

Fifteen-minute consultation: Approach to the child with an acute confusional state

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ABSTRACT

Acute confusional state (ACS) refers to sudden impairment of cognitive function and represents a major medical emergency. The impairment may be global or confined specifically to a particular faculty of higher mental function, such as memory. This review highlights the importance of relevant medical history and clinical signs and symptoms in reaching the correct diagnosis. In this review, we have presented a diagnostic approach to a child presenting with ACS and described commonly encountered causes, their treatments and outcomes. We have also presented an algorithm for the diagnostic approach to the child with ACS.

INTRODUCTION

Acute confusional state (ACS) represents a major medical emergency due to its possible association with serious underlying pathological process, some of which can be reversible with timely diagnosis and management, such as non-convulsive status epilepticus (NCSE) or basilar migraine. ACS remains a diagnostic and therapeutic challenge at presentation due to a wide variety of possible aetiologies (table 1) and the urgent need to rule out serious conditions.

ACS can be defined as the sudden impairment of mental state in a previously healthy child.¹ This impairment can be global and severe or could be very specific and mild, such as short-term memory impairment in 'transient global amnesia', in which only the memory faculty is impaired.¹

Clinically ACS can be divided into 'silent' or 'agitated' types.¹ Silent type can be more difficult to notice and sometimes only becomes apparent when specific mental status test is carried out (table 2). Assessment can be difficult

when there is pre-existent neurodevelopmental disability. In such situations parent/carer concerns should be sought, taken seriously and actively investigated. Agitated form manifests as variable degree of psychomotor unrest. Even mild deficit in intellectual function can lead to behavioural change owing to the frustration and anxiety.

The overall incidence of ACS in paediatric age group is not known but it is not a rare presentation in emergency departments. It is commonly encountered in conditions frequently seen in paediatric practice such as high fever, drug ingestion/intoxication, head trauma, nervous system infections and inflammations (table 1).

In this review, we have presented three interesting cases that posed diagnostic dilemma at presentation and highlighted the learning points. This is followed by brief discussions about other common aetiologies.

We have also proposed a diagnostic algorithmic approach to the child with ACS.

CASE REPORTS

Case 1

A girl, aged 9 years, required admission to hospital following a generalised convulsion lasting 20 min. She had been given one dose of rescue medication with buccal midazolam at home before being brought to hospital by ambulance. She had been alert, oriented and her usual self prior to the onset of the seizure. Mary has a diagnosis of four-limb cerebral palsy, moderate learning disability and epilepsy with multiple seizure types, including generalised motor seizures, focal motor seizures and absences. She is on sodium valproate with reasonable



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Table 1 Conditions associated with acute confusional state in childhood

| High fever | Fever-induced delirium |
|---|--|
| Sleep disturbances/parasomnias | Confusional arousal, night terrors, somnambulism |
| Head trauma | Bleeding Postconcussion syndrome even after mild injury |
| Central nervous system (CNS) infections and inflammations | Meningitis, encephalitis, brain abscess Parainfectious Autoimmune |
| Metabolic derangements | Hyponatremia Hypoglycaemia Hyperammonaemia Uraemia Severe acidosis Hyperglycaemia (in non-ketotic hyperglycaemia)—rare disorder |
| Intoxication | Drug abuse/accidents Alcohol Medication side effect |
| Epilepsy | Postictal state Focal seizures with impairment of consciousness Non-convulsive status epilepticus |
| Migraine | Basilar migraine, hemiplegic migraine, acute confusional migraine |
| Vascular, raised intracranial pressure | Arteriovenous malformation-bleed Hydrocephalus/blocked shunt CNS tumours |
| Medically unexplained (psychogenic) | More common in adolescent girls |
| Miscellaneous | Hypoxia Hypovolaemia Hypotension Hypertension (hypertensive encephalopathy) Septicaemia |

seizure control. Parents report that she has only occasional convulsions but does have a few vacant episodes in a week. On admission she was noted to be febrile and, after initial investigations, was started on antibiotics for a chest infection. In the next two days parents remained concerned that Mary seemed 'out of it' and not herself. She did not respond consistently to her name, did not seem to recognise family members, and was less vocal, drooling and struggling to eat. Further investigations for the 'encephalopathic presentation' showed normal blood biochemistry and a normal lumbar puncture, though her inflammatory markers were still raised. An electroencephalogram (EEG) showed continuous electrical seizures confirming a diagnosis of NCSE. Treatment with intravenous lorazepam terminated the electrical status and Mary's responsiveness improved. She was discharged from hospital after 5 days with a recovered chest and her normal happy persona.

