Part I
The Clinical Practice Guidelines for Epilepsy 2018

Chapter 1
Diagnosis, Classification and Differential Diagnosis of Epilepsies (Including REM Sleep Behavior Disorder)

CQ 1-1

What is epilepsy?

Summary

Epilepsy is a disease characterized by an enduring predisposition to generate epileptic seizures. In other words, epilepsy is a chronic brain disease, in which abnormal hyperexcitable neurons in the brain cause recurrence of seizure symptoms. Seizures occur suddenly, manifesting physical symptoms different from the normal state, altered consciousness, and motor and sensory changes. The possibility of epilepsy is adequately high if accompanied by seizures.

Comment

Cerebral neurons generate regular rhythm electrically, while maintaining synchronous neuronal activity in the brain. Epilepsy is caused by a sudden disturbance of this activity accompanied by abnormal, disorderly discharges of the electrical activities of neurons in the brain (excessive excitation or synchronization). This may occur in an afebrile state, and the seizure symptoms are diverse depending on the region of the brain that is involved in the abnormal electrical activity[1]. These symptoms include not only "convulsions and spasms" but also various symptoms such as "feeling black out", "jerking of the body", "moving around with loss of consciousness" (see CQ1-4 on page 10, and CQ1-5 on page 11). In addition, epilepsy is characterized by recurrence. Electroencephalography (EEG) has a central role in various examinations and is necessary to establish the diagnosis (see CQ1-6 on page 13).

Traditionally, epilepsy was defined as "two unprovoked seizures occurring at intervals of longer than 24 hours". In 2014, a task force of the International League Against Epilepsy Organization (ILAE) recognized that epilepsy may be present in special circumstances that do not meet the criteria of "two unprovoked seizures". In order to address this issue, the task force proposed to consider epilepsy as a disease of the brain defined by any of the following criteria[2]: (1) at least two unprovoked (or reflex) seizures occurring at intervals of longer than 24 hours; (2) one unprovoked (or reflex) seizure and a probability of further seizures similar to the general recurrence risk (at least 60%) after two unprovoked seizures, occurring over the next 10 years (see Note below); and (3) diagnosis of an epilepsy syndrome.

The term "unprovoked seizure" is a term that describes spontaneous seizure as a chronic disease without a definitive trigger. In contrast, "provoked seizure" is also known as acute symptomatic seizure or situation-related seizure, which occurs secondary to acute brain disorders such as encephalitis, trauma, cerebrovascular disorders, and metabolic disorders [3].

Note: Number (2) in the second paragraph signifies that if there is one unprovoked seizure and the risk of recurrence can be proven to be over 60%, then patient care should be initiated assuming a diagnosis of epilepsy. Some specific examples include patients with a single seizure occurring at least one month after onset of stroke, and children with a single seizure simultaneous with a structural or indirect symptomatic etiology for the symptom and an epileptiform EEG. Another example is patients in whom a specific epilepsy syndrome associated with persistent threshold change can be detected after a single seizure. Even when the first seizure manifests as status epilepticus, this by itself does not imply epilepsy [2].

References

1) Iinuma K, Fujiwara T, Ikeda A, et al. Japan Epilepsy Society, Task Force on Guideline Committee. Guideline for Diagnosis of Epilepsy. Tenkan Kenkyu. 2008; 26(1): 110-113 (in Japanese).
2) Fisher RS, Accvedo C, Arzimanoglou A, et al. ILAE Official Report. A practical clinical definition of epilepsy. Epilepsia. 2014; 55(4): 475-482.
3) 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: September 12, 2008
epilepsy [Mesh] and (define* OR definition*) = 2,382

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

PubMed search: June 28, 2015
(((((((epilepsy/classification [majr] OR epilepsy/diagnosis [majr])) AND ((define* OR definite*)))) AND (Humans [Mesh] AND (English [LA] OR Japanese [LA]))) AND ("2008" [Date-Publication]: "2015" [Date-Publication]))) AND (("ILAE") OR ("NICE" OR "National Institute for Health and Care Excellence")) = 17

Ichushi search: June 25, 2015
(((Differential diagnosis/TH) and (((REM sleep behavior disorder/TH or REM sleep behavior abnormality/AL) or (epilepsy/MTH)) and (Japan Epilepsy Society/AL)))) and (DT = 2008:2015 and PT = excluding proceedings and CK = human) = 6

CQ 1-2

What are the key clinical features to be included in history taking for epilepsy diagnosis?

