Case Report

Alien hand and leg as the presenting feature of probable sporadic Creutzfeldt-Jakob disease: A rare presentation of a rare disease

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Abstract

Sporadic Creutzfeldt-Jakob disease (sCJD) can have varied clinical presentation depending upon the genotype at codon 129. The common presenting clinical features of sCJD are rapid onset cognitive impairment, ataxia, psychosis and visual signs (field defects, distortion, cortical blindness). Alien limb sign was first described in patients with corpus callosal tumors and later with other neurodegenerative conditions like corticobasal degeneration. Alien hand complaints as the presenting feature of sCJD has been described in literature, but simultaneous alien hand and leg has been rarely described as presenting feature of sCJD. We describe here a case of a 55-year-old man who presented with progressive left alien hand and leg as the sole clinical manifestation of probable sCJD.

Key Words

Alien hand, Cruetzfeldt-Jakob disease, clinical presentation

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Introduction

The term "alien hand sign" (*le signe de la main etrangere*) was introduced by Brion and Jedynak[1] in three cases of tumour of the corpus callosum, to draw attention to their newly recognized clinical sign of the corpus callosum disconnection syndrome.

The term "diagnostic dyspraxia" was used by Akelaitis[2] in 1945 to describe an apparent conflict between the intended act and the act actually performed, in two patients who had undergone callosotomy for intractable epilepsy.

Fisher[1] described the inter-manual conflict between the dominant and non-dominant hand in a patient with ruptured *anterior communicating artery* (ACA) aneurysm.

Bogen,[3] first used the term "inter-manual conflict" to refer to a dissociative phenomenon seen post-callosotomy for epilepsy.

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Fisher[1] classified alien hand phenomenon (AHP) into two groups: Group I: lesions of the corpus callosum and /or anteromedial frontal cortex and Group 2: corticobasal degeneration.

Isolated alien hand as the sole presentation of CJD was first described by DJL Macgowan[4] in two female patients. One of the patients described by them also had alien leg.

sCJD is a rare disease and few case series are reported from India.[5] We present a case of alien hand and leg as the presenting feature of probable sCJD. This is to our knowledge the first case report of this rare presentation of probable sCJD from our region.

Case Report

A 55-year-old man with no significant past medical history presented to us with 1 month history of aimless wandering movements of his left hand. He said that he felt that his left hand was not under his control. It would act on its own will, in form of levitation of the arm, purposeless groping of objects in the surroundings. His left hand would hold objects in its vicinity and start using it, for example it would start to write if a pen was present. The left hand also showed interference in the activities of the right hand. Like when he would bring the food towards his mouth with the right hand, the left hand would try and stop it. There was also history of inter-manual conflict in form that whenever he would put his reading glasses with his right hand, the left hand would remove them. When

he would button his shirt with the right hand the left hand would unbutton it. When he would wear his cap with the right hand the left hand would pull off the cap and throw it on the ground. Many a times the patient had to use his right hand to control the activities of his left hand.

Over the last 20 days the patient started feeling that even his left leg was not under his control. While sleeping in the night the left leg would move out of the blanket and would make purposeless levitation movements. Whenever he started to walk he noticed that the left leg would step backwards. Hence he had great difficulty in walking and after effort he would drag the left leg to move forward. The patient did not feel any weakness in the left leg. There was no history of cognitive decline, myoclonus, ataxia, behavior changes, weight loss. There was no history of surgical intervention, or any toxin exposure like bismuth. Examination revealed normal speech and higher mental function. The cranial nerve and motor system examination was normal. The sensory examination showed loss of cortical sensation in form of graphesthesia, loss of two point discrimination, sensory extinction on left side of body including the face. Rest of the examination was within normal limits. Over the course of stay in the hospital (next 15 days) the patient also developed truncal ataxia, cognitive impairment, left arm myoclonus. The case was discussed as progressive left alien hand and leg syndrome. The MRI brain revealed cortical hyperintensities in bilateral frontal, bilateral parietal cortex, bilateral occipital cortex and cingulate gyrus on diffusion weighted images (DWI) [Figure 1]. The corresponding areas were also hyperintense on fluid attenuated inversion recovery (FLAIR) sequences but less than that on DWI. The electroencephalography (EEG) done using 10-20 system showed generalized periodic triphasic sharp wave complexes of 100-150 milli second (ms) duration and inter-complex interval of 500 ms to 1 second [Figure 2]. The cerebrospinal fluid (CSF) analysis showed proteins 32 g/dl, sugar 73 mg/dl (blood sugar was 80 mg/dl), Chloride 102 mM/L, cells were 2/cubic millimetre (all lymphocytes). The CSF Neuron Specific Enolase (NSE) done by enhanced chemiluminescence immunoassay was raised –143.2 ng/ml (normal below 16.3 ng/ml). CSF 14-3-3 was not done due to unavailability at our center. The CSF veneral disease research laboratory (VDRL) and tuberculosis polymerase chain reaction (Tb-PCR) were negative. The thyroid profile (including T3, T4, TSH and anti-thyroid peroxidase antibodies) was normal. Computed tomography (CT) chest, abdomen was normal. Stool for occult blood was negative. Upper and lower gastrointestinal tract endoscopy was normal. Serum levels of vitamin B12 and folate were normal. Serum HIV and VDRL were non-reactive. Carcinoembryonic antigen, alpha-fetoprotein, and prostate specific antigen were within normal limits. According to the Magnetic Resonance Imaging-Creutzfeldt-Jakob disease (MRI-CJD) Consortium criteria for sCJD the patient was diagnosed as a case of probable sCJD [Table 1].[6]

