THE PSYCHIATRIC ASPECTS OF WILSON'S DISEASE-A STUDY FROM A NEUROLOGY UNIT

RAJEEV KUMAR, SUNIL DATTA, L. JAYASEELAN, CHANDRAN GNANMUTHU, K. KURUVILLA

ABSTRACT
A series of 31 cases of Wilson's disease (WD) were assessed retrospectively on a range of variables including psychiatric, neurologic and biochemical data recorded at index admission over a period of 7 years. 18 patients (58%) showed psychopathological features. 5 patients (16.1%) were reported to have poor scholastic performance at the onset of illness and 1 patient (3.2%) had abnormal behaviour (mania like) many years prior to the appearance of neurological symptoms. The most common psychiatric features were cognitive impairment (45.2%), affective symptomatology (41.9%) and behavioural abnormalities (29%). Only one patient had a schizophrenia like psychosis. The psychiatric manifestation of Wilson's disease as they present in our setting and their clinical relevance are discussed.

Key words: Wilson's disease, psychopathology.

INTRODUCTION
Wilson's disease is an autosomal recessive disorder of copper metabolism leading to an excessive accumulation of copper in the liver, cornea, kidney and in the basal ganglia of the brain. It is a rare disorder with an incidence of 30 per million people and has a world wide distribution (Scheinberg, 1984). Psychiatric symptoms are important in WD (Dening, 1985). Literature shows that about half the patients will display some sort of psychopathological features and 20% would have a psychiatric consultation before a diagnosis of WD is made (Dening, 1989). The psychiatric symptoms of WD include confusional states, cognitive impairment, mental retardation or poor scholastic performance, anxiety, depression, mania, schizophrenia like states, non specific abnormalities of behavior, psychopathic personality disorders and alcohol abuse (Dening, 1991). Since WD can present with symptoms that mimic a variety of psychiatric disorders, diagnosis of the underlying disease can be missed. The ability of the psychiatrist to suspect WD early and request the appropriate test and consultations is vital, since treatment can reverse the symptoms of the disease and prevent further deterioration (Shoulson, 1983). Most of the clinical literature has been authored by non-psychiatrists who have tended to emphasise other features and psychiatric symptoms have been neglected or addressed in an unsatisfactory way (Walker, 1969; Dobyns, 1979). Dening reviewing nearly 650 cases reported since 1959 and divided the psychiatric symptoms of WD into four groups: affective, behavioral and personality, schizophrenia like and cognitive (Dening 1985). The published literature on the psychological manifestations of WD in India is very few. Pandey et al in a series of 21 cases reported psychoapthology in 48% of cases (Pandey, 1981).

We undertook the present study with the following aims:

1. To find out the frequency and nature of neurologic and psychiatric symptoms associated with WD.

2. To study whether these psychiatric symptoms fit into the syndromes described in literature on WD.

3. To assess the relationship of psychiatric symptoms associated with WD to clinical, biochemical and demographic parameters.
METHODOLOGY

Retrospective case record analysis of a consecutive series of inpatients admitted with a diagnosis of WD in the neurology unit, CMC, Vellore over a period of seven years (1983-1990) was done. The authors constructed a symptom check list which included a range of psychiatric symptoms covering four main syndromes: affective, behavioural and personality, schizophrenia like and cognitive. Another protocol was developed to rate the sociodemographic, neurologic and biochemical data. The diagnosis of WD was based on (1) low ceruloplasmin level (<20 unit per L), (2) raised 24 hour urinary copper excretion (>100 microgram per day). (3) presence of Kaysers-Fleischer ring on slit lamp examination. The charts were examined by two psychiatrists (RK&SD) and a neurologist (CG). For seven patients detailed psychiatric reports were available and for the rest of the patients psychiatric symptoms were obtained as recorded from the file. Where there was query regarding the presence or absence of a symptom, it was discussed and a mutual agreement between the raters were carried out. Where cognitive impairment was found to be present, it was assessed by a combination of an IQ assessment, history of poor academic performance and by evidence of intellectual deterioration. Data was collected on a range of psychiatric symptoms and from this data an attempt was made to classify patients with positive psychiatric symptoms into psychiatric "syndromes" as discussed above. The stages of analysis were descriptive analysis of sociodemographic, neurologic and biochemical data, analysis of psychiatric symptoms and inclusion of this under various syndromes and finally comparison of psychiatric cases and non cases on demographic, clinical and biochemical variables.

