CASE REPORT

Wilson disease: a most unusual patient

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Learning point for clinicians

All patients with Wilson disease are different.

It is generally believed that Wilson disease is an illness of children or young adults. Scheinberg and Sternlieb1 in their monograph 'Wilson’s Disease', based on a large series of patients seen over many years, reported only three patients over the age of 40. In my own series of over 300 patients seen between 1955 and 2000, the oldest patient referred was aged 39 years. However, it is now becoming clear that this disease can present in a much older age group, and, in the past, many patients must have been misdiagnosed. For instance, Peri et al.2 reported a patient presenting at the age of 60. Ala et al.3 examined even older patients, one presenting at the age of 70 and the other at 72 years. Walshe et al.4 in an article on the incidence of malignancies in patients with Wilson disease, noted two patients whose initial signs of Wilson disease occurred at the ages of 56 and 63 years. Ferenci et al.5 noticed 31 patients with initial neurological signs presenting over the age of 40 and Gow et al.6 detected 5 of 22 patients over the age of 40. Finally, I have had correspondence with a patient who claimed that her Wilson disease was diagnosed, with liver symptoms, at the age of 80, but it was not possible to get definite confirmation of this diagnosis. However, it is now clear that the age of onset can no longer be considered as eliminating this diagnosis. One patient in my series illustrates how difficult it can be in establishing the correct diagnosis and deciding on what, if any, treatment should be established.

Case report

The patient K first visited in November 1965 as a result of family screening. The reason for her referral was that her brother, who was 2 years older, had severe hepatic and neurological damage as a result of Wilson disease; his illness had presented at the age of 10 years with severe epistaxis, haemolysis and the finding of an enlarged liver and spleen. Splenectomy was performed and a lienorenal shunt constructed. A year later, neurological signs developed and Wilson disease was diagnosed.

When K was first presented, she was a healthy 14-year-old girl with no abnormal signs and no Kayser Fleischer pigment. Her routine laboratory tests were all normal, except that she has mild glycosuria and an inability to acidify her urine. Her serum caeruloplasmin was 14mg/dl, serum copper 86μg/dl, ‘free’ copper 34μg/dl and the urine copper was 164μg/24h. Isotope studies using 64Cu showed a reduced liver/plasma ratio and reduced incorporation of copper into caeruloplasmin. A diagnosis of Wilson disease was made and the patient was started on penicillamine.

She was then presented at regular intervals until 1986, and the results of the copper studies, during this period, show that her serum copper ranged between 49 and 96μg/dl and the caeruloplasmin between 10 and 31.5mg/dl. She admitted that her intake of penicillamine was irregular and infrequent, and in 2006 she admitted that ‘I stopped taking any penicillamine when I was 17 years old. If I told you I was taking penicillamine it was for a day or two only’. In other words the patient was, to all intents and purposes, untreated from 1968 onwards. Her routine laboratory tests of hepatic and renal function remained normal, and she never had any signs or symptoms of Wilson disease and Kayser Fleischer pigment was never seen.

She visited again in December 2006 when she remained free of signs and symptoms of Wilson disease. She had successfully brought up a family of two daughters, and her routine laboratory tests remained normal. At this time, her serum caeruloplasmin had returned into the normal range and her serum ‘free’ copper was not detectable. Her urine copper excretion remained abnormal at 114μg/24h. Therefore it might well seem that the diagnosis of Wilson disease was incorrect. However this was not the case. A liver biopsy in 1980 had shown a copper concentration of 322μg/g/wet weight (normal <10μg/gww) and the histological report read ‘There is widespread fatty vacuolation, glycogen nuclei and pleomorphic liver cells and widespread groups of inflammatory cells. The appearance is typical of early Wilson’s disease’. In 2002,
DNA studies showed that K and her severely affected brother were both homozygous for the common mutation Histidine 1069 Glutamine. Unfortunately after 2006, the patient complained of medical interference in her normal life and was lost to follow-up. The results of her copper studies between 1965 and 2006, the last available, show that between 1965 and 1983 the serum copper varied between 70 and 86 μg/dl and the caeruloplasmin between 13 and 22.5 mg/dl. The caeruloplasmin varied between 12.5 and 22.5 mg/dl. But the last determination in 2006 showed a serum copper of 96 and a caeruloplasmin of 29 mg/dl with a free copper of 9 μg/dl. Very recent correspondence with the patient resulted in a reply that she remained in excellent health and did not wish to be seen again.

Comment
The question remains, is this a case of late onset Wilson disease which has yet to present or is this patient never to develop signs and symptoms of the disease? The fact that, whilst virtually untreated, she successfully completed two pregnancies is unusual as miscarriage is the common result of pregnancy in untreated patients. It is also remarkable that, despite the very high concentration of copper in her liver, she has developed no clinical evidence of liver damage. Another possibility is that the Wilson disease gene does not have 100% penetrance. A recent study by the Sheffield team suggests that the frequency of pathogenic mutations for ATPase7B is much higher than had previously been believed so that many cases may have been misdiagnosed or that some carriers of the gene may not develop symptoms. It is unfortunate, but perhaps understandable, that the patient believes that her doctors have been overcautious in their attitude to her health and that they have tried to complicate her life with an illness that she does not have. Without further follow-up, the case will remain as an unsolved problem.

Conflict of interest: None declared.

References