Original Article

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Clinical Profile of Dementia Presenting before Age 25 Years: An Experience from a Tertiary Level Hospital in Mumbai

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Abstract

Background: Dementia is a decline in cognitive abilities of sufficient severity to interfere with activities of daily living and is not caused by delirium or other medical or psychiatric disorder. The subset of Very Young Onset Dementia (VYOD) with onset before 25 years is not studied well in India. In this study we aimed at describing the clinical profile, higher mental functions, investigations and etiological factors in these patients. *Methodology:* We conducted an observational, retrospective, single-cohort study to study the clinical profile of dementia patients presenting to the Department of Neurology at Topiwala National Medical College & BYL Nair Charitable Hospital, Mumbai. We searched for patients with dementia with onset between 10 to 25 years. We collected patient related demographic and clinical information from the records. All the collected data will be entered in Microsoft excel sheet and imported in to Statistical Package for Social Sciences (SPSS) version 16 for statistical analalysis. *Results:* 21 patients were included in the study, 18 males, average age of onset is 13.1 years. Subacute Sclerosing Panencephalitis, Hereditary Spastic Paraplegias, Wilson's disease were common aetiologies. 33% patients had Mini Mental Status Examination score of less than 10. 42% patients had Frontal Assessment Battery score less than 5. 42% patients had frontal, temporal and parietal lobes involvement. MRI brain was abnormal and revealed T2 hyperintensity in basal ganglia, brainstem and cerebellum. *Conclusion:* Early onset dementia is an underestimated problem in developing countries. Preventable conditions such as Subacute Sclerosing Panencephalitis (SSPE) and treatable condition such as Wilson's disease (WD) are leading causes in dementia with onset before 25 years. Awareness of these conditions is important while evaluating patients with VYOD.

Keywords: Dementia; Wilson's disease (WD); Very Young Onset Dementia (VYOD); Subacute Sclerosing Panencephalitis (SSPE).

Introduction

Dementia is defined as decline in cognitive abilities of sufficient severity to interfere with activities of daily living which the individual was able to do before. The cognitive decline is not due to delirium or altered sensorium, which can be distinguished from dementia by the presence of marked fluctuations and acute-to-subacute temporal pattern. Alzheimer's disease is the most common cause of dementia with onset after 65 years. Dementia in young onset (before 65 years) has not been studied well. Moreover Very Young Onset Dementia (VYOD) with onset before 25 years is not studied.

There were an estimated 35.6 million people worldwide living with dementia in 2010, with a prediction the number would double approximately every 20 years [1]. However, data from the Rotterdam study indicate the incidence of dementia may be declining [2], which in part may be due to improved treatment of vascular risk factors. The prevalence of early-onset dementia (EOD) is estimated at 40 to 100 per 100,000 individuals in developed countries, although no broad-based studies have been performed [3]. Risk factors for EOD may vary according to the underlying etiology of the dementia. Although genetic etiologies are more common in EOD compared with late-onset dementia, the majority of cases of both EOD and late-onset dementia do not

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have an identifiable monogenetic cause. Moreover, there is a higher rate of vascular disease in patients with EOD of any type. Many of the risk factors for EOD identified in population-based studies relate to increased vascular risk, including stroke, transient ischemic attack, chronic kidney disease, cardiovascular disease, hypertension, chronic alcohol use, and drug intoxication [4]. Patients with onset of dementia before 25 years has not been studied very extensively. We have defined this group as very young onset dementia (VYOD).

In this study we aimed at describing the clinical profile of such patients who presented to our hospital, along with their mental examination findings, results of their investigations and etiological factors. Management of progressive cognitive impairment in the younger adult requires a different approach than that of the older adult. Specifically, the differential diagnosis is much broader and therefore requires a more detailed evaluation that includes both common and rare disorders.

Methodology

We conducted an observational, retrospective, single-cohort study to study the clinical profile of dementia patients presenting to our hospital. All data from our medical record of Department of Neurology at Topiwala National Medical College & B.Y.L Nair Charitable Hospital, Mumbai was searched for patients with dementia with onset between 10 to 25 years.

We found 25 patients with dementia with onset between the specified ages between May 2008 and June 2016. We collected patient related demographic and clinical information from the records, like age, gender, age of onset of dementia, clinical signs, lobe affected, Mini Metal Status Examination (MMSE), Frontal Assesment Battery (FAB) etc.

Dementia was diagnosed using DSM IV criteria. We included those patients who were diagnosed with young onset dementia before the age of 25 years and had complete medical records.

We excluded those patients whose medical records were incomplete. MRI & EEG was also done in all patients. CSF study, genetic studies, metabolic study was done on case by case basis.

All the data was collected and abstracted from the patient records. All the collected data will be entered in Microsoft excel sheet and imported in to Statistical Package for Social Sciences (SPSS) version 16 for statistical analalysis.

Results

We included 21 patients in the study, 7 had age of onset less than 10 years and only 2 had age of onset between 20-25 years **(Table 1)**. Most common etiologies were Hereditary Spastic Paraplegias, Subacute Sclerosing Panencephalitis and Wilson's disease. Combined frontal, temporal and parietal lobe were most commonly affected. Majority of patients had MMSE score of less than 10 and FAB score of less than 5 **(Table 2)**. On CSF examination only 4 had abnormalities.

