Chapter 16
Acute Symptomatic Seizures

CQ 16-1

What is the definition of acute symptomatic seizure?

Summary

Acute symptomatic seizures are seizures that occur in close temporal association with acute central nervous system disorders, which include metabolic, toxic, structural, infectious, or inflammatory disorders.

Comment

The Commission on Epidemiology and Prognosis of the ILAE defined acute symptomatic seizures as "seizures occurring in close temporal association with an acute systemic, metabolic, or toxic encephalopathy or in association with an acute central nervous system disorder (infection, stroke, head injury, or acute alcohol intoxication or withdrawal)"[1]. This definition was also adopted by Beghi et al.[2].

Among acute symptomatic seizures, convulsive seizures mostly occur only once, but may be repeated or even develop to status epilepticus. Convulsive seizures may recur when the above disorders relapse.

Acute symptomatic seizure is clearly distinguished from epileptic seizure unprovoked by organic disorders (see CQ 1-1 on page 2).

■ References

1) Guidelines for epidemiologic studies on epilepsy. Commission on Epidemiology and Prognosis, International League Against Epilepsy. Epilepsia. 1993; 34(4): 592-596.
2) Beghi E, Carpio A, Forsgren L, et al. Recommendation for a definition of acute symptomatic seizure. Epilepsia. 2010; 51(4): 671-675.

■ Search formula and secondary reference sources

PubMed search: November 28, 2008
Acute symptomatic seizure = 222

Additional PubMed search: May 7, 2015
Acute symptomatic seizure (Filters: Clinical Trial; Multicenter Study; Randomized Controlled Trial; Systematic Reviews; Meta-Analysis;) = 28

No references that could serve as evidence were found in Ichushi Web.

CQ 16-2

What are the causes of acute symptomatic seizures?

Summary

The etiologies of acute symptomatic seizures include cerebrovascular disease, central nervous system infection, acute immune-mediated encephalopathies, head injury, metabolic or systemic disease, intoxication, withdrawal, post-neurosurgical operation, demyelinating disease, post-radiation therapy, and overlap of several etiologies.

Comment

The major etiologies for acute symptomatic seizures are shown in **Table 1**[1-4].

Acute symptomatic seizures differ from epilepsy in having clearly identifiable etiologies, having high mortality rates due to the acute diseases, and requiring short-term treatment with antiepileptic drugs[4, 5]. Acute symptomatic seizures often occur in the neonates and the elderly, similarly to epilepsy.

■ References

1) Annegers JF, Hauser WA, Lee JR, et al. Incidence of acute symptomatic seizures in Rochester, Minnesota, 1935-1984. Epilepsia. 1995; 36(4): 327-333.
2) Huang CC, Chang YC, Wang ST. Acute symptomatic seizure disorders in young children—a population study in southern Taiwan. Epilepsia. 1998; 39(9): 960-964.
3) Murthy JM, Yangala R. Acute symptomatic seizures-incidence and etiological spectrum: a hospital-based study from South India. Seizure. 1999; 8(3): 162-165.
4) Leung H, Man CB, Hui AC, et al. Prognosticating acute symptomatic seizures using two different seizure outcomes. Epilepsia. 2010; 51(8): 1570-1579.
5) Beghi E, Carpio A, Forsgren L, et al. Recommendation for a definition of acute symptomatic seizure. Epilepsia. 2010; 51(4): 671-675.

■ Search formula and secondary reference sources

PubMed search: November 28, 2008
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No references that could serve as evidence were found in Ichushi Web.

Table 1. Major acute symptomatic seizures.

Cerebrovascular disease	Seizure occurring within 7 days of cerebrovascular attack
CNS infection	Seizure occurring in the acute phase of CNS infection
Immune-mediated encephalopathies	See CQ16-6 (page 161)
Head injury	Seizure occurring within 7 days of head trauma
Metabolic or systemic disorders	Seizure occurring in association with systemic diseases including electrolyte imbalance, hypoglycemia, non-ketotic hyperglycemia, uremia, hypoxic encephalopathy, hepatic encephalopathy, hypertensive encephalopathy, eclampsia, posterior reversible encephalopathy syndrome (PRES), systemic lupus erythematosus (SLE), and mitochondrial encephalopathy
Intoxication	Seizure occurring when taking narcotics (such as cocaine), prescribed drugs (such as aminophylline and imipramine), dangerous drugs, drug overdose, environmental pollution (such as carbon monoxide, lead, camphor, and organophosphorus), and alcohol (such as acute alcohol intoxication).
Withdrawal	Seizure occurring within 1–3 days after discontinuation of alcohol and drugs (such as barbiturate and benzodiazepines) in patients who are addicted to those agents
Post-neurosurgical operation	Seizure occurring immediately after intracranial surgery
Demyelinating disease	Seizure occurring in the acute phase of acute disseminated encephalomyelitis or multiple sclerosis
Post-radiotherapy	Seizures occurring within 24 hours after radiation exposure
Multiple etiologies	Seizure related to several concomitant conditions

CQ 16-3

How to manage patients with acute symptomatic seizures?