Learning points

NCSE can present as an ACS.³ It may occur in the context of acute or chronic neurological insults, chronic neurodisability and in children with existent epilepsy, epileptic encephalopathies or epilepsy syndromes. It is often difficult to recognise due to pre-existent neurodevelopmental disability, particularly learning disability or pre-existent epileptic encephalopathy.³ Parent/carer report of a clear and persistent change in behaviour, arousal level, cognition or memory in 'at risk' contexts should always raise suspicion and trigger a request for an EEG, which can confirm the diagnosis. Prognosis tends to be good unless initial presentation is with coma or the NCSE is refractory to treatment.³

Case 2

A 14-year-old boy presented with a 24-hour history of acute confusion and vomiting. There was no history of trauma, infection or substance abuse. He had family history of migraine. On examination, his Glasgow Coma Scale Score (GCS) was 11 and he was mildly feverish (37.7°C). Neurological examination showed weak right side with right extensor plantar. Systemic examination was unremarkable. He was treated for encephalitis with antibiotics and antiviral medications. Twenty hours later, on review by a neurologist, it was clear that he had an expressive dysphasia rather than confusion. He could communicate clearly in writing, but was unable to initiate meaningful verbal conversation. MR imaging of brain 50 hours from onset showed mild cortical swelling in the left parietal region with no enhancement with gadolinium. Over the next 48 hours he understood some verbal commands, but clearly had difficulty finding some words. Right hemiparesis completely resolved. MRI 4 months later was normal. Clinical review at 6 months showed complete recovery. Subsequently, he did have further similar attacks.

Sequencing of the genomic DNA showed evidence of p[Thr666Mrt] mutation in exon 16 of the CACNA1A gene in this child and his father confirming diagnosis of familial hemiplegic migraine. (This case was previously published as one of the patients in the case series of three cases of familial hemiplegic migraine presenting with encephalopathy.⁴)

Learning points

Hemiplegic migraine is a rare disorder characterised by migraine attacks with hallmark unilateral motor weakness during the aura phase. Hemiplegic migraine may occur either in families (familial) or only in one individual (sporadic).⁵ Mutations in three genes (CACNA1A, ATP1A2, SCN1A) have been identified as causative factor for familial type.

A typical attack is characterised by motor weakness during the aura phase. Weakness is never the only aura during the attack, and various associated

Table 2 Suggested mini-mental state examination (adapted from Jain²)

| Functions | Tests |
|--|--|
| 1. Orientation | <ul style="list-style-type: none"> Sex/name/last name/recognises relative (one point for each, total score 4) Place/city/state/country (one point for each total score 4) Day/date/month/year (one point for each, total score 4) |
| 2. Attention and concentration | <ul style="list-style-type: none"> Minimum of 2 and maximum of 5 digits forward (one point for each, total score 4) Minimum of 2 and maximum of 4 digits backward (one point for each, total score 3) |
| 3. Registration and sensory perception | <ul style="list-style-type: none"> Identify three objects by name (one point for each, total score 3) |
| 4. Recall | <ul style="list-style-type: none"> Tell three objects presented previously (one point for each, total score 3) |
| 5. Language | |
| Name body parts | Points to five body parts (one point for each, total score 5) |
| Command (three steps) | Unwrap the toffee, give the wrapper to the doctor and then eat it (one point for each, total score 3) |
| Repeat sentence | Cat drinks milk (total score 1) |
| Reading | Reads his/her name (total score 1) |
| Writing | Writes own name (total score 1) |
| Copy a design | For example, circle (total score 1) |

- Scores 2 SD below normal for various ages may be used to pick up early encephalopathy. Scores at 2 SD for various age groups: 3–5 years, 24; 6–8 years, 28; 9–11 years, 30; 12–14 years, 35.²
- A score less than 10 on day 4 after therapy has a specificity of 100% and sensitivity of 68% in predicting poor outcome in children with encephalopathy.²

symptoms include visual field defect, scintillating scotoma, numbness, paraesthesia, aphasia and lethargy.⁵ Typically motor weakness starts in the hand and spreads up the arm to the face. Auras are usually prolonged, with nearly 50% lasting more than 1 hour and in nearly 5% of patients last even more than 24 hours.⁶

Headache typically occurs during the aura phase but may even occur before the aura. It may be mild or severe, unilateral or bilateral. The symptoms can last for hours to days, or rarely weeks, but most resolve completely.

