

Abdominal Migraine

Abstract

Abdominal migraine, previously referred to as a migraine equivalent is currently classified as one of the episodic syndromes that may be associated with migraine and is mainly characterized by recurrent attacks of abdominal pain, nausea and vomiting. Abdominal migraine, primarily a pediatric disorder, is often under diagnosed and misunderstood as it can mimic several other systemic and often potentially dangerous clinical entities. The aim of this review article is to provide the latest diagnostic criteria based on clinical features and the various management options available for abdominal migraine. It also stresses the importance of an early and a correct diagnosis of this treatable condition.

Keywords: Abdominal migraine; Abdominal pain; Childhood episodic syndrome; Migraine

Review Article

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Abbreviations: AM: Abdominal Migraine; ICHD: International Classification of Headache Disorders; IHS: International Headache Society

Introduction

AM, a term used by Brams close to a century ago to describe periodic attacks of 'epigastralgia' with symptom-free intervals between the episodes still remains an under-diagnosed cause of recurrent abdominal pain in the pediatric population [1].

However, in recent times, more precise criteria have been proposed to aid in the diagnosis of AM. ICHD-2 first published by the IHS in 2003 and then revised recently in 2013 as ICHD-3, identified AM as one of the "childhood periodic syndromes that are commonly precursors of migraine". Also, Rome III Diagnostic Criteria for Functional Gastrointestinal Disorders in 2006 separately proposed identifying markers for AM which succeeded the 1999 Rome II Gastroenterology Criteria.

At least 4-15 % of children visiting a pediatric gastrointestinal clinic for chronic, recurrent, idiopathic abdominal pain met diagnostic criteria for AM [2]. Rome III criteria for AM classified a greater percentage of children as meeting the diagnostic criteria for AM when compared to the use of Rome II criteria (23.1 % vs 5.7%) [3]. A UK study, however, demonstrated a slightly lower prevalence at 2.4 % [4].

The exact pathophysiology of AM, which is beyond the scope of this review, is not clearly understood but there is believed to be a great overlap between AM and migraine as there is between the various functional gastrointestinal disorders such as cyclic vomiting and irritable bowel syndrome. A recent study from Sri Lanka evaluated gastric emptying and antral motility parameters in children with AM and suggested a possible role of abnormal gastric motility in its pathogenesis [5].

Discussion

Clinical features and diagnostic criteria

ICHD-3 identifies AM as one of the "episodic syndromes that may be associated with migraine" [6].

ICHD-3 further describes AM as "an idiopathic disorder mainly seen in children as recurrent attacks of moderate to severe midline abdominal pain, associated with vasomotor symptoms, nausea and vomiting, lasting 2-72 hours and with normality between episodes. Headache does not occur during these episodes".

ICHD-3 proposes the following diagnostic criteria for AM:

- A. At least five attacks of abdominal pain, fulfilling criteria B-D
- B. Pain has at least two of the following three characteristics:
 - a. midline location, periumbilical or poorly localized
 - b. dull or 'just sore' quality
 - c. moderate or severe intensity
- C. During attacks, at least two of the following:
 - a) anorexia
 - b) nausea
 - c) vomiting
 - d) pallor
- D. Attacks last 2-72 hours when untreated or unsuccessfully treated
- E. Complete freedom from symptoms between attacks
- F. Not attributed to another disorder. In particular, history and physical examination do not show signs of gastrointestinal

or renal disease, or such disease has been ruled out by appropriate investigations.

As per Rome III Diagnostic Criteria for Functional Gastrointestinal Disorders, AM must include all of the following:

- 1) Paroxysmal episodes of intense, acute periumbilical pain that lasts for 1 hour or more
- 2) Intervening periods of usual health lasting weeks to months
- 3) The pain interferes with normal activities
- 4) The pain is associated with 2 of the following:
 - i. Anorexia
 - ii. Nausea
 - iii. Vomiting
 - iv. Headache
 - v. Photophobia
 - vi. Pallor
- 5) No evidence of an inflammatory, anatomic, metabolic, or neoplastic process considered that explains the subject's symptoms.

