CASE REPORT

DIAGNOSTIC DIFFICULTIES IN A PATIENT WITH HUNTINGTON DISEASE WITH SCHIZOPHRENIA LIKE PSYCHOSIS – A CASE REPORT

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Abstract

Objective: **Psychotic symptoms could be first presentation of neurological disorder before the appearance of cognitive and motor disturbance. This can lead to diagnosis of psychiatric illness in early phase and later appearance of motor disturbances could be seen as a side effect of anti-psychotic medications, leading to the delayed diagnosis of primary neurological disorder. The objective of this case to present a patient diagnosed initially with schizophrenia but careful consideration of pattern of motor abnormality and cognitive decline resulted in final diagnosis of Huntington disease behind schizophrenia.** ***Methods:*** **A patient of schizophrenia with cognitive decline and motor disturbance was investigated for the possibility of an undiagnosed neurological disorder.** ***Results:*** **Decline in patient's cognitive functions appeared to be rapid and severe as compared to relatively short duration of diagnosed psychiatric illness. Also motor abnormality of ataxia and choroeathtoid movements after improvement in features suggestive of antipsychotic induced parkinsonism, ie. bradykinesia, rigidity and tremors do not appear to be explained by psychotic illness only. Later, genetic testing for CAG trinucleotide repeats resulted in a primary diagnosis of Huntington disease.** ***Conclusion:*** **The index case suggests the need for analysis of motor abnormality and cognitive decline in a patient with a diagnosis of psychotic illness before attributing them to be the consequence of psychiatric illness. Whenever there is suspicion, further assessment for a neurological disorder should be performed, which may provide the opportunity for early diagnosis and accurate treatment of both entities.** ***ASEAN Journal of Psychiatry, Vol. 17 (1): January – June 2016: XX XX.***

Keywords: Antipsychotic, Huntington Disease, Schizophrenia

Introduction

Movement disturbances are common side effects of antipsychotic medication. Although risk of this side effect with atypical antipsychotic is less as compared to typical antipsychotic but risk is not completely obsolete. These side effects could be in the form of the features suggestive of drug induced Parkinsonism like bradykinesia, tremors and rigidity, or it could be in form of dystonia, akathasia and tardive dyskinesia. Proposed mechanism behind these side effects is the blockade of dopaminergic pathways in basal ganglia and hyperactivity of postsynaptic cholinergic neurons [1, 2]. Huntington disease may also present with psychotic symptoms first before motor disturbances begin. In such cases, these motor abnormalities could be seen as a side effect of antipsychotic medication

rather than the manifestation of primary neurological disorder, which remains undiagnosed.

Huntington's disease (HD) is neurodegenerative disorder with autosomal dominantly inheritance, which manifests in form of choreic movements, cognitive decline and psychiatric symptoms. These symptoms usually appear in the fourth to fifth decade [3, 4, 5]. Besides this abnormal involuntary movement such as chorea, other abnormalities of voluntary movement may also occur like bradykinesia, rigidity, and gait disturbances. Cognitive decline in form of loss of cognitive speed, flexibility and concentration is also seen [6]. The most common behavioural abnormality is personality changes, and others are depression, schizophrenia-like psychosis with apathy, irritability and aggressive manifestation [7, 8]. Psychosis is more commonly seen in an early-onset form of Huntington's disease [9].

This case study presents a male patient who developed schizophrenia-like psychosis in early forties and diagnosed initially with schizophrenia but further assessment for motor abnormality and cognitive decline, which were initially seen as a consequence of illness and treatment side effects resulted in final diagnosis of Huntington disease behind psychotic symptoms.

Case report

Thirty-two years-old male, unemployed, single brought by his uncle for treatment of his psychiatric illness. His illness started with suspiciousness and errors in records prepared by him. Later, he also developed hallucinations and anger outbursts. These symptoms resulted in impairment on both occupational and social functioning. He was initially treated with trifluoperazine. However, in view of inadequate improvement, antipsychotic was changed to risperidone up to 8 mg per day, which resulted in adequate improvement in psychotic symptoms. During this treatment, patient developed rigidity and bradykinesia, which were considered to be drug induced Parkinsonism features, and they improved after addition of trihexyphenidyl up to 4 mg per day. Over a period of one year, patient developed severe cognitive decline as compared to his previous level of functioning. His premorbid level of functioning was good. He attended until his post graduates from education in commerce and was working as account assistant in a firm. He could do all tasks related to his work like tax calculation, keeping record of transaction, auditing, analysis of financial records, writing and reporting. Now patient was not able to do even simple mathematical calculation and similarly his social functioning also declined to much lower level. He also developed abnormality in gait and involuntary movement, dominate on the left side.

