The treatment and management of alternating hemiplegia of childhood

Review

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Alternating hemiplegia of childhood has many factors that make it difficult to manage. These include its rarity of about one case per million, the variability of the manifestations, with seven characteristic features, and the potential for disabilities and acute, often severe, episodes in a disease that is of uncertain cause and for which treatment evidence is sparse. An integrated multidisciplinary team and emergency availability are key medical requirements, as well as an educational setting that understands the variations in performance that occur. The mainstays of treatment have been flunarizine, antiepilepsy drugs for the 50% of patients with epilepsy, attempts to avoid trigger situations, and the rapid encouragement of sleep when attacks begin. The diagnostic and management predicament of child, parent, and paediatrician in complex rare disorders are well illustrated by this condition.

The incidence of alternating hemiplegia of childhood (AHC) is about one in one million. This level of rarity creates problems. It is quite usual for the diagnosis to be delayed and, therefore, the local team at primary and secondary levels may well have misdiagnosed the condition. Once a firm diagnosis has been made it is very important that misunderstandings are settled and that the child and family have full access to local services, both for long-term surveillance and for acute problems.

Very often, parents find that they know more about this condition than the doctor they are seeing. This is inevitable and requires understanding and honesty from both parties. Certainly, even if the doctor has experience of AHC, the parents will know much more about their child. The doctor will often need to take advice but would have a broad knowledge of childcare, disability, and parental concerns, if given the opportunity to contribute. 'Overprotection' is, generally, an overused term but some parents of children with AHC are accused of this. It arises particularly because of parental attempts to prevent episodes. The condition is also not well named because bilateral attacks are common, and if hemiplegic attacks predominate they rarely alternate.

The diagnosis

The diagnostic process is a significant issue in the early management of AHC.[1] The seven accepted criteria are: (1) onset before 18 months of age; (2) repeated episodes of hemiplegia involving the right or left side of the body, at least in some episodes; (3) episodes of bilateral hemiplegia or quadriplegia, starting either as generalization of a hemiplegic episode or bilaterally; (4) other paroxysmal disturbances including tonic/dystonic attacks, nystagmus, strabismus, dyspnoea, and other autonomic phenomena occurring during hemiplegic attacks or in isolation; (5) immediate disappearance of all symptoms on going to sleep, with recurrence 10 to 20 minutes after awakening in long-lasting attacks; (6) evidence

of developmental delay, learning disability*, neurological abnormalities, choreoathetosis, dystonia, or ataxia; and (7) not attributable to another disorder. It is reasonable to categorize cases as typical, probable, and those that do not satisfy the criteria.

We suggest that typical cases should satisfy criteria 1, 2, 3, and 7. Criterion 7 can cause difficulty, and if the phenotype is typical but there is an abnormal finding (not just atrophy) shown by magnetic resonance imaging, we would still make the diagnosis of AHC.

For criterion 4, the eye movements seen early are highly characteristic, but in assessing an older child they may not have been noted or remembered. Other paroxysmal events are very common and supportive of this diagnosis.

Criterion 5 is very characteristic. In children who have somewhat equivocal attacks but have this sleep-related phenomenon, we would be suspicious that they had a condition closely related to AHC and call the diagnosis *probable* AHC.

Criterion 6, additional cognitive and motor impairments is, in our experience, universal in older children but may not be clear in those who are young; however, this could, be regarded as an obligatory component.

Epilepsy coexists in about 50% of patients and we suggest that epilepsy should be recorded as present or absent as part of the initial and subsequent diagnostic statements.

Disabling

Children with AHC are prone to several long-term disorders, which require management. They include selective and global cognitive impairments. A wide range of behavioural and psychiatric disorders are seen including impulsivity, lack of attention control, problems with communication, obsessionality, and short-temperedness.

Motor problems include weakness, spasticity, dystonia, and poor motor organizational skills (dyspraxia).

Very significant problems with speech, feeding, and airway protection occur commonly, both fixed and as part of an episode. Half of the children with AHC have epilepsy which is quite separate from the characteristic attacks. A major feature of the condition is variation within the day and over longer periods. A multidisciplinary and multi-agency service, which includes paediatric neurology, is required to meet these multiple needs.

Episodes with deterioration

The irregularly timed but often frequent occurrence of hemiplegia and four-limb episodes with bulbar (speech, feeding, and swallowing) problems in a child who already has fixed impairments is a major burden of AHC, both in terms of coping with the physical and emotional effects and with concerns about the long-term impact on function.

