Original Article

New-Onset Geriatric Epilepsy in China: A Single-Center Study

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Abstract

Background: Few studies have been published on new-onset geriatric epilepsy especially in older Chinese people. This study was to have a comprehensive understanding of new-onset geriatric epilepsy and find a more reasonable diagnosis and management of epilepsy in older people.

Methods: One hundred and three patients with onset age 60 years and older were admitted between January 2008 and December 2016. Electronic medical records were reviewed to collect information.

Results: There were 103 older patients with new-onset epilepsy. The mean age of the patients was 68.5 ± 6.4 years (range: 60–89 years), and there were 67 (65%) men and 36 (35%) women. The mean onset age was 67.9 ± 6.2 years (range: 60–89 years). The most common identifiable etiology of symptomatic seizures was autoimmune epilepsy in 43 (41.7%) patients. The second most common etiology was stroke in 15 (14.6%) patients. Seven (6.8%) older patients with acute seizures present with status epilepticus and 26 (25.2%) patients experienced clustered seizures (more than three events in 24 h) at seizure onset. Focal seizures (96.1%) were more common than generalized seizures (3.9%). Fifty-three (51.5%) patients had an abnormal brain magnetic resonance imaging (MRI) scan. Among them, video-electroencephalogram findings in 31 (30.1%) patients correlated with MRI abnormalities. Levetiracetam was the most used drugs before admission, in hospital, and during follow-up.

Conclusions: Autoimmune encephalitis is becoming an increasing risk factor of subsequent epilepsy in older people. Older patients with new epilepsy are more likely to respond to antiepileptic drugs, and drug-resistant epilepsy is uncommon.

Key words: Elderly; Electroencephalography; Epilepsy; Seizures

Introduction

Epilepsy is the third most common neurological condition in older people, following dementia and stroke.[1] By the age of 70 years, the incidence of epilepsy is almost double that of children, and at older than 80 years, it is over three times the rate in childhood.[2,3] The number of people aged 60 years or older had reached 241 million in China by the end of 2017. This figure accounted for 17.3% of the total population, according to the Office of the National Working Commission on Aging in China.[4]

Few studies have been published on new-onset geriatric epilepsy especially in older Chinese people. Clinical characteristics of epilepsy in older people are different from other age groups and diagnosis may be difficult. Therefore, this study aimed to examine new-onset geriatric epilepsy and attempt to find a more reasonable diagnosis and management of epilepsy in older people.

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Methods

Ethical approval

Informed consents were obtained from all the patients, and the study was approved by the Human Research Ethics Committee of Peking Union Medical College Hospital, Beijing, China.

Study setting and subjects

This study was conducted in the epilepsy monitoring unit (EMU) in Peking Union Medical College Hospital, which is a Class A tertiary comprehensive hospital in north China,

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with patients from all regions of the country. It offered over 2000 beds and reported a maximum of 17,300 outpatient visits a day and discharged 95,000 patients on yearly average.[5] Patients with new-onset epilepsy were admitted to the EMU, which had four beds, after an epilepsy clinic visit or they were referred by a general neurologist. We enrolled consecutive inpatients with new-onset epilepsy who were older than 60 years between January 2008 and December 2016, with a final confirmed diagnosis of epilepsy.

Measures

Electronic medical records were reviewed to collect information regarding sex, age at the time of admission, age at onset of the first seizure, laboratory examinations, risk factors of epilepsy, final diagnosis, antiepileptic drugs (AEDs), and neuroimaging and video electroencephalogram (VEEG) findings. Routine VEEG was performed for at least 1 h, using the international 10–20 system with 19 electrodes. Surveillance of patients during monitoring was conducted round the clock by an electroencephalogram (EEG) technologist or nursing staff who was experienced in response testing and acute management of seizures.

All VEEG data were independently reviewed in detail by a trained EEG technician and an attending epileptologist. Special attention was paid to the onset of events recorded by patients or caregivers. Two of the authors (JH Chen and XQ Zhou) independently reviewed ictal and interictal VEEGs.

Semiological seizure classification was performed according to Cleveland criteria[6] plus faciobrachial dystonic (FBD) seizures. Seizure frequency was classified as daily (one or more seizures per day), persistent (<1 seizure per day but at least one seizure in the last 6 months), rare (<1 seizure per 6 months), or undefined (seizure frequency could not be specified because of recent epilepsy onset).[7]

Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics 20.0 software (Armonk, New York, USA). Quantitative data are expressed as mean, median, standard deviation, and percentage. The Kruskal–Wallis *H*-test was used for intergroup comparison of continuous variables. The Chi-square test or Fisher's exact test was used for intergroup comparisons of categorical variables. A value of $P < 0.05$ was considered significant.