At this point, of time, patient presented for consultation in AIIMS (All India Institute of Medical Sciences), Jodhpur for detailed assessment. Psychological examination revealed minimal psychotic symptoms and no episodes of an anger outburst. Assessment for cognitive functions showed impairment in attention, intelligence, memory and visuo-motor coordination and also deficits in social skills. Neurologic examination revealed choreoathetoid involutory movements, involving trunk, shoulder and lower limb, dominantly lateralized in the left with obvious difficulties of movement and gait with no features of rigidity, tremors and bradykinesia. Medical records showed no abnormality in investigations done so far e.g. haematology, biochemistry, and Electro cardiogram. Electroencephalography, Computerized Tomography (CT) and Magnetic Resonance Imaging (MRI) of the brain showed no abnormality.

Family history revealed no similar illness in patient siblings and relatives on the paternal side. Mother died at early age of 50 years after suffered with similar illness for 10 years. Because of prevailing social stigma in local community, mother was separated from patient and his father after one year of onset of illness and lost contact with family. Whether any other relative on the maternal side also affected is not known because the tendency of her families not to reveal any information about a mentally ill person due to stigma and fear about effect on social image of family in society. Therefore, Family history on the maternal side was not completely available.

Although schizophrenia itself causes a cognitive decline specially after long duration [10, 11] but to such a lower level of decline in cognitive function as compared to his qualification and previous functioning as an accountant over a relatively short period of one year does not appear to be completely explained by his mental illness. Furthermore, motor abnormalities of ataxia and choreoathetoid movements were also not suggestive of antipsychotic induced parkinsonism (bradykinesia, rigidity and tremors). Considering above, family has been explained about the possibility of a primary neurological disorder, need for genotyping test and neurological liaison. Later, definitive diagnosis of Huntington's disease was confirmed by genetic validation of CAG trinucleotide repeat in size of 18/47 and patient was managed by closed liaison of both speciality psychiatry and neurology.

Discussion

In Huntington's disease, genetic defect is localized on the short end of chromosome 4 in form of expansion and instability of polymorphic trinucleotide repeat (CAG repeat) in gene IT15 [12]. Higher number of CAG-repeats in the gene for HD is correlated with earlier age of onset of illness [13]. The genotyping report of expanded allele with 47 CAG repeats (and unaffected allele with 18 repeats) in our patient confirm the diagnosis of Huntington's disease. Mutation of HD gene consisted of polyglutamine strech within the N-terminus of its protein product huntingtin (htt) with the resulting neuropathological features of formation of intraneuronal aggregates containing N-terminal fragments of mutated huntingtin and progressive degeneration of striatal neurons (selective atrophy of medium spiny neurons in the caudate and putamen) [12, 14].

Deficit in memory retrieval in HD is probably due to the decrease in cholinergic activity, and psychotic symptoms are considered to be due to the loss of inhibitory GABAergic function and an increase in dopamine turnover, because of selective survival of type II spiny interneurons [15]. Only few cases reported in literature, where in schizophrenia like symptoms along with the rapid cognitive decline appeared before in Huntington's disease long before occurred [16, 17, 18 , 19].

Our patient developed psychotic symptoms along with the rapid cognitive decline before the onset of neurologic manifestations. It is difficult to find whether motor abnormalities appeared as side effects of antipsychotic and later became the first manifestation of motor disturbances due to Huntington's disease. The more frequent occurrence of schizophrenia among HD carriers than in the general population could be explained by the co-occurrence of the HD gene and pro-schizophrenia gene or group of genes and also HD gene lowering the threshold for an onset of schizophrenic phenotype [19]. Irrespective of possible theories behind the relationship between schizophrenia and Huntington disease, need to be early diagnose and accurate treatment of both entities is very obvious with consideration of appropriate medication, which would have no negative consequences on the course and the treatment of both disorders.

