ejpmr, 2023, 10(9), 541-543

SJIF Impact Factor 6.222

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Case Study

ISSN 2394-3211

EJPMR

PSYCHIATRIC MANIFESTATIONS OF HUNTINGTON DISEASE: A CASE REPORT

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Article Received on 25/06/2023 **Article Revised on 15/07/2023** **Article Accepted on 05/08/2023**

ABSTRACT

Huntington disease is a rare chronic disorder of neurodegenerative nature in which cognitive and behavioural symptoms are seen along with choreatic movements. Main aetiology is unstable CAG repeats expansions in the geneIT15 which encrypts Huntingtin. It's mainly known for progressive motor and cognitive symptoms but also presents with psychiatric symptoms which are underrecognized. In recent years the neuropsychiatric symptoms have attracted the attention which are widely prevalent in Huntington disease. However, these psychiatric symptoms are still mistaken as psychiatric illness mainly in prodromal phase of illness which presents with depression, impulsivity and aggression. Clinical picture of patient is confused by this dilemma which leads to diagnostic delay leading to prognostic worsening and deteriorated quality of life. We present a case who presented with neuropsychiatric symptoms to start with. It helps to elicit the need for recognising early nonspecific psychiatric symptoms like irritability and depression along with other psychotic symptoms which do not respond typically to treatment in early presentation and also in progression of neurodegenerative disease like Huntington's disease.

INTRODUCTION

Huntington disease (HD) is an autosomal dominant disorder of neurodegenerative nature which shows motor symptoms in form of involuntary choreatic movements along with behavioural and cognitive symptoms.[1] It's main aetiology is mutation in Huntingtin gene which occurs due to trinucleotide repeats of cytosine, adenine and guanine (CAG) in short arm of chromosome 4.[2,3] Neurodegeneration is mainly due to unusually long extension of polyglutamine in HTT protein due to above said mutation.[4,5] Patients commonly have HTT alleles with CAG repeats between 36 to 55. Juvenile onset HD (onset before 20 years of age) have CAG repeats more than 60(1) which shows an inverse association among the age of onset and length of repeats. As far as onset is considered there are mainly three factors which have been associated with increased risk: the CAG repeats in the HTT gene, instability of CAG, genetic modifiers.[6] Degeneration is mainly seen in neurons at putamen, caudate and cerebral cortex. The motor symptom in form of chorea is indirectly due to degeneration in medium spiny neurons containing enkephalin in basal ganglia. Multiple hypothesis has been explained in the pathogenesis: 1) Aggregates in neurons, 2) Dysregulation in transcription, 3) Dysfunction in mitochondria, 4) Excitotoxicity, 5) Dysfunction in axonal transport and synapse.[5] It commonly affects patients between 30-50 years of age. Classic symptom cluster consist of cognitive, motor and psychiatric manifestations whereas other symptoms like sleep problems, weight loss and disturbances in autonomic nervous system are seen less commonly. Motor symptoms begin in distal muscles and gradually progress to axial and proximal muscles in form of involuntary choeatic movements which are progressive in nature. These symptoms start as hyperkinetic movements mainly chorea and progress to hypokinesia and dystonia in later stage. These lead to deterioration in quality of life. Along with these other neuropsychiatric and behavioral symptoms also present in early stage sometimes even before motor symptoms. Patients present with attention problems, irritability and impulsive behaviour which progress to emotional blunting and lack of drive and creativity along with cognitive decline. These symptoms are mainly owed to the fronto-striatal degeneration. Patients can also present with depression psychotic symptoms and even suicidal tendencies. In cognitive domain mainly executive functions leading problems in planning and multitasking which finally lead to dementia of subcortical type.[5] Clinically it can be diagnosed in a patient when there are classical motor and behavioural disturbances along with positive history of disease in family and confirmation can be done via genetic testing. As far as investigations are concerned Magnetic resonance imaging (MRI) is useful for the diagnosis before clinical manifestation appear; however, the gold standard is genetic evaluation. Which includes testing of repeat size of the CAG. 40 or more repeats of alleles is known to be associated with

clinical disease. Only treatment options available are mainly symptomatic like vesicular monoamine transporter inhibitors like tetrabenazine, antipsychotics and antidepressants which makes it a presently incurable disease.[4,7-9]

