**Supplemental data**

**Gerstmann-Sträussler-Scheinker disease (*PRNP* p.D202N) presenting with atypical parkinsonism**

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**Table e-1.** Clinical features and results of diagnostic investigations of the GSS patients carrying the p.D202N mutation reported to date.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **GSS (p.D202N) cases** | | | | |
| I [1] | II [2] | III [3] | IV [4] | V (present case) |
| **Country** | UK | Canada | US | Germany | Italy |
| **Sex/Age at onset (years)** | M/73 | M/60§ | F/70 | F/51 | M/59 |
| **Family history for neurodegenerative disorders** | - | positive (parkinsonism) | - | Negative | negative |
| **Disease duration** | 6 years | - | 3 years | 6 years | 6 years |
| **First diagnosis** | AD | PSP | PSP | PD^ | MSA-P or -C |
| **Symptom(s) at onset** | cognitive | - | parkinsonism | cognitive | cerebellar, parkinsonism |
| **Other clinical signs** | cerebellar | parkinsonism, cognitive | pyramidal, cognitive | parkinsonism, pyramidal, cognitive | pyramidal, cognitive |
| **PSWCs at EEG** | - | - | - | no | no |
| **Brain MRI** | - | - | atrophy of cerebellar vermis, midbrain, frontal and temporal lobes | normal | subcortical arteriosclerotic encephalopathy |
| **CSF positive 14-3-3/Total-tau >1250 pg/ml** | - | - | - | no/yes | yes/yes |
| **123I-ioflupane DaTSCAN** | - | - | - | abnormal | abnormal |
| ***PRNP* codon 129** | val/val | met/val | -\* | val/val | val/val |
| **Dominant PrP type** | 8, 18-19 and 27-29 kDa | - | 7 and 15 kDa | not done | not done |
| **Neuropathology** | absence of spongiform change. Abundant PrP-amyloid deposits in the cerebrum and cerebellum. Neurofibrillary tangles in the neocortex. | mild spongiosis and sparse neurofibrillary tangles in the neocortex. Multicentric PrP-plaques in the cerebellum, cortex and striatum. | PrP-deposits in the  neocortex, limbic structures, striatum, cerebellum, midbrain, inferior olivary nucleus. Tau-immunopositive  neurons, neuropil threads, and neurofibrillary tangles in all gray matter structures. | not done | not done |

§Age at death, \*mutation in *cis* with valine, ^atypical due to poor L-DOPA response, - not reported.

List of abbreviations: AD, Alzheimer’s disease; PSP, progressive supranuclear palsy; PD, Parkinson’s disease; MSA-P or C, Multiple System Atrophy (parkinsonism or cerebellar variants); MRI, magnetic resonance imaging; EEG, electroencephalography; PSWCs: periodic sharp-waves complexes, CSF, cerebrospinal fluid; val, valine; met, methionine; PrP, prion protein.

