that they have no competing interests.

Authors' contributions:

BMG, MG, WG, BAA, and GZ were involved in the concept design for the manuscript, manuscript preparation, critical analysis, and revision. They were also involved in the management of the patient.

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References

1. Moser AD, Epping E, Espe-Pfeifer P, Martin E, Zhorne L, Mathews K, *et al.* Juvenile Huntington's disease. Neurodegener Dis Manag, 2017;7(5):307–15.
2. 2. Mayo clinic. Huntington's disease. Mayo foundation for Medical Education and Research; 2014, Available from https://www.mayoclinic.org/diseases-conditions/huntingtonsdisease/symptoms-causes/syc-20356117
3. Nance MA. Genetics of Huntington disease. Handb Clin Neurol. 2017; 144:3-14. doi: 10.1016/B978-0-12-801893-4.00001-8. PMID: 28947123
4. Pringsheim T, Wiltshire K, Day L, Dykeman J, Steeves T, Jette N. The incidence and prevalence of Huntington's disease: a systematic review and meta-analysis. Mov Disord. 2012 Aug;27(9):1083-91. doi: 10.1002/mds.25075. Epub 2012 Jun 12. PMID: 22692795.
5. Rawlins MD, Wexler NS, Wexler AR, Tabrizi SJ, Douglas I, Evans SJ, Smeeth L. The Prevalence of Huntington's Disease. Neuroepidemiology. 2016;46(2):144-53. doi: 10.1159/000443738. Epub 2016 Jan 30. PMID: 26824438

6. Bower, James Howard, Mesfine Teshome, Zenebe Melaku and Guta Zenebe. “Frequency of movement disorders in an Ethiopian university practice.” *Movement Disorders* 20 (2005)
7. Myers RH. Huntington's disease genetics. NeuroRx. 2004 Apr;1(2):255-62. doi: 10.1602/neurorx.1.2.255. PMID: 15717026; PMCID: PMC534940.
8. Ranen NG, Stine OC, Abbott MH, Sherr M, Codori AM, Franz ML, Chao NI, Chung AS, Pleasant N, Callahan C, et al. Anticipation and instability of IT-15 (CAG)n repeats in parent-offspring pairs with Huntington disease. Am J Hum Genet. 1995 Sep;57(3):593-602. PMID: 7668287; PMCID: PMC1801258.
9. McColgan P, Tabrizi SJ. Huntington's disease: a clinical review. Eur J Neurol. 2018 Jan;25(1):24-34. doi: 10.1111/ene.13413. Epub 2017 Sep 22. PMID: 28817209
10. Koul RL. Huntington's disease in all (three) siblings and their one parent. Neurol India. 2007 Jan-Mar;55(1):78-9. doi: 10.4103/0028-3886.30435. PMID: 17272908
11. Osborne JP, Munson P, Burman D. Huntington's chorea. Report of 3 cases and review of the literature. Arch Dis Child. 1982 Feb;57(2):99-103. doi: 10.1136/adc.57.2.99. PMID: 6461298; PMCID: PMC1627539
12. Lesinskienė S, Rojaka D, Praninskienė R, Morkūnienė A, Matulevičienė A, Utkus A. Juve ile Huntington's disease: two case reports and a review of the literature. J Med Case Rep. 2020 Oct 1;14(1):173. doi: 10.1186/s13256-020-02494-7. PMID: 32998776; PMCID: PMC7528384.
13. Roos RA. Huntington's disease: a clinical review. Orphanet J Rare Dis. 2010 Dec 20; 5:40. doi: 10.1186/1750-1172-5-40. PMID: 21171977; PMCID: PMC3022767.
14. Jevtic SD, Provias JP. Case report and literature review of Huntington disease with intermediate CAG expansion. BMJ Neurol Open. 2020 Feb 9;2(1):e000027. doi: 10.1136/bmjno-2019-000027. PMID: 33681777; PMCID: PMC7871728
15. Julie S Snowden, The Neuropsychology of Huntington's Disease, *Archives of Clinical Neuropsychology*, Volume 32, Issue 7, November 2017, Pages 876–887
16. Foroud T, Gray J, Ivashina J, Conneally PM. Differences in duration of Huntington's disease based on age at onset. J Neurol Neurosurg Psychiatry. 1999 Jan;66(1):52-6. doi: 10.1136/jnnp.66.1.52. PMID: 9886451; PMCID: PMC1736160.
17. Eur J Hum Genet. Huntington disease in the South African population occurs on diverse and ethnically distinct genetic haplotypes, 2013 Oct; 21(10): 1120–1127
18. Magazi DS, Krause A, Bonev V, Moagi M, Iqbal Z, Dludla M, van der Meyden CH. Huntington's disease: genetic heterogeneity in black African patients. S Afr Med J. 2008 Mar;98(3):200-3. PMID: 18350222.