Summary

Accumulation of detailed information (medical history) and a witness of the actual seizure are most useful for the diagnosis of epilepsy. The chief complaint in most cases is a convulsive seizure (non-convulsive seizure in some cases). However, usually it is necessary to confirm the history of the seizure at least twice in order to diagnose epilepsy.

Comment

Detailed history taking of clinical features 1 to 3 described below is important for making a diagnosis[1, 2].

1. It is important to obtain seizure information from the patient and a witness of the seizure.

a. Frequency of seizure
b. Situation and trigger of the seizure (such as photosensitivity)
c. Symptoms before and during seizure (physical symptoms, psychological symptoms, and consciousness impairment)
d. Duration of symptoms
e. Symptoms after the seizure
f. Presence or absence of injury, tongue bite and urinary incontinence
g. Headache and muscle pain after seizure
h. Age of the first seizure for a patient with multiple seizures
i. Change and evolution of seizure and type of seizure
j. The last seizure
k. Relation between seizure and wake-sleep states

2. It is important to include the following clinical features in history taking from a witness of seizure.

a. Frequency of seizure
b. Detailed situations observed before and during seizure (patient's response, arm and leg movements, open or closed eyes, eyeball displacement, making sound, facial pallor, respiration and pulse)
c. Details of movements and behaviors after seizure
d. Video recorded by family members

3. When recording the medical history in the clinical record, it is important to include the following demographic characteristics.

a. Age (many epilepsies are age-dependent)
b. Sex
c. Past history (including perinatal abnormalities, febrile convulsions, head trauma, and mental illness)
d. Comorbid conditions (see **Table 1**)
e. History of alcohol consumption, regular medications, and history of narcotic use
f. Family history
g. Social history

References

1) Scottish Intercollegiate Guidelines Network. Diagnosis and management of epilepsy in adults. A national clinical guideline, 2003, p.3-7.
2) Stokes T, Shaw EL, Juarez-Garcia A, et al. Clinical Guidelines and Evidence Review for the Epilepsies: diagnosis and management in adults and children in primary and secondary care. London: Royal College of General Practitioners, 2004, p. 49-50, 85-95.

Search formula and secondary reference sources

PubMed search: October 30, 2008
((epileptic seizures or epilepsy) and diagnosis and (interview or (history taking)) and ("sensitivity and specificity" [mh] OR sensitivity [tiab] OR specificity [tiab] OR likelihood ratio* OR practice guideline [pt] OR likelihood functions [mh] or meta-analysis [mh] OR meta-analysis [pt] OR metaanaly* [tiab] OR "meta analysis" OR multicenter study [pt] OR evaluation studies [pt] OR validation studies [pt] OR systematic review* OR systematic [sb] = 58

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

PubMed search: June 28, 2015
(((((((epilepsy [majr]) AND medical history taking [mesh])) AND ("2008" [Date-Publication]: "2015" [Date-Publication])) AND (English [Language] OR Japanese [Language]))) AND Humans [Filter])) AND ("ILAE" OR "NICE") = 0

Ichushi search: June 25, 2015
(((((epilepsy/MTH)) and (SH = diagnosis)) and (history taking/MTH))) and (DT = 2008:2015 and PT = excluding proceedings) = 0

Table 1. Main comorbid conditions of epilepsy.

1. Birth asphyxia	8. Central nervous system infection
2. Brain malformation	9. Autoimmune encephalitis
3. Genetic abnormality	10. Cerebral hemorrhage
4. Chromosomal abnormality	11. Cerebral infarction
5. Developmental disorder	12. Brain tumor
6. Metabolic abnormality	13. Brain trauma
7. Hypoxia	14. Dementia

CQ 1-3

How are epileptic seizure types, epilepsies, epilepsy syndromes, and related seizure disorders classified?

Summary

Classification of epileptic seizures is indispensable for subsequent patient care, examinations, and choice of antiepileptic drugs. The ILAE classifications are widely used. Diagnosis of epilepsy for patients has important significance on physical, mental, social and economic status. Therefore, it is recommended that specialists conduct definitive clinical diagnosis of epilepsy.

Comment

Currently, the following ILAE classifications are widely used in Japan: the classification of epileptic seizures of 1981 [1] and the classification of epilepsies, epileptic syndromes and related seizure disorders of 1989 [2]. However, the ILAE task force proposed a new disease classification in 2010 [3]. **Tables 1 and 2** show the corresponding classification categories in the new and old classifications of 1981, 1989 and 2010 [4]. This guideline follows the classification of seizure types of 1981, in which epileptic seizures are divided into partial and generalized seizures. "Partial" is used to indicate "focal" or "localization-related".