Summary

In patients with acute symptomatic seizures, we promptly measure vital signs including consciousness level, take history, perform general and neurological examinations, and continue to perform these procedures.

Comment

Figures 1 and 2 show the flow chart of clinical investigation of patients suspected of acute symptomatic seizures.

In patients with convulsion, we first perform procedures to prevent injury or aspiration. Check vital signs and consciousness level, and perform respiratory and circulatory management if needed. Suspect inflammatory disease if the patient has a fever; and consider hypertensive encephalopathy, posterior reversible encephalopathy syndrome (PRES), or eclampsia if the patient has severe hypertension. In the case of status epilepticus, start treatment for status epilepticus (see Chapter 8).

For history taking, we should obtain information about symptoms at seizure attack, history of trauma, diseases under treatment (for example, hypoglycemia if receiving insulin injection for diabetes), current medications (for example, drug intoxication if taking massive dose of drug), alcohol drinking history (alcohol dependence, acute alcohol intoxication or withdrawal), and possibility of pregnancy.

For general physical examination, check for injury, incontinence, bite wound, skin conditions (color, rash, cyanosis, etc.), breath odor, and tachypnea. If arrhythmia, cardiac murmur, or cyanosis is present, consider the possibility of syncope, cerebral embolism or heart failure[1].

For neurological examinations, first check the level of consciousness, then suspect meningitis or encephalitis if meningeal irritation signs are present, brain tumor or cerebrovascular disease if focal neurological signs are present, and hypocalcemia if Trousseau signs or Chvostek signs are present.

■ References

1) National Collaborating Centre for Primary Care. The diagnosis and management of the epilepsies in adults and children in primary and secondary care. 2004.

■ Search formula and secondary reference sources

PubMed search: November 28, 2008
Acute symptomatic seizure = 222

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Figure 1. Procedures of investigation for patients suspected of acute symptomatic seizures, and examples.

Convulsive seizure, seizure with loss of consciousness	
↓	
Vital sign (conscious state) evaluation	Respiratory and circulatory management as necessary, treatment for status epilepticus
↓	
Medical history	Situation of seizure, past history including trauma, diseases being treated, drugs being used, drinking history, pregnancy, etc.
↓	
General physical examination	Injury, incontinence, bite, skin color, breath odor, tachypnea, etc. Arrythmia, heart murmur, cyanosis
↓	
Neurological examinations	Level of impaired consciousness, meningeal irritation sign, focal neurological signs, Trousseau signs, Chvostek signs
↓	
Other examinations	Blood tests, head CT or MRI, EEG, ECG, chest X ray, etc. If necessary, cerebrospinal fluid examination
↓	
Treatment	Treatment of underlying disease Antiepileptic drugs in case of high probability of relapse

