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PREMORBID COMBAT RELATED PTSD IN HUNTINGTON'S DISEASE
Case report

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SUMMARY

Huntington's disease (HD) is a neurodegenerative, autosomal dominant disease that manifests with a triad of symptom clusters including movement disorder, cognitive impairment and psychiatric symptoms.

We present a patient with HD who, prior to developing neurological signs and symptoms, had been exposed to war trauma and had developed posttraumatic stress disorder. Fifteen years later he manifested with dysarthria, difficulties with swallowing and involuntary movement. What brought him to psychiatrist was a heteroanamnestically noticed change in personality with irritable mood, impulsivity, aggressive outbursts in behavior and delusional ideation. Therapy was stared with haloperidol, but patient developed severe extrapiramidal side effects. Subsequent treatment with olanzapine, diazepam and omega 3 fatty acids lead to mood stabilization and better impulse control with even some improvement in motoric symptoms.

To our knowledge, this is the first case report on combat related PTSD as psychiatric disorder manifested prior to HD. We discuss a possible influence of psychological stress disorder on severity of psychiatric symptoms in the HD. The importance of personalized approach in both psychopharmacological and psychotherapeutical treatment of patients with HD is emphasized. If the influence of environmental stress on the psychiatric phenotype of the disease should be confirmed by clinical trials and further studies, both screening methods and interventions aimed to reduce psychological stress in carriers of Huntington gene could be considered.

Key words: *Huntington's disease – posttraumatic stress disorder - psychopharmacology*

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INTRODUCTION

Huntington's disease (HD) is an autosomal dominant inherited neurodegenerative disorder that results from an unstable expansion of the trinucleotide repeat cytosine-adenine- guanine (CAG) of the gene IT-15 on chromosome 4p16.3. It is characterized by movement disorders (usually chorea), cognitive impairment (resulting in dementia) and psychiatric disorders. Symptoms typically begin in the fourth decade of life and result in progressive deterioration in functional capacity and independence (Paulsen et al. 2001)

A prevalence of psychiatric morbidity in HD ranges from 35% to over 90%, depending on the study design. (Paulsen et al. 2001). Psychiatric disorders include affective disorders, schizophrenia-like states, behavioral and personality disorders, obsessive compulsive disorder, irritability and aggressive behavior (van Duijn et al. 2007). Psychiatric symptoms of HD constitute a major burden to patients and families, and are associated with more rapid functional deterioration (Marder et al. 2000) and greater disability (Nehl & Paulsen 2004).

Despite this fact, psychiatric aspects of the disease have not been comprehensively investigated yet. What has been proven is that unlike neurological and cognitive symptoms, psychiatric signs and symptoms are unrelated to the length of CAG repeats (Vassos et al. 2008). It is assumed that environmental factors play a role in the onset and spectrum of psychiatric symptoms.

We present a patient with clinically expressed HD who's premorbid environmental factors seem to have played a significant role a role in the onset and spectrum of psychiatric symptoms of the disease. Our aim is to underline the significance of investigating and understanding prior personal experiences and life context, thus using hollistic approach and creativity when planning psychopharmacological and psychotherapeutical treatment (Jakovljević 2009) of patients with HD and prominent psychiatric symptoms.

CASE REPORT

A 49- year-old patient was admitted to our Clinic with paranoid dellusions and aggressive behavior. This was his second psychiatric hospitalization, the first being 15 years before when he was treated from war related posttraumatic stress disorder (PTSD). He was the only member of his family exposed to combat trauma. At the time of the first psychiatric treatment the patient exhibited all of the cluster symptoms of PTSD. He was treated with a serotonin reuptake inhibitor, a mood stabilizer and a benzodiazepine. Concurrently, he received psychological councelling. With good support from his family and regular treatment, he was in good remission of PTSD symptoms.

Three years prior to current hospitalization, the patient started having slightly dysarthric and slowed speech, but didn't see a specialist for his symptoms. Couple of months prior to second psychiatric hospitalization his wife noticed a prominent change in his personality and behavior. His mood was unstable, irritable, he made some impulsive decisions regarding his finances, had concentration and memory impairment.

