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Case report

Creutzfeldt-Jakob disease in Oman: report of two cases

Euan M. Scrimgeour [a,*], Pratap R. Chand [b], Kimbra Kenny [c], Paul Brown [c]

[a] *Infectious Diseases Unit, Department of Medicine, Sultan Qaboos University, P.O. Box 35, Al-Khod (Muscat), Oman*
[b] *Neurology Unit, Department of Medicine, Sultan Qaboos University, Al-Khod (Muscat), Oman*
[c] *The Laboratory of Central Nervous System Studies, National Institutes of Health, Bethesda, MD, USA*

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Abstract

Sporadic Creutzfeldt-Jakob disease (CJD) was diagnosed in two Omani Arab men, aged 50 and 75 years respectively, both with a history of rapidly developing dementia and myoclonic jerks. Illness developed over a period of 3 months in the first case and over six months in the second. Electroencephalography in both subjects showed periodic triphasic sharp waves characteristic of CJD. In neither case was it possible to obtain a brain biopsy or perform autopsy (autopsy is contrary to Islamic practice in the Middle East), however, electrophoresis of cerebrospinal fluid from the second patient revealed the distinctive double protein spots characteristic of CJD. This is the first report of CJD from Oman.

Keywords: Creutzfeldt-Jakob disease; Oman-Arab race; Cerebrospinal fluid

1. Introduction

Creutzfeldt-Jakob disease (CJD) is one of the transmissible human spongiform encephalopathies, and the sporadic form of the disease occurs at a mean incidence rate of 0.5–1 case per million population per annum. Sporadic CJD is believed to result when a normally occurring amyloid protein precursor, present in neurological and other tissues, is transformed by an unknown stimulus, to produce a self-replicating molecule that can form insoluble fibrils of amyloid plaques (Brown, 1994). CJD typically presents with rapidly progressive dementia, generalized myoclonic jerks, and ends in death after a mean duration of 7.3 months of illness.

The diagnosis is supported by the characteristic electroencephalogram (EEG) recording of triphasic periodic waves at 1–2 cycles/s, and by histopathological evidence of spongiform changes with astrogliosis in brain tissue obtained by brain biopsy or at autopsy. The cerebrospinal fluid (CSF) is acellular with normal or mildly elevated protein levels, but electrophoresis may reveal abnormal proteins of diagnostic value which are present only in CJD and in herpes simplex encephalitis (Harrington et al., 1986). Transmission experiments in which inoculation of extracts of neurological or certain other tissues obtained by biopsy or autopsy into non-human primates leads to spongiform encephalopathy, constitute a further method of confirming CJD (Brown et al., 1994). We describe here two typical cases of CJD in Omani patients. Although neuropathologic evaluation was not possible, CSF from one patient revealed the double protein spots that are typically found in patients with CJD (Harrington et al., 1986).

2. Clinical reports

2.1. Case 1

A 50-year-old Omani Arab man from the town of Nizwa, 60 km west of Muscat, who had been previously well, developed trembling movements of the left upper limb. Over the subsequent three months, generalized myoclonic jerks appeared, and in addition, memory loss and disorientation developed. He became progressively obtunded and ultimately, unresponsive to speech. On admission to the Sultan Qaboos University Hospital (SQUH), he was conscious but unresponsive, and he reacted to pain only by withdrawal. The neurological features observed are documented in Table 1. Routine haematological, biochemical, and serological screening tests revealed no sig-

* Corresponding author. Tel: +968 515102. Fax: +968 513419.

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Table 1
Clinical characteristics of two Omani patients suspected to have CJD

Symptoms and signs	Patient 1 Male, 50 years	Patient 2 Male, 75 years
Mental deterioration		
Memory loss	++	++
Higher cortical function	++	++
Behavioural abnormalities	++	++
Primitive reflexes	++	++
Visual/oculomotor	−	++
Vertigo/dizziness	−	++
Headache	−	−
Pyramidal	−	−
Extrapyramidal (rigidity)	+	++
Cerebellar	+	+
Involuntary movements		
Myoclonus (stimulus sensitive)	++	++
Other including tremor	−	−
Sensory	−	−
Lower motor neuron: amyotrophy	−	+
fasciculations	−	+
Seizures	−	−
Periodic EEG		
Triphasic 1 cycle/s sharp waves	++	+
Burst suppression	+	−

Scale: ++, marked; +, present; −, absent.

nificant abnormality, and at lumbar puncture, the CSF was clear and acellular, with normal protein and glucose levels. Virus particles were not detected by electron microscopy of the CSF, and tissue culture of CSF failed to reveal evidence of viral infection. A computerised tomography (CT) scan of the brain demonstrated mild cerebral atrophy. The EEG showed background suppression, and generalised periodic triphasic sharp wave discharges at a frequency of 0.5 to 1 per second, associated with myoclonic jerks, supporting the clinical diagnosis of CJD. Further deterioration occurred, and the relatives elected to take him home where he died. An autopsy was not permitted by the relatives.