The feature of the 1981 classification of seizure types is based on an accurate correspondence between seizure symptoms and EEG findings (left column of **Table 1**), and the scheme is based on "epileptic discharge" on EEG, which is the information with the highest sensitivity and specificity. On the other hand, the feature of the 1989 classification of epilepsies and epilepsy syndromes is based on a 2 × 2 classification table (left column of **Table 2**). With this classification, idiopathic epilepsies and syndromes are not necessary only generalized epilepsies but also include some partial epilepsies. Conversely, within symptomatic epilepsies and syndromes, partial epilepsies and generalized epilepsies are both clearly classified. Furthermore, among these four categories, apart from symptomatic partial epilepsies, all the others have in principle age-dependent onset and reflect the element of onset age at the same time.

1. Idiopathic partial epilepsies are benign, (1) with childhood onset, (2) manifest localization-related seizure symptoms and localized EEG findings, (3) show no abnormal neuroimaging findings, and (4) remit by adolescence. This category includes benign epilepsy with centrotemporal sharp waves and Panayiotopoulos type with focus in the occipital region.
2. Symptoms suggestive of symptomatic partial epilepsies include: (1) a history of disease that may constitute the etiology, (2) aura, (3) local motor or sensory signs at onset or during seizure, and (4) automatism. However, even with absence seizures, automatism may sometimes occur.
3. Idiopathic generalized epilepsies rarely have onset older than at 25 years of age and show no other neurological symptoms. The symptoms suggesting this category include: (1) childhood onset (before adolescence), (2) induced by sleep deprivation and alcohol, (3) tonic-clonic seizure or myoclonic seizure immediately after waking, (4) seizure type is absence, with no other neurologic symptoms (5) spontaneous photoreaction on EEG, including generalized 3-Hz spike-and-slow-wave complexes or multiple spike-and-slow-wave complexes.
4. Symptoms suggestive of symptomatic generalized epilepsies include: (1) very early onset (neonatal period, infancy: under 1 year of age), (2) frequent seizures, (3) mental retardation and neurological symptoms from before onset, (4) progression and regression of neurological symptoms, (5) diffuse EEG abnormalities, and (6) organic morphological abnormalities in the brain.

The basic concepts for the 2010 classifications are as follows.

1. Modes of seizure manifestation and classification of seizures
   The term partial seizure is eliminated, and is replaced by "focal seizures" (with or without impairment of consciousness) (right column of **Table 1**). "Generalized" and "focal" are redefined. Generalized seizures are seizures that occur within the network of bilateral cerebral hemispheres, and this network is rapidly involved in seizure. Focal seizures are seizures that occur within the network limited to unilateral cerebral hemisphere and is either discretely localized or more widely distributed within unilateral hemisphere.
2. Classification of underlying causes
   Instead of the traditional terms "idiopathic", "symptomatic" and "cryptogenic", the 2010 classification recommends modified concepts using the new terms "genetic", "structural-metabolic" and "unknown".

This chapter is based on the classifications reported up to the time of this writing (2016), and the classifications published thereafter are not addressed.

■ References

1) Proposal for revised clinical and electroencephalographic classification of epileptic seizures. From the Commission on Classification and Terminology of the International League Against Epilepsy. Epilepsia. 1981; 22(4): 489-501.
2) Proposal for revised classification of epilepsies and epileptic syndromes. Commission on Classification and Terminology of the International League Against Epilepsy. Epilepsia.1989; 30(4): 389-399.
3) Berg AT, Berkovic SF, Brodie MJ, et al. Revised terminology and concepts of organization of seizures and epilepsies: Report of the ILAE Commission on Classification and Terminology, 2005-2009. Epilepsia. 2010; 51(4): 676-685.
4) Tobimatsu S. Chapter 1. Epidemiology of Epilepsy. 2. Classification (comparison of 1981, 1989 and 2010). In: Guidebook for Epileptologists, Japan Epilepsy Society (Ed.) Shindan To Chiryousha, Tokyo. 2014, p. 5-10 (in Japanese).

