MAR Neurology, Neurosurgery & Psychology (2023) 7:2
Case Report

ALS- PDC Complex - An Indian Perspective

Dr. Poornima Nair *[1], Dr. C.J Selvakumar [2]

1. Senior Resident, Department of Neurology, Government Medical College, Thiruvananthapuram, Pincode 695033, Kerala, India.

2. Senior Assistant Professor, Department of Neurology, Government Medical College, Coimbatore, Tamil Nadu, India.

***Correspondence to:** Dr. Poornima Nair, Senior Resident, Department of Neurology, Government Medical College, Thiruvananthapuram, Pincode 695033, Kerala, India.

Copyright

© 2023 **Dr. Poornima Nair.** This is an open access article distributed under the Creative Commons AttributionLicense, which permits unrestricted use, distribution, and reproduction in any medium, provided the originalwork is properly cited.

Received: 28 July 2023

Published: 01 August 2023

Introduction

Parkinsonism-dementia complex (PDC) is a unique, fatal disease of the CNS which was not clearly recognized as a disease entity before the description by Hirano in 1961 [4,5].PDC is known as Hirano's disease.Patients with this disorder exhibit features of Parkinsonism, akinesia, masked facies, dysarthria, mental slowness, apathy, depression and gait abnormalities and features of ALS. An environmental cause has been suggested.Parkinsonism-dementia complex (PDC) is a neurofibrillary tangle degeneration involving the deposition of Alzheimer-type tau, predominantly in the mesial temporal cortex, brainstem, and basal ganglia. It occurs in focal geographic isolates, including Guam and the Kii peninsula of Japan.

Case Presentation

A 37 year old healthy male who is a vegetable vendor by occupation, was admitted with a progressive cognitive decline over a period of two years. Patient initially had memory disturbances in the form of errors in money matters, which quickly started to interfere with his work. Subsequently he developed slowness in walking and taking more time to finish daily work. He developed difficulty in speaking in the form of reduced speech output, reduced loudness and slurring. He became mute by the end of second year of illness. There were no seizures/ myoclonic jerks/ bladder symptoms. There was no significant family history or drug intake. There was no history of consanguinity or similar illness in the family. There was no history of recent infection , fever or trauma.

On examination, the patient was restless, irritable with stable vitals. He was emaciated and had drooling saliva. There was no postural hypotension or skin lesions. He had camptocormic posture, expressionless starring facies and reduced blink rate. He was aphasic with occasional incomprehensible sounds.The MMSE score was 1/30. MOCA was 0/30(limited examination due to patient being anarthric). Detailed lobe function tests were not possible.

He had normal extraocular movements with hypometric horizontal saccades, broken pursuits. Fundus showed temporal pallor in both eyes and no cherry red spot. Visual fields were ormal with visual acquity of 6/12 in both eyes. Jaw jerk was exaggerated. There was no bulbar palsy. Tongue was flaccid, atrophic with frequent fasciculations. He had truncal rigidity with Cogwheel rigidity in both upper limbs and spasticity in both lower limbs.

Motor system examination showed predominant wasting in bilateral deltoid, biceps, triceps, thigh, thenar-hypothenar muscles, lumbricals and FDI. Fasciculations were noted from left deltoid and bilateral anterior thigh.

Normal strength was noted in all four limbs, except wasting and weakness in small muscles of both hands. There was differential involvement in lumbricals (2nd and 3rd more involved than 1st and 4th). All deep tendon reflexes including finger flexion reflexes were exaggerated with positive Babinski sign, Chaddock's sign and Gordon's sign. Hoffman's sign was present in left hand . Frontal release signs and primitive reflexes were noted.

There were no involuntary movements, cerebellar signs and peripheral nerve thickening.There was no organomegaly, bone tendernessor generalised lymphadenopathy. Neither gynecomastia nor testicular atrophy was noted.

Investigations revealed a normal blood picture with normal liver and renal function tests. Viral markers including retrovirus and VDRL was negative.

Reversible causes of dementia was considered ; Vit B12 level 586 IU/ L; TSH 4.12 mIU /L; parathyroid hormone 45 pg/ ml; CSF study showed no pleocytosis, sugar 40 mg/ dl, protein 54 mg/ dl. CSF was negative for the autoimmune antibody panel. ANA was negative and tumor markers were normal.CT chest and abdomen was done to rule out possibilty of occult malignancy; showed was no evidence of any solid organ malignancy or storage disorders or lymphoma.

Brain showed widespread cerebral atrophy. MRI brain showed bilateral frontal atrophy with no blooming & contrast enhancement. There was no diffusion restriction in any images.