Results

Patients' characteristics

There were 103 older patients with new-onset epilepsy. The mean age of the patients was 68.5 ± 6.4 years (range: 60–89 years), and there were 67 (65%) men and 36 (35%) women. The mean onset age was 67.9 ± 6.2 years (range: 60–89 years).

Etiology

Twenty-two (21.4%) patients had unknown etiology and 81 (78.6%) had symptomatic epilepsy. The most common identifiable etiology of symptomatic seizures was autoimmune epilepsy in 43 (41.7%) patients including 38 (36.9%) with autoimmune encephalitis and five (4.9%) with paraneoplastic neurological syndrome. The second most common etiology was stroke in 15 (14.6%) patients. Other etiologies were found in 10 (9.7%) patients with dementia or degenerative disorders, 5 (4.9%) with brain neoplasm, 4 (3.8%) with central nervous system infection, 2 (1.9%) with head trauma, and 2 (1.9%) with toxic or metabolic disorders.

Seven (6.8%) older patients with acute seizures presented with status epilepticus (SE) and 26 (25.2%) patients experienced clustered seizures (more than three events in 24 h) at seizure onset. Etiologies of these patients were autoimmune epilepsy in 17 (16.5%) patients, poststroke epilepsy in 5 (4.9%), unknown cause in 4 (3.9%), a brain tumor in 3 (2.9%), infectious encephalitis in 3 (2.9%), and metabolic encephalopathy in 1 (1.0%).

Neuroimaging findings

Fifty-three (51.5%) patients had an abnormal brain magnetic resonance imaging (MRI) scan. Among them, VEEG findings in 31 (30.1%) patients correlated with MRI abnormalities. Fifteen (14.6%) patients had stroke whose lesions were epileptogenic. The mean duration between stroke and the first seizure was 4.1 ± 6.0 years (range: 0–21.3 years). Four (3.9%) patients had head trauma or an operation history whose lesions were epileptogenic, and the duration between head trauma or an operation and the first seizure ranged from 1.7 to 29.0 years.

Seizure types and characteristics of epilepsy

All of the patients had a video EEG examination and the mean monitoring duration was 19.5 ± 15.3 h. A total of 71 (68.9%) patients had interictal epileptiform discharges. Focal seizures (96.1%) were more common than generalized seizures (3.9%). An aura (36.9%) was approximate with automatisms (35.0%). Auras were nonspecific, such as dizziness (16.1%), or a somatosensory aura (39.3%), psychic aura (14.3%), abdominal aura (12.5%), autonomic aura (7.1%), olfactory aura (3.6%), visual aura (3.6%), or gustatory aura (3.6%). Secondarily generalized tonic–clonic seizures occurred in 33% of the patients.

Among the seven patients with SE at onset, five had convulsive SE including four with secondarily generalized convulsive SE and one with focal motor SE. The other two patients had non-convulsive SE without a coma. Causes of convulsive SE included autoimmune encephalitis, viral encephalitis, vascular dementia, metabolic disturbances, and a brain tumor. Causes of nonconvulsive SE included stroke.

Comparison of patients with onset age at <60 and ≥60 years

According to onset age, older patients were divided into two groups: patients with an onset age at <60 years ($n = 103$) and those with an onset age at ≥60 years ($n = 31$). There was no significant difference in sex between these two groups.

Epileptic seizures were auras in 6.5% of patients with an onset age <60 years and in 14.6% in those with an onset

age ≥60 years. Furthermore, autonomic seizures occurred in 0 and 2.9%, dialeptic seizures in 9.7% and 7.8%, motor seizures in 83.9% and 63.1%, and FBD seizures in 0 and 11.7% of patients with an onset age <60 years and in those with an onset age ≥60 years, respectively. Immune and an unknown etiology were more common in patients with an onset age ≥60 years and in those with an onset age <60 years, respectively.

There were no significant differences in epilepsy types, interictal EEG, and ictal scalp EEG, between the two groups. There were also no differences in epilepsy risk factors and seizure semiology between the groups, except for a more positive family history of epilepsy in patients with an onset age <60 years, and more motor seizures in those with an onset age ≥60 years (both $P < 0.05$). There was a significant difference in cluster seizures or SE at onset between the two groups [$P = 0.002$; Table 1].

There were no significant differences in the number of AEDs before admission, in hospital, and during follow-up. However, carbamazepine was more frequently used in patients with an onset age <60 years ($P < 0.05$). Phenytoin ($P = 0.011$) was only more common in patients with an onset age <60 years before admission [Tables 2 and 3].