■ Search formula and secondary reference sources

PubMed search: October 17, 2008
((epileptic seizures) or epilepsy) and diagnosis and (classification or categorization) and ("sensitivity and specificity" [mh] OR sensitivity [tiab] OR specificity [tiab] OR likelihood ratio* OR practice guideline [pt] OR likelihood functions [mh] or meta-analysis [mh] OR meta-analysis [pt] OR metaanaly* [tiab] OR "meta analysis" OR multicenter study [pt] OR evaluation studies [pt] OR validation studies [pt] OR systematic review* OR systematic [sb] = 273

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

PubMed search: June 28, 2015
(((((((epilepsy/classification [majr]) AND classification [ti])) AND("2008" [Date-Publication]: "2015" [Date-Publication])) AND (English [Language] OR Japanese [Language])) AND Humans [Filter])) AND ("ILAE" OR "NICE") = 22

Ichushi search: June 25, 2015
(((epilepsy/MTH) and (classification/TI))) and (DT = 2008:2015 and PT = excluding proceedings) = 0

Table 1. International classifications of epileptic seizure types: corresponding categories for the 1981 classification and the 2010 revised classification.

1981 classification of seizure type [a]	2010 revised classification of seizure type [b]
Partial (focal, local) seizures	**Focal seizures**
A. Simple partial seizures (consciousness not impaired) 1. With motor signs 2. With somatosensory or special sensory symptoms 3. With autonomic symptoms or signs 4. With psychiatric symptoms (most experienced as "complex partial seizures"	A. Without impairment of consciousness With observable motor or autonomic components. This roughly corresponds to the concept of "simple partial seizure. "Focal motor" and "autonomic" are terms that may adequately convey this concept depending on the seizure manifestations). Involving subjective sensory or psychic phenomena only. This corresponds to the concept of an aura, a term endorsed in the 2001 Glossary.
B. Complex partial seizures 1. Simple partial onset followed by impairment of consciousness a. With simple partial at onset b. With automatism at onset c. With impairment of consciousness at onset	B. With impairment of consciousness This roughly corresponds to the concept of complex partial seizure. "Dyscognitive" is a term that has been proposed for this concept.
C. Partial seizures evolving to secondarily generalized seizures 1. Simple partial seizures (A) evolving to generalized seizures 2. Complex partial seizures (B) evolving to generalized seizures 3. Simple partial seizures evolving to complex partial seizures evolving to generalized seizures	Evolving to a bilateral, convulsive seizure (involving tonic, clonic, or tonic-clonic components). This expression replaces the term "secondarily generalized seizure.
Generalized seizures	**Generalized seizures**
A. 1. Absence seizures a. Impairment of consciousness only b. With mild clonic components c. With atonic components d. With tonic components e. With automatisms f. With autonomic component (b-f may be alone or in combination)	A. Absence seizures 1. Typical absence seizure 3. Absence with special features Myoclonic absence Eyelid myoclonia
2. Atypical absence seizure a. Changes in tone more pronounced than A1 b. Onset/offset not abrupt	2. Atypical absence seizure
B. Myoclonic seizures	B. 1. Myoclonic seizures 2. Myoclonic atonic seizure 3. Myoclonic tonic seizure
C. Clonic seizures	C. Clonic seizure
D. Tonic seizures	D. Tonic seizure
E. Tonic-clonic seizures	E. Tonic-clonic seizure (in any combination)
(no clearly corresponding entity)	
F. Atonic seizures	F. Atonic seizure
Unclassified epileptic seizures	**Unclassified epileptic seizures**
Neonatal seizures	Epileptic spasms
Rhythmic eye movements	
Chewing	
Swimming movement	
	Seizures that cannot be clearly diagnosed into one of the above categories should be considered "unclassified" until additional information allows their accurate diagnosis. However, "unclassified" is not considered a classification category.

[a] Modified from: Proposal for revised clinical and electroencephalographic classification of epileptic seizures. From the Commission on Classification and Terminology of the International League Against Epilepsy. Epilepsia. 1981; 22(4): 489-501.
[b] Modified from: Berg AT, Berkovic SF, Brodie MJ, et al. Revised terminology and concepts of organization of seizures and epilepsies: Report of the ILAE Commission on Classification and Terminology, 2005-2009. Epilepsia. 2010; 51(4): 676-685.

Table 2. International classification of epilepsy syndromes: 1989 classification and 2010 revised classification.