While taking a medical history, abnormal involuntary movements (chorea and tremor) were observed. Neurological examination revealed mild athetotic movements of the torso, slightly dysarthric and slowed speech and ataxia. Muscle reflexes were increased, partly cloniform. The Mini-Mental State Examination was preformed and the score was 22 of 30 points, suggestive of mild cognitive impairment. The MRI scan showed an atrophy of the cortex and the medulla.

The family history revealed that patient's mother, uncle, and two aunts from mother's side have had neurological manifestations consistent with Huntington's disease. In the uncle's case the illness was genetically confirmed. Consequently, a molecular genetic testing was performed.

Genetic analysis of our patient and his two asymptomatic brothers was carried out. The DNA analysis identified an abnormal IT 15 allele with 43 CAG repeats and a normal IT 15 allele with 16 CAG repeats in our patients. His two years younger brother was found to have an abnormal IT 15 allele with 44 CAG repeats and a normal IT 15 allele with 15 CAG repeats in. Third brother was not identified as a carrier of the mutation. The results indicated that the patient and his younger brother have the Huntington's disease CAG mutation with our patient already affected with the disease, and his brother predisposed to developing clinical symptoms. The brother was found free of psychiatric and cognitive symptoms with mild, HD non-specifical neurological signs.

Treatment was started with haloperidol (10 mg/day) for psychotic symptoms, but the patient developed extrapyramidal side effects. Combined treatment with olanzapine (20 mg/day), omega 3 fatty acids and diazepam lead to a satisfactory control of psychiatric symptoms. In addition to pharmacotherapy, patient has also received individual supportive psychotherapy. Three weeks after admission he was no longer delusional, his mood stabilized and even reported having fewer problems with swallowing. He was discharged and now remains in out hospital treatment, so far with good remission of psychiatric symptoms.

DISCUSSION

We presented a patient who has been exposed to combat trauma and developed posttraumatic stress disorder fifteen years prior to the onset of the disease. His two years younger brother, who is a verified carrier of the disease and has exactly the same number of CAG repeats, has not been involved in war actions and so far is free of psychiatric symptoms with only mild neurological signs.

In attempt to explain the underlying cause of different clinical presentation and severity of psychiatric aspects in HD prior studies had given inconclusive results (Vassos et al. 2008). Since the length of CAG repeats is found to be unrelated to psychiatric clinical presentation, environmental and other genetic factors are suggested to be the focus of future studies (Vassos et al. 2008). This case reports on the specific premorbid environmental factor, namely posttraumatic stress disorder. Mutual interplay between PTSD and psychiatric symptoms of Huntigton disease are disscussed: 1) premorbid stress disorder might influence the onset and severity of psychiatric symptoms later on in the disease; 2) a mutation carrier might be more sensitive to developing PTSD after exposure to combat.

It is known that psychological traumatic experience activates HPA axis leading to hypersecretion of glucocorticoids that regulate neuronal survival and neurogenesis (Herbert at al. 2006, Sapolsky et al. 2000). It could be that due to neuroendocrinological immbalance triggered by PTSD, our patient is more vulnerable to developing more prominent psychiatric symptoms within HD than his brother unaffected by psychological war trauma. Point prevalence of combat-related PTSD in studies of US military veterans ranges from approximately 2% to 17% (Richardson et al. 2010). Due to reported genetic predisposition to developing psychiatric disorders in of huntingtin mutation carriers (Duff et al. 2007), our patient might have been more sensitive to developing PTSD after exposure to combat.

Clearly, further rigorous studies are needed to clarify the complex interaction between genes and environment in creating diverse psychiatric syndromes in HD. To our knowledge, this is the first case report on combat related PTSD as psychiatric disorder manifested prior to HD.

We reported a positive effect of olanzapine and unsaturated fatty acids on the psychiatric and even motoric symptoms of HD. This is in accordance with several studies and case reports that have shown possitive effects of olanzapine (Bogelman et al. 2001; Squitieri et al. 2001, Grove et al. 2000, Dipple 1999, Etchebehere et al. 1999) and unsaturated fatty acids (Puri et al. 2005) on chorea and HD-psychosis. However, no double-blind, randomised, placebo-controlled trials have been conducted primary to assess symptomatic control of psychiatric or cognitive symproms of HD (Mestre et al. 2009). Further reaseach is necessary to determine a beneficial effect of these drugs on the psychiatric aspects of HD.