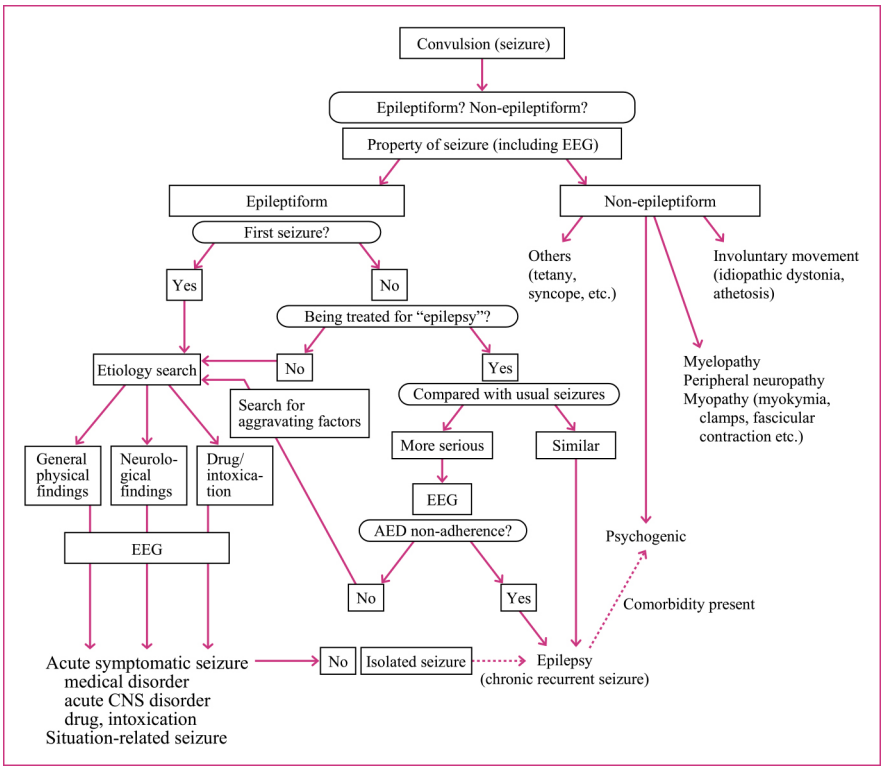

Figure 2. Flowchart for diagnosis of acute symptomatic seizures.
Situation-related seizure: seizure induced only in the presence of inducing factor.
Isolated seizure: unprovoked seizure occurring once in the lifetime.
Broken line in figure suggests the possibility of transition in some cases.
Note: "Epileptiform" in the figure signifies symptoms caused by a state of excessive activation in the brain, and does not necessarily mean seizure symptoms of epilepsy as a chronic disease.
(Modified from: Ikeda A, Shibazaki H. Convulsion; differentiation between syncope and epilepsy. In: Sugimoto T, Omata M (ed.) Differential Diagnosis in Internal Medicine, 2nd edition. Tokyo: Asakura Publishing Co. Ltd. 2003. p.87–96)

CQ 16-4

What kinds of examination are needed for acute symptomatic seizures?

Summary

Conduct blood test, brain CT or MRI, EEG, electrocardiogram, and chest X-ray, and perform cerebrospinal fluid examination if necessary.

Comment

Check for hypoglycemia, hypocalcemia, hyponatremia, high creatinine (uremic encephalopathy), high ammonia (hepatic encephalopathy), antinuclear antibody [systemic lupus erythematosus (SLE) and vasculitis], and antibodies of immune-mediated encephalopaties[1]. Brain CT or MRI is critical for the diagnosis of brain tumor, brain abscess, brain granuloma, and cerebrovascular disease[2, 3]. Perform cerebrospinal fluid examination if meningitis or encephalitis is suspected in febrile patients with headache or impaired consciousness.

■ References

1) National Collaborating Centre for Primary Care. The diagnosis and management of the epilepsies in adults and children in primary and secondary care. 2004.
2) Harden CL, Huff JS, Schwartz TH, et al. Reassessment: neuroimaging in the emergency patient presenting with seizure (an evidence-based review): report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. Neurology. 2007; 69(18): 1772-1780.
3) Krumholz A, Wiebe S, Gronseth G, et al. Practice parameter: evaluating an apparent unprovoked first seizure in adults (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology and the American Epilepsy Society. Neurology. 2007; 69(21): 1966-2007.

■ Search formula and secondary reference sources

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Acute symptomatic seizure = 222

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No references that could serve as evidence were found in Ichushi Web.

CQ 16-5

How to treat acute symptomatic seizures?

Summary

For acute symptomatic seizures, treat the underlying disease and start antiepileptic drugs if there is a high probability of seizure recurrence.

Comment

If seizure persists, treat as for status epilepticus (see Chapter 8). In the case of a highly probable seizure recurrence in the acute phase, intravenous injection of fosphenytoin, phenytoin, levetiracetam or phenobarbital is useful for patients who have difficulties in taking oral antiepileptic drugs[1, 2]. Conventional oral antiepileptic drugs are useful for patients capable of oral intake[3-5].

Avoid chronic prophylactic use of antiepileptic drugs and stop their administration after a short period, because continuous administration does not prevent transition to epilepsy[2].