Whether a child with an episode of AHC should be admitted to hospital will depend on the severity of the attack and on the plan that the family and medical advisors have agreed. However, a facility for rapid admission to the paediatric ward when the family or carers feel it appropriate is necessary. Specific issues that may require admission include: difficulty with maintaining hydration and feeding, breathing difficulties, concern about a chest infection, and epileptic seizures. Usually such indications have happened before in the individual child and a plan for in-patient management exists. If a problem occurs out of range of the unit that knows the child, the family need to have with them a file of information listing the problems, the normal management of episodes, and a contact number. For the most part, management of episodes at home or school is carried out with a previously agreed treatment schedule. After severe episodes there is sometimes a permanent loss of function and this is a cause of major concern to many families. AHC is probably not intrinsically a progressive disease but it can show stepwise deterioration with severe episodes. Early in the course of the illness characteristic episodes of AHC are often misdiagnosed as epileptic seizures. Family members mostly become familiar with the two different types of attack, but differentiation can be difficult on occasions and an urgent electroencephalogram (EEG) may be required. However, investigations into episodes are otherwise usually unhelpful, except to look for complications (e.g. chest X-rays for chest infections).

Less commonly, the child may need intensive care for breathing problems, inhalation, and chest infection, usually with whole-body attacks and severe seizures, which are the main life-threatening problems of AHC.

Despite the characteristic nature of the episodes there is considerable individual variation; the family will be familiar with the specific episodes that occur in their child and these should be described in the file or logbook that the family keeps.

Of uncertain cause

The lack of a definite cause for the condition has an effect on management; mostly, it creates some insecurity. There is no diagnostic test for AHC and it remains a clinical diagnosis requiring the child to fulfil certain diagnostic criteria. Early hypotonia and floppiness and abnormal eye movements precede the onset of hemiplegia, usually by several months. The early symptoms commonly resolve over time, and frequent attacks of hemiplegia emerge as the predominant manifestation in the first decade. Later they tend to be milder but never resolve spontaneously, with cognitive delay becoming more evident. There are many theories on the cause of the disorder but without anything definite being agreed upon. The child can undergo many biochemical, metabolic, neuroimaging, and angiographic studies to rule out other conditions with similar clinical features. These tests have usually been found to yield essentially normal results in children with AHC, although a lot more work needs to be done. The lack of a clear diagnosis, and having to wait to be seen by a specialist in the field, can be an ordeal for parents and carers. To add to the confusion, the complexity and fluctuation of the symptoms, as well as the lack of awareness, can result in a delay of several years before the correct diagnosis is made. Although a genetically-determined channelopathy is the most likely cause, this is as yet unproven but forms the basis of the advice given in genetic counselling, which is that there is a very low recurrent risk in AHC, no extra risk for the offspring of siblings, but a presumed 50% risk for any adult with AHC planning to have children. Management of severe episodes is largely of the secondary complications. Understandably, non-traditional treatments are used and may need medical discussion. Communication with education authorities and school has to take place with all of the above uncertainties included.

*North American usage: mental retardation.

Variability

The variation in function between times with and without attacks needs to be understood. A child may have a reasonable outdoor walk for part of the time but need for a chair or buggy may arise during the remainder of the trip. Thus, the requirements for mobility have to be assessed on the basis of a severe episode.

Feeding varies in attacks, and in whole-body episodes it is usually difficult. The first 15 to 20 minutes after waking, when the motor problems are minimal, is the opportunity that the family take to get food and particularly liquids into the child. An assessment of speech, feeding, or swallowing needs to take place at the appropriate time to answer relevant questions. For example, if a child is spending more than half of their life with feeding difficulty and we need to know whether it is safe to continue oral feeding, a cine swallow might need to be performed during an attack. Therefore, flexibility in the timing for such appointments is required. Any assessment of requirements for health or welfare benefits should be made on the basis of how a child is during an attack because the family have to plan every day for these to occur.

Treatment

Medical treatment can be divided into the following categories: (1) episode prophylaxis by avoiding triggers and long-term drug treatment; (2) the acute management of attacks; (3) epilepsy management; and (4) the use of sleep as a management tactic. Several studies have reported triggering events in about half of the children with AHC; these include exposure to cold, emotional stress, fatigue, bathing, hyperthermia/hypothermia, and upper respiratory infection. These factors may be patient-specific but problems may arise if the attempt to avoid stress or cooling severely limits the quality of the child's life. This has to be explored in detail by the medical team, school, and family so that the position can be agreed. This issue is the one over which concerns about 'overprotection' are raised.

The acute management of episodes is problematic. Any triggering situation should be removed, if possible, and the child managed in as quiet and relaxed a setting as possible. Very often there is an early phase or warning of tiredness, yawning, and appearing exhausted. Because of the uniform relief of symptoms by sleep we, and many parents, advocate the early induction of sleep. This may be by oral or rectal sedation but more recently two other methods have been used.