Severe attack with confusion—in addition to the typical attacks, some patients have more severe episodes manifesting with confusion, agitation, drowsiness and even seizures and coma.⁷ In majority these aura symptoms including hemiplegia and confusion last for days or even months before resolving completely.⁶

The acute presentation with confusion can be a diagnostic challenge, especially if it is the first severe attack. Thorough history and clinical examination along with family history is required. Relevant investigations including neuroimaging would be required to rule out the differentials. The diagnosis of hemiplegic migraine remains clinical and should meet the diagnostic criteria.⁸

The differential diagnosis should include cerebrovascular disease (eg, transient ischaemic attack and ischaemic or haemorrhagic stroke), seizure with post-ictal paralysis, and brain tumour.

Case 3

A 15-year-old girl presented with a 24-hour history of acute confusion and hallucination to emergency department. There was no history of infection or

trauma. Her GCS was 12. She was not feverish and neurological examination was normal. Her blood glucose and infection screen were normal. ‘Blood toxicology’ was normal. Her metabolic investigations and MRI brain were normal. On review by neurologist, she was confused, agitated but surprisingly drowsy and sleepy in between. She gradually made recovery without any treatment.

Urine toxicology revealed that she had raised levels of tetrahydrocannabinol. She then disclosed that she had taken cannabis with her friends at a party.

Learning points

Intoxication can be either exotoxins (overdose) or endotoxins (metabolic disorders). For exotoxins, the history will hopefully give some clues but urine and blood for toxicology should be obtained as soon as possible in any child with confusion. Blood should also be taken for paracetamol and salicylate levels, and a heavy metal screen where poisoning could be a possibility. Drug levels of anticonvulsants in known epileptic children should be done in situations of acute deterioration in conscious level as toxicity may be the cause.

Endotoxins are a broad category and children with suspected metabolic disease are at risk of being overinvestigated while missing the one crucial investigation necessary for diagnosis. Blood, urine and cerebrospinal fluid (CSF) are important in many cases and ammonia, lactate, venous blood gas, plasma amino acids, urine organic and amino acids and sometimes CSF lactate, glucose and amino acids should be done acutely. Early discussion with a metabolic specialist or neurologist is advised. Endocrine causes should also

be addressed in this category and blood glucose, blood gas and urine dipstick will identify diabetic ketoacidosis, and blood and urine electrolytes will point to adrenal insufficiency.

Case 4

An 11-year-old previously well boy presented with a 48-hour history of fever and confusion to emergency department. He had a viral prodrome 5 days prior to presentation. His general physician prescribed him oral antibiotics 24 hours before his presentation to hospital. His parents and teachers reported a 72-hour history of change of personality with episodic agitation and altered sleep pattern. On examination his GCS was 12, he was feverish (37.9°C) and had intermittent extreme agitation. His neurology examination was normal. His blood glucose, toxicology screen and metabolic investigations were normal. His urgent CT brain was normal. He was started on intravenous antibiotics and intravenous aciclovir on admission. Twenty-four hours later he had a left focal seizure. His EEG showed periodic lateralised epileptiform discharges suggestive of viral encephalitis. His blood and CSF investigations confirmed that he had herpes simplex virus positive on PCR and cultures. His MRI brain 3 days later showed changes in frontal lobe and temporal lobe on right side suggestive of viral encephalitis. He was treated with 2 weeks of high-dose intravenous aciclovir.

On discharge he made a full physical recovery but continues to have problems with behaviour with agitated depression needing treatment with fluoxetine and risperidone at 12 months follow-up.

Learning points

Infections are a common presentation of ACS. Early assessment and treatment with prophylactic antibiotics/antivirals are especially important until an alternative explanation is found for presentation of ACS to prevent morbidity and in rare cases mortality.⁹

OTHER COMMON AETIOLOGIES

Various aetiologies that can be associated with ACS in childhood are presented in [table 1](#). Review of all the causes is beyond the scope of this article. We have elaborated on some of the causes that can pose a greater diagnostic challenge.

Other migraine subtypes associated with confusion

*Acute confusional migraine (ACM):*¹⁰ ACM, a rare migraine variant, is a diagnosis of exclusion. The confusional state is hypothesised to be complex aura phenomenon secondary to cortical wave spreading leading to transient hypoperfusion and dysfunction in those brain areas. Manifestation can be as speech difficulties, agitation, hyperalertness and also amnesia. More sinister causes of acute confusion (see [table 1](#)) needs to be excluded first. Detailed history, clinical

examination, neuroimaging and EEG are often required.