1989 classification of epilepsy syndromes [a]	2010 revised classification of epileptic syndromes [b]
1. Localization-related (focal, local, partial) epilepsies and syndromes 1.1 Idiopathic (age-related onset) · Benign childhood epilepsy with centrotemporal spikes · Childhood epilepsy with occipital paroxysms · Primary reading epilepsy 1.2 Symptomatic · Chronic progressive epilepsia partialis continua of childhood (Kojewnikow's syndrome) · Syndromes characterized by seizures with specific modes of precipitation · Temporal lobe epilepsies · Frontal lobe epilepsies · Parietal lobe epilepsies · Occipital lobe epilepsies 1.3 Cryptogenic **2. Generalized epilepsies and syndromes** 2.1 Idiopathic (with age-related onset - arranged by age) · Benign neonatal familial convulsions · Benign neonatal convulsions · Benign myoclonic epilepsy in infancy · Childhood absence epilepsy (pyknolepsy) · Juvenile absence epilepsy · Juvenile myoclonic epilepsy (impulsive petit mal) · Epilepsy with grand mal (GTCS) seizures on awakening · Other generalized idiopathic epilepsies not defined above · Epilepsies with seizures precipitated by specific modes of activation 2.2 Cryptogenic or symptomatic (arranged by age) · West syndrome (infantile spasm, nodding spasm) · Lennox-Gastaut syndrome · Epilepsy with myoclonic-astatic seizures · Epilepsy with myoclonic absences 2.3 Symptomatic 2.3.1 Non-specific etiology · Early myoclonic encephalopathy · Early infantile epileptic encephalopathy with suppression burst · Other symptomatic generalized epilepsies not defined above 2.3.2 Specific syndromes **3. Epilepsies and syndromes undetermined whether focal or generalized** 3.1 With both generalized and focal seizures · Neonatal seizures · Severe myoclonic epilepsy in infancy · Epilepsy with continuous spike-waves during slow-wave sleep · Acquired epileptic aphasia (Landau-Kleffner syndrome) · Other undetermined epilepsies not defined above 3.2 Without unequivocal generalized or focal features **4. Special syndromes** 4.1 Situation-related seizures · Febrile convulsions · Isolated seizures or isolated status epilepticus · Seizures occurring only when there is an acute metabolic or toxic event such as alcohol, drugs, eclampsia, nonketotic hyperglycemia, etc.	**Electroclinical syndromes (arranged by age at onset) [c]** Neonatal period Benign familial neonatal epilepsy Early myoclonic encephalopathy Ohtahara syndrome Infancy Epilepsy of infancy with migrating focal seizures West syndrome Myoclonic epilepsy in infancy Benign infantile epilepsy Benign familial infantile epilepsy Dravet syndrome Myoclonic encephalopathy in nonprogressive disorders Childhood Febrile seizures plus (have infancy onset) Early onset benign childhood occipital epilepsy syndrome (Panayiotopoulos syndrome) Epilepsy with myoclonic atonic (previously astatic) seizures Benign epilepsy with centrotemporal spikes Autosomal-dominant nocturnal frontal lobe epilepsy Late onset childhood occipital epilepsy (Gastaut type) Epilepsy with myoclonic absences Lennox-Gastaut syndrome Epileptic encephalopathy with continuous spike-and-wave during sleep (CSWS)[d] Landau-Kleffner syndrome Childhood absence epilepsy Adolescence-Adult Juvenile absence epilepsy Juvenile myoclonic epilepsy Epilepsy with generalized tonic-clonic seizures alone Progressive myoclonus epilepsies Autosomal dominant epilepsy with auditory features Other familial temporal lobe epilepsies Less specific age relationship Familial focal epilepsy with variable foci (childhood to adult) Reflex epilepsies **Distinctive constellations** Mesial temporal lobe epilepsy with hippocampal sclerosis Rasmussen syndrome Gelastic seizures with hypothalamic hamartoma Hemiconvulsion-hemiplegia-epilepsy Epilepsy not belonging to these diagnostic categories are distinguished based on first, presence or absence of structural-metabolic disease (presumed cause), and second, mode of seizure onset (generalized vs. focal) **Epilepsies attributed to and organized by structural-metabolic causes (arranged by etiology)** Malformations of cortical development (hemimegalencephaly, heterotopias, etc.) Neurocutaneous syndromes (tuberous sclerosis complex, Sturge-Weber, etc.) Tumor Infection Trauma **Angioma** Perinatal insults Stroke Others **Epilepsies of unknown cause** **Conditions with epileptic seizures that are traditionally not diagnosed as a form of epilepsy per se.** Benign neonatal seizures Febrile seizures

[a] Modified from: Proposal for revised classification of epilepsies and epileptic syndromes. Commission on Classification and Terminology of the International League Against Epilepsy. Epilepsia.1989; 30(4): 389-399.

[b] Modified from: Berg AT, Berkovic SF, Brodie MJ, et al. Revised terminology and concepts of organization of seizures and epilepsies: Report of the ILAE Commission on Classification and Terminology, 2005-2009. Epilepsia. 2010; 51(4): 676-685.

[c] Classification of electroclinical syndromes does not reflect the etiology.

[d] Sometimes also called "electrical status epilepticus during slow sleep (ESES).

