Case Reports

Sporadic Creutzfeldt Jacob Disease

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ABSTRACT

نستعرض هنا حالة سيدة تبلغ من العمر 65 عاماً والتي حضرت إلى المستشفى بحالة خرف سريع التدهور، تم تشخيص المرض بأنه كروتز فلدت – جاكوب (CJD). على حد علمنا، ومن خلال مراجعة مصادر المعلومات والدوريات فإن حالتنا هذه هي الحالة الرابعة المصابة بمرض (CJD) التي يتم تسجيلها في المملكة العربية السعودية. هدفنا هو تسجيل هذه الحالة ليتم وضعها في التشخيص التفريقي لحالات الخرف سريعة التدهور.

We report a 65-year-old lady who presented with rapidly progressive dementia and was found to have Creutzfeldt-Jacob disease (CJD). On reviewing the literature, there have been only 3 case reports of CJD from Saudi Arabia. Our aim is to report this rare disease and to include it in the differential diagnosis of rapidly progressive dementia in our practice.

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Creutzfeldt-Jacob disease (CJD) is a rare and invariably fatal neuro-degenerative disorder. Part of a larger family of diseases called 'Prion diseases', this is a transmissible disorder with distinct clinical and pathological features. CJD is the commonest human prion disease with an approximate incidence of 1 per million. There have been only 3 case reports of CJD in Saudi Arabia.[1-3] Our aim is to emphasize the importance of knowing this fatal cause of dementia and to make the neurologist and internists familiar with its clinical presentations and prognosis.

Case Report. A 65-year-old female presented to the outpatient clinic with 3 months history of bilateral lower limb weakness associated with memory decline. The course was rapidly progressive until she was unable to walk without assistance or cope with activities of daily living. She has a history of numbness in her feet, imbalance, frequent falls, dysphagia, and dysarthria. She was hypertensive, diabetic and a former smoker on medications. There was no family history of similar illness. On examination, she appeared depressed and was overweight. Vital signs and systemic examination were normal. On neurological exam, the patient was conscious, disoriented to time, place and persons. She had poor concentration, calculation, and attention. Minimental status examination score was 22/30. Speech was slow with normal articulation. Cranial nerves from II to XII were normal. Motor examination showed generalized hypotonia and she had global symmetrical weakness, distally more than proximally at 4/5. Deep tendon reflexes were absent. Sensory examination showed impaired pinprick sensation in "gloves and stocking" distribution. She was unable to stand due to severe truncal ataxia. The patient was suspected to have paraneoplastic limbic encephalitis and full work up for an underlying malignancy was unremarkable. This included tumor markers, mammogram, and CT scan of the chest, abdomen, and pelvis. Magnetic resonance imaging of the the brain showed symmetrical bilateral hyperintensity of the caudate head and putamina, which are characteristic of CJD (**Figure 1**). Work up for other differential diagnosis including Hashimoto encephalopathy, vitamin B12 deficiency, syphilis, connective tissue diseases, vasculitis,

and HIV were unremarkable. Lumbar puncture was carried out twice and cerebrospinal fluid study showed normal biochemical and microbiological profile, however, protein 14-3-3 was persistently high. An EEG was carried out several times and showed diffuse symmetrical slowing bilaterally in the theta range, but failed to show classical triphasic waves. Her condition deteriorated over weeks with the development of myoclonic jerks, urine and stool incontinence, and a kinetic mute state. Tracheostomy was carried out and percutaneous endoscopic gastrostomy tube was inserted for feeding. Trial of steroids, intravenous immunoglobulin, acyclovir, and quinacrine were given while waiting for tests results with no improvement. The neurosurgery team and family refused performing brain biopsy. The patient was sent home with a private nurse and home health care. The patient and family failed to show up in the clinic for follow-up.

Discussion. Until 35 years ago, Creutzfeldt-Jacob disease (CJD) was an obscure form of rapidly progressive dementia unknown to most physicians. The name is now familiar to the medical community, including the internist and neurologist, as the major transmissible spongiform encephalopathy (or prion disease) in humans.[4] Once considered "slow virus" disease, prion diseases including CJD, are now thought to result from the accumulation within the brain of misfolded, host-encoded prion proteins (PrP). Creutzfeldt-Jacob disease, which is the most common variety of prion diseases was described in 1920.[5] A classic tetrad of progressive dementia, ataxia, myoclonus, and an abnormal EEG represent the salient clinical features of CJD. However, there is a wide variation in signs and symptoms observed, either at onset or during its course.[6] Creutzfeldt-Jacob disease is rare, affecting only one person per million each year worldwide.[4] There is no seasonal distribution or evidence of changing incidence over the years. There is no convening geographic clustering, except for areas with large numbers of familial cases. There are 4 types of CJD; sporadic, familial, iatrogenic, and new variant. Sporadic CJD accounts for most of the cases (approximately 85%).[7] The median age at time of disease onset is 60 years. Confusion and memory disturbances are the most common presenting features. Virtually all patients will develop frank dementia at some point in the disease and many will develop some degree of pyramidal and extrapyramidal and cerebellar features (**Table 1**). Prognostically, progressive mental and physical weakness leads to death within one year after the onset of symptoms in 90%, and a further 5% of patients die within the next year. Few have lived for more than 5 years, and there have been no reports of verified recoveries. Myoclonic jerks may appear at any time, but are more common in the middle to later stages of the disease. The myoclonic jerks are often stimulus-sensitive, clapping hands or turning on the light in a darkened room may induce this response.[5] Our case showed the classical cardinal features, which included dementia, myoclonic jerks, and ataxia. Interestingly, all cases reported in Saudi Arabia were females. Frequent EEG failed to show the classical periodic or semi periodic paroxysms of triphasic or sharp waves of 0.5- 2.0 Hz against a slow background. A negative EEG does not exclude the diagnosis, due to at least 30% of cases may not demonstrate the typical features.[8] In all the other 3 case reports coming from Saudi Arabia, the EEG changes were typical of CJD (**Table 2**). Although brain biopsy is the gold standard method for diagnosis, it was unfeasible in our case.[5] No brain biopsy was carried out for all other case reports coming from Saudi Arabia. The MRI changes in our case showed the characteristic marked hyperintensity of the caudate head and putamina, which is symmetrical bilaterally. This abnormality was not present in other case reports. The

