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Medicine in the elderly

Creutzfeldt-Jakob disease in the elderly

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Summary
Creutzfeldt-Jakob disease (CJD) is typically described as a pre-senile dementia. However, cases do occur in the elderly and a case of sporadic CJD in an 86-year-old patient is described. The database of the UK national surveillance unit has been studied, and the age-specific incidences for various age groups over the period 1980–93 calculated. Cases of CJD in those over 80 years old have been identified and their clinical characteristics examined. There is no evidence that CJD presents atypically in the elderly, or that large numbers of cases are being missed in the elderly due to poor ascertainment.

Keywords: Creutzfeldt-Jakob disease, prions, elderly

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Creutzfeldt-Jakob disease (CJD) is a rare neurodegenerative disease with a worldwide incidence of 0.5–1.0 case per million of the population per year.[1] Most cases occur sporadically, with no known causation. Around 15% of cases are familial, and linked with mutations of the 'prion protein' gene on the short arm of chromosome 20.[2] A very small number of cases (less than 100 worldwide) have been associated with the accidental intracerebral or parenteral inoculation of CJD-contaminated material.[3]

Clinical characteristics

The early features of affected cases are protean and can include personality change, cognitive impairment, dyspraxia, dysphasia, cortical blindness, cerebellar ataxia and extrapyramidal signs. There is relentlessly progressive central nervous system dysfunction, with the occurrence of primitive reflexes and the appearance of pyramidal signs, myoclonic jerks (sometimes in the form of a startle response) and akinetic mutism. Investigations are usually normal, although imaging of the brain may reveal slight cortical and/or cerebellar atrophy. The electroencephalogram (EEG) is the most useful investigation when abnormal, and characteristically shows periodic sharp wave complexes. When present throughout the recording and in the appropriate clinical context, this finding is diagnostic of CJD. However, in around 25% of cases (especially where the clinical presentation is atypical) the EEG is not characteristic.[4] Most patients (around 90%) succumb to their illness within a year. Macroscopically the brain is usually normal, or shows slight atrophy. On microscopy, CJD is characterised by the presence of vacuolation (spongiform change), neuronal loss, astrocytic hyperplasia and gliosis, microglial proliferation and, in some cases, the formation of amyloid plaques.[5]

Age of onset

Although the range of age of onset in sporadic CJD is wide, most identified cases are between 50 and 70 years old.[6] The explanation for the fall in age-specific incidence thereafter is unknown. It may represent an epidemiological characteristic of the disorder or it may be due to poor case ascertainment in the elderly, particularly if these cases present atypically and are misdiagnosed.

Case report

An 86-year-old woman was admitted with a two-week history of disorientation and self-neglect. She had sustained a minor head injury three months previously. Her mother had been confused for three years prior to death (at 84 years). On examination, she was frail and unkempt. Her Hodkinson mental test score was 15 out of 34. She had jerky limb movements, but otherwise her initial neurological examination was normal.

In hospital her level of awareness fluctuated. Computed tomography of the head showed no subdural haemorrhage. Routine biochemistry, haematology and chest radiograph were normal. EEG revealed slow background rhythms and periodic discharges. She deteriorated rapidly. Her jerky movements became more prominent and she 'startled' with the least stimulation. She became cortically blind and mute. Terminally she had frontal release signs, decorticate limb posturing and generalised rigidity. She died less than four weeks after admission.

At autopsy there was mild, mainly frontal cortical atrophy. Histological examination revealed spongiform change, most evident in the frontal, parietal and temporal lobes. In these regions, the vacuolation was confluent with accompanying reactive gliosis and neuronal loss. Immunocytochemistry for prion protein gave a positive result in the areas of confluent vacuolation. The neuropathological findings were typical of CJD.

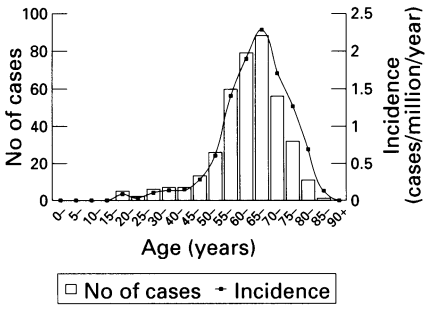

Figure Cases of CJD in the UK (1980–93) and age-specific incidence

Age of onset of cases referred to the surveillance unit

All definite (pathologically confirmed) and probable (with typical electrophysiological appearance) cases of CJD referred to the UK national surveillance unit[7] between 1980 and 1993 were identified. Of 400 cases, data pertaining to age of onset was available in 393 (figure). The mean age of onset for this population was 62 years (range 20 to 86, median 64). The age-specific incidence over the period of study fell from 2.28 cases/million/year between 65 and 69 years to 0.69 cases/million/year between 80 and 84 years.

