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Chronic abdominal pain in children: help in spotting the organic diagnosis

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CASE 1

Aisha, a 9-year-old Asian girl, was referred to the paediatric outpatient clinic by her general practitioner (GP) with a 4 month history of episodic central abdominal pain. Each episode would last a few hours, affecting her about three times per week, usually during the day, but also occasionally at night. This was associated with infrequent, non-bilious vomits but did not appear to be related to diet. She was missing some days of school because of her symptoms. She said she liked school, did not like missing days away from her friends and denied any bullying. Between episodes she was a well and active girl. She had no history of diarrhoea or constipation, was growing well, had no urinary symptoms and had not reached menarche.

She was born at term via normal vaginal delivery and had no neonatal problems. She had no significant past medical history, was not on any medications and was fully immunised. There was no history of foreign travel and no family history of bowel problems.

General physical examination was unremarkable. Abdominal examination revealed no distension, organomegaly, palpable masses or herniae and no tenderness on the day of her clinic visit. She was on the 75th centile for weight, which was consistent with previously documented weights.

Comment

Based on this history Aisha fulfils the criteria for a diagnosis of chronic abdominal pain (CAP), which is commonly defined as three or more episodes of abdominal pain over at least 3 months duration that is severe enough to affect daily activities in a child over 3 years of age. She has typical history and examination findings

of a patient with functional abdominal pain; the discomfort is localised around the peri-umbilical region, she is growing and developing normally, and there are no alarm symptoms or signs suggestive of underlying organic disease.

Alarm symptoms and signs associated with a higher prevalence of organic disease include:¹

- Involuntary weight loss/failure to thrive.
- Gastrointestinal bleeding.
- Chronic, severe diarrhoea or vomiting. Note—some vomiting can occur in functional abdominal pain.
- Persistent right upper quadrant or right lower quadrant (RLQ) abdominal pain.
- Unexplained fever.
- Family history of inflammatory bowel disease (IBD).
- Jaundice.
- Urinary symptoms, back or flank pain.
- Abnormal examination findings.

Note: There is no evidence that the frequency or severity of the pain, effects on lifestyle, or the presence of nausea, headache, joint pain, depression, anxiety, behavioural problems or recent negative life events can differentiate between functional and organic causes for CAP.¹

Constipation can present as CAP in children and should be excluded through a detailed history of bowel habits. Details on diagnosing, investigating and managing constipation in children can be found in the 2010 National Institute for Health and Clinical Excellence guidelines.

Aisha's parents were understandably worried that she may have a serious underlying pathology causing her pain. The paediatrician tried to reassure them that this was unlikely and said he would organise some investigations to try to rule out an organic cause for her pain. Urinalysis and blood tests including full blood count (FBC), urea and electrolytes (U&E), liver function tests (LFT),

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amylase, C-reactive protein and anti-tissue transglutaminase antibodies (coeliac screen) were taken in the clinic and a routine out-patient ultrasound scan was requested with a follow-up clinic appointment in 8 weeks time.

Comment

Although clinicians may be anxious not to miss a serious pathological cause there is no evidence that these investigations help distinguish between functional and organic abdominal pain in children in the absence of alarm symptoms or signs.

Dhroove *et al*² published a paper in 2010 on the cost-effectiveness of investigating children with CAP without alarm symptoms or signs. They concluded that investigations cost an average of US\$6104 (£3885) per patient with little yield. Of the 122 children in the study:

- Inflammatory markers (C-reactive protein/erythrocyte sedimentation rate) were raised in four children. On subsequent endoscopy three were normal and one confirmed *Helicobacter pylori*.
- FBC, U&E and LFTs did not change management in any patients.
- Pancreatic enzymes, stool studies, urinalysis all normal.
- Abdominal x-ray (AXR) was undertaken on 38.5% children—13% had retained stool, nothing else was identified. Note: one abdominal x-ray equates to a 0.12 mSv radiation dose (equivalent to 12 chest x-rays) with a potential cancer risk of 1/80 000.³ This poses a significant risk when considered in the context of 12 million children in the UK and an incidence of CAP of approximately 10%.