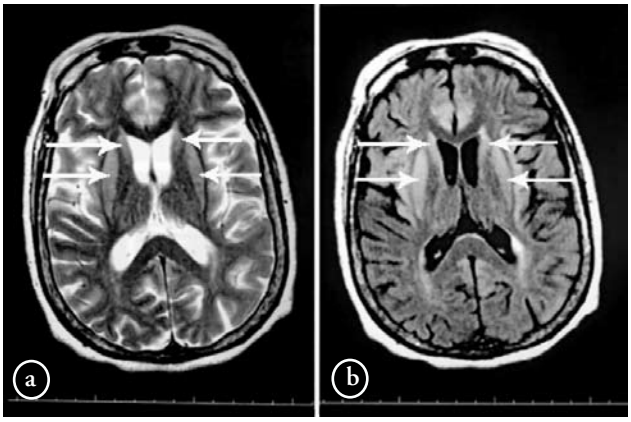

Figure 1 - **a)** T2 MRI axial images demonstrating increased signal intensity in both putamine and caudate nuclei. **b)** Similar finding in the fluid attenuated inversion recovery sequence.

Table 1 - Major clinical signs in sporadic Creutzfeldt Jacob disease.

Signs	Frequency (%)
Cognitive deficits (dementia), including psychiatric and behavioral abnormalities	100
Myoclonus	>80
Pyramidal tract signs	>50
Cerebellar signs	>50
Extra pyramidal signs	>50
Cortical visual effects	>20
Abnormal extra cortical movement	>20
Lower motor neuron signs	<20
Vestibular dysfunction	<20
Seizures	<20
Sensory deficit	<20
Autonomic abnormalities	<20

Table 2 - Summary of Creutzfeldt Jacob disease cases reported in Saudi Arabia.

Reporter	Gender	Age (years)	Clinical feature	EEG	MRI	Protein 14–3-3	Brain biopsy	Outcome
Algahtani et al 2007	Female	65	Subacute dementia, pyramidal and extrapyramidal signs, cerebellar signs	Encephalopathic changes with lack of classical PSWC	Classical basal ganglia abnormalities	Positive	Not done	Unknown
Dahbour et al 2002[3]	Female	55	Subacute dementia, myoclonic jerks, cerebellar features, visual disturbances, brisk reflexes	Encephalopathic changes with super added PSWC	Normal	Positive	Not done	Patient died after discharge
Al-Suliman et al 1996[2]	Female	45	Subacute dementia, myoclonic jerk, pyramidal and extrapyramidal symptoms	Characteristic PSWC	Marked cortical atrophy	Not done	Not done	Patient died after 18 months from symptom onset
Al-Tahan et al 1991[1]	Female	60	Subacute dementia, walking difficulty, visual hallucination, pyramidal and extrapyramidal signs, myoclonic jerk	Characteristic PSWC	Not done	Not done	Not done	Patient died after 18 weeks from symptoms onset

PSWC - periodic sharp wave complexes, EEG - electroencephalogram, MRI - magnetic resonance imaging

Table 3 - Tests used in diagnosis of sporadic Creutzfeldt Jacob disease.

Test	Comments
MRI (T2 and diffusion weighted images)	Sensitivity 79%, Specificity 93-100%
EEG (periodic complexes)	Sensitivity 67%, Specificity 86%
EEG (repeated)	More than 90% show changes
Protein 14-3-3	Sensitivity 96%, Specificity 99%
Brain biopsy	The gold standard method

MRI - magnetic resonance imaging, EEG - electroencephalogram

specificity of this sign in sporadic CJD is approximately 90% (**Table 3**).[9] An elevated level of 14-3-3 protein in the CSF was demonstrated in our case. This was also noticed in case reported in a previous study. The sensitivity of this test is 96%, and the specificity is 99%. False positive results have been reported in cases of viral encephalitis, stroke, Hashimoto's encephalopathy, Alzheimer's disease, and even multiple sclerosis.[10] In our case, all these causes have been excluded.

In conclusion, we report the fourth case of CJD from Saudi Arabia confirming the worldwide occurrence of this disease. It should be included in the differential diagnosis of rapidly progressive dementia.

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