

CREUTZFELDT-JACOB DISEASE: FIRST BIOPSY PROVEN CASE IN IRAN

Hossein Kalanie,* MD

Abstract—A biopsy diagnosed patient with Creutzfeldt-Jacob disease is reported in Iran. This 53-year-old hunter presented in May 1994 to Mehr Hospital with typical clinical manifestations of Creutzfeldt-Jacob disease and died 4 months later. Brain biopsy revealed severe neuronal loss, spongiosis and gliosis of cerebral cortex. Exposure of this hunter to the brain tissue of animals may explain the route of transmission of the disorder.

Acta Medica Iranica 33(1&2): 47-51; 1995

Key words: Creutzfeldt-Jacob disease; Prion disease; Iran; occupational transmission

INTRODUCTION

Creutzfeldt-Jacob disease is a transmissible neurodegenerative disease of prion infection which has been reported throughout the world (1). Eventhough the triad of progressive dementia, myoclonia and periodic electroencephalographic pattern are suggestive of the disease process (2), proven diagnosis basically will remain on biopsy findings. However, this procedure is not too often performed in Iran due to cultural barriers. In this report a biopsy proven case is presented and the clinical and diagnostic aspects of the disease are discussed.

CASE REPORT

A 53-year-old male hunter was admitted to Mehr Hospital on May 1994 because of rapid deterioration of

his mental state over the past six weeks. His medical history was unremarkable. He had never been abroad and there was no family history of dementing illness. On admission, his general medical examination was negative. On neurological examination, he laughed inappropriately at times. He was awake and oriented with respect to person and place; he knew the month but not the date. He was not highly knowledgeable. His reply to questions was often inconsistent and incorrect. He obeyed simple commands with preservation, poor concentration, and impersistence. He could not perform serial subtractions and confused his right side from his left. All cranial nerve functions were preserved, and his strength, coordination and sensations were intact. Deep tendon reflexes were slightly hyperactive but were symmetrical and had bilateral Babinski sign. He had a masked face with monotonous speech. He had 2⁺ cogwheel rigidity in his limbs and 1⁺ rest tremor in his hands with poor associative movements and retropulsion. Glabellar, suck, and snout reflexes were present but he had no grasp reflex. The CBC, ESR, FBS, liver function tests, BUN, creatinine, urine analysis, calcium, phosphorous, vitamin B¹² and folate level, and thyroid function tests as well as serum protein electrophoresis all were within the normal range. Lupus erythematosus (LE) cell and VDRL were negative.

A lumbar punure yielded clear, colorless, acellular cerebrospinal fluid; the glucose was 75 mg and the protein 44 mg per deciliter, microscopical examination of the specimens of the fluid disclosed no fungi, acid fast-bacilli, or other microorganisms. Test for cryptococcal antigen and a serologic test for syphilis were negative; culture remained sterile. Chest x-ray was normal. An electroencephalographic study was performed with patient awake. This showed background activity that consisted of diffuse moderate voltage of 4 to 5 Hz, intermixed anteriorly with intermittent delta activity of 2 to 3 Hz. Photic stimulation provoked no activation; and

*Associate Professor and Neurologist, Mehr and Shohada Hospitals, Faculty of Medicine, Shahid-Beheshti University of Medical Sciences, Tehran, Iran.

hyperventilation was not performed (Fig. 1). Cranial CAT scanning with and without contrast injection and an MRI scan of the brain did not reveal any abnormalities (Figs. 2 and 3), however both were of poor quality due to irritability of the patient and movement artefact. While in the hospital and during the third week of admission he became unmanageable with bouts of bizarre and uncontrollable agitation and had shaking spells suggestive of a seizure. At this stage he alternated between laughing and crying and had episodes of urinary incontinence. A brain biopsy was performed upon wife's consent, which showed neuronal loss, gliosis and spongiform changes of the gray matter compatible with Creutzfeldt-Jacob disease (Fig. 4).

At the end of his fourth week of hospitalization he was discharged to be cared for at home where his speech gradually deteriorated, myoclonic jerks appeared; he became speechless and died of aspiration, pneumonia, three months after his discharge from the hospital.

