J Neurol (2001) 248 : 1106 – 1108

Shinji Ohara

Dressing and constructional apraxia in a patient with dentato-rubro-pallido-luysian atrophy

Received: 16 April 2001
Received in revised form: 21 June 2001
Accepted: 28 June 2001

Sirs: Dentato-rubro-pallido luysian atrophy (DRPLA) is an autosomal dominant multisystem neurodegenerative disease, most commonly found in Japan, that is clinically characterized by chorea, cerebellar ataxia, and dementia as well as progressive deterioration [1, 2]. The genetic defect of DRPLA is a cytosine-adenine-guanine (CAG) triplet nucleotide expansion of the atrophin-1 gene on chromosome 12. The dementia seen in DRPLA is typically subcortical without focal cognitive impairments such as aphasia, apraxia, and agnosia [3]. We describe here a patient with DRPLA who presented with constructional apraxia and cortical sensory deficits and improved after the administration of neuroleptics.

A 50-year-old man was brought to our clinic by his wife with the chief complaint of difficulty in carrying out daily routines. He had retired from his job as a laboratory worker 6 months earlier because of a decline in his performance. He had a positive family history of dentato-rubro-pallido-luysian atrophy (DRPLA), his mother and his two sons having been affected. His two sons both had seizure disorders and mental retardation and had been diagnosed with DRPLA upon genetic analysis.

The patient had difficulty in manipulating learned objects such as the phone or a semi-automated toilet. He could not use a touch-phone anymore because he confused the numbers on the keypad, although he had correct verbal recall of the numbers. When using the toilet, he would push the wrong button to flush the water. He would also light the wrong end of a cigarette. Dressing by himself had become particularly difficult as he would insert an arm in the neck aperture or try to fit both legs in one leg of the trousers. It was as if he could not distinguish parts of the clothing or could not remember how to dress.

On examination, he was somewhat irritable. His speech was slightly explosive and uninhibited, and the content of his speech was often incoherent and slightly delusional, but without deficits in articulation and fluency. His language was normal. He could follow 3-step commands across the midline. He was fully oriented and was able to remember 3 out of 3 items after 5 minutes. His long-term memory was well preserved. Smooth-pursuit eye movement was slightly jerky; otherwise, the rest of the cranial nerve examination was normal. When speaking, his head showed a slight rotational tremor. His muscle strength and bulk were normal. Finger nose-to-finger testing was accurate but was interrupted by some choreic movement. He was astereognosic despite normal sensations to light touch, pinprick, and vibration on both hands. For example, he was able to describe the tactile features of an eraser (soft, light), but could not recognize it. The sense of graphesthesia was mildly decreased over his palm. There was no finger agnosia, right-left disorientation, dyscalculia, or tactile or visual neglect. His color perception was normal. He performed poorly on tests of spatial construction, such as drawing a clock or copying a cube (Fig. A, C). He was unable to imitate specific finger postures. He was able to pantomime how to blow a match, salute militarily, smoke a cigarette, and kick a ball. However, he rubbed his thumb on his teeth when pantomiming how to brush the teeth and pounded his fist on the table while showing how to hammer a nail. His praxis improved with real tools. His gait was wide-based and unsteady. His deep tendon reflex was diffusely hyperactive, and planter reflexes were in flexion bilaterally. He did not suffer from urinary incontinence or orthostatic hypotension.

Routine hematological and chemical laboratory results were normal. Upon genetic analysis, a CAG repeat expansion was confirmed. Brain MRI showed slight cerebral and cerebellar atrophy. Single Photon Emission Computed Tomography (SPECT) with N-isopropyl-p [I-123]-iodoamphetamine revealed hypoperfusion of the parietal areas. Motor and sensory nerve-conduction studies were within normal range. Electroencephalogram and auditory-evoked responses were normal, while somatosensory-evoked potentials after stimulation of the median nerves at the wrist revealed normal N20 latency on both sides.

The patient was started on haloperidol 0.75 mg twice a day, which was then increased to three times a day after a month. Two months later, he was once again able to use a touch-phone without much difficulty. He was also able to dress by himself without assistance. His wife thought that his previous level of activity had almost returned. On examination, he was cooperative and spoke sensibly. His choreic movement and rotatory head jerks were improved, and his gait was less ataxic.

At this time, he was tested with the revised Wechsler Adult Intelligence Scale (WAIS-R). His verbal

IQ was 119, while his performance IQ was only 63. He scored 15 out of 61 in a block-design test, and 14 out of 47 in a picture-combination test. He scored 35/36 in the Raven Matrix, and his drawing of a cubic was improved (Fig. D). Four months later, his daily living activities remained improved. Upon examination, his drawings were further improved (Fig. B, E). Still, he could not recognize small objects by touch. He was able to imitate hand posture more easily, but he had still problems in imitating how to brush his teeth, or to hammer a nail. At the 6-month follow-up visit, his neurological findings remained unchanged and the repeated SPECT study did not show significant interval changes.

