A CASE WITH RAPIDLY DETERIOATING COGNITION AND MYOCLONUS

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Case Presentation

W is a 89 years old lady. She has history of fracture with closed reduction and internal fixation performed three years prior to the index admission. Post operatively she manages to mobilize with quadripod independently. She was not on any regular medication. She was noted to have progressive memory impairment for 6 months. She presented to the Accident and Emergency Department with clumsiness on right side, associated with slurring of speech for 4 days. Examination showed lead pipe rigidity of four limbs and a mask face. Power was graded 4/5 at right upper and lower limbs power. She was slow in responding to questions. MMSE was at 6/30 and Barthel Index at 4/20. An urgent plain CT Brain was reported to have generalised cerebral atrophy compatible with age only. She was managed as acute ischemic stroke. Despite a course of rehabilitation for 3 weeks, she had progressive mental dullness, became non-communicable and developed tetraparesis with BI at 0/20. She was noted to have persistent myoclonus involving right upper limbs. Repeated plain CT Brain did not provide additional information. EEG was performed and showed generalized slow waves and frequent triphasic waves. Neurologist was consulted with a working diagnosis of diffuse encephalopathy and that Creutzfeldt-Jakob Disease has to be considered. A MRI was arranged which showed bilateral occipito-parietal hyperintense signal highly suggestive of CJD. Retrospectively there is no family history of neurological or psychiatric disease. The diagnosis is probable sporadic Creutzfeldt-Jakob Disease (sCJD).

Discussion

To the best of our knowledge, the patient is the oldest patient reported to have sCJD locally. CJD was previously recognized either a neuro-degenerative condition, or a disease transmitted by slow virus. In the past decade, there is a revolutionary change of concept in the disease, and the condition is now recognized as a prion disease. Following sections will focus on the concept of prion diseases, clinical features of sCJD, and the diagnosis of the condition.

Prion Disease

Prions are infectious proteins and are the etiological agents to a wide range of "neuro-degenerative" conditions[1]. In mammals, prion protein is encoded by a gene at short arm of chromsome 20. Usually a cellular isoform of the prion protein (PrP^c) is produced. This PrP^c can be hydrolysed and does not cause disease. Through a (some) unknown mechanism(s), the gene mutates and the disease-causing isoform PrP^{Sc} is produced instead. In the central nervous system, this PrP^{Sc} undergoes incomplete proteolysis to form PrP 27-30 which in turn polymerizes into amyloid and deposit as amyloid plaques in the CNS. It is hypothesizes that the different conformation of the PrP^{Sc} structure and its anatomical deposition results in different phenotypes of "neuro-degenerative" conditions[1].

Epidemiology and Clinical Features of sCJD

sCJD occurs in about 1 per million population worldwide[2]. It was difficult to ascertain the age of onset, but the reported age at death[3] ranged from 30-79 with a mean age of 65. There was a slight female predominate with a female to male ratio at 1.68:1[3]. Reportable death cases in England and Wales UK had increased from about 0.4 per million in the early 1970s to about 1.4 per million in the mid 90s[4]. This has attributed to an ageing population and increase surveillance rather than a reflection of true increase in its incidence.

The hallmarks of the disease are rapidly progressive dementia, myoclonus and death within few months[5]. These features can be associated with other focal cortical deficits. In the series of 152 cases[3], Wills RG reported that the commonest presenting symptoms were dementia (21%), followed by ataxia (19%) and behavioral disturbances (18%). On examination, 100% has evidence of dementia, 82% has myoclonus, 79% has upper motor neuron signs and 62% has dysphasia. Cerebellar signs were detected in 42% of patients and akinetic mutism occurred in 39%. The mean duration of illness is 4 months, although 10% of cases survive for more than 1 year[5].

It should be noted that sCJD represents a phenotype and comprises about 85-90% of the TSE (Transmissible Spongifiorm Encephalopathies). The other phenotypes include the variant (vCJD), familial type and iatrogenic types. With the similarity of pathological features with the Bovine Spongiform Encephalopathy (BSE), vCJD has aroused much concern over the past decades. Typically vCJD affects younger patients (average age 29 years)[6], has relatively longer duration of illness (mean 14 months before death), and is strongly linked to exposure. vCJD also presented predominately with progressive neuro-psychiatric disorder.

Diagnosis

Definite diagnosis of sCJD rests on histological proof from brain biopsy. "Probable sCJD" or "Possible sCJD" can be diagnosis with a combination of clinical features and laboratory findings[7]. In essence, a probable case of sCJD is made if they have progressive dementia, a typical EEG, and at least two of the following: myoclonus; visual or cerebellar signs; pyramidal or extrapyramidal signs; akinetic mutism.

EEG is an important investigation in sCJD. Typically it shows a generalized periodic complex. A validation study[8] using the criteria developed by Steinhoff BJ[9] demonstrated a sensitivity of 65% and specificity at 86%.

Routine CSF may show mild elevation of protein without increase in cell count. This elevated CSF correlates with the increase in CSF 14-3-3 protein which occurs in over 90% of sCJD cases. However, this CSF 14-3-3 is a non-specific marker of neuronal damage and can also be found in about 50% of vCJD cases[5].

Although CT brain is typically unrevealing, MRI may be the tell tale investigation. The classical picture is the presence of symmetrical high signal changes on T2-weighted images in the caudate and putamen regions. The test has a sensitivity of 67% and specificity of 93%[10]. The test is especially useful in the differentiation of vCJD, of which the high signal T2 weighted changes occur likely in the pulvinar region of the posterior thalamus[11]. It is promising that MRI will emerge as important criterion for diagnosis of sCJD though further validation studies need to be done.

Others issues - Infection Control

With the nature of prion transmission, it is understandably that anxiety arises as to the infection control measures after a case is diagnosed to have CJD. Guideline has been issued by WHO[12]. In essence, the highly infective tissues are the brain, spinal cord and eyes. Studies on infectivity of blood showed conflicting results. Rest of body fluids show no detectable infectivity. Accordingly, normal social and clinical contacts do not represent a risk to healthcare workers, relatives or the community. No special precautions are required for feeding utensils, feeding tubes, suction tubes or items involved in bed sore care. Special precautions may be taken in handling high risk specimens. This can be referred to the WHO guideline.

Summary

A case of sCJD is presented. Classically patients presented at their 5 or 6 decades with sub-acute onset and rapidly progressing cognitive impairment. Myoclonus also occurs in about 80% of cases though it may not the presenting feature. Median survival is about 4 months, though 10% survive beyond 1 year. Diagnosis is by combination of clinical features and investigations (EEG, MRI, CSF 13-4-4) though definite diagnosis rests on a brain biopsy. The infectivity is low except in brain, spinal cord and eye. General infection control measures suffice except for handling of tissue specimens.

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