

Seizure in Iranian patients with multiple sclerosis

Mohammad Zare, Rasul Norouzi, Vahid Shayegannejad, Fereshteh Ashtari, Majid Ghasemi, Hemaseh Tavahen, Ali Masaali

Department of Neurology, Isfahan Neurosciences Research Center, Isfahan University of Medical Sciences, Isfahan, Iran

Background: There is a broad variation in reported frequencies of seizure in multiple sclerosis (MS). In this study, the seizure and its characteristics analyzed among a large group of patients with MS. **Patients and Methods:** We reviewed the medical records of all definite MS patients referred to the MS Clinic of Kashani hospital, Isfahan, Iran, between 2007 and 2011. **Results:** Altogether, 34 cases with seizure activity identified among the 920 definite MS subjects (3.69%). Five excluded due to the other probable etiologies rather than MS. In the remained 29 patients (3.15%), the type of seizure was mostly generalized (79.3%); interictal electroencephalography showed an abnormal pattern in 84.6%, brain magnetic resonance imaging revealed subcortical white matter lesions in 84.6% of patients. The mean duration of MS onsets was 8.17 years and the mean interval between MS onset and the first seizure occurrence was 3.7 years. In general, response to antiepileptic treatment was excellent. **Conclusion:** Seizures can occur at any stage during the course of MS, but it is more common during the early stages.

Key words: Electroencephalography, multiple sclerosis, magnetic resonance imaging, seizure

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INTRODUCTION

Multiple sclerosis (MS) is the most common cause of neurological disability in adults^[1] with an unpredictable clinical course and variable manifestation.^[2] Seizure has reported as one of the less common manifestations of MS.^[3] Uncommon incidence of seizure in MS makes it difficult for an appropriate assessment, and the accurate prevalence of seizure in patients with MS is still in doubt.^[4,5] To our knowledge, no studies have yet been carried out on the association between seizure and MS in Iranian patients. The purpose of our study was to analyze the seizure and its characteristics in patients with MS.

PATIENTS AND METHODS

A descriptive, cross-sectional study was performed. The ethics committee of the Isfahan University of Medical Sciences approved the study. We conducted a general study in medical records of all definite MS patients referred to MS Clinic of Kashani hospital, Isfahan, Iran, from March 2007 to June 2011. The collected data included demographic information, the characteristic of a decisive seizure occurrence, the course of MS, degree of disability, related electroencephalography (EEG) and magnetic resonance imaging (MRI) finding, and information about the prescribed antiepileptic

drugs (AED) until now. Report of the International League against Epilepsy Commission on Classification and Terminology^[6] and McDonald criteria^[7] were used to verify seizure and MS respectively. To assess the extent of disability, the Kurtzke Expanded Disability Status Scale (EDSS)^[8] utilized. The Clinical course of MS was defined as relapsing-remitting (RR), secondary progressive, or primary progressive.^[9]

The statistical analysis was done using SPSS 17 for Windows (SPSS, Inc., Chicago, IL, 1996).

RESULTS

From 920 subjects with definite MS who referred to MS Clinic of Kashani hospital, Isfahan, Iran, between 2007 and 2011, we identified 34 cases (3.69%) with definite seizure activity. Five patients excluded due to other probable etiologies rather than MS, including one with the history of brain tumor, one with central nervous system infection and three with febrile seizure. 29 patients (3.15%) remained for analysis with the mean age of 32.7 years (range 22-44) and most were female (25 case; 86.2%). Seven patients (24.1%) had the history of seizure before MS onset and 22 patients (75.9%) had experienced seizures after that. The mean duration of MS onset was 8.17 years (range 1-20) and the mean of the interval between MS onset and the first

Address for correspondence: Dr. Hemaseh Tavahen, Isfahan Neurosciences Research Center, Alzahra Hospital, Sofeh Blvd, Isfahan 81744-176, Iran. E-mail: h.tavahen@gmail.com

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seizure occurrence—when occurring after MS onset—was 3.7 years (range 0-11).

Seizure classification

We had no report of status epilepticus. Seizure was general tonic clonic in 23 patients (79.3%), complex partial in 4 (13.8%) and simple partial in 2 (5.9%). We could not truly establish whether those with generalized seizure were primary or secondary.

EEG pattern

Findings of the 26 available interictal EEG showed abnormal EEG pattern in 84.6% of patients, including: Focal epileptiform discharge or focal slowing in 10 records (38.5%), generalized discharge (spike-wave, polyspike or general paroxysmal fast activity) in 10 records (38.5%) and general slowing activity in 10 record (38.5%), which these patterns may exist together in one EEG recording.

MRI review

A review on 26 available brain MRI showed subcortical white mater lesions in 22 (84.6%), cortical lesions in 13 (50%), and cortical plus subcortical in 12 patients (46.2%). No other structural intra-axial lesions reported. All MRIs performed after the first seizure episode but in some instance, there was a long interval time from seizure occurrence.

