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A Case of Creutzfeldt-Jakob Disease

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Creutzfeldt-Jakob disease (CJD) is presumably caused by a slow infectious pathogen or prion. The principal clinical features of Creutzfeldt-Jakob disease are dementia, pyramidal and extrapyramidal symptoms and signs, cerebellar dysfunction, and myoclonus. The patient rapidly deteriorates, declines to a vegetative state, becomes comatous, and is ultimately dead within several months. The authors present a case of Creutzfeldt-Jakob disease, proved by clincal findings, typical serial EEG, and pathologic features.

Key Words : *Creutzfeldt-Jakob disease*

INTRODUCTION

Creutzfeldt-Jakob disease is known to be a transmittable disease. In the course of the disease,clinical manifestations of CNS involvement are presented progressive dementia, motor and sensory disturbance, and cranial nerve dysfunctions. A pathological feature of this disease is characterized by spongiotic change in the cerebral cortex. Recently, we experienced a case of CJD, proven by clinical features, serial EEGs, and pathological findings.

CASE

A 54-year-old female was admitted to Hanyang University Hospital on July 10, 1990 because of general weakness, headache, sleep disturbance, and behavior change. She had no specific familial or personal history. On admission, her blood pressure was 160/90mmHg, body temperature .37C, pulse rate 100/min, and respiratory rate 20/min. On neurologic examination, she was alert and her memory was intact, but she was disoriented in time and place. Visual acuity and field were intact. The extraocular muscle movement showed a full range of motion. No facial palsy and no evidence of pathologic reflexes were noted, but she kept raising both her arms in a repeated motion, as if trying to catch something. Peripheral blood count revealed Hgb 12mg%, WBC 10900, and platelet 240,000. Blood chemistry, routine urine analysis, liver function test,and thyroid function test were within normal limits. On CSF study, WBC was 0, protein 63mg%, and sugar was normal. Computerized tomography demonstrated no specific finding (Fig. 1). Magnetic resonance imaging also revealed normal brain architecture (Fig. 2), Fifteen days later, the patient became confused, disoriented, and spastic, and intermittent myoclonic seizure in all extremities developed. She fell into a progressively bed-ridden state. Electroencephalo-graphy showed periodic sharp waves with 1-1.2Hz (Fig. 3). A brain biopsy was performed in the frontal, temporal, and parietal lobes.

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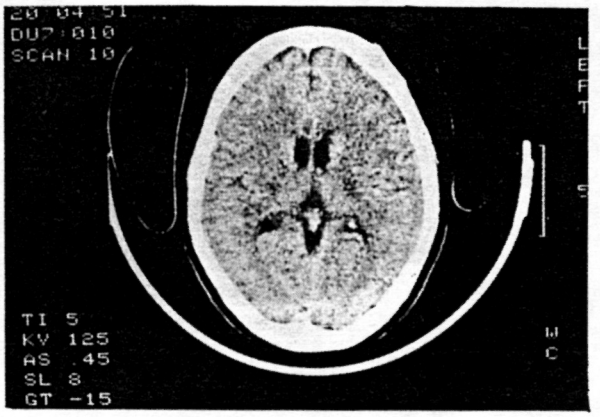

Fig. 1. No specific finding in brain CT can be seen.

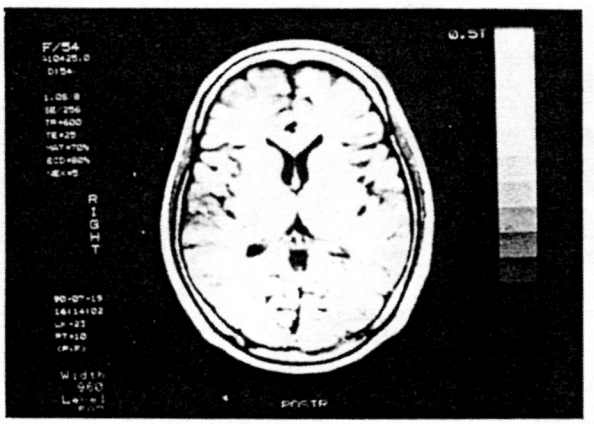

Fig. 2. Axial MR image also reveals normal brain architecture (600/25).