Abdominal pain can vary in character and location. 'Colicky' and diffuse pain is reported in 22 % and 16 % of patients respectively [7]. Behavior, mood changes or other nonspecific prodromal symptoms can precede the pain in about 14 % patients. In children, differentiating anorexia from nausea may be difficult. Pallor may be accompanied by dark shadows under the eyes. Flushing may be the predominant vasomotor symptom in a subset of patients [8].

Typical age of presentation ranges from 3-10 years with a peak prevalence at 5-7 years of age. Boys and girls are mostly equally affected; but, a female preponderance has been reported by many authors [4]. A strong family history is noted. 90 % of patients have a history of migraines in a first-degree relative, especially their mothers [4]. Also, a history of motion sickness is commonly found amongst either the patients with AM or their family members [4].

Children with AM are believed to develop migraine headaches either concurrently or later in life; but AM itself rarely persists into adulthood [4]. Hence, essentially, AM is a disorder of childhood and therefore it is of interest not only to pediatric neurologists but even the general pediatricians in the community should be aware of it.

Management

Differential diagnosis and investigations

AM, just like migraine, remains a clinical diagnosis. Hence, eliciting a good clinical history and performing a thorough physical examination are crucial. General physical examination including a neurological examination during the symptom-free interval is usually entirely unremarkable.

Children with AM will usually first present either to the general pediatrician or a gastroenterologist for evaluation

before they see a pediatric neurologist which sometimes leads to a diagnostic delay. During the initial evaluation of a child with recurrent episodes of abdominal pain, it is extremely important that the health care provider does not miss a potentially grave underlying *gastrointestinal* (pancreatitis, intermittent small bowel obstruction, chronic idiopathic intestinal pseudo-obstruction), *renal* (obstructive uropathy), *neurologic* (brain tumor with raised intracranial pressure, brainstem tumor, subdural hematoma, familial dysautonomia), *endocrine* (adrenal insufficiency) or *metabolic* disease (ornithine transcarbamylase deficiency, methylmalonic acidemia, acute intermittent porphyria) which can mimic symptoms of AM [8].

Laboratory, radiological and procedural investigations, if any, should be performed to rule out a serious clinical condition at the earliest. Identifying certain "red-flags" which indicate the presence of an organic disease can be crucial in directing relevant investigations to avoid diagnostic delay. These "red-flags" are summarized in Table 1 [9,10]. Table 2 provides a list of investigations that could be considered in a child presenting with clinical features suggestive of AM [11]. The list is exhaustive but by no means complete and each case merits its own set of investigations, if any.

Interestingly, for the pediatric neurologists, electroencephalography findings have been reported in patients with AM. Benign focal or rolandic spikes have been reported and this may mislead some into believing that the clinical presentation is consistent with an epileptiform phenomenon [12]. Similarly, in children with clinically diagnosed AM when compared to normal controls, a study found significant differences in the fast wave activity in the visual evoked response to a red and white flash [13].

Treatment

Very little is concluded regarding the treatment of children with AM. Not all children require treatment; especially, if the frequency and severity of the episodes does not affect the quality of life or school work. In these cases, in addition, to providing reassurance; risk-benefit ratio of different treatment options should be explained to the family and they should be totally involved in the decision-making process.

Broadly, management of AM is divided into non-pharmacological and pharmacological modalities and both are largely extrapolated from the treatment of migraine headaches in children.

Non-pharmacologic therapy

A basic understanding of the disease process and also the fact that AM rarely persists into adulthood should be given to the families. It is necessary to emphasize that a dangerous gastrointestinal, renal, metabolic, endocrine or neurologic disease process is absent in these children.

Theoretically, avoidance of triggers may help in a small group of patients; although, evidence is minimal for it. Russell et al. suggested avoidance of triggers viz., stress, travel, prolonged fasting states, dehydration, exposure to flickering or strobe lights, physical exertion or exercise, and, alterations in sleep patterns [14].

