Early Psychiatric Manifestations of Huntington's Disease: More Than Just a Movement Disorder

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ABSTRACT

Huntington's disease (HD), a neurodegenerative condition of the central nervous system, poses a major challenge for clinicians. The clinical presentation is variable and consists of cognitive, psychiatric and motor symptoms. The psychiatric manifestations often appear many years before the movement disorder. Lack of recognition of the psychiatric mani-festations may lead to delays in diagnosis and multidisciplinary interventions. The aim of this article is to highlight the psychiatric aspects of HD, particularly focusing on the early presenta-tion. Two cases of HD with prominent psychiatric symptoms are used to illustrate the preva-lence of these aspects of the disease. In the absence of treatment directly influencing the course of HD, psychiatrists remain central to the multidisciplinary team diagnosing and treating this debilitating condition.

Huntington's disease (HD), which was first described by George Huntington in 1872, is a neurodegenerative disorder which presents as a syndrome of motor abnormalities, cognitive decline and neuropsychiatric symptoms. HD has an autosomal dominant pattern of in-heritance with complete penetrance. The gene for the disease was identified in March, 1993 (1,2), enabling predictive and prenatal testing for those at risk of inheriting the disease (3). The disease affects 5 to 8 per 100,000 in North America (4,5). The average age of onset is be-tween 35 and 40 years of age, however, juve-nile forms of the disease can result in symp-toms as early as age 4 (6).

The course of HD is progressive and is marked by increasing motor difficulties, in-cluding chorea, dystonia and athetosis, as well as bradykinesia, dysarthria, dysphagia, and urinary incontinence (7). Death results an average of 17 years after onset of the disease and is caused by cardiac and pulmonary complica-tions, suicide, nutritional deficiencies and self-destructive behaviours (8).

The HD gene (referred to as IT15), found on the short arm of chromosome 4, partly consists of an unstable triplicate repeat (CAG) sequence. The number of triplicate repeats is higher (more than 38 repeats) in those with HD than in the normal population, which has 11-38 repeats. The mRNA transcribed from the HD gene can be found in all organs of an affected person and codes for a protein which has been called "huntingtin". The relationship between this protein and the development of the pathological changes in HD is still unclear, although several studies have attempted to define the neurophysiology and neuropathology. Neuropathology reveals early and promi-nent degeneration of the caudate nucleus. Later cell loss occur in the globus pallidus, subthalamic nucleus, nucleus accumbens, cerebellum and parts of the cortex (9). Within the caudate nucleus, abnormalities of small-to-medium sized spiny neurons result in loss of the inhibitory neurotransmitter gamma aminobutyric acid (GABA) as well as substance P and enkephalins. There is relative sparing of somatostatin and dopamine (10).

HD is generally considered a "neurologic" illness, falling under the rubric of "movement disorders. Many clinicians are well-versed in the motor manifestations of HD, whereas the psychiatric aspects are often underrecognized. This stands in contrast to the fact that the psychiatric burden of the illness is severe and it is the psychiatric, rather then the motor symptoms, which often lead to hospitalization (11). The prevalence of psychiatric symptoms in HD ranges from 35% to 73% (12). These symptoms include mood, anxiety, and psychotic disorders as well as personality change and aggressive behaviour. The psychiatric symptoms often precede the characteristic movement disorder. There are also cognitive abnormalities which have a progressive course and are characteristic of a dementia syndrome. McHugh and Folstein (13) delineate two features of the dementia syndrome: impaired cognitive functioning and progressive mental apathy. In this article, we report two cases of patients with HD who had prominent psychiatric symptoms requiring psychiatric hospitalization. Our aim is to draw attention to the variable presentations of psychiatric symptoms in HD and illustrate how the psychiatric symptoms are often early symptoms or harbingers of the motor presentations of the disease.