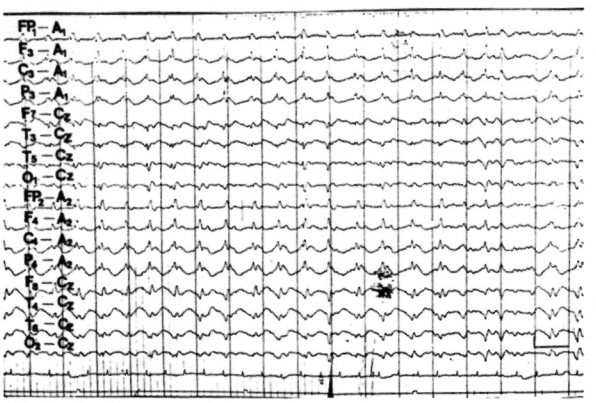

Fig. 3. EEG shows periodic sharp wave with 1 HZ (90 hospital day).

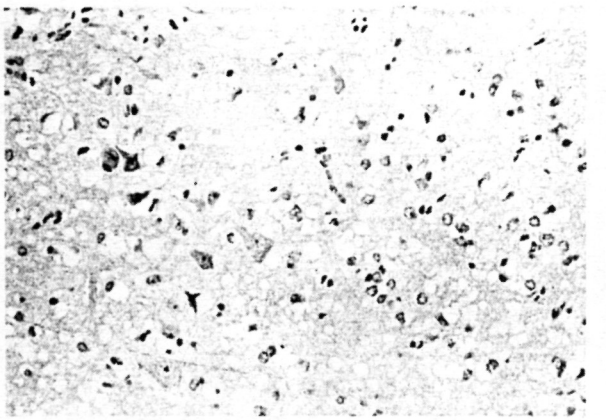

Fig. 4. Extensive spongioform change in the cortex is seen (H and E, X 200).

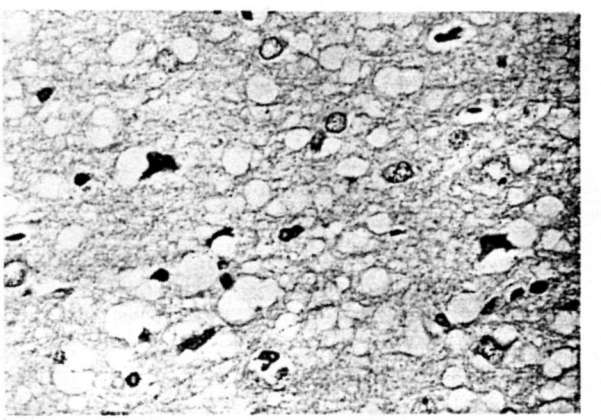

Fig. 5. Higher magnification reveals intracytoplasmic vacuoles and the degenerated and angulated nuclei of neuronal cells (H and E, X 400).

All three specimens showed similar histologic features. Diffuse and marked spon-giform changes throughout the cortex were noted (Fig.4). The vaculoes varied in size, and some of them were confluent. They were intraneuronal or freely scattered in the neuropil. Neuronal degeneration was marked, and their nuclei were pyknotic and angulated by stuffed cytoplasmic vaculoes (Fig.5).

Astrocytic gliosis was not so prominent and seemed to be inversely related to the degree of vacuolation (Fig.6). Inflammatory reaction was notably absent throughout the brain substance.

Electron microscopic study revealed typical membrane-bound vacuoles, which were curled

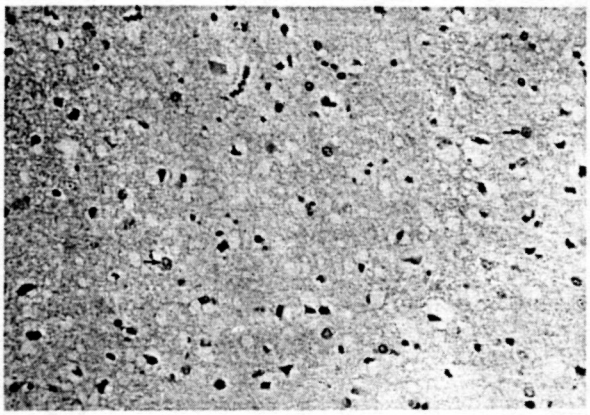

Fig. 6. Proliferation of reactive astrocytes is shown (arrows). Vaculolization is not so marked (H and E, X 200).