In the presence of jaundice, urinary symptoms, back or flank pain, significant vomiting or abnormal examination, ultrasound has been shown to detect an abnormality in 10% of those scanned.¹ However, in those with no alarm symptoms or signs, ultrasound identifies pathology in less than 1%.¹ The cost of investigations commonly undertaken in children with CAP are highlighted in table 1.

At 8 week follow-up Aisha was still having the same symptoms, which had now been persisting for 6 months. Her examination findings were again normal and she remained on the 75th centile for growth. All her investigation results were normal.

Having spent several weeks worrying about the results, Aisha's parents were extremely anxious by the time of her clinic appointment. They had undertaken research on the internet and had a number of possible diagnoses in mind. Her parents found it hard to accept there was no physical explanation for her pain and were keen for further investigations. The investigations she had already undergone had cost approximately £193.46 and had failed to reassure either Aisha or her parents.

Table 1 Approximate costs for commonly used investigations in children with chronic abdominal pain

Investigation	Cost (£)*
Full blood count	7.99
Urea & electrolytes	6.48
Liver function tests	8.10
Amylase	1.62
C-reactive protein	5.68
Glucose	1.62
Coeliac screening: Anti-Transglutaminase antibodies	18.20
Urinalysis	10.00
Stool microscopy, culture and sensitivity	20.51
Abdominal x-ray	69.55
Abdominal ultrasound	135.39
Upper Gastrointestinal Endoscopy±Biopsy	1714.97

*Costings are for elective investigations; non-electively they can be considerably more expensive.

Comment

The only investigation that is indicated for CAP in the absence of alarm symptoms and signs is a coeliac screen. This is because coeliac disease is relatively common and presents with non-specific abdominal symptoms. The 2012 European guidelines recommend that children should be screened using anti-transglutaminase type2 IgA (anti-TG2) and IgA.⁴ If the anti-TG2 is positive the child should be referred to a paediatric gastroenterologist for further investigation. If the anti-TG2 is negative and IgA levels normal the parents can be reassured the child does not have coeliac disease and no further investigations are required. In cases where the anti-TG2 is negative in association with IgA deficiency refer to the European guidelines for further investigation or a paediatric gastroenterologist.

The paediatrician spent a long time trying to reassure Aisha's parents that CAP is common in children and normally does not have an underlying organic pathology. He explained that further investigations were not indicated and could cause more harm than good. With reluctance they agreed to hold off further investigations at this stage, but were keen to have some treatment to try to improve her symptoms. They were particularly worried that her time off school was affecting her studies. They had tried paracetamol and ibuprofen, which had made little difference. On a presumptive diagnosis of abdominal migraine the paediatrician commenced Aisha on nasal sumatriptan.

Comment

Rome III Criteria have been produced to sub-categorise children with functional abdominal pain into five distinct groups based on symptoms: functional abdominal pain, functional abdominal pain syndrome, functional dyspepsia, irritable bowel syndrome and abdominal migraine.⁵ These are detailed in table 2.

Table 2 Rome III criteria for functional abdominal pain⁵

Diagnosis	Rome III criteria*
Functional abdominal pain	<ul style="list-style-type: none"> ■ Episodic or continuous abdominal pain ■ Insufficient criteria for other functional gastrointestinal disorders
Functional abdominal pain syndrome	<ul style="list-style-type: none"> ■ Functional abdominal pain for at least 25% of the time and one or more of the following: <ol style="list-style-type: none"> 1. Some loss of daily functioning 2. Additional somatic symptoms such as headache, limb pain, or difficulty sleeping
Functional dyspepsia	<ul style="list-style-type: none"> ■ Persistent or recurrent pain or discomfort centred in the upper abdomen ■ Not relieved by defecation or associated with a change in stool frequency or form
Irritable bowel syndrome	<ul style="list-style-type: none"> ■ Abdominal discomfort or pain associated with two or more of the following at least 25% of the time: <ol style="list-style-type: none"> 1. Improved with defecation 2. Onset associated with a change in frequency of stool 3. Onset associated with a change in form of stool
Abdominal migraine	<ul style="list-style-type: none"> ■ Paroxysmal episodes of intense, acute peri-umbilical pain that last for one or more hours. ■ Intervening periods of usual health lasting weeks to months ■ The pain interferes with normal activities ■ The pain is associated with two or more of the following: anorexia, nausea, vomiting, headache, photophobia, pallor

*There must be no evidence of an inflammatory, anatomical, metabolic or neoplastic process to explain symptoms. Criteria must be fulfilled at least once a week for at least 2 months before diagnosis, except abdominal migraine where criteria must be fulfilled two or more times in the preceding 12 months.

