



Masked Neurodegenerative Disease

Marc Borner*, Ulrike Grieben, Friedrich C. Luft, Simone Spuler and Oliver Peters

Experimental and Clinical Research Center, A Joint Cooperation between the Charité-Universitätsmedizin Berlin and Max Delbrück Center for Molecular Medicine in the Helmholtz Association, Germany

Clinical Image

A 27-year-old woman presented to our muscle outpatient clinic accompanied by her foster parents. She complained about generalized muscle weakness, modest weight loss, and an accompanying depression; both had progressed over the past 2 years. Facioscapulohumeral dystrophy had been diagnosed elsewhere. The parents had observed forgetfulness and a withdrawn behavior. The patient was adopted making a family history impossible. She had successfully completed German secondary schools, had enrolled at a university but had abandoned these plans to successfully complete a 3-year apprenticeship. Nonetheless, she was currently unemployed. On examination, the right-handed patient had no localizing neurological findings. Cranial nerves were not remarkable; speaking was a little inarticulate. We detected no movement disorders. Trendelenburg and Romberg testing were not specifically abnormal; however, gait- and station appeared unstable. There was no specific proximal or distal muscle weakness or signs of atrophy. We could not confirm the presence of facioscapulohumeral dystrophy. Referring colleagues had expected a skeletal muscle disease, but we could not settle on that diagnosis. Muscle stretch reflexes were non-localizing and there were no pathological reflexes except brisk patellar and left-sided Achilles tendon reflex, but no Babinski sign. We viewed the responses as less common for muscle disease and considered the likelihood of a neurodegenerative disease. Depression still appeared possible, because of her withdrawn behavior, lack of drive, loss of interest, and weight loss. However, her mood appeared appropriate and there were no sleep disturbances. We performed clinical neuropsychological testing. The baseline mini-mental-status-test gave 26 of a possible 30 points. An intelligence test based on vocabulary revealed a normal score. The Hamilton depression scale was also nonspecific. The patient was cooperative and motivated. Her speech was fluid and appropriate. However, her memory and repetition skills seemed impaired, she occasionally perseverated, and appeared slightly dysarthric. In the clock completion test (Figure 1A), she required corrections and constructed the clock hands as a single line. The Trail-making Test and the requirement to alternate between numbers and letters were slowed and not without errors. When attempting to achieve a certain number or letter she often did not achieve her aim but instead performed these tests with quick spontaneous correction loops (Figure 1B and 1C). We were uncomfortable with the diagnoses of skeletal-muscle and depressive disorders. We considered the possibility of a neurodegenerative disease, including Huntington's disease. However, generally that diagnosis does not rest on solely psychological symptoms. Our psychiatric consultant regarded that diagnosis as unlikely.

Analysis of CAG repeats at the HTT locus on chromosome 4p revealed 14 CAG repeats on one allele and 53 CAG repeats on the other. CAG is the triplet codon for glutamine. A series of glutamines results in a polyglutamine tract (polyQ tract). Generally, persons have fewer than 36 CAG repeats. More than this number alters the characteristic of the Huntingtin protein resulting in the neurodegenerative condition termed Huntington's disease [1]. We obtained additional relevant history contact with both biological parents and four siblings had been lost. The patient was always

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*Correspondence:

Marc Borner, Charité-
Universitätsmedizin Berlin, Campus
Berlin Mitte, Charitéplatz 1, 10117
Berlin, Germany,
E-mail: Marc.Borner@charite.de

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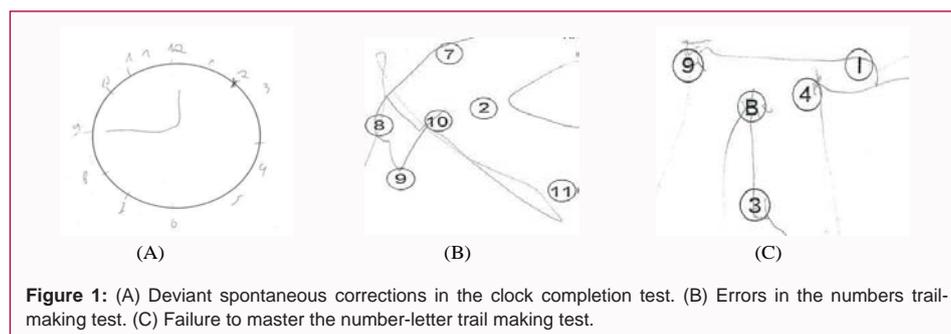


Figure 1: (A) Deviant spontaneous corrections in the clock completion test. (B) Errors in the numbers trail making test. (C) Failure to master the number-letter trail making test.

petit but had been athletic as a child and loved her bicycle. For two years, she had been unable to ride because of difficulties maintaining her balance. She reported falling frequently but was able to get up unassisted. Since she had received neurological care elsewhere, we inquired about imaging. An earlier brain magnetic resonance imaging study had been performed. In retrospect, very small alterations in the corpus striatum were identified (appendix). Huntington's disease is an autosomal-dominant genetic disorder affecting muscle coordination, leading to mental decline and behavioral symptoms [1]. The condition generally becomes symptomatic beyond 35 years; however, 6% of cases begin prior to 21 years. Our patient exhibited subtle changes in mood and cognition [2]. In retrospect, a general lack of coordination was apparent. Our patient showed no clear movement disorder, which probably led to a delay in diagnosis. We have counseled our patient and her foster parents, who gave us consent to report her findings. Unfortunately, there is no approved treatment for Huntington's disease. Histone deacetylase (HDAC) [4] is a transcriptional repressor containing a glutamine-rich domain could possibly be developed as a therapeutic target [3]. Even green tea has shown some promise [4]. Our patient underscores the role

of clinical-pattern building and thorough testing when confronting unusual psychiatric presentations of genetic conditions.

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