■ References

1) Minicucci F, Muscas G, Perucca E, et al. Treatment of status epilepticus in adults: guidelines of the Italian League against Epilepsy. Epilepsia. 2006; 47(Suppl 5): 9-15.
2) Koppel BS. Treatment of acute and remote symptomatic seizures. Curr Treat Options Neurol. 2009; 11(4): 231-241.
3) Temkin NR. Antiepileptogenesis and seizure prevention trials with antiepileptic drugs: meta-analysis of controlled trials. Epilepsia. 2001; 42(4): 515-524.
4) Marson AG, Williamson PR, Clough H, et al. Carbamazepine versus valproate monotherapy for epilepsy: a meta-analysis. Epilepsia. 2002; 43(5): 505-513.
5) Glauser T, Ben-Menachem E, Bourgeois B, et al. ILAE treatment guidelines: evidence-based analysis of antiepileptic drug efficacy and effectiveness as initial monotherapy for epileptic seizures and syndromes. Epilepsia. 2006; 47(7): 1094-1120.

■ Search formula and secondary reference sources

PubMed search: November 28, 2008
Acute symptomatic seizure = 222

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No references that could serve as evidence were found in Ichushi Web.

CQ 16-6

How to diagnose and treat anti-NMDA receptor encephalitis?

Summary

(1) If acute symptomatic seizures are suspected to be caused by anti-NMDA receptor encephalitis, perform brain MRI and cerebrospinal fluid examination and consider to measure anti-NMDA receptor antibody. Perform a systemic search for the presence of neoplastic disorders including ovarian teratoma.

(2) After starting appropriate circulatory and respiratory management, consider surgical resection of the tumor in the early stage if paraneoplastic syndrome is suspected. Also consider steroid pulse therapy, high-dose intravenous immunoglobulin therapy, plasmapheresis, and immunosuppressants (currently not covered by medical insurance).

Comment

Anti-*N*-methyl-D-aspartate (NMDA) receptor encephalitis is more prevalent in young women. It initially manifests diverse psychiatric symptoms such as emotional disorder, memory impairment, hallucination, and delusion; and later shows convulsive seizures and involuntary movements such as dyskinesia, respiratory failure, and autonomic nervous system symptoms[1, 2]. Convulsive seizures may be the initial symptom[3].

Brain MRI shows high signal intensity regions in mesial temporal lobe, cerebral cortex, and cerebellum on T2-weighted images. Cells and proteins increase in cerebrospinal fluid. However, these abnormal findings are absent in some cases[1, 2]. Measurement of autoantibodies including anti-NMDA receptor antibody in blood and cerebrospinal fluid specimens is requisite for the diagnosis[1, 2]. However, these tests can be done only in a limited number of facilities. Systemic search for malignancies is recommended because tumors such as ovarian teratoma may be involved in the pathophysiology[1, 2, 4].

We should consider early surgical resection of a tumor when its involvement is suspected[1, 2]. When acute anti-NMDA receptor antibody encephalitis is strongly suspected, consider steroid pulse therapy, high-dose immunoglobulin therapy, plasmapheresis, and immunosuppressants[1, 3, 4]. There is no high level evidence for the choice of treatment method.

■ References

1) Dalmau J, Gleichman AJ, Hughes EG, et al. Anti-NMDA-receptor encephalitis: case series and analysis of the effects of antibodies. Lancet Neurol. 2008; 7(12): 1091-1098.
2) Titulaer MJ, McCracken L, Gabilondo I, et al. Treatment and prognostic factors for long-term outcome in patients with anti-NMDA receptor encephalitis: an observational cohort study. Lancet Neurol. 2013; 12(2): 157-165.
3) Viaccoz A, Desestret V, Ducray F, et al. Clinical specificities of adult male patients with NMDA receptor antibodies encephalitis. Neurology. 2014; 82(7): 556-63.
4) Iizuka T, Sakai F, Ide T, et al. Anti-NMDA receptor encephalitis in Japan: long-term outcome without tumor removal. Neurology. 2008; 70(7): 504-511.

■ Search formula and secondary reference sources

PubMed search: December 11, 2014

"anti-n-methyl-d-aspartate receptor encephalitis" [MeSH Terms] OR ("anti-n-methyl-d-aspartate" [All Fields] AND "receptor" [All Fields] AND "encephalitis" [All Fields]) OR "anti-n-methyl-d-aspartate receptor encephalitis" [All Fields] OR ("anti" [All Fields] AND "nmdar" [All Fields] AND "encephalitis" [All Fields]) OR "anti nmdar encephalitis" [All Fields] = 399 Among the 399 papers, the above references were reviewed.

No references that could serve as evidence were found in Ichushi Web.