Aisha fulfils the Rome III criteria for a diagnosis of functional abdominal pain, but not specifically abdominal migraine at present because she has been symptomatic for less than a year.

Current evidence suggests that the optimal management for Aisha and children with all types of functional abdominal pain is as follows:^{1 2}

- Following a thorough history and examination, if no alarms symptoms or signs are present, a positive diagnosis of functional abdominal pain should be made.
- The primary treatment is reassurance and education on functional abdominal pain.
- It should be explained that functional abdominal pain is a common condition, affecting up to 10–14% of children in the UK, and that it has been extensively studied.
- Reassurance should be given that the pain is real; however, there is no evidence of dangerous underlying pathology. For illustration the analogy of a headache may be helpful where there is real pain that does not necessarily result from organic disease.
- Identify for the parents the criteria for which you have based the diagnosis of functional abdominal pain: the

periumbilical or epigastric nature of the pain, their continued normal growth and development (show a growth chart if available), their normal activity level and well-being between episodes, and the absence of any symptoms or signs suggestive of organic disease.

- It should be stressed that there is evidence that investigations are not useful in this condition and often result in more harm to the child than good—both psychologically and physically if more invasive procedures such as endoscopy are undertaken which inevitably come with risks. It should be explained that the only condition which needs to be excluded is coeliac disease, which is less common than functional abdominal pain, but can present with similar non-specific abdominal symptoms.
 - Offer follow-up to provide advice, support and re-assessment. Alternatively, if the parents are satisfactorily reassured and happy to manage independently, offer an open appointment. Reassure them that if alarm symptoms or signs were to arise in the future then appropriate investigations could be undertaken at that stage.
 - It should be recommended that the parents and their child focus on trying to return to normal functioning rather than a complete disappearance of pain. Attainable goals include: normal school attendance, involvement in extra-curricular activities enjoyed by the child, normal growth and normal sleep patterns. Advise liaising with staff at the child’s school to gain support in improving attendance and a graded exercise programme if physical activity is affected.
 - Highlight that sometimes the pain can be exacerbated by anxiety and stress, which can result in the physical symptom of abdominal pain, similar to how it can result in other physical changes such as sweating, changes in heart and respiratory rate, urinary frequency and urgency, constipation, diarrhoea and headaches. Encourage the parents to explore potential stressful contributing factors with their child.
 - Discuss the impact of any illness models within the family and address any specific concerns the parents and child may have for example, cancer, IBD.
 - If possible, have information leaflets on functional abdominal pain available in clinic. This not only provides further education for the parents and child, but also reinforces that it is a well known, clearly defined condition. A patient information document is available on www.uptodate.com entitled ‘CAP in Children and Adolescents’.
 - There is some evidence for the use of psychological and pharmacological interventions in the management of functional abdominal pain in children as highlighted in table 3.^{1 6–12}
- There is good evidence that hypnotherapy can significantly reduce pain intensity and frequency over standard medical therapy alone.¹¹ Similarly, other psychological therapies, particularly cognitive-behavioural therapy and relaxation therapies, have been shown to be effective.¹² Care should be taken when approaching the subject of psychotherapy with parents and

Table 3 Current evidence for the management of functional abdominal pain in children

