A 66-YEAR-OLD WOMAN WITH SUBACUTE DEMENTIA

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Summary
We report a 66-year-old woman who suffered from dementia of subacute onset. The diagnosis of Creutzfeldt Jakob disease was reached clinically after some delay. The clinical criteria of diagnosing this rare cause of dementia are discussed. Updated information on some useful investigation e.g. magnetic resonance(MR) imaging of brain and other methods in experimental stage is also provided.

Introduction
Dementia in elderly people is usually due to Alzheimer’s disease and vascular dementia in over 80% of cases. Such high prevalence may blunt our alertness to look for rare causes of dementia in elderly people. Patient suffering from dementia of rapid onset is certainly uncommon and worth detailed examination and investigation as illustrated by the following patient.

Case Report
A 66-year-old woman was admitted to our hospital with the suspicion of suffering from extrapyramidal side-effects of major tranquilizers. She was well all along and had no significant medical, surgical nor family history. She had two-month history of increasing forgetfulness. According to her relatives, she became increasingly dull and failed to perform her usual duties as a housewife. She stopped going to market, used wrong words during conversation, failed to cook, launder and even to open the door with keys. The patient claimed that she forgot how to do these things. She was noted to have difficulties in using her hands especially the right side.

Both the patients and her relatives had been shopping around in town for specialist consultation. Various diagnoses were offered: stroke, dementia, hysteria and catatonic psychosis. A private computerised tomography (CT) scan of her brain was reported to be normal. A number of cerebral activators and major tranquilizers were prescribed to improve her condition but in vain. Her body and limbs gradually became rigid and she became chair and bed bound. Feeding was also difficult. She developed involuntary limb and body movements several days after fluphenazine decanoate depot injection which led to the hospital admission.

Physical examination on admission revealed that the patient was alert but mute. She had marked lead-pipe rigidity of body and limbs without any spontaneous movement. Myoclonic jerks of the limbs were detected. Motor power of limbs could not be assessed because of the rigidity and the absence of voluntary movement. Deep tendon reflexes were also not elicited because of the rigidity. Primitive reflexes were absent. The plantar reflexes were down going. Examination of other systems was normal. Basic blood and cerebrospinal fluid (CSF) investigation results were also normal. A second cerebral activators and major tranquilizers were prescribed to improve her condition but in vain. Her body and limbs gradually became rigid and she became chair and bed bound. Feeding was also difficult. She developed involuntary limb and body movements several days after fluphenazine decanoate depot injection which led to the hospital admission.

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CT scan of brain (three months after presentation) showed mild cerebral atrophy. Electroencephalogram (EEG) of the patient showed generalized periodic sharp waves, bilateral and synchronous, one to three phases, 1-2 Hz with a background of theta slow waves (Fig. 1). The diagnosis of sporadic type of Creutzfeldt Jakob disease (CJD) was made. The patient survived ten months more in a bed bound state with nasogastric tube feeding in a convalescent setting. A magnetic resonance (MR) scan of brain was performed ten months after presentation. It showed generalized cerebral and cerebellar atrophy with prominent sulci and ventricles. Marked atrophy of the basal ganglia and diffuse high signal abnormality in the periventricular regions and centrum semiovale were also noted on T2 weighted images. In addition, bilateral decreased signal intensity in the thalamus on T2 weighted images was evident (Fig. 2 a, b, c). The patient’s relatives declined any brain biopsy nor post-mortum examination.

Discussion

There has been concern that the diagnosis of CJD might be missed in elderly patients as dementia are easily labelled by the unwary to be due to Alzheimer’s disease or other psychiatric orders. In UK, a significant increase in the incidence of CJD since 1990 was largely due to an increase in the number of cases in patients aged over 75.

Our patient fulfilled the clinical criteria of definite CJD (mental deterioration, myoclonus, 1-2 Hz periodic EEG complexes) according to Brown, et al. CJD is a form of transmissible spongiform encephalopathies (TSE) or prion disease which is transmissible within and between mammalian species. CJD in human is classified as inherited, acquired or sporadic types. The inherited types, being autosomal dominant, contributed about 15% of cases. The acquired type is usually iatrogenic. Transmission of the disease in human has been reported to be via human growth hormone or gonadotropin, dura mater, corneal graft and neurosurgical instruments. Effective methods of sterilization and disinfection for the etiologic agent remained unknown. The sporadic type, as in our case, has a prevalence of one per million worldwide, affecting both sexes equally with peak plateau between age 55 and 75 years. The median duration of illness was 4 months and 90% of patients died within a year of onset. However, better nursing care of patients in vegetative state nowadays may lengthen the survival as our case.

