WILSON'S DISEASE PRESENTING WITH OBSESSIVE-COMPULSIVE DISORDER

HARPREET S. DUGGAL & S. HAQUE NIZAMIE

ABSTRACT

Wilson's disease, a disorder of copper metabolism, is known to be associated with psychiatric symptoms. Psychiatrists see about 20% of these cases before they are labeled as Wilson's disease. Reports of these patients treated mistakenly as primary psychiatric illnesses exist in literature. This report thus emphasizes a thorough underpinning in this disease on the part of psychiatrists in order to arrive at the correct diagnosis at first contact. Besides this, the emergence of obsessive-compulsive symptoms in a case of Wilson's disease is described, which is a rare association. Finally, the authors discuss the role of basal ganglia in obsessive-compulsive disorder.

Key words: Wilson's disease, obsessive-compulsive disorder, basal ganglia

Wilson's disease (WD) is an autosomal recessive inherited inborn error in copper metabolism and storage. Its prevalence is about 4 to 30 per million (Lang et al., 1990). WD may manifest as post-necrotic liver cirrhosis or as a degenerative basal ganglia lesion. As a rule, however, both brain and liver are involved (Lang et al., 1990). In addition, occurrence of psychiatric symptoms is well recognized in WD (Dening, 1985). Amongst its manifold psychiatric presentations four major groups have been recognized (Dening, 1985) - affective disorders, behavioural/personality abnormalities, cognitive impairment, and schizophrenia-like states.

Treatment with penicillamine potentially can reverse the neurologic and psychiatric manifestations of the disease if started early but psychiatric symptoms are less responsive (Skuster et al., 1992). The Indian account on psychiatric aspects of WD has remained mainly anecdotal (Dastur et al., 1968; Pandey et al., 1981a, 1981b; Jayaswal et al., 1984; Sagar & Saxena, 1989). A case of patient with WD is reported who besides other psychiatric symptomatology, also developed obsessive-compulsive disorder (OCD), a hitherto unreported association. This report also highlights the role of basal ganglia as a neuroanatomic correlate of OCD.

CASE REPORT

M.K., an 18-year-old right handed male, with normal birth and developmental history, presented with a multitude of physical and psychiatric complaints. His illness started 15 months prior to the current psychiatric consultation with dysarthria being the initial symptom. Subsequently, he developed progressive dystonic posturing of extremities, trunk, neck and face, which interfered with his daily activities. He also developed intention tremors over his hands. Other than these features, for the past four months parents observed that patient was remaining inordinately cheerful and was talking in excess. Furthermore, he had become irritable and impulsive and would frequently argue with his parents. For about two months prior to his admission with us, patient was also observed to be repetitively washing his
WILSON'S DISEASE PRESENTING OCD

hands. This occurred 8-10 times a day, each episode lasting about 10 minutes, with the purpose of preventing the risk of germ contamination. In the hospital, he would repetitively dust off his bed sheet. He realized that these thoughts were his own and were unreasonable. Though he tried to resist them, he could not. His behaviour gradually increased in amount and intensity to an extent where it starting hampering his activities of daily living. Past and family history were unremarkable.

On admission, examination revealed a well-nourished oriented youth having marked dystonic posturing of his body. There was no hepatosplenomegaly and the only positive finding on general examination was the presence of Kayser-Fleischer (KF) rings in both the corneas. The latter observation was confirmed by a slit-lamp examination. Central nervous system examination revealed broken eye pursuit movements, cogwheel rigidity of all limbs, truncal and limb dystonia, intention as well as resting pin-rolling tremors, bradykinesia and a shuffling and festinant gait. His speech was scanning in quality and he had micrographia. Deep tendon reflexes were preserved and plantars were downgoing. Mental status examination showed over-familiarity, increased psychomotor activity, circumstantial speech with overabundant productivity, euphoric and inappropriate affect, grandiose ideas of ability, obsessions of contamination and compulsions of hand washing. There was no evidence of any overt psychotic phenomenology, including hallucinations, delusions, or other Schneiderian first rank symptoms. He appeared to be of average intelligence though a formal psychological testing was not possible considering his severe dysarthria and tremors. Nevertheless, he had no gross cognitive deficits as indicated by a score of 28 on mini-mental state examination (total score=30).

There was no evidence to suggest hepatic involvement either in history or examination. A normal abdominal ultrasonography and normal liver function tests corroborated this. His other routine blood and urine investigations were normal. The only significant abnormality on laboratory investigations was a low ceruloplasmin level of 10 mg/dl (normal=20-40 mg/dl). A CT scan of brain revealed mild cerebellar atrophy with bilateral hypodense areas in basal ganglia (putamen and globus pallidus). Patient was diagnosed as having Wilson's disease and treatment with D-penicillamine was contemplated. However, patient chose to leave the hospital before the treatment could be initiated and unfortunately failed to return on follow-up.