Probable CJD

Two out of 1 and atleast one out of 2.

Possible CJD

Two out of 1 and duration less than 2 years.

The patient was put on sodium valproate 500 mg twice a day for myoclonus and discharged. The patient and his relatives were not willing for a brain biopsy. The prognosis of the disease was explained to the relatives.

Discussion

The first description of isolated alien hand as the sole presentation of pathologically established CJD was given by

Table 1: MRI-CJD Consortium criteria for sporadic CJD[6]

MRI-CJD Consortium criteria for diagnosis of sporadic CJD
Clinical signs
Dementia
Cerebellar or visual signs
Pyramidal or extrapyramidal signs
Akinetic mutism
Tests
Periodic sharp wave complexes (PSWC) in EEG
14-3-3 detection in CSF (in patients with a disease duration less than 2 years)
High signal abnormalities in caudate nucleus and putamen or at least two cortical regions (temporal-parietal-occipital) either in DWI or FLAIR.

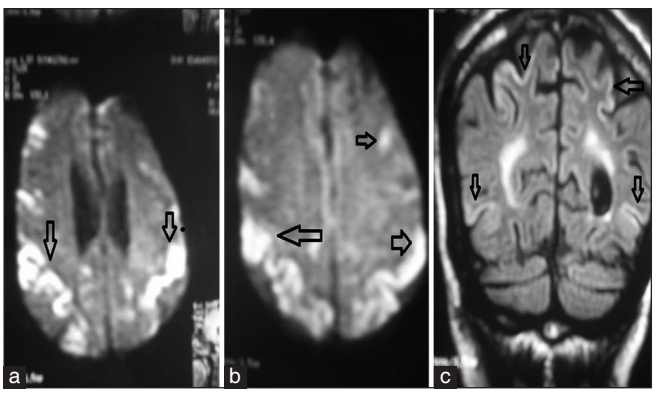

Figure 1: (a) MRI Diffusion Weighted image (DWI) showing cortical hyperintensities in bi-lateral parietal cortex.(arrows) (b) MRI DWI showing cortical hyperintensities in bi-lateral frontal and parietal cortex. (arrows) (c) MRI FLAIR showing hyperintensities in bi-lateral frontal cortex (arrows). Cortical hyperintensities in DWI>FLAIR

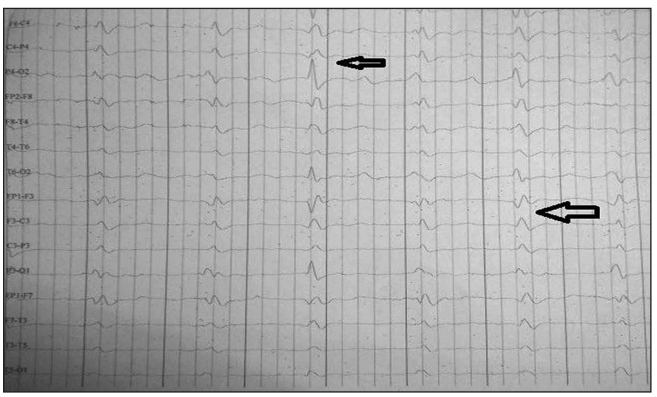

Figure 2: 16- channel EEG showing generalized periodic triphasic waves of 100-150 ms duration recurring after 500 ms^{-1} s (arrows)