**Table e-2.** Results of serial neuropsychological evaluations.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Test** | **Evaluation** | | | |
| **I** | **II** | **III** | **IV** |
| **Age at evaluation (years)** | 59 | 60 | 60 | 61 |
| **Time from the onset (months)** | 25 | 31 | 36 | 40 |
| **Screening** |  |  |  |  |
| Mini-Mental State Examination [/30] | 28 | 27 | **25** | 29 |
| **Attention** |  |  |  |  |
| Attentional matrices [/50] | 31 (1) | **19 (0)** | 33 (1) | **19 (0)** |
| Trial Making Test |  |  |  |  |
| Test A | 48 (3) | 65 (2) | 44 (4) | 76 (1) |
| Test B | 145 (2) | **306 (0)** | 192 (1) | 233 (1) |
| Test B-A | 97 (2) | **241 (0)** | 148 (1) | 157 (1) |
| **Short-term memory** |  |  |  |  |
| Span |  |  |  |  |
| Digit span | **4 (0)** | **4 (0)** | **4 (0)** | **4 (0)** |
| Visual span | 4 (1) | 5 (2) | 4 (1) | 4 (1) |
| Digit span backward | 4 (2) | 3 (1) | 3 (1) | 4 (2) |
| Visual span backward | 5 (4) | 4 (2) | **3 (0)** | **3 (0)** |
| **Long-term memory** |  |  |  |  |
| Babcock [/28] | 10 (1) | 14,5 (4) | - | - |
| Mauri Auditory Verbal Learning Test |  |  |  |  |
| Immediate Recall [/80] | **25 (0)** | 28 (1) | 31 (1) | 35 (2) |
| Delayed Recall [/16] | **4 (0)** | 5 (1) | 9 (4) | 11 (4) |
| Recognition [/32] | **16 (0)** | 28 (2) | 31 (4) | 31 (4) |
| **Visuospatial functioning** |  |  |  |  |
| Rey-Osterrieth complex figure - Copy [/36] | 32 (3) | **28 (0)** | 31 (2) | 33 (4) |
| Rey-Osterrieth complex figure - Delayed recall [/36] | 13,5 (2) | 20 (4) | 15,5 (3) | 22 (4) |
| Judgment of Line Orientation [/30] | 20 | 19 | 9 | 19 |
| Clock Drawing [/10] | 10 | 7 | 9 | 9.5 |
| **Language** |  |  |  |  |
| Verbal fluency |  |  |  |  |
| Phonemic | **15 (0)** | **25 (0)** | **16 (0)** | **13 (0)** |
| Semantic | 33 (1) | 34 (2) | 34 (2) | 35 (2) |
| **Executive functioning** |  |  |  |  |
| Raven CPM 47 [/36] | 31 (3) | 29 (3) | - | - |
| Stroop Test |  |  |  |  |
| Interference time | 35 (1) | 27,5 (3) | 32,5 (2) | **41 (0)** |
| Interference errors [/30] | 0 (4) | 0 (4) | 0 (4) | 0 (4) |
| Frontal Assessment Battery [/18] | **14 (0)** | 17 (3) | 15 (1) | **13 (0)** |
| Cognitive Estimation Task |  |  |  |  |
| Errors | 13 | 15 | 17 | - |
| Oddness | 1 | 1 | **16** | - |
| **Mental health screeners** |  |  |  |  |
| Hospital Anxiety and Depression Scale |  |  |  |  |
| Anxiety | 4 | 8 | - | 6 |
| Depression | 3 | 3 | - | 2 |
| Neuropsychiatric Inventory | 6 | 10 | - | 28 |
| **Activities of daily living** |  |  |  |  |
| Activities of daily living | 6/6 | 6/6 | - | **1/6** |
| Instrumental activities of daily living | 5/5 | 5/5 | - | **3/5** |
| Neuropsychological raw scores are reported for each test. The maximal value of each test is bracketed. Abnormal values, after correcting for age and education level, are noted in bold. Equivalent scores (from 0 to 4) are reported after each score, when available from normative data. Equivalent score equal to 0 means more than 2 SD below the norms. | | | | |

**Figure e-1.** Sanger sequencing electropherogram.

**e-References**

e1. Risacher SL, Farlow MR, Bateman DR, et al. Detection of tau in Gerstmann-Sträussler-Scheinker disease (PRNP F198S) by [(18)F]Flortaucipir PET. Acta Neuropathol Commun 2018;6:114.

e2. Foutz A, Appleby BS, Hamlin C, et al. Diagnostic and prognostic value of human prion detection in cerebrospinal fluid. Ann Neurol 2017;81:79-92.

e3. Bongianni M, Orrù C, Groveman BR, et al. Diagnosis of Human Prion Disease Using Real-Time Quaking-Induced Conversion Testing of Olfactory Mucosa and Cerebrospinal Fluid Samples. JAMA Neurol 2017;74:155-162.

e4. Franceschini A, Baiardi S, Hughson AG, et al. High diagnostic value of second generation CSF RT-QuIC across the wide spectrum of CJD prions. Sci Rep 2017;7:10655.