RAPIDLY PROGRESSIVE DEMENTIA A CASE OF SPORADIC CREUTZFELDT-JAKOB DISEASE (SCJD)

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ABSTRACT

Sporadic CJD is a rare and fatal spongiform encephalopathy characterized by rapidly progressive dementia and myoclonus. It is a rare cause of dementia with an estimated incidence of the disease in one patient per million per year worldwide, however, no data is available for Pakistan. As it is a rare cause of dementia, so rarely considered in differential diagnosis of rapidly progressive dementia.

INTRODUCTION: CJD is a rare degenerative brain disorder which is almost always fatal, it is characterized by progressive brain dysfunction.[1] CJD falls into four categories, sporadic, iatrogenic, familial and variant.[2] Sporadic CJD is most common and accounts for 85% of all cases. It occurs worldwide and its incidence ranges from 0.5 to 1.5 cases per million per year. Of the remaining 15% of cases, 10 percent (%) is familial and iatrogenic and variant comprise 2 to 5 percent. CJD should be suspected in patients who presented with cerebellar signs, myoclonic jerks, and rapidly progressive dementia. However, these symptoms and signs are usually preceded by Psychiatric symptoms, which could be easily ignored.

Case Report:

A 75 years old man, with no previous history any significant medical or surgical disease, presented with two months history of dementia that started with delusion of persecution followed by worsening mobility, lack of coordination and cognitive issues. Over a course of four weeks he was not able to mobilize, started having visual hallucination, and myoclonic jerks. On examination patient was non-communicative, drowsy and had myoclonic jerks. Primitive reflexes were present in the form of palmer grasp and snout reflexes. He had moderate to severe axial and cogwheel rigidity in both upper and lower limbs. Reflexes were symmetrically brisk and plantars were bilaterally up going. Patient was admitted in neurology unit for further investigations. Base line blood tests were performed with normal results of liver and renal function tests, complete blood count, ESR, Serum Electrolytes. MRI brain showed gyriform cortical hyperintensity in both cerebral hemispheres and restricted diffusion in the same areas with corresponding low ADC values (cortical ribboning). Restricted diffusion was also observed in the caudate head bilaterally (figures 1a and 1b). EEG showed slow background rhythm with periodic sharp wave complexes with a frequency of 1-2 hz (figure.2). MRI-CJD consortium diagnostic criteria was applied to diagnose the case of sporadic CJD (Table.1)[3]. Patient remain admitted in our unit for three days, after excluding all the treatable causes, patient's attendants were counseled about the prognosis of disease and transmission of this fatal disorder.

Discussion:

CJD is prion disease that is transmittable. Diagnosis of CJD in early stages is fairly challenging due to very low incidence and high variability of initial presenting symptoms. Other rapidly progressive dementias can resemble sCJD due to overlapping of clinical presentation, and thus make the diagnosis of sCJD difficult especially in the early stage of presentation. The predominance of psychiatric symptoms and/or extrapyramidal usually mask the early onset of dementia. Nearly twenty six percent patients first present with "behavioral symptoms" such as agitation, irritability and depression initially.[4] Myoclonus may be

absent in early stages of disease and may appear in advanced stages of disease. Akinetic mutism is usually manifested at the end of disease.

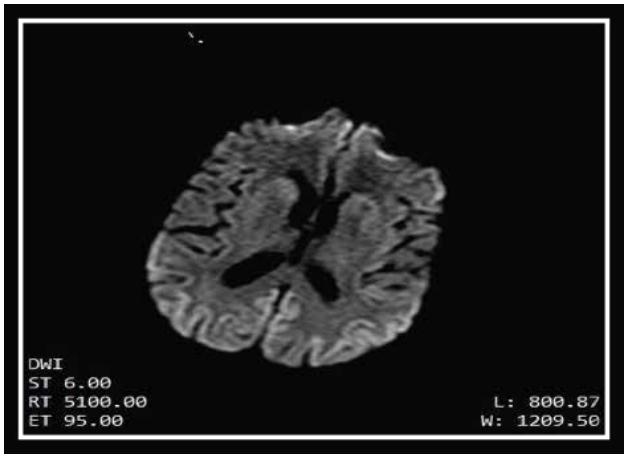
The definitive neuropathological diagnosis of sCJD, which is not feasible in clinical practice, depends on biopsy/autopsy characterized by loss of neuron, gliosis, spongiform, degeneration or the presence of protease-resistance prion protein (PrPSc) on histolopathology of brain tissue. Center of disease control (CDC) has proposed a probable diagnosis of sCJD based on the following four criteria. 1) Progressive dementia 2) at least two out of the following four clinical features: a)Myoclonus b) Visual or cerebellar signs c) Pyramidal/extrapyramidal signs d)Akinetic mutism. 3) typical EEG and/or positive 14-3-3 CSF assay and/or MRI high signal abnormalities on DWI or FLAIR. 4) Unremarkable alternative diagnosis on dementia screening. [5]