DISCUSSION

Creutzfeldt-Jacob disease is rare with an estimated yearly incidence of less than one case per million

population (3). It affects men and women equally (4). Unlike Alzheimer's disease, Creutzfeldt-Jacob disease has been reported in all age groups, although the median age at onset is in the seventh decade. It is considered a sporadic illness, although in about ten percent of the cases it is familial. Occupational transmissions have been reported in a neurosurgeon, a pathologist, two histology technicians and an orthopedic surgeon (5). Also, the disease has been reported in several people working in occupations where exposure to neural tissue could have happened, (for example, butchers, farmers and various health professionals (4), to name a few). In some children who received cadaveric pituitary growth hormone (6), and a few other patients who received corneal and dural grafts (7), the disease was also evident.

In identifying the nature of the infective agent, Prusiner (8) ushered in the molecular era of neurology in Creutzfeldt-Jacob disease. He coined the term "prions" to denote small proteinaceous infectious particles that are apparently devoid of nucleic acid.

There are three human prion diseases—the infectious disease kuru, the genetic illness Gerstmann-Straussler-Scheinker and Creutzfeldt-Jacob. Because abnormal isoforms of prions accumulate in brain of patients with all these conditions (9), it is not surprising that they share clinical features.

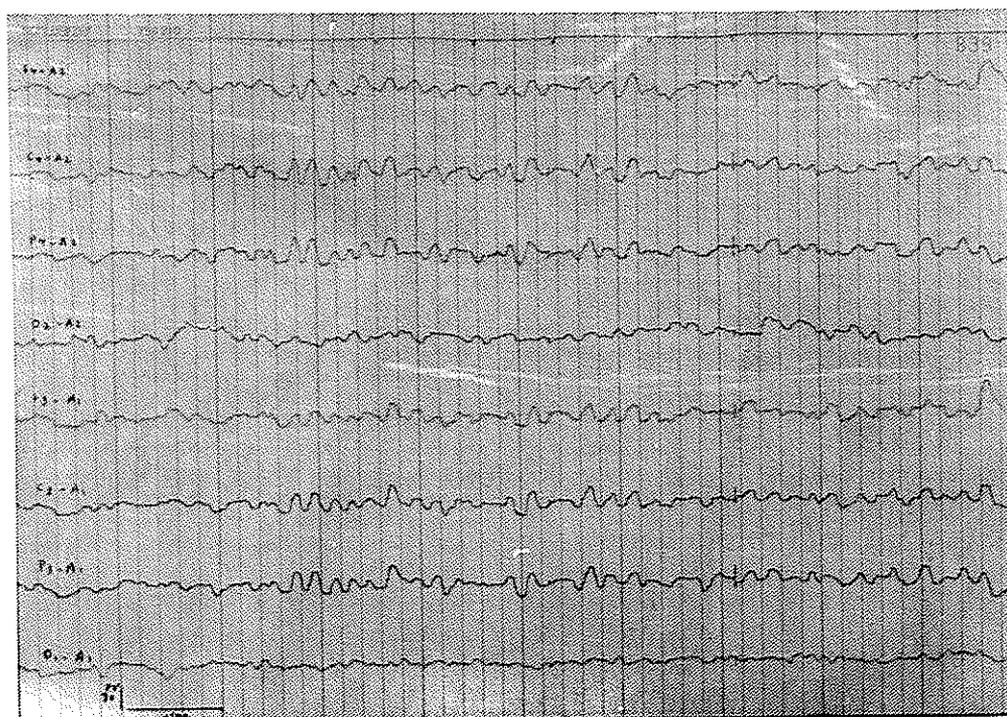


Fig. 1. EEG of the patient which shows 4-5 Hz rhythm mixed with 2-3 Hz anteriorly.