Follow-up and prognosis

A total of 73 (70.2%) patients with new-onset epilepsy had a follow-up longer than 12 months. The mean follow-up time was 24.1 ± 10.8 months (range: 12–54 months). The most common AEDs in hospital and during follow-up were levetiracetam (50.9%), followed by oxcarbazepine (33.3%), valproic acid (14.0%), lamotrigine (12.3%), carbamazepine (5.3%), topiramate (3.5%), phenobarbital (3.5%), and clonazepam (1.8%). Levetiracetam was the most used drugs before admission, in hospital, and during follow-up. Sixty-nine (92.8%) patients' seizures were well controlled with monotherapy or two AEDs, except for 4 (7.2%) patients with an onset age ≥60 years and one (6.3%) older patient with an onset age <60 years. Only one (1.8%) patient was referred to have a presurgical evaluation for refractory epilepsy. Thirty-six patients with seizures related to autoimmune encephalitis were followed up for at least 12 months, and their seizures were well controlled after immunotherapy.

Discussion

Old age is the most common time to develop epilepsy. Results from epidemiology have shown that geriatric epilepsy and older people with epilepsy have a two to three times greater mortality rate than that in the general population.[8-10] However, few studies have examined seizure characteristics and long-term follow-up in older people.[11-13] We collected data from a single center over 9 years to analyze epidemiology, presentation, etiology, and management to prognosis of epilepsy in older people to obtain a comprehensive understanding of Chinese geriatric epilepsy.

Older people are generally defined as those aged older than 60 or 65 years.[11] Some studies and reviews have included people aged older than 60 years.[11] The United Nations agreed on a cutoff of 60+ years for older people. Similarly, in China, the age of 60 years is used as a definition of older people. Therefore, we enrolled patients who were older than 60 years in our study.

New-onset geriatric epilepsy has some characteristics that are different from young adult-onset epilepsy, which makes diagnosing and managing new-onset geriatric epilepsy difficult. Some of these characteristics are as follows. First, older patients can have episodes that mimic seizures but are actually the result of syncope, a sleep disorder, or a psychiatric illness.[12] Differentiating nonepileptic seizures from epileptic seizures can be difficult. Chen *et al*.[13] found that 73.9% of older patients who were admitted to the EMU were admitted for diagnosis of paroxysmal events, which were usually nonspecific. Among these events, 63.2% were confirmed as epileptic seizures.[13] As many as 21% of patients with new-onset geriatric epilepsy had no underlying etiology in our study. This rate is similar to that of 25–40% of new epilepsy cases in the older people in the literature.[14] One patient in our study who presented with syncope was diagnosed with psychogenic nonepileptic seizures after negative MRI and VEEG findings and then suffered from seizure clusters 4 months after withdrawal of AEDs. Second, 33% of our patients had secondarily generalized tonic–clonic seizures. This rate is lower than previously reported data, which showed that secondarily generalized tonic–clonic seizures occurred in 65% of younger adults.[11] Third, geriatric patients usually had more comorbidities and a higher mortality rate. We found that hypertension, diabetes mellitus, and coronary heart disease were common in our patients. One patient with an onset age <60 years had obstructive sleep apnea syndrome (OSAS), and two patients with an onset age ≥60 years had OSAS. Two patients died during admission for the reason of deterioration of the original disease. One patient experienced SE on the first night of admission. Considering the high prevalence of symptomatic epilepsy and the probability of worsening condition in older people, more attention should be paid to patients who are in the acute stage of disease. Fourth, there are special considerations when considering AEDs in older people. We found that the most common AEDs was levetiracetam, followed by oxcarbazepine and valproic acid. Over 90% of geriatric epilepsy in our study was well controlled with monotherapy or two AEDs. However, 7% of patients needed three or more AEDs to control seizures, and only one patient was referred to have a pre-surgical evaluation for refractory epilepsy. This finding is in agreement with the literature that epilepsy in older people generally responds well to treatment and drug-resistant epilepsy is uncommon.[15] The prevalence rate of SE in our study was 6.8% including five convulsive and two nonconvulsive cases of SE. Our findings suggest that SE is more frequent in the older patients and is almost twice that seen in the general population.[11] Episodes of SE tend to be more prolonged and associated with an increased mortality rate when occurring in patients aged older than 60 years.[16,17]