CASE 1

Mrs E., a 52 year old divorced woman who lives in a group home, was admitted to a psychiatric unit with unmanageable aggressive outbursts, persecutory delusions, agitation, suicidal ideation, and tearful episodes. She had been diagnosed with HD 1 year previously. Family history revealed a high risk for HD; 5 members on the maternal side were affected. Mrs E.'s problems began 10 years prior to admission. At that time, she was admitted to a psychiatric institution for depression and anxiety. She was subsequently hospitalized on 2 further occasions as an involuntary patient for psychosis and depression. Her psychosis was marked by persecutory delusions of her children wanting to harm her. On the second of these admissions, she was noted to have abnormal movements of her mouth and lips as well as mild cognitive decline. A referral for genetic testing was made and she was found to be positive for the HD gene. Neurologic exam did not reveal any chorea. CT of the head revealed mild generalized atrophy; EEG was normal. After a course of electroconvulsive therapy (ECT), Mrs E. returned to a euthymic state, however, due to the cognitive decline, she was declared personally incompetent and was discharged to the care of a group home. Medications on discharge were paroxetine 20mg/d, loxapine 70mg/d and lorazepam 3mg/d. Her past medical history was otherwise negative. Her fourth and most recent admission to the psychiatric unit was due to a relapse in her mental state. On admission, she was noted to have marked motor abnormalities with choreiform movements of her face and upper limbs. She was clumsy and had repetitive eye blinks. Her speech was slightly slurred. Mood and affect were depressed and anxious. No perceptual abnormalities were present although she was once again experiencing persecutory delusions. On mini-mental status testing, she had deficits on short-term memory, attention and concentration. About a week after admission, Mrs. E. started to be-come very needy, constantly demanding attention and reas-surance. She perseverated excessively on concerns about her future. At one point, she struck a co-patient. Her mood became even lower than on admission and she attempted sui-cide by running into the ocean. She then developed obsessions about running into the men's washroom and flushing herself down the toilet. Mrs. E. was subsequently treated with trazodone 300mg/d, propranolol 30mg/d, and

perphenazine 12mg/d. Psychotic, mood and aggressive symptoms partially resolved to the point at which she could return to the group home.

CASE 2

Mr K, a 43 year old divorced man who lives in a group home, was admitted to the psychiatric unit for an increase in agitation and physically aggressive behaviour. He had attacked workers and residents in his group home. The patient had first been diagnosed with HD at the age of 33 when he started developing personality changes, marked by irritability and antisocial behaviour. Minor motor abnormalities appeared 5 years later. He had no other medical or psychiatric history. There was a significant family history of 5 paternal relatives with a diagnosis of HD. His three immediate siblings were unaffected. This man's course of illness was marked by episodes of low mood, an increasing distrust of people, chronic insomnia and worsening alcoholism. At the onset of the ill-ness, he had been working in construction, however, following the loss of his job and with the changes in personality, he began to have significant marital difficulties. He became violent towards family members to the point that his wife had to leave with the children. The ensuing legal problems around his divorce caused him constant worry and distress. On admission, Mr K. appeared well-groomed and dis-played prominent choreiform movements. His speech was slurred and hesitant. He was preoccupied with feelings of anger and frustrations toward his wife, but had otherwise normal thought form and content. There were no perceptual abnormalities. Mood was low and affect anxious. Mini-mental status exam revealed significant problems with attention, calculation and short-term memory. CT head and EEG were not undertaken. Aside from the chronic insomnia, Mr K. denied any recent changes in neurovegetative functioning. Medications on admission included tetrabenazine 100mg/d and lorazepam 2mg/d.

DISCUSSION

The reason for the early manifestations of psychiatric illness in HD is unclear. It may be related to the progression of neural damage which proceeds from the caudate to the putamen resulting in damage to fronto-caudal and fronto-limbic circuits. These circuits underlie psychiatric symptoms. In contrast, the motor abnormalities result from damage to motor-putamen circuits which occurs at a later stage in the disease (15). Several investigators have examined whether there exists a temporal association between the onset of psychiatric symptoms and cognitive decline; the data do not support such a relationship (16,17). There was no evidence of cognitive decline coinciding with the initial psy-chiatric presentation in either of our two cases. Mood symptoms and disorders in HD have been well described in the literature (4,18). One study found that in a HD population, up to 32.5% met DSM III-R criteria for major affective disorders and 9% for dysthymia (4). Depression is frequently one of the first psychiatric symptoms to occur, as was the case in Mrs. E's presentation. However, as both cases illustrated, the mood symptoms may appear atany stage of the disease (19). The presence of depression in the context of a progressive illness raises the issue of suicide risk. Suicide is significantly more common (8.2x) in patients with HD compared to the general population and accounts for up to 2.3% of all HD deaths (20). Psychosis was seen in both cases presented. The first case, Mrs. E., had psychosis in the context of a depressive episode, whereas the second case, Mr. K., had more subtle symptoms of distrust and suspiciousness in the context of personality change. 3-12% of patients with HD present with schizophrenia-like psychosis (21). All the subtypes of schizophrenia have been reported as well as cases of isolated delusional states (12) and poorly systematized paranoia (22). As with the mood symptoms, the psychotic symptoms appear earlier on in the course of the illness. These symptoms tend to decline after the cognitive deficits become apparent (21).