Buccal midazolam is rapidly absorbed and has been developed for seizure rescue, but it is also a sedative and might be expected to take effect within a few minutes. However, it is not licensed for any use currently. Melatonin, the sleep-inducing hormone, taken orally may take 20 minutes or so to have an effect and the dose may be increased in subsequent attacks if it is not effective. Again, it is not licensed for this use but is widely used on an individual patient basis, and because it is not sedating it can be used with a sedative. If the child cannot swallow at this stage, the value of buccal midazolam is clear, or rectal diazepam may be used. This is such an important measure but because it is being used in a rare disorder it is usually helpful to bring the child and parent into hospital to try out and refine the management strategy and reassure everyone that it is safe. Benzodiazepines can temporarily make swallowing worse, and such an adverse reaction should be anticipated. We suggest trying to involve the school in using a similar tactic early in the episodes. There is no definite evidence of the efficacy of early sleep induction on outcome, but shortening and minimizing the attacks has to be worthwhile and can at least be tried. There is no published evidence to suggest that giving oxygen during attacks has any value but, to our knowledge, this has not been studied.

Some children complain of pain or seem to be in pain in attacks and some parents use paracetamol or ibuprofen with relief of distress. Again, there is no study on this treatment of which we are aware, but this seems a reasonable line of management in such circumstances.

Epilepsy

Half the children with AHC have epilepsy, and these seizures are usually quite distinct from AHC attacks in their manifestations, although they may occur simultaneously. If an EEG is recorded during the seizure it usually shows an appropriate abnormality, but between seizures the EEG is normal. Seizures may be prolonged in two forms: either minor motor jerking in one part of the body (epilepsia partialis continua) or a more generalized convulsive status epilepticus. Such an occurrence requires urgent medical attention, usually by calling an ambulance and giving agreed rescue medication. There is no agreed specific drug for seizure prevention in AHC, and indeed, the epilepsy is often resistant to treatment. It is usual to give antiepilepsy drugs (AEDs) if the child has epilepsy, but one should monitor their effect and not continue in the face of side effects and poor efficacy.

Prophylaxis for episode of AHC

There is general agreement that AEDs have no effect on the episodes of AHC. A wide range of drugs have been tried, particularly antimigraine treatments including propranalol, methysergide, pyzotyline, amantidine/memantidine, and nimodipine, but these have not been adopted in regular use. We have reviewed the reports of drug prophylaxis.[2–18] However, flunarizine, a drug with blocking effects on calcium channels, has been used widely despite it being agreed that it rarely stops attacks. In a review of 20 reports of 230 patients treated with flunarizine, more than 50% of the patients reported reduced duration and severity of attacks and 25% reported a reduced frequency. These are not, however, randomized studies and are subject to reporting bias and of not taking note of natural fluctuation of all aspects of the attacks. Nevertheless, flunarizine in doses of 5 to 20mg daily remains the mainstay of treatment.

Motor management

Motor impairments commonly persist between attacks and need assessment and management. These problems include: (1) mobility seen in a broad context; (2) dyspraxia requiring occupational therapy and remedial educational input; (3) dystonia that requires management and may benefit from medical treatment; (4) chorea; (5) tremor and ataxia; (6) weakness and hypotonia; and (7) spasticity.

It is unusual for radical (e.g. surgical) treatments to be used in this condition because of uncertainty about the effect in relation to acute episodes.

Nutrition

Most children with AHC are small and underweight. This is almost certainly because of lack of sufficient calorie intake

during bilateral episodes. It is helpful for a dietician to review the intake and the tactics for dealing with bulbar palsy, to make recommendations, and then to review them periodically. Where a fixed feeding difficulty exists, seating, food consistency, and method of feeding should be reviewed as discussed above, with an understanding of the variability of these functions. If the situation cannot be adequately managed, a gastrostomy should be considered.

Medical requirements of AHC

It seems appropriate for doctors to acknowledge the limitations of their understanding of this condition, but they must sustain their professional role for intercurrent illness and review of the child and family functioning. Families need good individual documentation to take with them, and they require agreed guidelines for managing events. Such issues as having sleeping facilities available at school are important. The need for admission and expert consultation is clear, but the best outcome is if the family can develop trust in the local team's ability to cope with attacks.

The children need to be seen in a multidisciplinary setting. Medically, it seems that AHC is best placed for specialist opinion and advice within a comprehensive epilepsy programme. This is because 50% of affected children have epilepsy, which is often intractable to treatment. This assumes that the epilepsy service is multidisciplinary with integrated behavioural and educational input. However, this specialist unit should not supercede the local community-based service, if it is present in the country and region concerned: the theme should be 'shared care' between specialist centre and community-based services.

Transition to adult services can be problematic and there is need both for centres of special expertize and a community-based service as attacks continue into adult life.

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