Table 1: Red flags in a child presenting with symptoms of AM.

Changes in Growth Curve or Delay in Puberty
Recurrent and Unexplained Fevers
Abdominal Pain Radiating to the Back
Bilious or Bloody Emesis
Visible or Occult Blood in Stool
Chronic Diarrhea
Oral Ulcers
Dysphagia
Unexplained Rashes
Nocturnal Symptoms
Pallor or Anemia
Warm, Tender, Swollen Joints
Organomegaly
Localized Abdominal Tenderness, Away from the Umbilicus
Dysuria
Family History of Inflammatory Bowel Disease

Table 2: Initial diagnostic studies that can be considered in a child presenting with symptoms of AM.

Blood Studies
Hemoglobin, White Blood Cell Count and Differential
C-Reactive Protein
Erythrocyte Sedimentation Rate
Electrolytes, Urea, Creatinine and Glucose
Liver Function Tests
Amylase and Lipase
Celiac Antibodies
Urine and Stool Studies
Pregnancy Test
Urinalysis with Microscopy and Culture
Stool Occult Blood and Microscopy
Stool Test for <i>Helicobacter Pylori</i> Antigen
Radiological Studies
Ultrasound of the Abdomen and Pelvis
Contrast Study of Upper Gastrointestinal Tract and Small Bowel
Magnetic Resonance Imaging of the Brain (Computed Tomography of Brain in Urgent and Resource-Limited Settings)
Endoscopic Studies
Esophagogastroduodenoscopy, Colonoscopy with Ileoscopy (To Exclude Crohn's Disease)

Dietary modifications with increased fiber, reduced lactose and avoidance of certain food items have been proposed by various authors; again evidence is scarce to support these dietary changes. Feldman et al reported a significant benefit when fiber was increased in the diet of 52 children with AM studied by them. They concluded that 50 % of the children in the fiber group had a 50 % reduction in the number of episodes with abdominal pain, compared to only 27% in the control group [15]. Barr and Liebman demonstrated that eliminating lactose in the diet of children with AM, a significant proportion of whom had an abnormal lactose tolerance test, provided a complete symptom resolution [16,17]. Russell et al. also proposed that avoidance of certain food items ('few-foods or 'oligo-antigenic' diet) known to trigger AM is helpful especially in children with frequent attacks (>2 per week) [14]. Most notable items included chocolates, citrus fruits, caffeine, cheese, and colorings.

Other non-pharmacologic options include psychotherapy in particular cognitive behavioral therapy. These therapies involve introducing the child to the concept of pain and help build various coping strategies. Sanders et al studied forty-three children with recurrent abdominal pain between the ages 7-14 years and randomized them to either the cognitive behavior therapy group or the standard pediatric care group without cognitive therapy. Clearly, the percentage of pain-free children as assessed by a diary and by families was higher in the cognitive behavior therapy group both at a 6 month and at a 12 month evaluation [18]. Hypnotherapy or guided imagery is another therapeutic distraction technique that has shown promising results in the treatment of children with chronic pain conditions such as migraine headaches and recurrent abdominal pain [19,20].

Pharmacologic therapy

This is usually considered in children who fail non-pharmacological measures or in those with frequent and disabling symptoms where drug therapy can be combined with the non-pharmacologic measures discussed above.

Abortive agents used for acute management in AM are similar to those used in migraine headaches and include acetaminophen or ibuprofen which is usually most effective when given early during the attack. Symptomatic treatment with anti-emetics is indicated in those with nausea or vomiting. Minimal evidence suggests a response to triptans and valproic acid [21,22]. In a cohort study of 10 adult patients with AM, triptans were used as abortive medications in 2 patients. While one patient was able to successfully use 10 mg of rizatriptan to abort infrequent mild episodes of abdominal pain and nausea; the other patient failed to respond to sumatriptan. The authors', however, concluded that a positive symptom response to a triptan could be helpful in the diagnosis of AM in adults and could be useful in differentiating AM from other periodic forms of abdominal pain [23].