DISCUSSION

In patients with a psychiatric illness who are found to have a low serum ceruloplasmin, the diagnosis of WD is confirmed by the detection of KF rings on slit-lamp examination (Dening, 1985). Besides having a clinical picture resembling that of hypomania, our patient also met the DSM-IV criteria for obsessive-compulsive disorder (American Psychiatric Association, 1994). An interesting observation in this patient's presentation was a total absence of overt hepatic involvement which was supported by the normal investigative procedures, though in all instances, the first expression of the disease is a deposition of copper in the liver, leading to an acute or chronic hepatitis (Scheinberg & Sternleib, 1984). This may, however, be asymptomatic, which accounts for hepatic dysfunction being the initial presentation in only 40% of cases (Beam, 1957). In the realm of psychiatric manifestations of WD, in one study 51% of patients of WD were stated to have some psychopathologic findings at the time of their index admission and 20% were seen by psychiatrists before the diagnosis of WD (Dening & Bernos, 1989). The latter statistical figure calls for a thorough underpinning in the myriad presentations of WD, the onus of diagnosing which may occasionally rest on the psychiatrist. In a similar vein, it is disconcerting to note that cases of WD have been treated for primary psychiatric illnesses for years prior to
accidental discovery of the KF rings (Cartright, 1978; Jayaswal et al., 1984). Lishman (1998) thus rightly states that the KF ring is a diagnostic sign of great importance, the absence of which makes the diagnosis of WD improbable in the presence of neuropsychiatric symptoms. However, KF rings may be absent in the purely hepatic forms of the disease (Adams et al., 1997) or may be a part of other hepatic conditions such as primary biliary cirrhosis (Scheinberg, 1998). Hence, low ceruloplasmin coupled with KF rings are considered as diagnostic of WD (Scheinberg, 1998). Dening & Berrios (1989) even recommend that serum ceruloplasmin should be measured in all psychiatric patients who show personality change, especially towards disinhibited, bizarre, or restless behaviour, in those who show neurologic signs not accounted for by medications, and in patients with unexplained hepatic disease. Moreover, dysarthria strongly corroborates with neuropsychiatric symptoms in WD and in a patient below middle age should prompt investigations for WD (Lishman, 1998).

Another aspect of this report is to throw some light on the role of basal ganglia in OCD. There is a reasonable body of evidence to suggest the involvement of basal ganglia in obsessive-compulsive symptoms. Besides mannerisms associated with Tourrette's syndrome, obsessional thoughts and compulsive stereotypic routines can also develop in patients with basal ganglia diseases such as Sydenham's chorea, Parkinson's disease, and progressive supranuclear palsy (Escalona et al., 1997). Cummings & Cunningham (1992) provide a brief review of studies implicating basal ganglia in OCD. In another review, Cummings (1993) explores the frontal-subcortical circuits as the basis for the various behavioural syndromes, including OCD. Structural lesions of caudate, globus pallidus along with orbitofrontal cortex and anterior cingulate cortex have been associated with OCD. Support for the involvement of these brain structures in OCD comes from the functional neuroanatomic studies of OCD (Insel, 1992). However, WD per se has not been reported to be associated with the emergence of obsessive-compulsive (OC) symptoms (Cummings, 1993) which makes the presentation of our patient a rare one.

The biochemical basis of emergence of OC symptoms in basal ganglia pathology derives largely from studies on Huntington's disease (HD). Such studies reveal reduction in neostriatal concentration of acetylcholine and choline acetyltransferase, with a relative increase in dopamine concentration in these structures (Spokes, 1979; Cummings & Cunningham, 1992). This increase in dopamine may be important in the mediation of OC symptoms as evidenced by the reports of amphetamine-induced stereotype ritualistic behaviours (Frye & Arnold, 1981) and the precipitation of compulsions in parkinsonian patients treated with levodopa (Hardie et al., 1984). Other investigators have proposed models of the neurochemical basis for OCD, which include an important role for the globus pallidus (Modell et al., 1989; Baxter, 1992).

In summary, this case adds to the sparse Indian literature on the psychiatric aspects of Wilson's disease. Moreover, while sensitizing the psychiatrists to harbour a high index of suspicion and clinical acumen to diagnose WD, this report also encourages further studies to decipher the neuroanatomic correlates of OCD focussing particularly on the basal ganglia.