Table 1: Comparison of epilepsy characteristics according to onset age

Characteristics	Onset age <60 years old (n = 31)	Onset age ≥60 years old (n = 103)	t or χ^2	P
Age at admission (years)	62.5 ± 3.0	68.5 ± 6.4	-7.234	<0.01
Age at onset (years)	41 ± 17.9	67.9 ± 6.2	-8.228	<0.01
Female:male	14:17	36:67	1.062	0.303
Epilepsy risk factors				
Family history of epilepsy	3	0	10.196	0.011
Head trauma	5	5	4.386	0.051
Central nervous system infection	1	3	0.008	1.000
Stroke	7	30	0.511	0.505
Brain tumor	0	5	1.563	0.589
Alzheimer's disease	0	1	0.303	1.000
Cerebral vascular disease	0	10	3.252	0.116
Seizure semiology				
Aura	2	15	1.415	0.358
Autonomic seizure	0	3	0.924	1.000
Dialeptic seizure	3	8	0.115	0.716
Motor seizure	26	65	4.714	0.030
Faciobrachial dystonic seizure	0	12	3.967	0.068
Epilepsy types				
Focal seizure	30	99	0.029	1.000
Generalized seizure	1	4	0.029	1.000
Interictal EEG				
Normal	7	32	0.832	0.362
Focal IEDs	22	71	0.047	0.829
Multifocal IEDs	1	0	3.348	0.231
Generalized IEDs	1	0	3.348	0.231
Ictal scalp EEG				
Clinical seizure without clear EEG change	4	16	0.130	1.000
Temporal lobe onset seizure	7	26	0.093	0.763
Frontal lobe onset seizure	4	19	0.515	0.473
Parieto-occipital lobe onset seizure	1	2	0.180	0.549
Generalized discharges	1	4	0.029	1.000
Magnetic resonance imaging positive				
Temporal lesion	6	27	0.604	0.487
Frontal lesion	2	13	0.912	0.519
Parieto-occipital lesion	1	4	0.029	1.000
Multilobar lesions	0	14	4.705	0.039
Other loci (basal gangalion/brainstem)	0	14	4.705	0.039
Seizure frequency at onset				
Daily	14	56	0.810	0.368
Persistent	16	44	0.762	0.383
Rare	1	3	0.008	1.000
Cluster/Status epilepticus	1	32	9.951	0.002
Etiology of epilepsy				
Structural	9	36	0.374	0.541
Infectious	1	5	0.148	1.000
Metabolic	0	1	0.303	1.000
Immune	4	44	9.214	0.002
Unknown	17	17	18.492	<0.01

Data are presented as mean ± SD or n. IEDs, interictal epileptiform discharges; EEG: Electroencephalography; SD: Standard deviation.

DeLorenzo[18] found that the incidence of SE in older people was twice that of the general population and associated with at least 50% mortality by the age of 80 years.

Some findings, in our study, are different to those in previous studies. We found that the most common identifiable etiology of symptomatic seizures was autoimmune epilepsy, and the second most common was stroke. However, previous studies have indicated that the most common cause of symptomatic seizures is stroke, which accounts for 40–54%.[3,19,20] Brodie *et al*.[10] considered that stroke was the

Table 2: Comparison of AEDs according to onset age

Characteristics	Onset age <60 years old (n = 31)	Onset age ≥60 years old (n = 103)	χ^2	P
AEDs before admission				
None	12	47	0.463	0.496
Monotherapy	13	42	0.013	0.908
Two AEDs	3	10	0.000	1.000
Three or more AEDs	3	4	1.616	0.352
Type of AEDs before admission				
Valproate	4	21	0.880	0.348
Lamotrigine	1	4	0.029	1.000
Levetiracetam	7	25	0.037	0.846
Carbamazepine	7	5	9.183	0.006
Oxcarbazepine	3	14	0.330	0.761
Topiramate	3	3	2.549	0.136
Phenytoin	3	0	10.196	0.011
Phenobarbital	1	1	0.824	0.411
Clonazepam	0	6	1.890	0.336
AEDs in hospital				
None	1	5	0.148	1.000
Monotherapy	19	69	0.343	0.558
Two AEDs	9	23	0.589	0.443
Three or more AEDs	2	6	0.017	1.000
Type of AEDs in hospital				
Valproate	5	29	1.820	0.177
Lamotrigine	3	10	0.000	1.000
Levetiracetam	9	43	1.622	0.203
Carbamazepine	11	8	15.043	<0.01
Oxcarbazepine	8	35	0.731	0.393
Topiramate	4	5	2.464	0.211
Phenytoin	1	0	3.348	0.231
Phenobarbital	1	3	0.008	1.000
Clonazepam	1	5	0.148	1.000

Data are presented as n. AEDs: Antiepileptic drugs.