DWI and FLAIR imaging of brain MRI can be utilized for the early diagnosis of sCJD with a sensitivity of 91% and specificity of 95%.[6] MRI shows cortical signal increase and hyperintensities in the basal ganglia and thalamus.[7] Hyperintensities in DWI greater than FLAIR imaging and restricted diffusion are more common in sCJD than in any other rapidly progressive dementia disease which may facilitate differentiating sCJD from other prion disease. EEG can be used as an adjunctive non-invasive method to diagnose sCJD. The periodic sharp wave complexes (PSWCs) in the EEG are typical for sCJD, however in early stages of the disease there may only be nonspecific findings such as diffuse slowing and frontal rhythmic delta activity (FIRDA) and non-convulsive status [8] The sensitivity and specificity of periodic sharp wave complexes on EEG is 67 % and 86 % respectively.[9] CSF 14-3-3 protien analysis has a relatively high sensitivity but a moderate specificity. One study showed that CSF 14-3-3 protein possessed a sensitivity of 97% and a specificity of 87% in diagnosing sCJD.[10]

We could not perform the CSF 14-3-3 protein analysis because of the lack of the availability of the test at our country and higher chance of transmission during the intervention. Diagnosis can only be confirmed by histological examination of brain tissue obtained either by the brain biopsy or after autopsy which was not possible in our set-up.

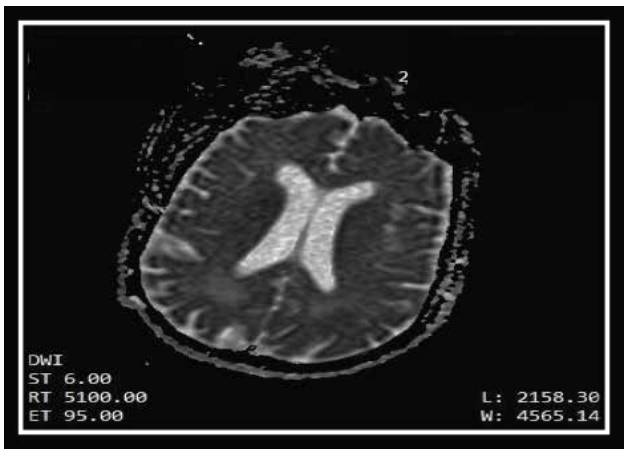
Conclusion:

sCJD is a fatal disorder and it is transmittable from person to person , therefore unnecessary interventions should always be avoided. Although a rare disease, it should be considered in the differential diagnosis of rapidly progressive dementia along with other disorders.



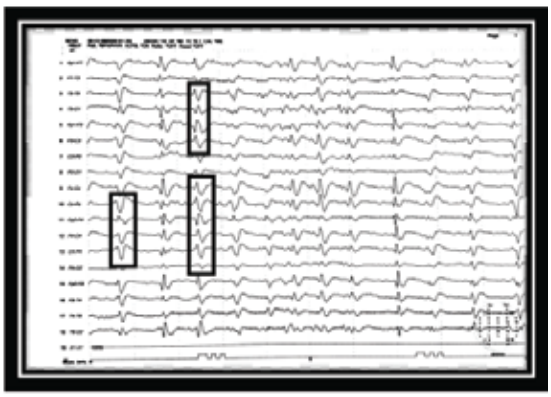
(FIGURE.1a DWI)

INCREASE UPTAKE IN CORTICAL AND BASAL GANGLION



(FIGURE.1b, ADC)

LOW UPTAKE ON ADC IN THE FRONTOPARITAL CORTEX



(FIGURE.2) POSITIVE SHARP WAVE COMPLEXES OF 1-2 HZ ON EEG

Table-1

[3]MRI-CJD CONSORTIUM DIAGNOSTIC CRITERIA (2009)

A)! CLINICAL SIGNS
1.! Dementia 2.! Cerebellar or Visual signs 3.! Pyramidal or extra-pyramidal signs 4.! Akinetic mutism
B)! LABORTOARY TESTS
1.! EEG: Periodic sharp wave complexes 2.! CSF: Positive 14-3-3 proteins in patient with a disease duration of less than 2 years 3.! MRI: high signal abnormalities in caudate nucleus and putamen or at least two cortical regions (temporal-parietal-occipital) either on DWI or FLAIR
Probable sCJD at least 2 of A + at least 1 of B **Possible sCJD** at least 2 of A + duration < 2 years

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Author's contribution:
Harwindar Kumar; concept, data collection, data analysis, manuscript writing, manuscript review
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Amjad Iqbal; data collection, data analysis, manuscript review
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