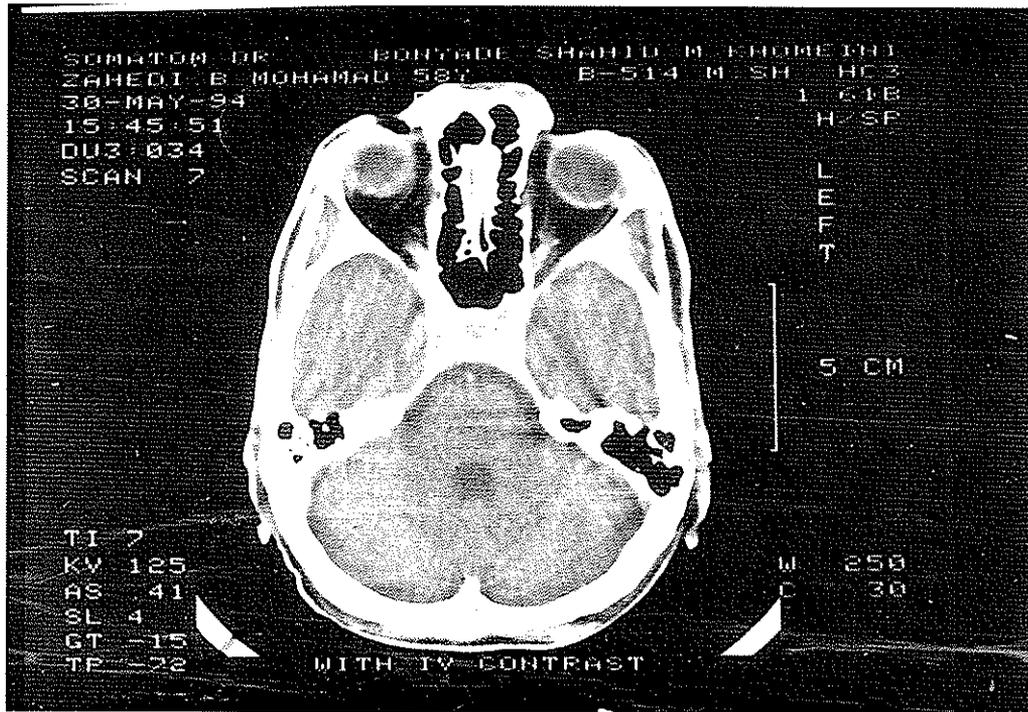


Fig. 2. Normal brain CAT scan.

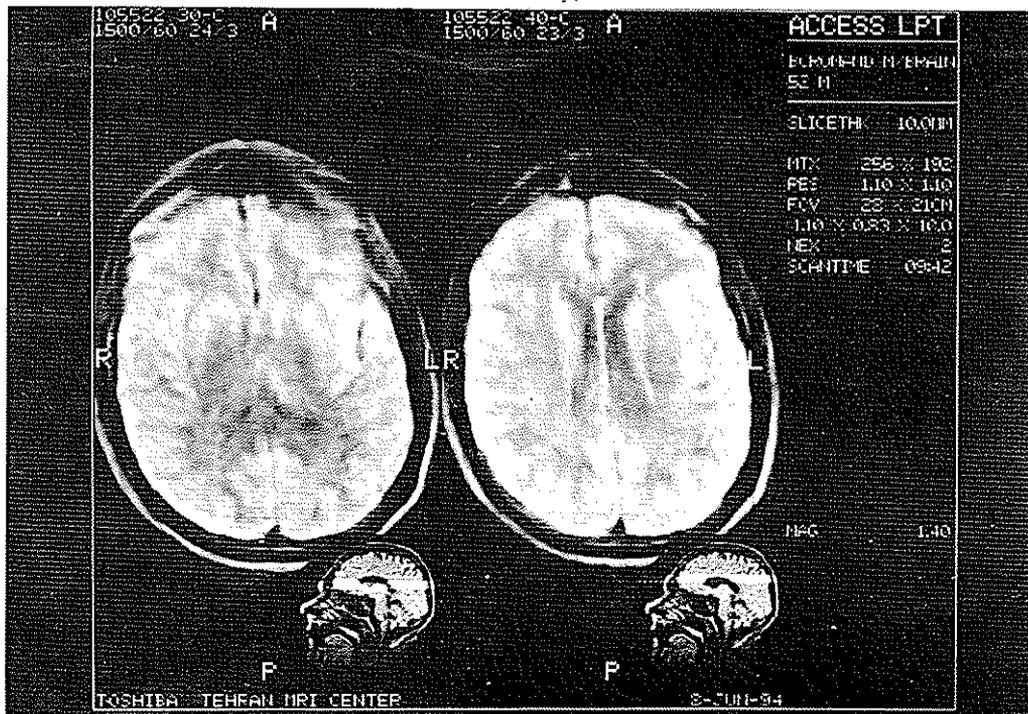


Fig. 3. Normal MRI of the brain.

