Wilson’s Disease - A Rehabilitation Perspective

Introduction
Wilson’s disease (WD) is a rare autosomal recessive inborn error of metabolism due to a defective WD gene, ATP7B, located on Chromosome 13q1, which causes low levels of the copper binding protein, ceruloplasmin. Spontaneous mutations are common. Copper accumulates in the liver, cornea and basal ganglia due to loss of the binding protein, reduced hepatic transport and reduced biliary secretion of copper.

Untreated Wilson’s disease (hepatolenticular degeneration) is a relentlessly progressive and ultimately fatal disorder. A timely diagnosis and co-operation with lifelong specific treatment removes the copper, prevents re-accumulation and prevents or treats the liver and brain damage.

Wilson’s disease is not usually presented from a rehabilitation perspective. This account describes the clinical journey of a 23-year-old man with WD, who deteriorated catastrophically after initial penicillamine therapy. He needed intensive long-term neurorehabilitation for severe neurological and cognitive impairment that for some time looked irreversible. Although there are excellent reviews of the initial medical treatment of Wilson’s, there is little available on rehabilitation outcomes14 and even less on evidence-based practice.

Case history
Presentation and treatment
This man presented with a six-month history of mild dysarthria, an asymmetric ‘tapping’ tremor at rest in his right hand, incoordination on walking and running, minor personality changes and uncharacteristic under-performance in his preceding year at University.

He moved stiffly, spoke softly and had variable rigidity of the right upper limb with dystonic hypertenstion of the right thumb and tremor. Kayser-Fleischer (KF) corneal rings were seen and confirmed on slit lamp examination. His serum ceruloplasmin was very low at 4mg/dl (normal >20); serum copper was low, 5mmol/L. (normal 11-24) and 24hr urinary copper excretion (with precautions to avoid contamination) was high with an average of 16.6mmol/24hr (normal<0.9). MRI brain scans showed typical abnormalities. His full blood count, renal parameters, and liver function tests were normal.

His parents were unrelated and there was no relevant family history. A diagnosis of Wilson’s disease was confirmed. UK experts were consulted and involved in due course. Genetic testing found he was a compound heterozygote for two mutations of the Wilson gene, 524_525delAA and H1069Q and his siblings were then screened. He was prescribed penicillamine, and tolerated this combination well, although compliance was erratic with therapy interventions and suspicious of hospital and doctors.

Further management
Trientine, an alternative chelating agent was started, and benzhexol was continued. UK experts were consulted repeatedly over his management. He was severely disabled, was referred urgently for neurorehabilitation, and began intensive treatment 19 days after the onset of his reaction to the penicillamine.

Neurorehabilitation
He had inpatient neuro-rehabilitation for over twelve months with goal setting, regular case conferences and involvement of his family. Initially there was no significant change in his severe disability. Reference to a few case reports on the potential for late neurological and cognitive recovery encouraged the team and family that an intensive rehabilitation programme was worth pursuing.11

Verbal output was whispered, dysarthric and perseverative. He had severe antecollis with drooling and unsafe swallowing. Botulinum toxin injections into neck muscles improved head positioning from a marked tilt to the right to a lesser tilt to the left. The complexities of dealing with this dystonic, akinetic rigid state with cognitive impairment were becoming apparent.

Strategies to deal with mood swings, disinhibition and mildly sexualised behaviour were introduced by the psychologist and were partially successful. He remained distractible with poor concentration and attention skills for many months. Insight was slow to improve, as was his speed of information processing which came up from <1st percentile two months after diagnosis to the 16th percentile some eight months later.

Zinc acetate was introduced, after careful consideration and wide consultation, some seven months after his diagnosis was made, to try and speed up an intractably slow rate of change in his condition. This appeared to be associated with a faster rate of recovery. Zinc induces enterocyte metallothionein, promoting enteral binding of copper and slowly increases faecal copper excretion.2 Careful dosing schedules avoiding interaction between trientine and zinc are necessary for maximal effect. He tolerated this combination well, although compliance was to become a significant issue.

His dominant right thumb was painfully dislocated at the MCP joint and was severely dystonic. After much discussion it was wired and splinted after a trial of Botulinum toxin. Botulinum toxin injections were also used repeatedly to reduce dystonia in the short and long flexors of his right foot, neck muscles, and forearm and hand muscles, with overall success. Throughout, he had serial splinting to his contractures, intensive physiotherapy and bespoke orthoses. The early goals were to maintain, or regain, muscle length and passive range of movement at all joints. A powered wheelchair helped his mobility and mood, and reduced his social isolation.

His initial Barthel ADL (Activities of Daily Living) Index score was 1/20 (totally dependent) and had only improved to 6/20 after three months of intensive reha-
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Rehabilitation centre he was keen to stay on. This distressed him, his family and his local outpatient therapy services were inadequate, while sometimes erratic, was reasonable. At the end of a year, he was discharged home.

Outcomes

When his University were made aware of his illness they reconsidered his University record and decided to award him his degree. His family was pivotal in anchoring his recovery and was tenacious in its management. At the start of this man’s rehabilitation journey his future looked bleak. An unwritten goal was to secure his full cooperation, that of his family and the treating team. The evidence as there, was suggested that a good outcome could be achieved. Four years after becoming symptomatic he is still improving.

2. Do no harm

Another unwritten goal was to do no harm — good clinical practice. The ease with which one dystonic deformity could be converted into another with Botulinum toxin, introduced a high degree of caution into our practice. Early hand surgery to correct deformities without addressing function, e.g. cosmetic tenotomies, could have been destructive. Frequent inter-specialty discussions maximised his prospects for a better recovery of muscular control.

3. Early treatment is not simple — consult the experts

Initial treatment of Wilson’s disease presenting with neuro-psychiatric symptoms is controversial.1-3,10 Penicillamine has been the mainstay of treatment but there is a risk of early neurological worsening, possibly due to rapid mobilisation of copper from the liver and its redistribution to the brain. It may be transient but can be catastrophic. In penicillamine intolerance or as first line treatment, monamine oxidase inhibitors may be considered.

Discussion points

1. Recovery is slow and protracted

Wilson’s disease is rare, affecting 1:30,000 of the population worldwide.3 Few neurorehabilitation teams have experience in its management. At the start of this man’s rehabilitation journey his future looked bleak. An unwritten goal was to secure his full cooperation, that of his family and the treating team. The evidence as there, was suggested that a good outcome could be achieved. Four years after becoming symptomatic he is still improving.

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References