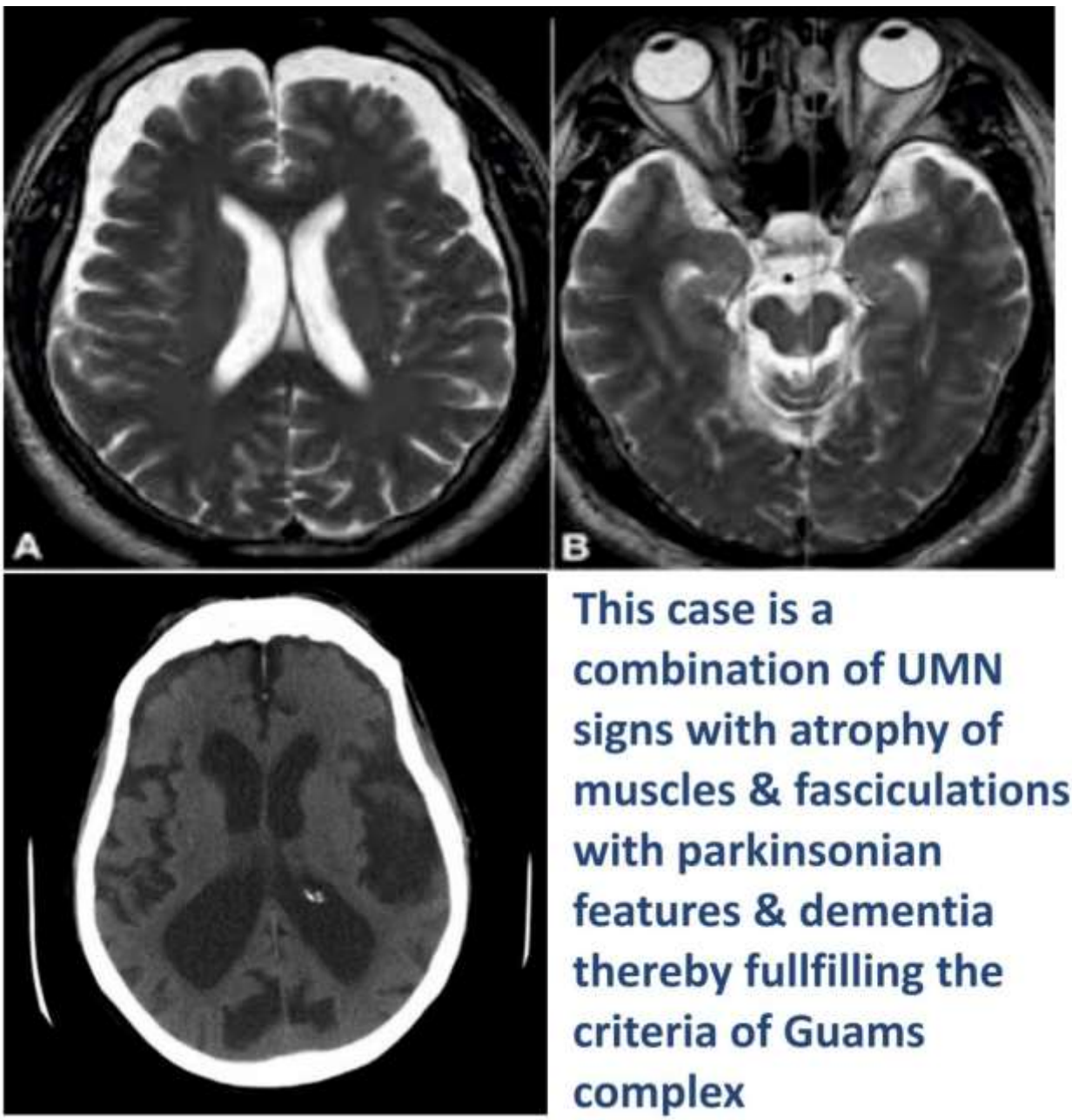

Figure 1: MRI Brain Axial T2 section

The electromyogram (EMG) revealed a decrease of compound muscle action potential (CMAP) and relatively decreased motor nerve conduction velocity (NCV) but normal sensory NCVs and sensory nerve action potential (SNAP) amplitudes.

Needle EMG showed frequent fasciculations, fibrillations, and high-amplitude polyphasic motor-unit potentials in the bilateral FDI, left Deltoid, left Extensor digitorum communis & tongue. Fibrillations were noted in left tibialis anterior, and lower extremities, thereby satisfying the El-escorial revised criteria for ALS.

EEG study showed mild electrophysiologic disturbance in the form of generalized theta slowing without any inter epileptiform discharges. Sleep study was normal. Genetic analysis was done for PARK 2, PINK 1 and GBA genes which were negative.

Patient had features of parkinsonism, with dementia and ALS based on the clinical presentation and investigations. He was given supportive therapy in the form of physiotherapy and locomotor rehabilitation. Levodopa was initiated and titrated however stopped due to unresponsiveness. The prognosis was explained to the wife and the patient was kept under neurology follow up.