CQ 1-4

Which diseases should be differentiated from epilepsy in adults?

Summary

The conditions that may be misdiagnosed as epilepsy are as follows.

(1) Syncope (vasovagal, cardiac, etc.)
(2) Psychogenic nonepileptic seizures
(3) Hyperventilation or panic disorder
(4) Stroke (cerebral infarction, cerebral hemorrhage), transient ischemic attack
(5) Parasomnia (REM sleep behavior disorders, non-REM parasomnia)
(6) Acute intoxication (drugs, alcohol), drug withdrawal, alcohol withdrawal
(7) Acute metabolic disorders (hypoglycemia, tetany, etc.)
(8) Acute renal failure
(9) Head injury (within one week)
(10) Involuntary movements (tic, tremor, myoclonus, paroxysmal dyskinesia, etc.)
(11) Episodic ataxia

Comment

Among patients visiting the emergency room with acute onset of loss of consciousness, the most common causes are vasovagal syncope or psychogenic nonepileptic seizure (40%), followed by epilepsy (29%) and cardiac syncope (8%) [1]. In the diagnosis of epilepsy, we should exclude or consider an associated cardiovascular factor [2]. A syncope attack is characterized by no change in consciousness level, fatigue, and malaise after an attack [3, 4]. Patients who develop acute convulsion within 1 week after head injury have an overall risk of approximately 25% for developing epilepsy in the future [3]. Alcohol withdrawal may also cause a convulsive attack [3, 4].

■ References

1) Day SC, Cook EF, Funkenstein H, et al. Evaluation and outcome of emergency room patients with transient loss of consciousness. Am J Med. 1982; 73(1): 15-23.
2) Zaidi A, Clough P, Cooper P, et al. Misdiagnosis of epilepsy: many seizure-like attacks have a cardiovascular cause. J Am Coll Cardiol. 2000; 36(1): 181-184.
3) Japanese Society of Neurology Ad Hoc Committee of Treatment Guidelines. Guideline for Treatment of Epilepsy 2002. Rinsho Shinkeigaku. 2002; 42(6): 549-597 (in Japanese).
4) Scottish Intercollegiate Guidelines Network. Diagnosis and management of epilepsy in adults. A national clinical guideline, 2003. p.3-5.

■ Search formula and secondary reference sources

PubMed search: October 30, 2008
((epileptic seizures) or epilepsy) and diagnosis and (distinguish or differentiate or "Diagnosis, Differential" [Mesh]) and ("sensitivity and specificity" [mh] OR sensitivity [tiab] OR specificity [tiab] OR likelihood ratio* OR practice guideline [pt] OR likelihood functions [mh]) and (meta-analysis [mh] OR meta analysis [pt]OR metaanaly* [tiab] OR "meta analysis" OR multicenter study [pt] OR evaluation studies [pt] OR validation studies [pt] OR systematic review* OR systematic [sb]) = 32

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

PubMed search: June 28, 2015
((((((“Epilepsy” [Major Mesh]) AND “diagnosis, differential” [MeSH Terms]) AND (English [Language] OR Japanese [Language])) AND (“2008”[Date-Publication]: “2015” [Date-Publication])) AND adult [MeSH])) AND (“ILAE” OR “NICE”) = 4

Ichushi search: June 25, 2015
(((((epilepsy/MTH)) and (SH = diagnosis)) and (differential diagnosis/TH))) and (DT = 2008:2015 and PT = excluding proceedings and CK = adult (19–44), middle-aged (45–64), elderly (65–), elderly (80–)) = 3

CQ 1-5

Which diseases should be differentiated from epilepsy in children?

Summary

Confirm that there are no features suggestive of the following pathological conditions. Especially, take history carefully about the situation before and after the attack. In the case of children, check for fever, crying, diarrhea, sleep-wake rhythm, and whether the child is hungry.

(1) Febrile convulsion
(2) Breath-holding spells
(3) Benign convulsions with mild gastroenteritis
(4) Convulsion during sleep/sleep myoclonus
(5) Non-REM parasomnia (night terror/sleepwalking)
(6) Tic
(7) Syncope (vasovagal, cardiac, etc.)
(8) Psychogenic nonepileptic seizures
(9) Masturbation
(10) Acute metabolic disorders (hypoglycemia, tetany, etc.)