2.2. Case 2

A 75-year-old Omani man from Ibra, a rural district north of Muscat, had been well until 6 months earlier, when he began to complain of dizziness, vertigo, and ataxia with falls. He became forgetful, and reported visual impairment. Over the subsequent three months, he exhibited increasing memory loss, disorientation, and inability to recognize relatives and friends. He became inert and dysphasic, and developed sporadic jerking movements of the left arm and leg. Incontinence became established. In the four weeks prior to admission, he had become mute and unresponsive to speech. Generalized myoclonic jerks involving the trunk and all limbs were now prominent. He was evaluated initially in a rural hospital, where lumbar puncture revealed clear, acellular CSF with a protein level of 54 mg%.

On admission to the SQUH, he was conscious but mute, and he did not respond to speech. On examination, significant clinical abnormalities were confined to the neurological system (Table 1). Routine haematological, biochemical, and serological investigation revealed no significant abnormality. A repeat lumbar puncture again revealed clear, acellular CSF, with a normal glucose level but a mildly raised protein level (96 mg%). Further investigations included CT of the skull and brain which revealed advanced cerebral atrophy with dilated ventricles. The EEG showed periodic, generalised, sharp wave discharges at a frequency of 1 Hz, predominant over the left mid-temporal regions, supporting the clinical diagnosis of CJD.

The feasibility of obtaining a diagnostic brain biopsy was being assessed when the patient abruptly deteriorated and died. The relatives at once removed the body for burial in their own district, and autopsy was not possible. However, a specimen of cerebrospinal fluid was preserved at −80°C, and subsequently evaluated in the Laboratory for Central Nervous System Studies, the National Institutes of Health, Bethesda. Two-dimensional gel electrophoresis followed by silver staining revealed the presence of two protein spots (130 and 131) that have to date been found only in patients with CJD or herpes simplex encephalitis; in particular, the spots have not been seen in any patient with other chronic neurological illnesses, including Alzheimer's disease (Harrington et al., 1986). As our patient's clinical history was typical of CJD and not at all consistent with a herpes infection, the CSF result provides diagnostic confirmation of CJD.

3. Discussion

It might be anticipated that Oman, with a population of some two million individuals, would have an incidence rate of sporadic CJD in the range of one to two cases per annum. During a period of four years (1991–1995), the patients described here were the only suspected cases of CJD to be diagnosed in the SQUH. No cases of CJD were diagnosed by the neurologists of the major Ministry of Health hospital in Muscat (the Sultan Hospital) over this period. As these are the two tertiary referral hospitals for neurological patients from all over Oman, it is likely that most patients with rapidly developing dementia and myoclonus would be evaluated in one of these centres. Thus the incidence of CJD in Oman is unlikely to be more than one or two cases per million population per annum, in keeping with the incidence rate in most populations. Elsewhere in the Middle East, sporadic CJD appears to be equally rare: in Saudi Arabia, only a single case has been reported; here, histopathology was not obtained (Al-Tahan et al., 1991).

The diagnosis of CJD was made in our patients on the basis of a rapidly developing dementia with myoclonus,

and supported by typical EEG abnormalities. A number of conditions may resemble established CJD clinically, including herpes simplex encephalitis, multiple cerebral abscesses, cryptococcal meningoencephalitis, hyperparathyroidism, and syndromes associated with administration of bismuth, lithium and tricyclic antidepressive drugs (Brown, 1994), but the characteristic EEG is absent in these cases. There was no evidence that any of these conditions were present in our patients, neither of whom had previously been taking medication. When these conditions are excluded, the clinical presentation of CJD is so distinctive that in most cases a confident diagnosis can be made on the basis of the history and examination alone, supplemented by the results of the EEG.

Histopathology is the most conclusive method of confirming diagnosis; however in the Middle East, including Oman, it is often very difficult or impossible to obtain consent from relatives to perform brain biopsy, and permission to carry out autopsy is almost never granted in these very conservative, traditional Islamic societies (Al-Tahan et al., 1991). Without histopathological proof of CJD, most physicians would be unwilling to document cases. In this setting, the availability of diagnostic CSF tests becomes especially important, and in our second case, the demonstration of the distinctive double protein spots made a convincing contribution to our diagnosis. An additional procedure, the demonstration of neuron-specific enolase in the CSF (Zerr et al., 1995), is yet a further method of supporting the clinical diagnosis. With the availability of diagnostic CSF tests, it is possible that more cases of CJD will be reported from the Middle East, and a more accurate estimate of the incidence of the condition in this region will then be obtained.

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