Discussion

We are presenting the case of a young male who had akinetic rigid mute state with features of Parkinsonism, Dementia and ALS.

Our patient was a young male who presented with episodic memory disturbances, inattention and subsequently developed bradykinesia and following speech abnormality. This is in contrast to the average age of onset of around 53 years [3].Over the years, the age of onset has increased[2]. The syndrome appears most frequently in middle life but can occur in almost any decade.

The sex ratio for PDC in Murakami's report [5] in 1980 was 1.8:1, against 3:1 in Hirano's report[4]. Male dominance is a characteristic of the disease, in ratios varying from 2:1 to 4:1. The durations of the disease ranged from 1 to 15 years, with an average duration of 5.0 ± 2.6 years [6], indicating the rapidity of progression as compared to Parkinson"s disease.

The rigidity is more marked as compared to what we see in Parkinson's disease. This was evident in our case. As the disease progresses, ambulation deteriorates due to the combined influences of rigidity, akinesia, and the loss of postural reflexes. Festination and propulsion are not common features of , possibly because they are masked by the limb deformities and gait apraxias.[1].

Hirano classified PDC into 3 groups: 1) Parkinsonism- dementia complex, 2) Parkinsonism dementia with clinical evidence of upper motor neuron disease, and 3) Parkinsonism- dementia with clinical evidence of upper and lower motor neuron disease (ALS).

Parkinsonism-dementia complex shows no evidence of association with markers corresponding to known neurodegenerative disease loci, with the exception of the marker adjacent to FT33.[7].

Literature also suggests that amyotrophic lateral sclerosis and parkinsonism-dementia patients may suffer from a basic defect in mineral metabolism. This defect is provoked by chronic nutritional deficiencies of calcium, leading to secondary hyperparathyroidism and increased intestinal absorption of toxic metals and the deposition of calcium and other metals in central nervous system tissues[8]. As a consequence of increased acculturation and westernization, with decreased isolation, known changes in dietary habits and local water supplies, and much less dependence on locally grown food, it is anticipated that the incidence rates of both amyotrophic lateral sclerosis and parkinsonism-dementia on Guam will continue to decrease despite the apparent possibility of a genetic susceptibility, which in the absence of detrimental environmental conditions (or triggers) would not result in the expression of clinical disease.

MRI Brain showing cortical atrophy, with clinical and EMG evidence of denervation and the relatively rapid progression of the disease are points favoring the diagnosis in our patient. Due to widespread atrophy and involvement of the brain, the prognosis is extremely poor. Additional neuropathological and molecular studies will be helpful in analyzing this disease further.

Conclusions

A combination of dementia with parkinsonism & evidence of upper motor neuron with lower motor neuron involvement is rare and points to the diagnosis of Guam's complex in our patient. Reports of ALS- PDC complex is very sparse in literature. A case of Guam's complex has not yet been reported from India to the best of our knowledge since it's a primitive neurodegenerative disease prevalent in the other part of the world. To our knowledge, this is the first report of a non-Guamanian, non-caucasian patient from the Indian subcontinent, supporting a possible non-environmental, genetic cause.

Reference

1. Chen KM, Chase TN (1985) Parkinsonism- dementia. In: Vinken PJ, Bruyn GW (eds) Handbook of Clinical Neurology. Extrapyramidal Disorders, Elsevier Sci- ence, Amsterdam 49: 167–183

2. Elizan TS, Hirano A, Abrams BM et al. (1966) Amyotrophic lateral sclerosis and Parkinsonism-dementia complex of Guam: Neurologic reevaluation. Arch Neurol 14: 356–368

3. Hirano A, Kurland LT, Krooth RS, Lessel S (1961) Parkinsonism-dementia complex: an endemic disease on the island of Guam. I. Clinical Features. Brain 84: 642–661

4. Hirano A, Malamud N, Kurland LT (1961) Parkinsonism-dementia complex: an endemic disease on the island of Guam. II. Pathological Features. Brain 84: 662–679

5.Murakami N (1980) A study on the natural history of amyotrophic lateral sclerosis in Japan and Guam. Nagoya-Igaku 103: 154–163

6. Murakami N. Parkinsonism-dementia complex on Guam – overview of clin- ical aspects. J Neurol (1999) 246(Suppl 2):II16–8. doi:10.1007/BF03161077

7. Morris HR, Steele JC, Crook R, et al. Genome-Wide Analysis of the Parkinsonism-Dementia Complex of Guam. Arch Neurol. 2004;61(12):1889–1897. doi:10.1001/archneur.61.12.1889

8. Garruto RM. Elemental insults provoking neu- ronal degeneration: the suspected etiology of high incidence amyotrophic lateral sclerosis and par- kinsonism-dementia of Guam. In: Hutton JT, Kenny AD, eds. Senile dementia of the Alz- heimer's type. Neurology and neurobiology. Vol 18. New York: Alan R. Liss, 1985:319-36.