The diagnosis of CJD can only be confirmed by neuropathological presence of the classic triad in brain biopsy or at necropsy: spongiform vacuolation, astrocytic gliosis and neuronal loss. However, this is not usually available before patient’s death, especially in elderly people. Thus, diagnosis in lifetime depends a lot on the clinical features and investigative findings.

The clinical criteria derived from 230 neuropathologically verified cases by Brown were: rapidly progressive dementia, myoclonus and characteristic EEG periodic sharp-wave complexes (PSWC). It has been proven by experimental transmissibility in primates that clinical diagnosis is highly accurate, particularly if there is a charac-
teristic appearance on an EEG. However, not all cases are typical. Unusual clinical features included cerebellar ataxia, extrapyramidal rigidity, cortical blindness, pyramidal signs, oculomotor disorders, paresthesias, central sensory disturbances, seizures and vegetative dysfunction⁵. Other atypical presentations have been reported e.g. progressive aphasia without dementia and persistence of unilateral neurological deficits. About 10% of patients have a protracted clinical course which makes the distinction from Alzheimer’s disease difficult.

The typical EEG findings as in our case usually arouse the clinical suspicion. The presence of PSWC was shown to have high diagnostic value in CJD³. However, the characteristic PSWC may not be apparent in the early and final phase of the disease. Nonspecific alpha activity disappearance with replacement by generalized theta and delta activity (may be asymmetrical and focal) are the usual early EEG features. Levy, et al⁶ found that development of PSWC was usually within twelve weeks of onset of clinical symptoms. The absence of PSWC is a point strongly against the diagnosis of CJD unless it is a rare subtype of long duration. The presence of PSWC was found to be more linked with myoclonus and severe neocortical involvement and at least mild thalamic involvement⁵.

Brain imaging such as CT scan is considered not very useful in diagnosing CJD and usually shows no abnormality or nonspecific cortical atrophy. Recently, MR scan of brain was found to show some specific diagnostic features for CJD patients, making it a useful investigative option. It was shown that bilateral & symmetrical increased signal intensity in caudate nuclei and putamina on long-repetition-time MR images in elderly patients with acute dementia was suggestive of CJD (present in 80% of 29 pathologically proven cases)⁸. The scans were performed at three months on average after presentation. The hyperintense signals were due to gliosis, spongiform changes and neuronal loss early in the course of CJD. In our case, the MR scan did not show such features. However, it was performed ten months after the onset and near the end of the disease course. Marked atrophy of the cerebral cortex, basal ganglia, diffuse white matter demyelination and mineralization in the thalami were shown. Recently, a case report⁷ of pathologically proven case of CJD showed that MR picture at fifteen months after presentation could be global cortical atrophy of the cerebrum and cerebellum accompanied by white matter degeneration. The initial MR signal abnormalities in the basal ganglia may be subtle⁷. Bilateral decreased signal intensity in the thalamus on T2 weighted images due to mineralization also have been reported⁸. These findings are very similar to that of our case.

Thus, MR of brain should be performed early in suspected cases of CJD in order to detect the characteristic diagnostic features.

The recent suspicion of a new variant CJD causing the “Mad Cow Disease” in young people in UK pressed for the development of reliable and safe pre-mortem methods of diagnosing CJD. A new test based on immunoassay of a special protein (named 14-3-3) in CSF was found to have high specificity and sensitivity for CJD in demented patients⁹. The recent report of early detection of prion protein in tonsillar tissues¹⁰ also aroused interest. It raised the possibility of diagnosing the disease in the preclinical stage. However, generalized usage of these methods in daily practice requires further evaluation.

The diagnosis of CJD is made more challenging when a recent report showed that AIDS-dementia complex could mimic the clinical and EEG features of CJD which improved dramatically after zidovudine treatment¹¹. Thus, checking the HIV status in clinically suspected cases appears mandatory.

References