Aggression and irritability are common symptoms in HD and may be the main reason for a psychiatric hospitalization (18). A range of presentations from irritability to intermittent explosive disorder may characterize the aggression. The aggression may be related to the personality change which is often an early occurrence, as was illustrated by Mr. K. in case 2. Alternatively, another underlying psychiatric problem such as persecutory delusions, depressed or manic states may precipitate aggressive outbursts (23). In case 1, Mrs. E. became more aggressive with the onset of her depressive episode. In addition, the needy, clinging and intrusive behaviour described has been conceptualized by some as being similar to aggression in that both may be manifestations of disinhibited anxiety caused by minor frustrations (24). Few systematic attempts at quantifying types and degrees of aggression have been attempted in the neuropsychiatric literature, although one study by Burns et al. (25) used a scale to measure apathy and irritability in 26 patients with HD. Compared to a group of patients with Alzheimer disease, the HD patients were more aggressive. 58% of the sample had elevated scores for irritability and 59% had elevated scores for aggression. The authors found no interrelationship between apathy, a symptom common in HD, irritability and aggression, although there was a correlation between premorbid "bad temper" and irritability in the HD group.

Other psychiatric problems include anxiety disorders, sexual disorders and sleep abnormalities. The literature is sparse with regards to reports of the prevalence of anxiety disorders in HD. Dewhurst et al. (18) found that anxiety was the commonest early psychiatric symptom of HD, however, obsessive symptoms, such as those which arose in Mrs E. following admission, are not common in HD. To our knowledge, only two cases of obsessive-compulsive disorder in HD have been reported (26). Sexual disorders including promiscuity, incest, indecent exposure and voyeurism have been well-documented in HD (18), although neither of the cases presented here displayed such difficulties. One study found that 15% of a sample of 39 male patients with HD had paraphilias (27). Sleep disorders have also been reported in HD. Wiegand (28) demonstrated polysomnographic findings similar to other dementing illnesses including decreased slow-wave sleep, prolonged sleep latency, and decreased sleep efficiency. As have other authors (29), this study found a higher density of sleep spindles in HD subjects compared to control subjects. Mr. K., in case 2, suffered from chronic insomnia. Unfortunately, no sleep studies had been undertaken to determine the exact polysomnographic abnormality present in his case. Chronic insomnia can significantly add to a patient's psychiatric morbidity and may even precipitate abnormal mood states.

Finally, the psychosocial burden of HD is heavy. Case 2 is an example of the complex psychosocial difficulties arising in a family with HD. Divorce is common in HD and in one sample, up to 38% of marriages broke up after the onset of the disease in one partner (18). Reasons for break-up included social and intellectual deterioration of the affected partner as well as an increased incidence in sexual aberrations and antisocial behaviour. As was also illustrated in case 2, the increased incidence of alcoholism in HD populations (18) adds to the psychosocial difficulties includ-ing marital, occupational and social functioning. Dewhurst (18) found 19 cases of alcoholism in a sample of 102 HD patients and this was considered an underestimation of the true prevalence.

CONCLUSION

The above cases have illustrated the significant and varied burden of psychiatric symptoms which manifest in HD. These symptoms have been conceptualized in various ways including a DSM-based classification (23), which divides the disorders into personality alterations,

aggressive behaviour, depression and suicide, mania and hypomania, psychosis, obsessive-compulsive disorder and paraphilias, and altered sexual behaviour, as well as a cluster approach which classifies all the psychiatric symptoms in two groups, either episodic mood disorder or a delusionary hallucinatory state (13).

Many of the psychiatric symptoms and disorders described above appear early in the course of the illness, often before the onset of the more characteristic motor abnormalities. Recognition of psychiatric symptoms as early manifestations of the disease may lead to earlier detection and intervention. Such intervention would allow multidisciplinary involvement at an earlier stage and provide the possibility of genetic counseling, family support and individual psycho-therapy to guard against the psychosocial complications of the illness. These interventions are crucial as current management is symptomatic only.

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