Comment

In children, some diseases or conditions with paroxysmal symptoms are often misdiagnosed as epileptic seizures. The symptoms and the diseases/conditions that may show these symptoms are as follows: (1) generalized tonic convulsions and tonic-clonic convulsion: febrile convulsions, benign convulsions with mild gastroenteritis, some psychogenic seizures, acute metabolic disorders, and prolonged cyanotic breath-holding attacks; (2) loss of consciousness and atonic attack: breath-holding spells, vasovagal syncope, some psychogenic seizures, some acute metabolic disorders, and some febrile convulsions; (3) muscle jerks: sleep myoclonus and some psychogenic reactions; (4) strange behaviors such as fear and wandering: night terror, sleepwalking, and psychogenic reactions. Medical history, symptoms, and onset age help differentiate these diseases from epilepsy, and EEG examination is sometimes needed [1, 2]. Note that some febrile convulsions (especially in children over 3 years of age) or some of the acute metabolic disorders may show epileptic discharges (epileptiform EEG) (**Table 1**).

■ References

1) Iinuma K, Fujiwara T, Ikeda A, et al. Japan Epilepsy Society. Task Force on Guideline Committee. Guideline for Diagnosis of Epilepsy. Tenkan Kenkyu 2008; 26(1): 110-113 (in Japanese).
2) Scottish Intercollegiate Guidelines Network. Diagnosis and management of epilepsy in adults. A national clinical guideline, 2003.

■ Search formula and secondary reference sources

PubMed search: October 30, 2008
((epileptic seizures) or epilepsy) and diagnosis and (distinguish or differentiate or "Diagnosis, Differential" [Mesh]) and ("sensitivity and specificity" [mh] OR sensitivity [tiab] OR specificity [tiab] OR likelihood ratio* OR practice guideline [pt] OR likelihood functions [mh]) and (meta-analysis [mh] OR meta analysis [pt] OR metaanaly* [tiab] OR "meta analysis" OR multicenter study [pt] OR evaluation studies [pt] OR validation studies [pt] OR systematic review* OR systematic [sb]) = 32

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

PubMed search: June 28, 2015
(((((("Epilepsy" [Major Mesh]) AND diagnosis, differential [MeSH Terms])) AND (English [Language] OR Japanese [Language])) AND ("2008" [Date-Publication]: "2015" [Date-Publication])) AND "child" [Filter])) AND ("ILAE" OR "NICE") = 1

Ichushi search: June 25, 2015
((((((epilepsy/MTH)) and (SH = diagnosis)) and (differential diagnosis/TH))) and (DT = 2008:2015 and PT = excluding proceedings and CK= infancy (2–5), children (6–12), young adult (13–18))) and (Japan Epilepsy Society/AL) = 1

Table 1. Diseases that have to be differentiated from epilepsy in children – benign convulsions and related disorders.

