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Research paper

Correlation of medial temporal lobe atrophy with seizures in Alzheimer's disease and mild cognitive impairment: A case control study

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ABSTRACT

Background: Seizures are common accompaniment of neurodegenerative disease. Though, Alzheimer's disease (AD) is the most common cause, but seizures also occasionally occur in mild cognitive impairment (MCI).

Material & methods: We studied patients of Subjective Memory Complaints coming to the Department of Neurology of a Tertiary Care Hospital in Northern India from July 2012 to July 2015. A total of 171 patients were studied. Those with a diagnosis of AD/MCI with seizures were taken for the current study. A total of 30 controls with chronic diseases were taken for comparison. Medial Temporal Lobe Atrophy (MTA) Rating was done using Sheleten's Visual Rating Scale.

Results: A total of 256 patients were screened and 171 had dementia of Alzheimer's type (n = 75; M:F = 60:15) and 96 patients had MCI (M:F = 76:20). The mean MMSE of those with AD was 18.5 ± 3.3 was and that of the MCI was 26.6 ± 2.4. A total of 9 cases with AD had seizures and 6 had seizures in MCI group (total n = 15). Moderately strong correlation was obtained between MMSE of AD patients having seizures and MTA scoring.

Conclusions: Seizures are common in dementia of Alzheimer's type and not uncommon in MCI. They have the potential to worsen the cognitive profile of the patient and need attention in these patients.

1. Introduction

Late life seizures occur in patients with Alzheimer' disease (AD)[1] and Mild Cognitive Impairment (MCI). It has been observed that seizure occurrence in AD is more common than previously thought.[2] Notably, advanced age carries a higher risk for development of seizures in patients with AD.[2] In the absence of proper drug management, seizures have the potential to cause deterioration of dementia[3].

AD is the most common cause of dementia while MCI is a precursor to dementia.[3] Patients with AD are at a high risk of developing seizures, upto 10 folds.[2] Ongoing seizures can worsen the cognitive status in these patients. It has been observed that AD and other neurodegenerative conditions are the presumed etiology of upto 10% of New onset Epilepsy in patients older than 65 years.[3] Also, the lifetime prevalence of seizures in AD has been estimated to be 1.5–64%.[4] Appearance of a new onset seizure is associated with cognitive worsening and seizures also contribute amnestic wandering.[5] Though AD is common in Indian elderly, but no systematic study is there on seizures in AD/MCI patients.[6] The present study was done to study the frequency and factors associated with seizures in patients with AD/MCI. Also, an attempt was made to correlate Medial Temporal Lobe Atrophy (MTA) with various predictors in patients of AD/MCI.

2. Material & methods

Patients attending to the Department of Neurology of a Tertiary Care Hospital in Northern India from July 2012 to July 2015 were enrolled for the present study. The study represents >6000-person-years of observations. A total number 256 with memory complains were screened in last 3-years. The patients were selected randomly from the outpatient department of Neurology and were asked to attend the specialized memory clinic. Those selected underwent through general physical, neurological and neuropsychological evaluation. The diagnosis of MCI and dementias was made as per the established criteria (Clinical Dementia Rating score = 0.5 for MCI and Diagnostic & Statistical Manual DSM-

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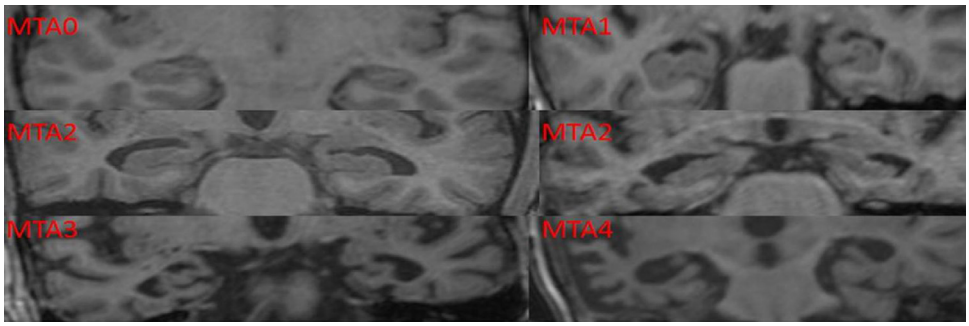

Fig. 1. Sheletens Medial Temporal Lobe Atrophy (MTA) Rating Scale. Scoring was done as follows (0) (0) scores on left and right sided were given if there was no visible atrophy on T1 weighted coronal MRI images. The scores of (1) (1) left sided were given to those with minimal atrophy. Those with moderate atrophy were rated as (2) (2) left and right sided respectively. Those with moderate atrophy were given the score of (3) (3) and scores of (4) (4) were given to those with marked atrophy.