These abnormalities reflected either increased CSF IgG index or increased CSF antimeasles antibodies. Investigations revealed 6 Wilson's disease, 1 leukodystrophy and 1 HIV patient **(Table 3)**. EEG

Table 1: Characteristics of patients included in the study

Sample size	**21**
Males	18
Age of onset distribution	
Less than 10 years	7
10-15 years	5
15-20 years	7
20-25 years	2
Etiological causes	
Hereditary Spastic Paraplegias	5
Subacute sclerosing panencephalitis	4
Wilson's disease	5
Leukodystrophy	1
HIV	1
Undiagnosed	5
Clinical signs	
Pyramidal signs	11
Extrapyramidal	9
Cerebellar	4
Axial myoclonus	3
No signs	1
Lobe affected	
Parietal	2
Subcortical	3
Frontal + Temporal + Parietal	9
Generalized	7

Table 2: Clinical assessment scores of patients

Mini Metal Status Examination	
Less than 10	7
10-15	2
16-20	3
21-25	5
More than 25	4
Frontal Assessment Battery	
Less than 5	9
6-10	3
11-14	5
15-18	4

Table 3: Results of investigations in patients

Cerebrospinal fluid examination	
Normal	17
Abnormal	4
Blood investigations	
Wilson's disease	6
Leukodystrophy	1
HIV	1
EEG findings	
Normal	15
Subacute sclerosing panencephalitis	4
Diffuse encephalopathy	2
Magnetic Resonance Imaging findings	
Normal	8
Thinning of dorsal cord and thinning of corpus callosum	4
T2 hyperintensity in basal ganglia, brainstem and cerebellum	5
White matter lobar hyperintensity	3
Others	1

was abnormal in 6 patients showing periodic pattern of Subacute sclerosing panencephalitis and diffuse encephalopathy. MRI revealed abnoramlities in 13 patients **(Table 3)**.

Discussion

Kelly et al reported neurodegenerative etiologies being the most common cause of cognitive decline and dementia in adults age 35 and older [5]. Frontotemporal dementia (FTD) and vascular dementia are more prevalent at the younger end of the spectrum. Hereditary Spastic Paraplegia (HSP) was one of the most common causes of EOD in our patient population. Some forms of HSP are associated with impairment in childhood followed by gait impairment and spasticity in the second and third decades of life [6].Symptoms of autosomal dominant HSP usually start before the age of 10 years and the course may be nonprogressive. Because of this early onset, sporadic cases have been misdiagnosed as cerebral palsy. Wilson's disease was the other most common cause of EOD in our patient population. The majority of patients with Wilson disease are diagnosed between the ages of 5 and 35 years (mean age of 12 to 23 years), though this disorder has been diagnosed in younger patients and in patients in their 70s.[7] Two main categories of cognitive impairment in Wilson disease have been described, a frontal syndrome and subcortical dementia, with some patients having features of both. In patients with cognitive impairment, the findings can be subtle and may only be recognized retrospectively. In addition, some have suggested that the apparent cognitive impairment may be primarily the result of psychiatric and motor manifestations of Wilson disease [8].

MRI brain is an important component of the initial evaluation of suspected EOD, both to exclude structural pathologies and to look for clues to the underlying dementia etiology. In our sample of patients, majority had abnormalities on MRI brain, 5 had T2 hyperintensities in basal ganglia, brainstem and cerebellar, 4 had thinning of dorsal cord and thinning of corpus callosum and 3 had white matter lobar hyperintensities. Excluding a space occupying lesion is the main objective of doing imaging studies in dementia patients. After appropriate brain imaging, cerebrospinal fluid analysis has been suggested [9]. Early-onset alzheimer's disease is supported by a CSF profile of low Aβ42 and elevated tau and phospho-tau levels. Additional laboratories to consider depending upon the specifics of the individual case include: CSF for either 14-3-3 or total tau (elevated in CJD), serum copper, ceruloplasmin, and 24-hour urine copper (for Wilson disease), plasma HIV immunoassay, CSF herpes simplex virus 1/2 polymerase chain reaction (PCR), CSF varicella PCR, CSF Whipple PCR, and a serum paraneoplastic panel. In our sample patients, we performed hematological tests to diagnose Wilson's disease, leukodystrophy and HIV.

Genetic testing may be helpful in establishing a cause for early-onset dementia (EOD) in selected patients. Among the neurodegenerative dementias, genetic testing is most often pursued for CADASIL, Huntington disease, autosomal-dominant forms of AD, and in patients with FTD, particularly when there is concomitant motor neuron disease. The role of brain biopsy is very limited in the management of dementia. Despite being an invasive test with a significant risk of serious complications, the diagnostic yield is very low. In one series of 90 consecutive biopsies undertaken for the investigation of dementia, 57% were diagnostic, although biopsy obtained information led to specific treatment interventions in only 11% [10].

Conclusion

Our study gives us a clinical profile of early onset dementia patients who presented to a tertiary level hospital in Mumbai in a comprehensive manner and highlights the problem of dementia in yonger age groups. EOD is an underestimated problem with difficult to diagnose cases. The general issues of management of behavioural issues, non-pharmacological methods, and support for caregiver all apply in young-onset dementia. Future research should focus on ways to identify and diagnose cases ar an early stage. We also need novel ways to manage such cases with specific needs of younger patients.

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