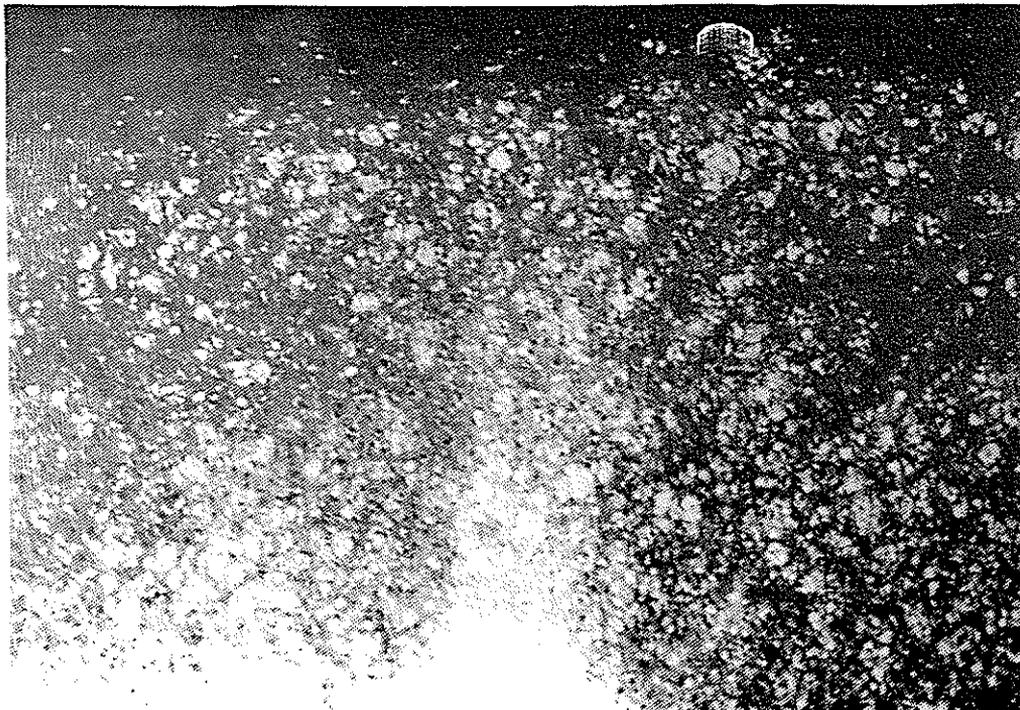


Fig. 4. Brain biopsy which shows spongiosis and gliosis.

The onset of the disease is often heralded by a prodrome of behavioral abnormalities, including personality changes, depression, and amnesia. Alterations in mental state occur in all the patients and are often the first signs of the disease. As noted in this case and in contrast to Alzheimer's disease, motor abnormalities due to dysfunction of the pyramidal tract, cerebellum, and basal ganglia are common. Evidence of pyramidal tract damage, including Babinski sign, is almost always present, whereas lower-motor-neuron signs are unusual, cerebellar function is impaired, often early in the disease, and is manifested by ataxia and intention tremor. Signs referable to involvement of basal ganglia include rigidity, bradykinesia, tremor, dystonic posture, and choreoathetosis. In this case clinical findings were of progressive dementia with signs of basal ganglia dysfunction. The brain imaging studies were normal, however nonspecific cerebral atrophy and hyperintense MRI signals in the basal ganglia and thalamus have been emphasized in recent reports (11,12). The electroencephalogram is always abnormal in cases of Creutzfeldt-Jacob disease. Initially, as in this case, there is generalised slow wave activity which usually gives way to a characteristic tracing of paroxysmal sharp-wave activity against the slow background rhythm. In about 88

percent of the cases the EEG displays periodic sharp-wave activity and slow wave burst suppression (2). In the present case only the early changes were recorded.

It is concluded that, the patient exposure to infected brain tissues of the animals might have been the transmission route.

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