The prophylactic agents found useful in AM, again, are those primarily used in migraine headaches in children - beta blockers (propranolol), serotonin antagonists (cyproheptadine, pizotifen) and calcium channel blockers (flunarizine). Their overall response rate is highly variable and ranges from 8-75 % as outlined below.

A study by Worawattanakul et al. concluded that propranolol or cyproheptadines are effective prophylactic agents in majority of AM patients [24]. The authors retrospectively reviewed records of 53 patients who underwent treatment for AM for six months or until migraine cycles had stopped. Among the children given propranolol (10-20 mg, 2-3 times daily), 75 % had an excellent response identified as complete cessation of symptoms, 8 % had a fair response which meant persistence of symptoms but which were milder and less frequent and 17 % had no response. In those treated with cyproheptadine (0.25-0.5 mg/kg/day), 33 % had an excellent response while 50 % had a fair response while the non-responders remained the same at 17 %. 46 % patients in the propranolol group took the medication for less than six months and 50 % in the cyproheptadine group took medication for less than 10 months while rest of the patients in both the groups continued the respective therapy for three years.

Propranolol is typically started at 10 mg divided in two or three daily doses. Propranolol is best avoided in children with asthma as it can cause bronchospasm. Cyproheptadine is used in doses of 2-8 mg divided in two doses; increased appetite, weight gain and sedation are the most common side-effects.

Symon and Russell in a double-blind crossover trial of fourteen children with AM using pizotifen or placebo demonstrated pizotifen to be clearly superior to placebo. Pizotifen with its antiserotonin, antihistamine and anticholinergic properties, widely used in Canada and Europe; was found to be an effective prophylactic drug in 70 % of the children with AM [25]. Some authors have reported continued benefit even after the drug is stopped [26].

Pizotifen is started at 0.5 mg/kg/day and titrated based on the clinical response up to 4-6 mg/day. Common side-effects are similar to cyproheptadine.

Flunarizine, a calcium-channel blocker was found to be a safe, once-daily option for AM prophylaxis in a study by Kothare [27]. Ten children with AM were treated with a mean dose of 7.5 mg/day and were followed up after a mean average of 13 (6-24) months. 61 % reported a reduction in frequency and 51 % a reduction in the duration of the attacks. Flunarizine, not available in the US, is typically given at a dose of 5 mg at bedtime. Common side effects include constipation, weight gain and hypotension.

Scarce literature is available to support use of topiramate, valproate, amitriptyline, nortriptyline, verapamil, nadolol, lynesternol (progestin not available in the US), flumedroxone (progesterone derivative not available in the US) in the preventive treatment of AM [22,23,28,29]. The response is believed to be due to similarities in the pathophysiology of migraine and AM.

Treatment of AM is briefly summarized in Table 3.

Conclusion

AM is a well-established, yet, often an under diagnosed condition. Complications from mistaking an underlying serious condition for AM and vice-versa can be devastating. An incorrect diagnosis involves subjecting the child to unnecessary and often expensive investigations. A delay in diagnosis can cause

significant impairment in the quality of life of both children and their parents, with school and work absenteeism respectively. Hence, early and correct diagnosis is the key. AM as a diagnosis should be on the radar in any child presenting with unexplained and recurrent abdominal pain especially in the setting of a strong family history of migraines. This disorder is of interest to both

pediatric neurologists as well as pediatric gastroenterologists but should also be well-known to general practitioners caring for children in the community; as, abdominal pain is an extremely common pediatric symptom. Treatment is possible with both non-pharmacological and readily available medication options.

Table 3: Current therapy options for AM.

Non-Pharmacologic
Avoidance of Triggers
Dietary Modifications
Non-Invasive Pain Management Techniques e.g Cognitive Behavior Therapy, Hypnotherapy Etc.
Pharmacologic
Abortive agents* - Simple Analgesics, Anti-Emetics
Preventive Agents** - Beta Blockers, Serotonin Antagonists, Calcium Channel Blockers

Limited data for *Triptans, Valproic Acid; **Topiramate, Valproic Acid

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