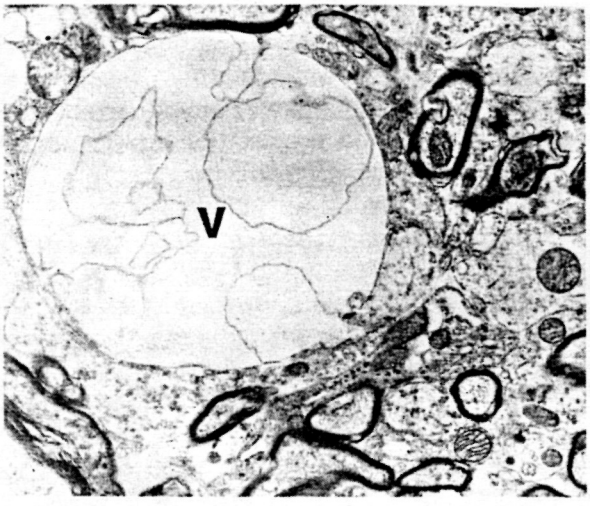

Fig. 7. Eletron micrograph shows a large vacuole (V0 in the neuropil. The vacuole is membrane-bound and curled with multiple buddings into the vacuole (X 10,000).

or coiled making multiple budding daughter cysts within the vacuole (Fig.7). The axonal and dendritic processes were swollen, and the neuronal cells were degenerated (Fig.8). Viral inclusions or virus-like particles could not be found. Recently, the patient has become stuporous, with intermittant myoclonic seizure involving all the extremities.

DISCUSSION

Creutzfeldt-Jakob disease was recognized by Creutzfeldt (1920) and Jakob (1920) as a

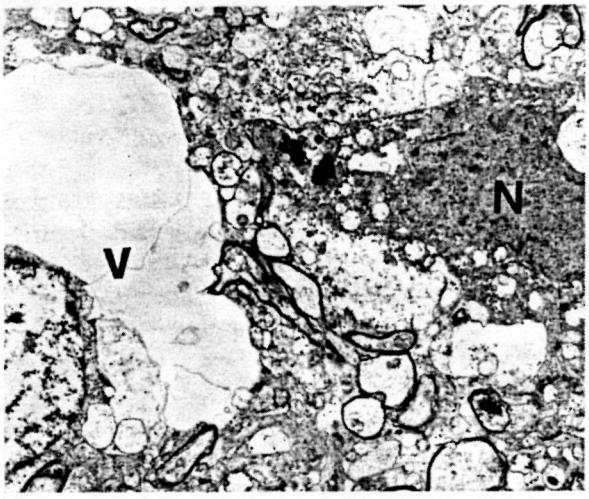

Fig. 8. An electron micrograph shows a degenerated neuronal cell (N) with cytoplasmic clearing. Axonal and dendritic swellings are also present. No virus-like pare present within the vacuole (V) (X 4000).

clinicopathological entity and was named by Spielmeyer (1922). Others reported this disease as corticopallidospinal degeneration, or corticostriatospinal degeneration (Davison, 1932). This disease has been reported to be worldwide in distribution. The vast majority of cases are sporadic, but perphaps as many as 10% to 15% have affected other family members (Masters et al., 1979). Its cause has been thought to be a common exposure factor rather than genetic. Creutzfeldt-Jakob disease is rare ; incidence in France (Cathala et al., 1986) and in England and Wales (Metthews and Will, 1982) is 0.45/million, i.e., less than half the figure of 1 million often cited. In Korea, 2 cases have been reported (Kon et al., 1983 : Jung et al, 1985).