Table 3: Comparison of AEDs according to onset age during follow-up

Characteristics	Onset age <60 years old (n = 16)	Onset age ≥60 years old (n = 57)	χ^2	P
AEDs during follow-up after 1 year				
None	1	5	0.105	1.000
Monotherapy	11	37	0.082	0.775
Two AEDs	3	11	0.002	1.000
Three or more AEDs	1	4	0.012	1.000
Detailed AEDs during follow-up				
Valproate	1	8	0.701	0.673
Lamotrigine	2	7	0.001	1.000
Levetiracetam	6	29	0.896	0.344
Carbamazepine	4	3	5.613	0.037
Oxcarbazepine	6	19	0.096	0.756
Topiramate	1	2	0.238	0.530
Phenytoin	0	0	-	-
Phenobarbital	0	2	0.577	1.000
Clonazepam	0	1	0.285	1.000

Data are presented as n. AEDs: Antiepileptic drugs.

most important risk factor for development of subsequent epilepsy in older people and could account for up to 50% of cases in whom a cause can be identified. Whether the difference between our and previous studies is related to a higher prevalence of autoimmune encephalitis or to a lower incidence of post-stroke epilepsy in Chinese older people is still unknown. We found that most studies on epilepsy in older patients were published in the 1990s, and autoimmune

encephalitis was not emphasized as a cause of symptomatic epilepsy at this time. Autoimmune antibody-associated syndromes were reported from 1980 to 2000, and many new autoimmune antibodies have been discovered since 2000.[21-23] Seizures are a common symptom in autoimmune neurological disorders. Autoimmune encephalitis first became recognized in China in 2010.[24] During the past several years, diagnosed autoimmune encephalitis cases have increased in number in China. Our hospital has begun to detect antineuronal antibodies since 2011, and the spectrum of antineuronal antibodies has broadened. Hence, the actual number of symptomatic seizures secondary to autoimmune encephalitis might be higher. There were 43 older patients with autoimmune epilepsy over 9 years in our study. Quek *et al*.[25] identified 32 patients who were diagnosed with autoimmune epilepsy in the Mayo Clinic during 6 years. Although the enrolled patients in our study were from one center, we found that autoimmune encephalitis was becoming an increasing risk factor of subsequent epilepsy in older Chinese people. More attention should be paid to autoimmune epilepsy in older people with new-onset seizures.

This study has some limitations. Only patients who were admitted to the EMU were registered in our study. However, for a comprehensive understanding and detailed recording of the patients' clinical characteristics and follow-up, patients in the EMU were the best choice. The retrospective nature of our study is also a limitation.

In conclusion, autoimmune encephalitis is becoming an increasing risk factor of subsequent epilepsy in older people. Geriatric patients might experience risks of SE or clustered seizures at onset. Older patients with new epilepsy are more likely to respond to AEDs and drug-resistant epilepsy is uncommon.

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Conflicts of interest

There are no conflicts of interest.

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中国人群新发老年癫痫：一项单中心研究

摘要

背景: 中国人群新发老年癫痫的研究报道较少。本研究的目的是全面了解中国人群新发老年癫痫，以便对其更好地诊断及治疗。
方法: 2008年1月至2016年12月期间收入院的所有发病年龄大于等于60岁的老年癫痫患者，回顾分析其临床资料。
结果: 共103例患者为新发老年癫痫。平均入院年龄为68.5±6.4岁 (范围: 60–89 岁) ，其中男性67例 (65%) ，女性36例 (35%)。平均发病年龄 67.9±6.2 岁 (范围: 60–89 岁)。 症状性癫痫最常见病因为自身免疫性癫痫，共43例 (41.7%) 患者。第二大常见病因是卒中，共15例 (14.6%) 患者。新发急性老年癫痫患者中7例 (6.8%) 经历了癫痫持续状态，26例 (25.2%) 患者起病时经历了丛集发作 (24小时发作次数大于3次) 。局灶性癫痫 (96.1%) 比全面性癫痫 (3.9%) 更常见。 53例 (51.5%) 患者头颅核磁共振异常。其中，31例 (30.1%) 患者视频脑电结果与核磁共振异常一致。左乙拉西坦是老年癫痫人群中，包括入院前、住院时及出院后随访期间最常用的抗癫痫药物。
结论: 自身免疫性脑炎正成为老年人群癫痫的一大危险因素。新发的老年癫痫患者对抗癫痫药物疗效反应较好，难治性癫痫不常见。