Isolated visual symptoms at onset in sporadic Creutzfeldt-Jakob disease: the clinical phenotype of the “Heidenhain variant”

S A Cooper, K L Murray, C A Heath, R G Will, R S G Knight

Background: The Heidenhain variant of sporadic Creutzfeldt-Jakob disease (sCJD) is commonly understood to represent cases with early, prominent visual complaints. The term is clarified to represent those who present with isolated visual symptoms. This group may pose diagnostic difficulties and are likely to present to ophthalmologists with risks of onward unnecessary ocular intervention, with risks of onward needless ocular intervention, with risks of onward unnecessary ocular intervention, with risks of onward needless ocular intervention.

Method: A retrospective review of 594 pathologically proved sCJD cases referred to the UK National CJD Surveillance Unit over a 15 year period to identify Heidenhain cases.

Results: 22 cases had isolated visual symptoms at onset with a mean illness duration of 4 months. The mean age at disease onset was 67 years. Most displayed myoclonus, pyramidal signs, and a delay in the onset of dementia for some weeks. 17 (77%) were referred initially to ophthalmology.

Conclusions: This rare, but clinically distinct, group of patients with sCJD may cause diagnostic difficulties. Because ocular intervention carries with it the risk of onward transmission awareness of this condition among ophthalmologists is important.

MATERIALS AND METHODS

A retrospective case file review was performed on all pathologically proved cases of sCJD referred to the UK National CJD Surveillance Unit (NCJDSU) between January 1990 and March 2005 inclusive. Case files comprised clinical and epidemiological information collected by NCJDSU staff and copies of hospital and general practitioner records. A clinical assessment and interview with patients’ relatives was conducted by a surveillance neurologist whenever possible.

RESULTS

Twenty two patients out of 594 (3.7%) with pathologically proved sCJD had clearly documented purely visual symptoms for at least the first 2 weeks of the illness. The nature of these initial symptoms is summarised in table 1.

Fourteen (64%) cases were women. Mean age at onset was 67 years (median 66 years, range 50–88 years). Mean duration of illness was 4 months (median 3 months, range 1–17 months). Seventeen patients (77%) lived for 3 months or less.

Clinical features

Throughout the illness myoclonus was observed in 21 (95%), pyramidal signs in 19 (86%), cerebellar signs in 12 (55%), psychiatric symptoms in seven (32%), other involuntary movements in six (27%), sensory symptoms in four (18%).

Abbreviations: EEG, electroencephalogram; MRI, magnetic resonance imaging; NCJDSU, National CJD Surveillance Unit; sCJD, sporadic Creutzfeldt-Jakob disease
and extrapyramidal signs in one (5%). None had documented seizures. A rapidly progressive dementia was observed in all after the initial period of cognitive preservation which lasted from 2–6 weeks.

Case 1
A 73 year old man complained of difficulty reading, with blank spaces appearing in words. He also complained of colours appearing abnormally enhanced. He was assessed by an ophthalmologist when there was normal visual acuity but dense scotomata lying to the right of fixation bilaterally. A provisional diagnosis of an occipital infarct was made. Six weeks after onset he developed myoclonus, followed by ataxia and ultimately dementia. His vision deteriorated with oculomotor apraxia and cortical blindness. He died 3 months after disease onset.

Case 2
A 62 year old woman presented with deteriorating visual acuity. She felt that her vision was “fogging up” and complained of tunnel vision. She attended an optician but no abnormality was identified. A week later she complained that everything appeared green. An MRI brain scan was ordered following referral to the ophthalmology department but no diagnosis made. Over the next month her gait became unsteady and she was increasingly forgetful. By the time she ordered following referral to the ophthalmology department. Two underwent cataract extrac- tion after the onset of symptoms and before a diagnosis of sCJD was considered. Previous work has highlighted the incidence of oculary surgery in sCJD cases with visual symptoms. Although there have not been any reports of CJD transmission following cataract surgery, it has been reported after corneal grafting. Abnormal prion protein has been isolated from ocular tissue. It is important that ophthalmologists are aware of the condition despite its rarity as it may or may not be identified a distinct subgroup of cases as reflected in the genotype findings.

Defining a group of cases with isolated visual symptoms at onset may aid future recognition of similar cases. By clarifying the definition of Heidenhain cases we have identified a group who generally exhibit short illness duration, myoclonus, and a PRNP codon 129 MM genotype. As well as aiding diagnosis these findings may contribute to the understanding of the how abnormal prion protein causes disease within the central nervous system.

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