But the cases were reported by only clinical manifestations and EEG findings without pathological confirm. CJD is of initial onset but with rapid and relentless clinical deterioration. The first symptoms are nonspecific-depression, fatigue, forgetfulness, anxiety, lassitude, alteration of personality and behavior, mood swings, sleep disturbance, and difficulty with calculation. In our case, patient had non-specific symptoms, for example headache, sleep disturbance, behavior change. We considered her complains as a

somatiform disorder. However, it usually becomes apparent that the progression of CJD is more rapid, and signs appear indicating involvement of other parts of the neuraxis. Spasticity, clonus, and extensory plantars indicate pyramidal disorder. Rigidity and tremor, indicate disorders of extrapyramidal system. As the disese progresses further, evidence of cerebral disease with myoclonic seizure, vegetative dysfunction, and eventual coma and physical disintegration ensues, leading to death from intercurrent infection within 6 to 12 months.

Our patient fell into vegetative state within 3 month. The EEG is abnormal in virtually all cases during the course of the disease, but it may be normal or nonspecifically abnormal with diffuse slow-wave activity in the earlier stages. Rhythmic periodic bursts of high-voltage biphasic or triphasic sharpwave complexes, sometimes with spike and wave activity, appear, which is characteristic but not pathognomic (Burger et al.,1972; Chiofalo et al., 1980). At necropsy, the brain shows generalized cerebral atrophy, although grossly detectable abnormalities can be absent when the disease has been rapidly progressive. Three histologic features are diagnostic hallmarks of subacute spongiform encephalo-pathy. There are 1) marked spongiform changes throughout the cortex, especially in the deeper cortical layers, 2) neuronal degeneration and loss, and 3) astrocytic proliferation. The spongiform change is prominent in the early stage or in rapidly fatal cases. In contrast, astrocytic proliferation is more prominented in the later stage of the disease (Masters and Richardson, 1978). The spongiform change is the result of a swollen neuronal and astrocytic process, as well as membrane-bound vacuoles. Also, amyloid plaques are found much less frequently than in Alzheimer's disease (Beck et al., 1969; Manuelidis, 1985; Masters and Richardson, 1978) and have been shown to be composed of prion-proteins (De Armond et al., 1985). In our patient, amyloid plaque was not found at biopsy. The source of infection and the transmission method of the disease are unknown. Iatrogenic transmission has been reported by corneal transplantation (Duffy et al., 1974), by intracerebral electrode implantation (Bernoulli et al., 1977), and by administration of growth hormones from the pituitary gland (Brown et al., 1985; Gibbs et al., 1985; Koch et al., 1985; Powell-Jackson et al., 1985). Prion is the name given to the group of slow infectious agents which are distinct from viruses and viroids which are thought to cause the transmissible encephalopathies (Prusiner, 1987). Prion is proteinaceous infectious particle containing no nucleic acid. It has been demonstrated that an agent of CJD is similar to scrapie proteins (Bendheim et al., 1985; Bockman et al., 1985; Manuelidis et al., 1985). Hsiao(1990) classified it as an inherited prion disease ; Kurn, Creutzfeldt-Jakob disease, Gerstmann-Straussler-Scheinker syndrome. Recently an immunological test using antiserum against a purified fraction of scrapie-infected hamster brain can detect antigen in purified preparation of CJD brain in 81% of the cases using the Western blot technique (Brown et al., 1986).

Differential diagnoses from CJD are listed in (Table 1.) Treatment is unsuccessful, although there have been occasional claims that partial remission may be induced by antiviral agents such as amantadine (Sanders

Table 1. Differential Diagnosis of Creutzfeldt-Jakob disease

Kuru
Herpes Encephalopathy
SSPE
General Paresis
Alzheimer's Disease
Parkinsonism with Dementia
Wilson's Disease
Huntington's Chorea
ALS with Dementia
Common Vascular Disease
Subacute Diencephalic Angioencephalopathy
Hepatic Coma
Cerebral Anoxia
Drug Intoxication
Genetic Storage Disease
Multiple Sclerosis
Schizophrenia

and Dunn, 1973) or vidarabine (Furlow et al., 1982), which have been uncleared. We used vidarabine for our patient during 1 month. But it was no benefit effect. The most recent recommendations are that infectivity can be abolished either by autoclaving for 1 hr at 132℃ or by exposure to 1-N sodium hydrochloride for 1 hr at room temperature. Disposable items should then be burnt (Committee on Health Case Issue, 1986.)

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