The clinical presentation of hereditary DRPLA is quite diverse, depending on the age of onset. In patients with adult onset, cerebellar ataxia or choreoathetoid movements tend to dominate the clinical picture, whereas in patients with juvenile onset, seizures and myoclonus are more common. A progressive intellectual impairment and/or personality changes are also commonly observed in the adult-onset form, and those often precede the appearance of motor manifestation. The dementia in DRPLA is "subcortical", primarily consisting of psychomotor slowing without cortical dysfunction such as aphasia or apraxia. Our case presented with bilateral astereognosia, dressing and constructional apraxia, and less prominently ideomotor apraxia. All of these cortical deficits occurred in the context of normal memory, abstractions, and language comprehension. To our knowledge, this presentation has not been reported in a case of adult-onset DRPLA.

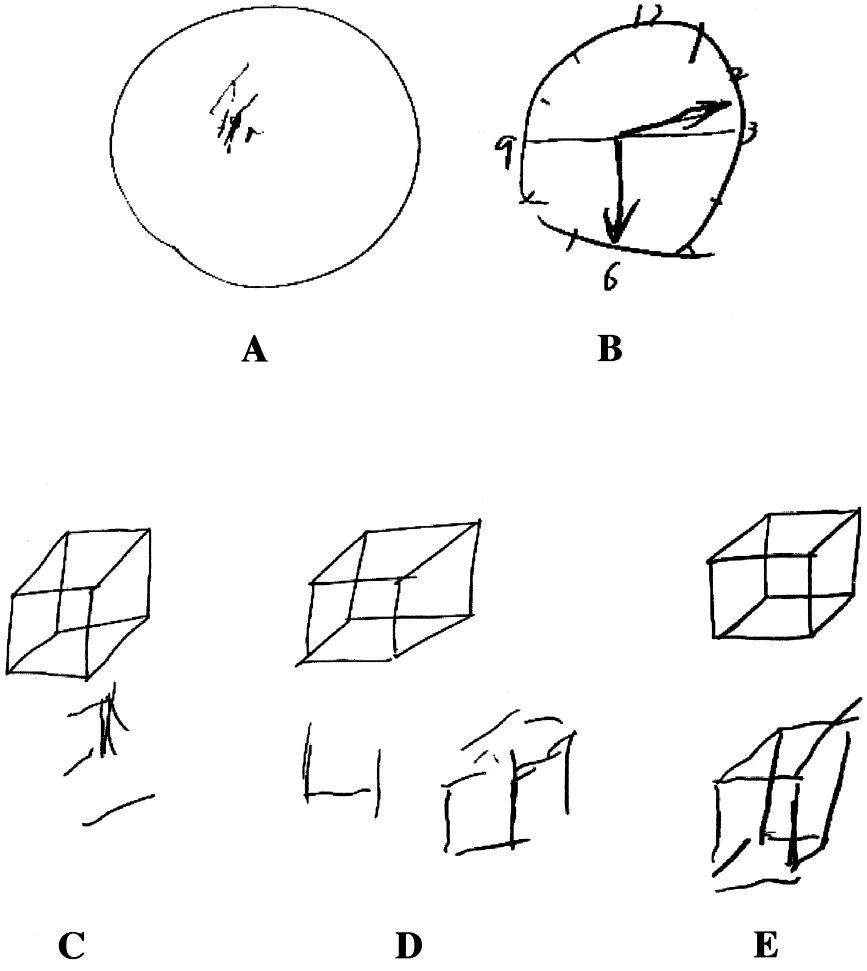

Fig. A, B Drawing of a clock by the patient. A) Before starting on neuroleptics. The patient was asked to put numbers and arms on the circle drawn. B) 4 months later. The patient was asked to draw a clock showing a time of 2:30. **C, D, E** Copy of a cubic figure by the patient. C) Before starting neuroleptics. D) 2 months later. E) 4 months later. The sample presented at the time of each drawing is shown above. Original x 0.5

The site of cortical dysfunction can be localized to the parietal cortex based on the clinical presentation. It is generally accepted that the parietal lobes are the principal cortical areas involved in visual-motor integration responsible for constructional ability [4]. Dressing apraxia is rarely reported in combination with constructional disturbance. However, Yamaguchi et al. have reported a 60-year-old Japanese man with possible corticobasal degeneration who presented with a 2-year history of slowly progressive dressing apraxia and constructional apraxia without other apraxia or aphasia [5]. They postulated a common underlying disturbance in visual-spatial recognition to explain this association. Recent evidence indicates that astereognosia is related to a focal lesion in the contralateral parietal cortex, which receives direct input from the finger joints [6].