RESULTS

The mean age of the patients studied was 17.3±9.4 years. There were 13 females and 18 males. The mean age of onset of illness was 15.2±9 years. The duration of index admission was 14.9±6.9 days. There was a positive family history among first degree relatives in 4(12.9%) patients. 6(19.4%) patients had psychiatric symptoms as their first symptom of the illness along with neurological symptoms. Among these 5 patients had poor scholastic performance and 1 patient had abnormal behaviour (mania like) prior to the onset of neurological symptoms. Seven patients had psychiatric consultation and the rest were not assessed psychiatrically. The mean serum copper was 49.2±18.2 microgram% (normal value for males is 70-140 and for females 85-155 microgram%). The mean serum ceruloplasmin level was 9.1±1.45 units/L (normal value is 23-58 unit/L). The mean urinary copper was 504±65.4 microgram per day (normal value is 15-50 microgram per day) at the time of diagnosis. 18 out of 31 patients (58%) were found to have some psychopathological features at the index admission. The symptoms most frequently recorded were cognitive impairment (45.2%), inappropriate affect (29%), irritability (16.1%), overactivity (12.9%), depression (12.9%) and aggression (9.7%). Delusions and hallucinations were uncommon (see table 1). When the symptoms were clustered based on Denings classification, affective and cognitive syndromes were the commonest types followed by behavioural disorders. Schizophrenia like psychosis was extremely rare (see table 2). When psychiatric cases were compared with non-cases, age, sex and age of onset were not found to be statistically significant. Patients with psychiatric symptoms had a prolonged hospital stay. Tremor was surprisingly a common symptom in patients with psychiatric symptoms, although the association did not reach levels of significance. Rigidity, dysarthria, dyskinesia, KF ring, serum ceruloplasmin and urinary copper did not show any significant difference.

DISCUSSION

The findings of this study indicate that psychiatric manifestations are a significant compo-
THE PSYCHIATRIC ASPECTS OF WILSON'S DISEASE

It was found that 58% of patients had some psychopathological features. Dening and Berrois in 1989 reported a similar figure of 51% in a series of 195 cases and Pandey et al reported 48% in a series of 21 cases (Dening, 1989; Pandey, 1981).

In our series 19.4% of patients had psychiatric symptoms at the onset of illness along with neurological symptoms. This shows that when patients present with psychiatric symptoms and with history of neurological symptoms and/or a family history of WD, a diagnosis of WD should be considered because an early diagnosis and treatment could prevent further progression or even lead to a reversal of the process. Once the diagnosis is suspected, ceruloplasmin level should be obtained. Since that level is low in only 90% of cases, 24 hour urine copper also should be measured; this is usually elevated. Slit lamp examination can detect Kayser-Fleischer rings that are pathognomonic. Patients who had psychiatric symptoms at index admission had a prolonged hospital stay. Inspite of this fact only 7 out of 18 patients had a psychiatric consultation. We found that cognitive and affective syndromes were the commonest types followed by behavioural and schizophrenia like psychosis. This is contrary to the findings observed by Dening which showed a preponderance of behavioural and personality syndromes (Dening, 1989). Schizophrenia like psychosis was rare in our series as well as in many other studies (Dening, 1989; Akil, 1991). Liver function test was done for all patients and was reported as normal in all patients except 2 in the present series. This again confirmed the fact that psychiatric manifestations are important accompaniments in patients with neurological symptoms (Dening, 1989), rather than with liver pathology. Limitations of the present study are the retrospective nature of study design and underreporting bias. However, the records at the hospital have meticulous and detailed entries, and we feel that it did not contribute to any substantial bias. The other limitations are that CMC Hospital is mainly a tertiary care centre and by the time a patient reaches, he may already be in a more advanced stage of the illness.