Course and prognosis

The mean duration of MS onset was 8.17 years (range 1-20) and the mean EDSS was 3.3 (ranged 0-8.5). At the time of the first seizure occurrence and at the time of study; MS type was predominantly RR type (61.7% and 58.8% respectively).

AED treatment

Among these 29 patients with seizure activity; one case (3.4%) was self-limited and got seizure free without any treatment, two cases (6.9%) reported an intractable seizure disorder (despite adequate treatment), 25 cases (86.2%) had an excellent response (controlled with mono-therapy) and one case (3.4%) had a good response to AEDs (controlled with poly therapy). Mostly used drugs were sodium valproate and carbamazepine (41.4% and 34.5% respectively).

DISCUSSION

Seizure is reported as one of the less common manifestations of MS.^[3] Seizure itself can be both physically and psychosocially disabling, and these can be intensified when occur in patients with MS.^[10] Uncommon incidence of seizure in MS makes it difficult to assess properly.^[4,5] In previous studies, a broad discrepancy of seizure frequency has been reported from 0.89% to 17%.^[3] We have no data about the prevalence of seizure in the Iranian general population, and so we cannot discuss whether the prevalence of seizure in MS is higher or not. The mean age of MS patients with

seizure was 32.7 years (range 22-44) and most of the patients were female (86.2%). However, this predominance of young feminine may reflect the nature of the MS.

Pathophysiology of seizures in MS is not clear^[5,11] and the exact causative relation between seizure and MS has not been found.^[12,13] However, the increase of seizure frequency among MS patients raises the probability of a causal relation between them.^[12] Some investigators suggest that the seizure activity in MS may be correlated to the cortical pathologies and inflammation,^[12-14] some suggest a causative role for subcortical plaques^[15] and others showed that the accumulation of cortical and subcortical lesions are greater in patients with MS and seizure. In this study, we found subcortical white mater lesions in 84.6%, cortical lesions in 50% and cortical plus subcortical in 46.2% of available MRIs. Our data support the hypothesis that a relationship exists between the subcortical plaques of MS and seizures.

Seizures may occur at any stage during the course of MS,^[14,16] and even can occur before the diagnosis of MS.^[3,11,17-19] Indeed, in some patients, it may be the first and only manifestation of MS.^[5,18] Based on the finding of previous studies, seizure activity in MS is more commonly presented in early stages of the disease, mostly within the first 5 years after MS onset.^[14] We also found the mean interval between MS onset and the first seizure occurrence of 3.7 years. Indeed, seizures were the initial clinical manifestation of MS in 24.1% that is higher than the results of similar studies.^[5] It is unclear that whether seizure influences the clinical course^[12,15] and long-term prognosis of MS.^[14] Some investigators have reported a good prognosis for seizures in MS,^[16-17] but others have reported unpredictability in long-term prognosis.^[14] About the course of MS in most studies, there is no evidence that seizure could be related to severity and course of the disease,^[3,4,14,17] but some authors suggested a correlation between them.^[18] In our study the mean EDSS of patients with seizure was 3.3. However, as we did not have any control group, we cannot discuss in severity and course of the disease in presence of seizure activity. At the time of first seizure occurrence and at the present time; MS type was RR in most of the patients. A probable relationship between type of MS and seizure activity may be supposed, however, it can be related to the influence of RR superiority in MS.

Several retrospective researches have studied medication for seizure in MS,^[4,10,15,20-22] however, the reported drug, dosage, duration and response to treatment were not in agreement with each other. However, as concluded by some investigators,^[10,14] seizure in MS usually has a benign nature with a good response to antiepileptic drug therapy or occasionally may be self-limited. Among our 29 MS patients with seizure activity; most of them were controlled with mono-therapy and had an excellent response. Mostly used drugs were valproate sodium and carbamazepine.

All types of seizures may have seen as a part of MS.^[11] There are variable reports regarding to the most common types of seizure in MS. Some studies reported that generalized seizures are more common than partial^[10,23] while results of more others^[3,11,15,17,18,21,24] suggests that partial seizures are more common. In studies with dominance of partial seizures, there is a high report of secondary generalization; however, in those with dominance of generalized seizure, the state of primary or secondary onset is not clearly described. Although our data showed that generalized seizure was more common than partial seizure, we also could not truly determine whether those with generalized seizure are primary or secondary.

In a review by Kelley *et al.*^[14] EEG abnormalities were identified in most MS patients with seizure activity. However, there is no report of specific EEG pattern in MS patients with seizure activity. Indeed, existing evidence could not specify whether in MS patients without seizure disorder, these abnormalities would be seen or not.^[14] In our study findings of the available interictal EEG showed abnormal EEG pattern in most of the patients, including: Focal discharge, generalized discharge and slowing activity. Interpretation of EEG abnormalities was not straight forward, as the time of EEG recording in relation to the first seizure onset and anticonvulsant treatment was incongruent between patients.

CONCLUSIONS

Seizures can occur at any stage during the course of MS; however, it is more common during the early stages. The subcortical plaques may bring about seizure activity in patients with MS and seizure; however, it should be proven in a large study regarding MRI findings.

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