Migraine with brainstem aura (MBA): Previously called basilar-type migraine is a rare subtype of migraine with aura presenting with brainstem symptoms and signs without weakness.¹¹ Diagnosis should be suspected when presenting with episodic attacks of vertigo, dysarthria, visual symptoms, ataxia and confusion particularly when associated with more typical features of migraine. MBA remains a diagnostic challenge and requires fulfilment of diagnostic criteria.⁸

Detailed personal and family history and clinical examination is required and neuroimaging (MRI with MR angiogram) is strongly advised during the first presentation to rule out posterior fossa structural or vascular abnormalities.

Epilepsy

Postictal state: Confusion is well recognised following the convulsive epileptic seizure. It can pose diagnostic difficulties if the patient is not known to have epilepsy and especially if the seizure was not witnessed. Confusion is usually short lasting for 30–45 min with gradual complete recovery. In the case of diagnostic uncertainties, relevant investigations to rule out other causes are often required. EEG may show features of postictal slowing or interictal epileptiform discharges, which may be of supporting value.

*Focal seizures with impairment of consciousness or awareness (previously referred to as complex partial seizures):*¹² Confusion and memory impairment are features of ictal phenomenon and may well be the only manifestations of the epileptic seizure. Epileptogenic focus is most commonly in the temporal lobe but can be in frontal lobe, parietal or occipital lobes. Typical attack from temporal lobe origin lasts for 2–3 min and manifests as impairment of consciousness, psychomotor arrest, vacant staring and automatism. Postictal confusion is often prolonged (minutes), which distinguishes it from absence seizures. EEG is often helpful for diagnostic confirmation and neuroimaging is required to look for any structural causes.

*Absence status:*¹³ This is defined as a prolonged generalised absence seizure usually lasting for at least 30 min but can go on for hours and even last for days. This is a type of NCSE. Main feature is the impairment of consciousness in a patient who is alert but only partially responsive. It is rare before 10 years of age and majority of the patients suffer from idiopathic generalised epilepsy, although it may be the only seizure type. Diagnosis is established by ictal EEG recording of 3 Hz/sec spike and wave discharges.

Infection/parainfection

Inflammatory markers would be expected to be raised in meningitis, encephalitis and cerebral abscesses, though not invariably.⁹ One should not be reassured

by unremarkable values when there is good clinical suspicion of central nervous system infection. Blood cultures and viral serology (including mycoplasma and Borrelia) are useful as is blood PCR for suspected viruses. Viral throat swab, urine and stool samples can also help identify a precipitant. In demyelinating conditions, it would also be important to send blood

oligoclonal bands (paired with CSF). Aquaporin-4 antibodies are becoming increasingly used but are not as sensitive for neuromyelitis optica as in adults. Lumbar puncture is the gold standard for diagnosis and should be performed as soon as is safe. Microscopy, culture and sensitivity, protein and glucose should be sent in addition to viral samples.