REFERENCES

Adams, R.D., Victor, M. & Ropper, A.H. (1997) Principles of Neurology, Edn. 6, pp 969-971, New York : McGraw-Hill.

American Psychiatric Association (1994) Diagnostic and Statistical Manual of Mental Disorders (DSM-IV). Washington, DC : American Psychiatric Association.

Baxter, L.R. (1992) Neuromaging studies of obsessive-compulsive disorder. Psychiatric Clinics of North America, 15, 871-884.

Bearn, A.G. (1957) Wilson's disease: an inborn error of metabolism with multiple
manifestations. *American Journal of Medicine*, 22, 747-757.

Cartright, G.E. (1978) Diagnosis of treatable Wilson's disease. *New England Journal of Medicine*, 298, 1347-1350.

Cummings, J.L. & Cunningham, K. (1992) Obsessive-compulsive disorder in Huntington's disease. *Biological Psychiatry*, 31, 263-270.

Cummings, J.L. (1993) Frontal-subcortical circuits and human behaviour. *Archives of Neurology*, 50, 873-880.

Dastur, D.K., Manghani, D.K. & Wadia, N.H. (1968) Wilson's disease in India, I: geographic, genetic and clinical aspects in 16 families. *Neurology*, 18, 21-23.

Dening, T.R. (1985) Psychiatric aspects of Wilson's disease. *British Journal of Psychiatry*, 147, 677-682.

Dening, T.R. & Berrios, G.E. (1989) Wilson's disease: psychiatric symptoms in 195 cases. *Archives of General Psychiatry*, 46, 1126-1134.

Escalona, P.R., Adaor, J.C., Roberts, B.B. & Graeber, D.A. (1997) Obsessive-compulsive disorder following bilateral globus pallidus infarction. *Biological Psychiatry*, 42, 410-412.

Frye, P.E. & Arnold, L.E. (1981) Persistent amphetamine-induced compulsive rituals: response to pyridoxine (B6). *Biological Psychiatry*, 16, 583-587.

Hardie, R.J., Lees, A.J. & Stern, G.M. (1984) On-off fluctuations in Parkinson's disease. *Brain*, 107, 487-506.

Insel, T.R. (1992) Toward a neuroanatomy of obsessive-compulsive disorder. *Archives of General Psychiatry*, 49, 739-744.

Jayaswal, S.K., Lal, P., Nepal, M.K. & Wig, N.N. (1984) Wilson's disease presenting with schizophrenia-like psychosis: a case report. *Indian Journal of Psychiatry*, 26, 245-247.

Lang, C., Muller, D., Claus, D. & Druschky, K.F. (1990) Neuropsychological findings in treated Wilson's disease. *Acta Neurologica Scandinavica*, 81, 75-81.

Lishman, W.A. (1998) Movement disorders. In: *Organic Psychiatry*, Edn.3, pp 661-666, London: Blackwell Science.

Modell, J.G., Mountz, J.M., Curtis, G.C. & Greden, J.F. (1989) Neuropsychologic dysfunction in basal ganglia/limbic striatal and thalamocortical circuits as a pathogenetic mechanism of obsessive-compulsive disorder. *Journal of Neuropsychiatry*, 1, 27-36.

Pandey, R.S., Sreenivas, K.N., Patil, N.M. & Swamy, H.S. (1981a) Dopamine beta hydroxylase inhibition in a patient with Wilson's disease and manic symptoms. *American Journal of Psychiatry*, 138, 1628-1629.

Pandey, R.S., Swamy, H.S., Sreenivas, K.N. & John, C.J. (1981b) Depression in Wilson's disease. *Indian Journal of Psychiatry*, 23, 82-85.

Sagar, R.S. & Saxena, S. (1989) Capgras syndrome with disorder of copper metabolism: a case report. *Indian Journal of Psychiatry*, 31, 344-346.

Scheinberg, I.H. & Sternlieb, I. (1984) Wilson's disease. *Major Problems in Internal Medicine*, Vol.23, Philadelphia: Saunders.

Scheinberg, I.H. (1998) Wilson's disease. In: *Harrison's Principles of Internal Medicine*, Edn.14, (Eds.) Fauci, A.S., Braunwald, E.,
Skuster, D.Z., Digre, K.B. & Corbett, J.J. (1992) Neurologic conditions presenting as psychiatric disorders. *Psychiatric Clinics of North America*, 15, 324-325.

Spokes, E.G.S. (1979) Dopamine in Huntington's disease: a study of post-mortem brain tissue. In: *Advances in Neurology*, Vol. 23, (Eds.) Chase, T.N., Wexler, N.S. & Barbeau, A., pp 481-493, New York: Raven Press.