Clinical characteristics of elderly cases

The clinical features of the 12 cases that presented at or after 80 years are presented in the table. Their disease characteristics were typical of sporadic CJD. The mean disease duration was 3.0 months, also consistent with the disease duration reported in sporadic cases.[6]

Is CJD in the elderly missed?

In line with previous observations, a fall in age-specific incidence of CJD after around the age of 70 has been demonstrated. Is this due to cases of CJD being missed in the elderly? The rapidity of cognitive decline and the associated neurological abnormalities (exemplified by the reported case) should militate against this condition being missed or misdiagnosed. Furthermore, appraisal of very elderly (80 years and over) cases has revealed that their clinical characteristics are no different from the 'norm'. Atypical presentations of CJD do of course occur, but they are not numerically significant[8] and in any case there is no evidence that they occur more commonly in the elderly.[4]

There is further evidence to refute this contention from unselected postmortem series. In a systematic study of dementia in the elderly, 137 demented patients from a psychiatric hospital (mean age 80.3 years) and 308 demented patients from a geriatric hospital (mean age 80.8 years) had autopsy examinations consecutively after death. Only one case of CJD was identified.[9] In a smaller series of 46 cases (age range of disease onset 17 to 80 years) with a variety of neurodegenerative features referred to a specialist laboratory investigating spongiform encephalopathy, CJD could not be confirmed in a single case.[10]

It is likely therefore that the current observation, which is consistent with all previous studies on age of onset in CJD, represents a key epidemiological characteristic of this disorder. If so, it brings into question a recent hypothesis generated to account for the causation of sporadic CJD. Based on the observation that transgenic mice over-expressing the 'prion protein' gene develop spontaneous neurodegeneration including spongiform encephalopathy, it has been argued that the chance physicochemical alteration of the nascent sialoglycoprotein encoded by this gene to an abnormal form (with a capacity to further convert normal protein autocatalytically) causes sporadic CJD.[11] If this is the case, the chance of this alteration occurring should increase, not decrease, with increasing age.

Summary points

- CJD is a rare, progressive and invariably fatal neurodegenerative condition
- the annual worldwide incidence is 0.5–1.0 case/million
- most cases are sporadic (with no known causation), but up to 15% may be familial and a very small number are iatrogenic
- the disease presents typically in the pre-senile age group (median age at onset approximately 64 years)
- there is no evidence of increasing incidence with age. The currently popular model for the causation of sporadic CJD accounts poorly for this epidemiological characteristic

Table Cases of CJD presenting at 80 years and older

Age at onset (years)	*Duration of illness (months)*	*Clinical course*	*EEG**
80	3	disorientated/muddled, unsteady, myoclonus	not typical
80	2	poor memory, dysphasic, lethargic, labile affect, involuntary movements	typical
80	1	forgetful, scared, gait disturbance, incontinence, myoclonus, mutism	typical
80	1	personality change/confusion/forgetful/incontinent, unsteady, myoclonus	typical
81	1	confused, myoclonus, parkinsonism, pyramidal signs, coma	not typical
82	4	occipital blindness, ataxia, confusion, pyramidal signs, coma	not typical
82	5	cognitive decline, myoclonus, unsteadiness, akinetic mutism	not typical
82	3	spatial disorientation, immobile/uncommunicative, personality change, unsteady, myoclonus, rigidity	not typical
83	5	odd behaviour, cognitive loss, visual hallucinations, myoclonic jerks	typical
83	2	confusion, memory loss, poor balance, dyspraxic, mute, startle	typical
84	1	personality change, ataxic, rigid	typical
86**	2	cognitive and personality change, myoclonus, akinetic mutism	not typical

*confirmed pathologically where EEG atypical; **present case.

Note added in proof

Recently, in a study from Austria, annual incidence values for CJD of up to 1.25 cases/million/year (in 1995) were recorded, implying near-perfect case ascertainment. In this study also a fall in the number of cases of CJD *dying* after the age of 65 was demonstrated. Over the entire period of study between 1969 to 1995, there were 19 deaths in the age group 60–64 years, falling progressively to two deaths in the age group 80–84 years.[12]

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Medical Anniversary

SAMUEL GEE, 13 September 1839

Samuel Gee (1839–1911) was born in Enfield, UK, and graduated in medicine from University College Hospital London in 1861. He became a physician at Great Ormond Street Children's Hospital and St Bartholomew's, both in London. He was the first person to identify coeliac disease but he is best remembered for Gee's cough mixture. Dr Robert Bridges was best man at his marriage. He was appointed physician to the Prince of Wales (later King George V) in 1901. — *DG James*