Conclusion

The diagnostic difficulties we faced in our case were whether schizophrenia is a genuine entity or just a part of primary Huntington's disease and motor side effects were antipsychotic induced or manifestation of Huntington Disease. However, this case emphasizes the need to have caution while treating a patient with schizophrenia like illness and attributing cognitive decline and motor abnormalities to psychotic illness and its treatment antipsychotic medication only. We need to be aware that neurological disorder like Huntington disease could present first with psychotic symptoms before the motor abnormality and so treating physician has to exercise care regarding therapy in order to avoid possible complications.

References

1. Folnegović-Šmalc V, Jukić V, Kozumplik O, Uzun S,Mimica N. Side effect profile of atypical antipsychotic agents and comparation to conventional antipsychotics. Soc Psihijat 2003;31:19-24.

2. Uzun S, Kozumplik O, Mimica N, Folnegović-Šmalc ,V. Nuspojave psihofarmaka, Zagreb: Medicinska aklada i Psihijatrijska bolnica Vrapče; 2005.

3. Watt DC, Seller A. A clinico-genetic study of psychiatric disorder in Huntington's chorea. Psychol Med Suppl 1993;23:1-46.

4. MacMillan J, Snell R, Tyler A, Houlihan G, Fenton I, Cheadle J, Lazarou L, Shaw D, Harper P. Molecular analysis and clinical correlations of the Huntington's disease mutation. Lancet 1993;342:954-958.

5. Quinn N, Schrag A. Huntington's disease and other choreas. J Neurol 1998;245:709-716.

6. Hayden MR. Huntington's chorea. London: Springer-Verlag, 1981.

7. Schiwach R. Psychopatology in Huntington's disease patients. Acta Psychiatr Scand 1994;90:241-246.

8. Cummings JL. Behavioural and psychiatric symptoms associated with Huntington's disease. Advances in Neurology 1995;65:179-186.

9. Rosenblatt A, Leroi I. Neuropsychiatry of Huntington's disease and other basal ganglia disorders. Psychosomatics 2000;41:24-30.

10. Bowie CR, Harvey PD. Cognitive deficits and functional outcome in schizophrenia. Neuropsychiatric Disease and Treatment. 2006;2(4):531-536.

11. Y. Vishnu Gopal, Hannele Variend, First-episode schizophrenia: review of cognitive deficits and cognitive remediation, Advances in Psychiatric Treatment Jan 2005, 11 (1) 38-44.

12. 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.

13. Andrew SE, Goldberg YP, Kremer B et al. The relationship between trinucleotide (CAG) repeat length and clinical features of Huntington disease. Nat Genet 1993;4:398-403.

14. DiFiglia M et al. Aggregation of huntingtin in neuronal intranuclear inclusions and dystrophic neurites in brain. Science1997;277:1990-1993.

15. Amann B, Sterr A, Thoma H, Messer T, Kapfhammer HP, Grunze H: Psychopathological changes preceding motor symptoms in Huntington's disease: A report on four cases. World J Biol Psychiatry 2000; 1:55-58.

16. Ljiljana Radanović-Grgurić1, Anamarija Petek1, Davor Laufer1, Oliver Koić1, Branko Radanović2 & Pavo Filaković1 , Psychiatria Danubina, 2009; Vol. 21, No. 4: 575–578.

17. Lovestone S, Hodgson S, Sham P, Differ A-M, Levy R. Familial presentation of Huntington's disease.J Med Genet 1996;33:128-131.

18. Tsuang D, DiGiacomo L, Lipe H, Bird TD. Familial aggregation of schizophrenia-like symptoms in Huntington's disease. Am J Med Genet 1998;81:323-327.

19. Tsuang D, Almqvist EW, Lipe H, Strgar F, DiGiacomo L, Hoff D, Eugenio C, Hayden MR, Bird TD. Familial aggregation on psychotic symptoms in Huntington's disease. Am J Psychiatry 2000;157:1955-1959.

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