CASE REPORT

We have presented a case of 38 years old married male presenting with psychotic symptoms along with cognitive decline and behavioural symptoms was brought to psychiatry out-patient setting. His symptoms started 12 years prior to presentation characterised by agitation, delusion of persecution, delusion of infidelity, hallucinatory behaviour and suicidal attempt with insidious onset and continuous and progressive course. Initially, he responded to antipsychotic medications for 4 years but over the course his condition deteriorated. As the disease progresses, he developed involuntary rapid jerking motor movements. Patient was admitted in the psychiatry ward in view of potential harm to others and new set of symptoms characterized by involuntary rapid jerking motor movements. There was no family history of similar complaints and no history of any substance use. He was started on T. olanzapine 7.5mg in divided doses, T. Divalproex sodium 500mg in divided doses and T. clonazepam 4mg in divided doses with provisional diagnosis of unspecified non-organic psychosis (F29-ICD 10) with possibility of tardive dyskinesia.

Clinical examination revealed normal vital signs and patient was conscious and oriented. Neurological examination revealed choreiform movements, incomprehensible speech, absent reflexes, inability to perform complex motor tasks. Neurological consultation was taken.

Laboratory investigations showed low Vitamin B12 levels (183 pg/ml) and low Vitamin D levels (6.90 ng/ml). The remaining laboratory tests including complete hemogram, glucose, electrolytes, liver function and kidney function tests were within normal range. Magnetic Resonance Imaging of brain showed diffuse cerebral atrophy with bilateral atrophy of head caudate and putamen. PCR fragment analysis detected presence of 17 CAG repeats in one allele and 44 repeats in the other allele of HUNTINGTON gene. At this point, based on history, physical examination and laboratory findings diagnosis of Huntington disease was made. T. haloperidol 0.75mg in divided doses was added and gradually increased to 1.25mg in divided doses, T. Tetrabenazine 25mg in divided doses was also. T. olanzapine was increased to 20mg in divided doses. Patient showed 20% improvement in behavioural symptoms with the treatment.

DISCUSSION

George Huntington described Huntington Disease in 1872 and didn't report even a single case which presented with motor symptoms before third or fourth decade of life. Earlier onset of symptoms can be seen if higher number of CAG repeats are present. Classically, neuropsychiatric abnormalities often come first followed by neurological signs as seen in index case. Major therapeutic hurdle are Psychotic symptoms which are rare and often resistant to treatment. Presence of psychotic symptoms can be linked to young age of onset and less CAG repeats in HTT gene. Our case demonstrates the presence of psychiatric manifestations before motor symptoms. Index case validates the massive role of neuroimaging in patients presenting with a psychosis and disturbance in executive functions along with motor symptoms. We detected diffuse cerebral atrophy with atrophy of bilateral caudate head and putamen in MRI Brain. For confirmation of the diagnosis, PCR fragment analysis was done which showed presence of 17 CAG repeats in one allele and 44 repeats in other allele of Huntington gene. Patient showed approximately 20% improvement with the treatment and family members were counselled about the condition.

CONCLUSION

The presented case adds to the suggesting a clinical overlap in symptomatology and presentation of Huntington's disease and psychotic disorders. The neuropsychiatric symptoms have attracted the attention which are widely prevalent in Huntington disease. However, these psychiatric symptoms are still mistaken as psychiatric illness mainly in prodromal phase of illness which presents with depression, impulsivity and aggression. Clinical picture of patient is confused by this dilemma which leads to diagnostic delay leading to prognostic worsening and deteriorated quality of life. This case helps to elicit the need for recognising early nonspecific psychiatric symptoms like irritability and depression along with other psychotic symptoms which do not respond typically to treatment in early presentation and also in progression of neurodegenerative disease like Huntington's disease.

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