CONCLUSION

With this case report we wish to emphasize the significance of environmental influences and thus personalized approach in both psychopharmacological

and psychotherapeutical treatment of patients with HD and prominent psychiatric symptoms. When evaluating these patients, clinicians are advised to take a thorough family and personal history, with special consideration on examination of psychological stressful events. If the influence of environmental stress on the psychiatric phenotype of the disease should be confirmed by clinical trials and further studies, psychological interventions aimed to reduce stress, improve coping skills and defense mechanisms could be planned in individuals genetically predisposed to HD.

REFERENCES

1. *Bogelman G, Hirschmann S & Modai I: Olanzapine and Huntington's disease. J Clin Psychopharmacol 2001; 21:245–246.*
2. *Dipple HC: The use of olanzapine for movement disorder in Huntington's disease:a first case report. J Neurol Neurosurg Psychiatry 1999; 67:123–124.*
3. *Duff K, Paulsen JS, Beglinger LJ et al: Psychiatric Symptoms in Huntington's Disease before Diagnosis: The Predict-HD Study. Biol Psychiatry 2007; 62:1341-1346.*
4. *Etchebehere EC, Lima MC, Passos W, Maciel Junior JA, Santos AO, Ramos CD & Camargo EE: Brain SPECT imaging in Huntington's disease before and after therapy with olanzapine. Case report. Arq Neuropsiquiatr 1999; 57:863–866.*
5. *Grove VE, Jr,Quintanilla J & DeVaney GT: Improvement of Huntington's disease with olanzapine and valproate. New Engl J Med 2000; 343:973–974.*
6. *Herbert J, Goodyer IM, Grossman AB, Hastings MH, de Kloet ER, Lightman SL, et al. Do corticosteroids damage the brain? J Neuroendocrinol 2006;18:393–411.*
7. *Jakovljević M: The side effects of psychopharmacotherapy: conceptual, explanatory, ethical and moral issues – creative psychopharmacology instead of toxic psychiatry. Psychiatria Danubina 2009; 21:86-90.*
8. *Marder KS, Zhao H, Myers RH, et al.: Rate of functional decline in Huntington's disease: Huntington Study Group. Neurology 2000; 54:452–458.*
9. *Mestre T, Ferreira J, Coelho MM, Rosa M & Sampaio C: Therapeutic interventions for symptomatic treatment in Huntington's disease. Cochrane Database Syst Rev 2009;(3):CD006456.*
10. *Nehl C, Paulsen JS, et al: Cognitive and psychiatric aspects of Huntington disease contribute to functional capacity. J Nerv Mental Dis 2004;192:72–74.*
11. *Paulsen JS, Ready RE, Hamilton JM, Mega MS & Cummings JL: Neuropsychiatric aspects of Huntington's disease. Journal of Neurology. Neurosurgery and Psychiatry 2001;71:310–4.*
12. *Puri BK, Leavitt BR, Hayden MR, Ross CA, Rosenblatt A, Greenamyre JT, Hersch S, Vaddadi KS, Sword A, Horrobin DF, Manku M & Murck H: Ethyl- EPA in Huntington disease: a double-blind, randomized, placebo-controlled trial. Neurology 2005;65: 286–292.*
13. *Richardson LK, Frueh BC & AciernoR: Prevalence estimates of combat-related post-traumatic stress disorder: critical review. Australian and New Zealand Journal of Psychiatry 2010; 44:4–19.*
14. *Sapolsky RM., Romero LM & Munck AU: How do glucocorticoids influence stress responses? Integrating permissive, suppressive, stimulatory, and preparative actions, Endocr. Rev. 2000; 21:55–89.*
15. *Squitieri F, Cannella M, Piorcellini A, Brusa L, Simonelli M & Ruggieri S: Short-term effects of olanzapine in Huntington disease. Neuropsychiatry Neuropsychol Behav Neurol 2001; 14:69–72.*
16. *Van Duijn E, Kingma EM, Van der Mast RC: Psychopathology in Verified Huntington's Disease Gene Carriers. The Journal of Neuropsychiatry and Clinical Neurosciences 2007; 19:441–448.*
17. *Vassos E, Panas M, Kladi A & Vassilopoulos D: Effect of CAG repeat length on psychiatric disorders in Huntington's disease. Journal of Psychiatric Research 2008; 42: 544–549.*

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