Table 2: Causes of Alien Hand Syndrome[1]

Causes of Alien Hand Syndrome[1]
Group I (lesions of the corpus callosum and/or the anteromedial frontal cortex)
Surgical section of corpus callosum (for epileptic seizures)
Anterior Cerebral Artery (ACA) territory infarction
Ruptured saccular aneurysm of the ACA
Marchiafava-Bignami disease
Angioma of the corpus callosum
Group II
Corticobasal degeneration (CBD)
Group III (Alien hand cases of special types)
Sensory type-
Occlusion of right posterior cerebral artery
Thalamo-capsular hemorrhage
Seizure related
Medial frontal lobe focus
Parietal lobe focus
Transient Ischemic Attack (TIA) in the ACA territory

DJL MacGowan *et al*.[4] Both their patients had associated left hemiparesis, sensory ataxia and left upper limb myoclonus at presentation. The MRI brain of both the patients was normal, however the EEG did show periodic sharp wave complexes. The CSF 14-3-3 was positive in the second patient. Our patient had both alien hand and leg at presentation, and within 15 days of admission developed truncal ataxia and cognitive decline. The common causes of alien hand syndrome have been described in Table 2.

The MRI brain in our patient showed DWI hyperintensities >FLAIR in three cortical regions (cingulate gyrus, frontal, parietal and occipital gyrus). According to University of California Sanfrancisco (UCSF 2011)[7] criteria for diagnosis of sCJD based on MRI findings, DWI > FLAIR hyperintensities in classic pathogonomic: cingulate gyrus, striatum and > 1 neocortical gyrus (precuneus, angular, superior, or middle frontal gyrus is suggestive of MRI definte CJD. According to this criteria our patient comes under MRI Probable CJD (<= 3 cortical areas involved). The sensitivity of DWI to detect early CJD is 92.3% and specificity is 93.8%.[8]

The CSF showed significantly increased levels of NSE. The sensitivity and specificity of increased value of CSF NSE (> 20 ng/ml) in s CJD is 80% and 92% respectively.[9] CSF 14-3-3 was not done due to unavailability at our center.

The EEG in our patient showed generalized periodic triphasic sharp wave complexes of 100-150 ms duration and inter-complex interval of 500 ms to 1 second. The sensitivity of PSWC in detection of early sCJD is 50%.[8]

Fisher[1] has divided the manifestations of alien limb phenomenon into two groups: I) Those included under complex, unwilled motor acts: which include inter-manual conflict, mirror movements, interference, enabling synkinesis, reversal of complex acts. II) Includes Utilization behavior in form of reaching out to objects in the environment, grasping groping. Our patient had features of inter-manual conflict, interference, reversal of complex acts (like stepping back when intended to walk) and utilization behavior. The pathological basis of this phenomenon is the damage to the supplementary motor area and the adjacent cingulate gyrus, usually in association with the interruption of the anterior corpus callosum.

Decety *et al*.,[10] have attempted to replicate the movements of an alien hand using PET imaging. They proposed that the clinical alien hand represents a release phenomenon resulting from processes interfering with the coordinated function of motor execution and motor learning.

Alien hand as the presenting feature of sCJD has rarely been describe from India.

In a series of 10 patients of CJD from north India by Mehndiratta *et al*.,[11] the most common presentation was abnormal behavior and psychosis (70%). None of their patients developed alien hand phenomenon as the initial presentation or any time during the course of the disease.

In a series of 10 patients of probable sCJD from east India by Atanu Biswas *et al*.,[5] the most common presentation was psychosis, ataxia and visual complaints. None of their patients developed alien hand phenomenon as the initial presentation or any time during the course of the disease.

This case report highlights two important things. First, sCJD may have atypical presentations before the development of classic progressive dementia and startle myoclonus. Alien hand and leg can be the only initial manifestation of sCJD and hence the differential of sCJD should always be kept in mind while dealing with isolated alien hand sign. Second, DWI MRI brain changes and CSF biomarkers like NSE may help in early diagnosis of sCJD even when full blown clinical picture is not present.

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