| PSYCHIATIC SYMPTOMS (N=31) |
|---------------------------|
| Symptoms                  | Present n | %  | Absent n | %  |
| Cognitive impairment      | 14.0(45.2)| 17.0(54.9)|
| Inappropriate affect      | 09.0(29.0)| 22.0(71.0)|
| Irritability              | 05.0(16.1)| 26.0(83.9)|
| Poor scolaric perf.       | 05.0(16.1)| 26.0(83.9)|
| Over activity             | 04.0(12.9)| 27.0(87.0)|
| Depression                | 04.0(12.9)| 27.0(87.0)|
| Aggression                | 03.0(09.7)| 28.0(90.3)|
| Insomnia                  | 03.0(09.7)| 28.0(90.3)|
| Hallucinations            | 02.0(06.5)| 29.0(93.5)|
| Delusions                 | 01.0(03.2)| 30.0(96.8)|
| Disorientation            | 02.0(06.5)| 29.0(93.5)|
| Incongruous behaviour     | 01.0(3.2) | 30.0(96.8)|

| PSYCHIATIC SYNDROMES IN PRESENT STUDY |
|--------------------------------------|
| Syndromes                           | n  (%) |
| Cognitive                            | 14(45.2)|
| Affective                            | 13(41.9)|
| (Emotional Lability, Depression)     |        |
| Behavioral                           | 09(29.0)|
| (Aggression, irritability, Incongruous behaviour) | |
| Schizophrenia like                   | 01(03.2)|
CONCLUSION

Psychopathological findings are important constituents of WD and psychiatrists tend to be involved at two stages: either early in the disease when patients present with psychiatric symptoms and do not as yet have a physical diagnosis, or in the psychiatric management of the established cases. In our series of cases the most common psychiatric syndromes were cognitive, affective and behavioural disorders. When clinicians evaluate young patients with history of psychiatric and neurological symptoms and especially if there is a family history of a neurological disorder, WD should be considered as one of the differential diagnoses and appropriate neurological and biochemical tests should be ordered to confirm or rule out WD.

REFERENCES

Akil M, Schwartz JA, Dutchak D, Gurkan VY, Brewer GJ. (1991) The psychiatric presentations of Wilson's disease. The Journal of Neuropsychiatry and Clinical Neurosciences, 3, 3777-382.

Dening TR. (1985) Psychiatric aspects of Wilson's Disease. British Journal of Psychiatry, 147, 677-682.

Dening TR, Berrios GE. (1989) Wilson's Disease: psychiatric symptoms in 195 cases. Archives of General Psychiatry, 46, 1126-1134.

Dening TR. (1991) The Neuropsychiatry of Wilson's disease. A review. International Journal of Psychiatry in Medicine, 21(2) 135-148.

Dobyns WB, Golstein NP, Gordon H. (1979) Clinical spectrum of Wilson's disease. Mayo Clinic Procedure, 54, 35-42.

Pandey RS, Swamy HS, Sreenivas KN, John CJ. (1981) Depression in Wilson's Disease. Indian Journal of Psychiatry, 23, 82-85.

Shoulson I, Goldbatt D, and Plassche W. (1983) Some therapeutic innovations in Wilson's disease. Advances in Neurology 37, 239-246.

Walker S. (1969) The Psychiatric presentation of Wilson's disease with an aetiological explanation. Behavioural Neuropsychiatry, 1, 38-43.

Rajeev Kumar, M.D, D.P.M*; Sunil Datta, M.D.; D PM; L Jayaseelan, M.Sc, Ph.D; Chandran Gnanamuthu, M.D, D.M4 and K. Kuruvilla, M.D, F.R.C. Psych*; 1, 2 and 5 formerly in the Dept of Psychiatry, 3 Dept of Biostatistics, 5 Dept of Neurological Science, of Christian Medical College, Vellore - 632 002.

*Correspondence, Royal Park Hospital, Private bag no 3 P.O. Parkville, Victoria 3052, Australia