Benign convulsion		Seizure symptoms	EEG abnormality	Diagnosis
Febrile convulsion		Generalized tonic convulsion accompanied by fever of over 38°C; tonic-clonic convulsions. From medical history and clinical examinations, convulsion seems not attributed to central nervous system infection, metabolic abnormalities, or other obvious causes. Atonic febrile convulsions such as atonia, staring, and upward rolling of eyeballs 5%; familial onset 20-30%. EEG may show epileptiform waves.	+/-	Convulsions occurring only during fever. No symptoms suggestive of other disorders.
Breath-holding spells	cyanotic	Child cries uncontrollably due to pain, anger, or bad mood. Suddenly stops breathing resulting in cyanosis. Loses consciousness, becomes limp. If prolonged, whole body becomes tonic.	-	Medical history. If anxious, perform EEG
	pallid	Suddenly loses consciousness without crying, due to sudden pain, surprise, or fear. Becomes limp, face turns pale.	-	
Benign convulsions with mild gastroenteritis		Generalized afebrile tonic-clonic convulsions caused by diarrhea or vomiting for 2 to 5 days with mild or no dehydration. Convulsions may be caused by vomiting alone before diarrhea occurs. If no abnormalities found in EEG and electrolyte tests, the possibility is high. Commonly seen in rotavirus infection. 80% of patients show cluster of 2 or more spasms, lasting 2-3 days in 20%.	-	Medical history, rotavirus antigen in feces (other viruses too), (EEG)
Convulsion during sleep / sleep myoclonus		Convulsion during sleep: brief and minor convulsions occurring at the beginning of sleep; single or repetitive. Although commonly left-right asymmetric affecting lower limbs, may be seen in upper limbs and head muscle. Sleep myoclonus: can occur in all sleep stages, not only asynchronously but also left-right symmetrically; not only in distal muscles but also in proximal muscles and trunk.		Symptoms, time of occurrence. If anxious, perform EEG
Non-REM parasomnia (night terror/sleepwalking)		Night terror: strong fear that happens suddenly during sleep; showing screams, crying, excitement, tachycardia, etc.; lasting 1 to 10 minutes. One-half of patients also show sleepwalking. Sleepwalking: suddenly rising during sleep, walking or running around, etc., lasting 1 to 40 minutes. Both occur during the first one-third of sleep at night, and are common among 4-12 year-old children. Do not wake up even when someone tries to wake them. Patient does not remember the episode. There may be a family history.	-	Symptoms, time of occurrence. If anxious, perform EEG and poly-somnography
Tic		Abrupt movements noticeable in the face, neck, shoulders, upper limbs, etc., which repeat regularly and constantly. Also occurs in eyeballs. Increase with mental tension. Does not disturb other movements while the tic occurs. Does not bother the patient. Does not occur during sleep.	-	Symptoms
Vasovagal syncope		Suddenly loses consciousness and collapses; becomes atonic. May be postural dysregulation occurring during postural change or standing; vagal reflex due to fear and pain; or reflex due to cough, urination, or swallowing. The duration of consciousness loss is short.	-	Medical history and symptoms
Psychogenic nonepileptic seizures		Diverse seizure symptoms, difficult to diagnose from symptoms alone. Tends to occur under the same situation. Usually does not occur where nobody is watching. In the case of only psychogenic reaction, the reaction may be concomitant with epilepsy. Ictal EEG is necessary for a reliable diagnosis. See the section of "Psychogenic nonepileptic seizure" (CQ14-1 on page 123).	-	Symptoms Ictal EEG
Masturbation		Repeated motion of extending lower limbs with force over a long time. Conscious. When looking closely, the thighs and pelvis are rubbing against the bed or something. Symptoms are interrupted when the thighs are separated. Sometimes red face can be seen.	-	Observe motions carefully
Acute metabolic disorders (hypoglycemia, tetany, etc.)		Hypoglycemia may cause loss of consciousness and tonic-clonic convulsion. Hypocalcemia may cause tonic convulsion or tonic-clonic convulsion. Hyponatremia may cause tonic-clonic convulsion. Hyperammonemia may cause loss of consciousness and tonic-clonic convulsion.	-/+	Blood glucose, serum calcium, serum sodium, blood ammonia, etc.

CQ 1-6

What are the practical procedures for the diagnosis of epilepsy?

Summary

The main procedures of diagnosis of epilepsy are summarized in Figure 1 [1]. It is recommended that a neurology specialist should make a definitive clinical diagnosis of epilepsy.

Comment

In patients presenting with the first unprovoked seizures, EEG recording (including photic stimulation, hyperventilation, and sleep) is recommended [1, 2]. Sleep-deprived EEG increases the detection rate of epileptic discharges [2]. Neuroimaging study [1] and video-EEG monitoring are necessary.

■ References

1) Krumholz A, Wiebe S, Gronseth G, et al. Practice Parameter: Evaluating an apparent unprovoked first seizure in adults: Report of the Quality Standards Subcommittee of the American Academy of Neurology and the American Epilepsy Society. Neurology. 2007; 69(21): 1996-2007.
2) van Donselaar CA, Schimsheimer R-J, Geerts A, et al. Value of the electroencephalogram in adult patients with untreated idiopathic first seizures. Arch Neurol. 1992; 49(3): 231-237.

■ Search formula and secondary reference sources

PubMed search: October 30, 2008
((epileptic seizures) or epilepsy) and diagnosis and (distinguish or differentiate or "Diagnosis, Differential" [Mesh]) and ("sensitivity and specificity" [mh] OR sensitivity [tiab] OR specificity [tiab] OR likelihood ratio* OR practice guideline [pt] OR likelihood functions [mh]) and (meta-analysis [mh] OR meta analysis [pt] OR metaanaly* [tiab] OR "meta analysis" OR multicenter study [pt] OR evaluation studies [pt] OR validation studies [pt] OR systematic review* OR systematic [sb]) = 32

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

PubMed search: June 28, 2015
((((epilepsy/diagnosis [majr]) AND diagnosis/methods [majr]) AND ((procedure* OR protocol*)))) AND ("2008" [Date-Publication]: "2015" [Date-Publication])) AND (English [Language] OR Japanese [Language]) = 116

Ichushi search: June 25, 2015
(((((epilepsy/MTH)) and (SH = diagnosis))) and (DT = 2008:2015 and PT = review)) and (Japan Epilepsy Society/AL) = 2

Figure 1. Procedures for the diagnosis of epilepsy.