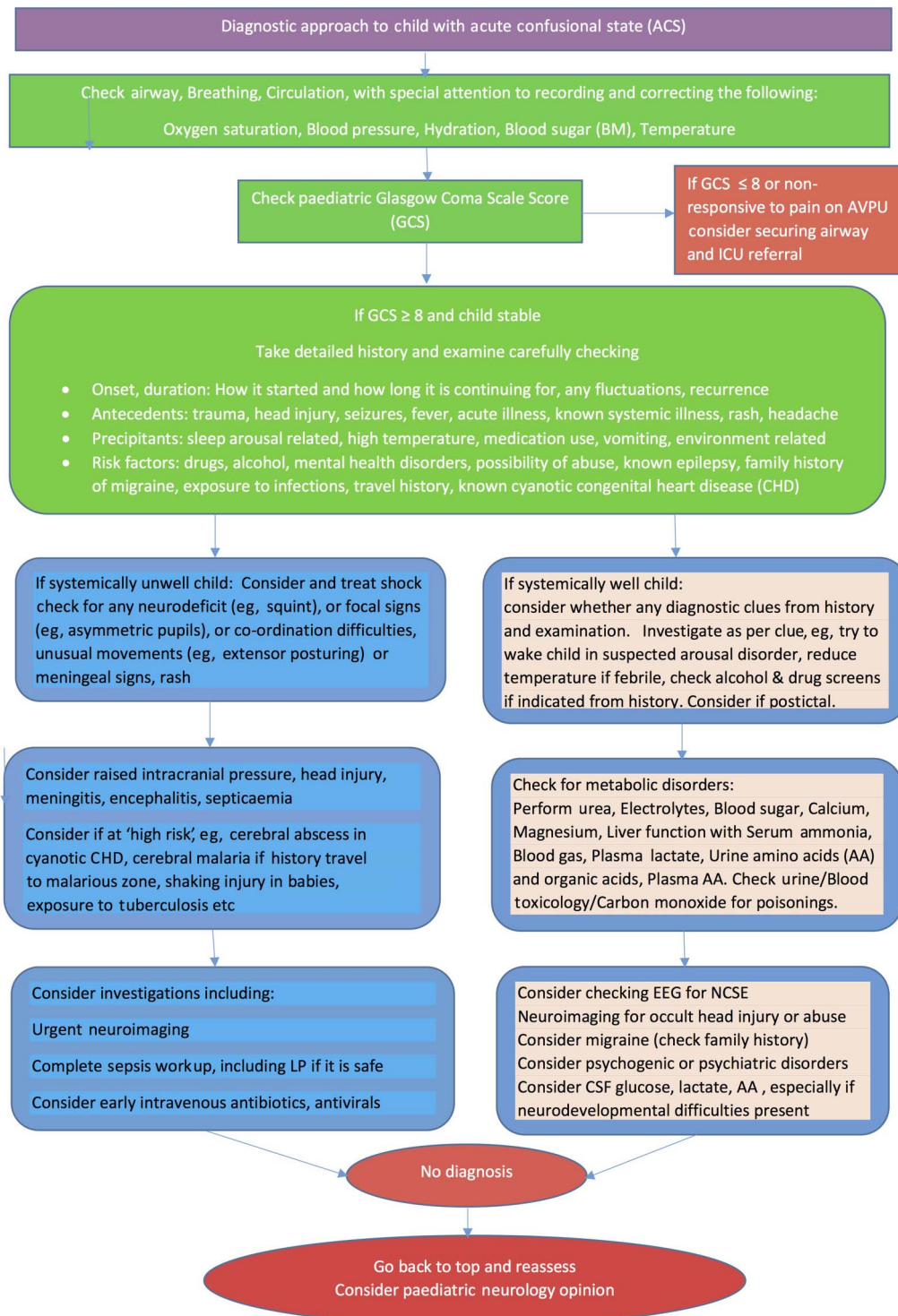


Figure 1 Algorithm for diagnostic approach in child with acute confusion state. AVPU, alert voice pain unresponsive; CSF, cerebrospinal fluid; ICU, intensive care unit; LP, lumbar puncture; NCSE, non-convulsive status epilepticus.

The list of viruses causing encephalitis/acute disseminated encephalomyelitis is long and pointers in the history, and results from throat/stool/urine will allow targeted testing of the CSF.

ACS in teenagers

This is a commonly encountered presentation in paediatric practice. Every attempt should be made to get detailed history from the patient and the family and friends. Drug/alcohol intoxication is particularly common in this age group and therefore should be sought even when the history is not forthcoming, as highlighted in case 3. ACM may also present for the first time in teenage years posing diagnostic dilemma. As mentioned before, this is a diagnosis of exclusion and other causes should first be ruled out. Autoimmune encephalitis, especially anti-N-methyl-d-aspartate (NMDA) receptor antibody encephalitis, can also pose diagnostic challenge. Investigation should include autoimmune screening (anti-NMDA receptor antibody, anti-voltage-gated potassium channel antibody, anti-glutamic-acid-decarboxylase antibody) along with all the investigations mentioned in the section Infection/parainfectious causes.

Once the organic disorders are ruled out with confidence, one should think about 'medically unexplained (psychogenic) confusion' as the likely diagnosis, as this is very common in this age group. History of abuse and bullying, mental health problems, adverse life events, difficulties with peer and social relationships, and insecure or sensitive personality are often reported and may provide the clue towards the diagnosis. Early diagnosis and prompt involvement of child and adolescent mental health services is paramount.

Diagnosis and management: Please refer to [figure 1](#), which presents the algorithm for diagnostic approach to a child with ACS. Initial management is as directed in the algorithm. Subsequent management is dictated by the diagnosis made. Regular close monitoring including vital signs, Paediatric GCS and neuro-observations is essential till the diagnosis is reached, as some of the underlying causes can be life threatening. Refer to the Royal College of Paediatrics and Child Health-produced guideline 'The Management of children and young people with an acute decrease in conscious level' (2015 update)¹⁴ and National Institute for Health and Care Excellence guidance on 'Meningitis (bacterial) and meningococcal septicaemia in under 16s: recognition, diagnosis and management'¹⁵ for more detailed advice on assessment and management.

CONCLUSION

ACS is not an uncommon presentation in children and should be considered a medical emergency. A detailed history, systemic and neurological examination

and routine laboratory tests may help in diagnosing majority of the cases in children. For those posing diagnostic dilemma, less frequent causes should be considered and further investigations should be undertaken urgently to avoid diagnostic delays.

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