Previous neuropathological studies of DRPLA brains have consistently revealed predominant subcortical foci of degeneration, whereas the anatomical correlates of the progressive dementia in DRPLA have not been fully clarified [7]. It is possible that the anatomical damage is predominantly subcortical, causing parietal symptoms via known basal-thalamo-cortical connections. Potentially similar cortical deficits and metabolic abnormalities after the appearance of subcortical lesions have both been described in other neurodegenera-

tive diseases such as Alzheimer's disease and in stroke [8]. It is possible that the subcortical pathological changes of DRPLA may affect relevant cortical functions through their connections. Recently, however, it has been shown that a diffuse accumulation of mutant atrophin–1 in the neuronal nuclei is the predominant pathological condition of the DRPLA brain and involves a wide range of CNS regions far beyond the combined degeneration of the dentatorubral and pallidoluysian systems [9]. In that study, the cerebral cortex was among the sites preferentially affected, suggesting the primary role of cortical pathology in producing a variety of clincal features of DRPLA, including dementia and epilepsy. Since the clinical improvements in our patient included both automatic and non-automatic tasks requiring more attention and concentration, it seems unlikely that his visuospatial deficit was simply due to his chorea/or psychiatric illness.

The medical treatment of DRPLA is limited. It is usually directed to the symptomatic improvement of movement and emotional deficits with neuroleptics and/or anti-depressants. In our case, the response to treatment with the neuroleptics was quite remarkable, since not only chorea but also visuospatial abilities were improved. It remains unclear at present whether these deficits were related to chorea, with difficulty with sequential motor programs, which has well disappeared with the treatment, or can such a deficit be reversible with this type of drug. Further case studies of DRPLA seem warranted, with special attention being paid to visuospatial function and its response to treatment with neuroleptics.

Acknowledgments We thank Dr.Kunihiro Yoshida, Department of Medicine (Neurology), Shinshu University School of Medicine, for conducting the genetic analysis, and Dr. Maurizio Corbetta, Department of Neurology, Washington University School of Medicine, for his invaluable discussion and critical reading of the manuscript.

References

1. Kanazawa I (1998) Dentatorubral-pallidoluysian atrophy or Naito-Oyanagi disease. Neurogenetics 2:1–17
2. Tsuji S (1999) Dentatorubral-pallidoluysian atrophy (DRPLA): Clinical features and molecular genetics. In Advance in Neurology. Vol. 79, eds. AV Delgado-Escueta, WA Wilson, RW Olsen and RJ Porter. 399–409
3. Naito A (1995) Clinical picture of DRPLA. No to Shinkei 47:931–938. (In Japanese)
4. Benton A, Tranel D (1993) Visuoperceptual, visuospatial, and visuoconstructive disorders. In Clinical neuropsychology. 3rd ed. Oxford Univ. Press 165–213
5. Yamaguchi H, Kawamura M, Yokochi M, Yano Y (1998) Slowly progressive dressing and constructional apraxia: symptomatological study, especially for dressing apraxia. Clin Neurol 38:897–903 (in Japanese, English abstract)
6. Tomberg C, Desmedt JE (1999) Failure to recognize objects by active touch (astereognosia) results from lesion of parietal cortex representation of finger kinaesthesis. Lancet 534:393–394
7. Takahashi H, Ohama E, Naito H, Takeda S, Nakashima S, Makifuchi T, Ikuta F (1988) Hereditary dentatorubral-pallido-luysian atrophy: Clinical and pathologic variants in a family. Neurology 38:1065–1070
8. Perani D, Di Piero V, Lucignani G, Gilardi MC, Pantano P, Rosetti C, Pozzilli C, Gerundini P, Facio F, Lenzil GL (1988) Remote effects of subcortical cerebrovascular lesions: a SPECT cerebral perfusion study. J Cereb Blood Flow Metab 8:5607
9. Yamada M, Wood JD, Shimohata T, Hayashi S, Tsuji S, Ross CA, Takahashi H (2001) Widespread occurrence of intranuclear atrophin–1 accumulation in the central nervous system neurons of patients with dentatorubral-pallidoluysian atrophy. Ann Neurol 49:14–23

Dr. S. Ohara, MD (✉)
Department of Neurology
National Chushin-Matsumoto Hospital
811 Kotobuki
Matsumoto 399–0021, Japan
Fax: +81-263/86-3190