V criteria for diagnosis of dementias respectively).[7] A total of 171 patients with diagnosis M:F (136:35) with mean age 71 ± 0.6 years and the mean duration of illnesses 3.2 ± 0.3 years were recruited for the present study. The MTA rating was done using Sheleten Visual Rating Scale.[8] This scale has a high inter and intra-rater reliability. For the purpose of the study, the standardization of rating was performed using the figures given below (Fig. 1). T1 oblique coronal image was used for MTA rating and confirmed using T2 weighted coronal images. A total of 30 controls with chronic diseases were taken for comparison. Comparison with controls was done to know the relative risk of seizures in controls and diseased group and also to see if there is any correlation that exists in between controls and diseased group and MTA.

The controls (n = 30) were the patients with Osteoporosis (n = 12), Diabetes and Hypertension (n = 6), and Psychiatric illnesses which included anxiety disorders, depression and psychosomatic disorders (n = 12). Mean duration of illness in case of controls was 3.5 ± 0.6 years. The mean age of controls was 56 ± 5.53 years.

3. Results

A total of 75 patients had dementia of Alzheimer's type and 96 patients had MCI out of the total number 256 screened in last 3-years (Tables 1 & 2). The duration of illness in AD was 3.6 ± 0.3 years and that of the MCI was 2.8 ± 0.2 years. The mean MMSE of those with AD was 18.5 ± 3.3 and that of the MCI was 26.6 ± 2.4 The MMSE of those with AD having seizures has been plotted using Box and Whisker plot (Fig. 2). There were a total of 15 cases with seizures in this study sample [(AD = 9, MCI = 6), Fig. 3].

There was a significant difference between the MMSE of MCI, AD without seizures and AD with seizures were statistically different using one way ANOVA (p-value = <0.001).

The prevalence rate of the Alzheimer's disease was 2.08%. It was calculated as the total number of AD cases during last 3 years divided by the number of elderly at risk (>60 years) reporting to the neurology outpatient department during this period (July 2012–July 2015), multiplied by 100. This prevalence rate is not significantly different from the prevalence rate of dementias reported from urban Indian population.[2] Likewise, the prevalence rate for seizures in AD was calculated to be 9/75 × 100 = 12%, which is in range with the reported prevalence rate for seizures in AD (1–64%).[4] The odds ratio (OR) at 95% confidence interval in AD was almost twice to that in MCI group (OR = 1.94, 95% confidence interval = 0.6545–5.6327). That means, patients with AD are twice more likely to have seizures compared to those with MCI. Likewise, the OR of having seizures in patients with AD was 7.6 compared to controls (95% confidence interval = 0.4331–136.0228). Similarly, OR in MCI compared to controls was 4.1 (95% confidence interval = 0.2249–75.0607). A total of 7 patients in the AD group had generalized seizures and 2 had partial seizures; in the MCI group a total of 4 had generalized seizures and 2 had partial seizures. The mean duration of seizures was 3.2 ± 0.3 years in AD and 2.5 ± 0.3 years in MCI respectively.

Table 1
Demographic features of the patients in the present study.

Category	Sample size (n = 171)	Mean Age (years)	Sex Ratio	MMSE
AD	75	75 ± 5	60:15	18.5 ± 3.3
MCI	96	67 ± 7	76:20	26.6 ± 2.4

Table 2
Breakup of screened cases of cognitive impairment/dementia from July 2012 to July 2015.

Type of Cognitive Impairment/Dementia (n = 256)	Sample size (n)
MCI	96
AD	75
Vascular dementia	30
Dementia with Levy Body	6
Mixed dementias	12
Fronto-temporal dementias	8
Normal pressure hydrocephalous	4
Pseudodementias	3
Thyroid dementias	5
B12 deficiency	5
Drug-Induced dementias	5
Crutzfelt-Jacob's disease	2
Corticobasal dementias	1

The mean and standard deviation of MTA rating score was 2.40 ± 0.63 and 0.87 ± 0.35 in AD with seizures compared to those without seizures (p- < 0.001). There was no significant correlation between the MMSE and MTA ratings in MCI group (Pearson Correlation Coefficient = 0.19, p-value = >0.05). However, correlation between MMSE and MTA rating in the AD group was significant (Pearson Correlation Coefficient = 0.59, p-value = < 0.05).

The mean duration of antiseziure treatment in patients with AD/MCI in the current study was 2.9 ± 0.3 years. All (n = 15) but 2 cases had controlled seizures in the current study population of AD/MCI. Two cases, one with MCI, another with AD had breakthrough seizures while being on antiseziure drugs. A total of 7 cases were taking sodium valproate (1000 mg/day) and two cases were on levetiracetam (1000 mg/day) in AD group, and 4 cases in MCI group were on sodium valproate (1000 mg/day) compared to 2 cases who were on levetiracetam (1000 mg/day).