Intervention	Evidence source	Outcome/conclusion
Psychological therapies	Meta-analysis 2011 ¹²	10 controlled studies were reviewed demonstrating psychological therapies are effective in treating children with chronic abdominal pain ($p < 0.01$)
	Cochrane systematic review 2009 ¹⁰	There is evidence that cognitive behavioural therapy (in person and online) and relaxation treatments, such as yoga and hypnosis, are effective at reducing CAP in children
	RCT of 53 children in 2007 ¹¹	At 1-year successful treatment was accomplished in 85% of the hypnotherapy group and 25% of the standard medical treatment group ($p < .001$)
Pharmacological treatment	Cochrane systematic review 2011 ⁸	There is no evidence that anti-depressants (amitriptyline trialled) are beneficial in the treatment of recurrent abdominal pain in children and there is a risk of adverse events, some potentially life-threatening
	Cochrane systematic review 2009 ⁶	There is weak evidence that pizotifen reduces the mean number of days in pain in those with abdominal migraine and famotidine with CAP associated with dyspepsia. There is no significant benefit to using peppermint oil capsules in CAP associated with IBS. The overall lack of evidence suggests there is little reason to prescribe drugs unless the pain is severe or used within a clinical trial
	APP & NASPGHAN* clinical guidelines for CAP in children 2005 ¹	There is weak evidence for the use of peppermint oil in CAP associated with IBS based on a RCT of 42 children showing an overall reduced pain score in the treatment group at 2-weeks. However, there was no significant difference in the frequency or duration of pain or impact on daily life
Dietary interventions	Meta-analysis 2011 ⁷	<i>Lactobacillus rhamnosus</i> GG moderately increases treatment success in children with recurrent abdominal pain, particularly those diagnosed with IBS. For IBS subgroup ($n=167$) NNT 4. There was no benefit for children with functional abdominal pain or functional dyspepsia
	Cochrane systematic review 2009 ⁹	There is no evidence that fibre supplements, lactose free diets or lactobacillus supplements are effective

*APP, American Academy of Paediatrics; CAP, chronic abdominal pain; IBS, irritable bowel syndrome; NASPGHAN, North American Society for Paediatric Gastroenterology, Hepatology & Nutrition; RCT, randomised controlled trial.

children since they often do not appreciate the suggestion that a psychological pathology is responsible for the pain. Hence, it may be beneficial to introduce the idea of psychological therapy during later consultations once a rapport has been established. Explain that in recommending these therapies you are not suggesting the pain is in their head; on the contrary the therapies are focused towards coping with and managing real pain and helping the child return to normal activities.

Pharmacological interventions should be considered on an individualised basis as part of a multifaceted approach to help reduce symptoms and disability. Subcategorising functional abdominal pain using the Rome III Criteria could help optimise treatment outcome for instance using pizotifen for those with abdominal migraine, an H₂-receptor antagonist for those with functional dyspepsia and *Lactobacillus rhamnosus* GG in those with irritable bowel syndrome.⁵⁻⁷

Aisha continues to be followed-up in clinic on a 3 monthly basis. She says the nasal sumatriptan provides her with some relief, but she continues to have symptoms. Despite this she continues to grow well and is achieving a higher attendance at school through the support of social work and teacher liaison.

Comment

Studies show that a third of children with CAP will go on to have persisting abdominal pain in adulthood, half of whom also develop non-abdominal pain such

as headaches.¹³ Of the two thirds whose abdominal pain resolves, a quarter develop chronic non-abdominal pain. Hence, only about 50% become pain-free. There is evidence that parental gastrointestinal problems are a risk factor for persistence of pain, but the hypothesis that psychological factors are predictive of persistence of symptoms is not supported by current evidence.¹⁴

CASE 2

Lucy, a previously well 7-year-old girl, was referred by her GP to paediatric out-patient clinic with a 3 month history of abdominal pain. She described the pain as crampy and generalised, with no localisation or radiation. It typically lasted for a few hours once or twice a week. She had missed a few days from school. Between episodes she was pain free. She had experienced two episodes of 'yellowy-green' vomiting and diarrhoea containing some fresh blood, each lasting 2-3 days. There was no history of infectious contacts or foreign travel.

She was born at term, had no significant past medical history and no family history of IBD.

On the referral letter the GP had documented a normal examination and a weight of 22.5 kg (50th centile). He had sent stool samples for microscopy, culture and sensitivity, which was negative, and faecal occult blood, which was positive.

The paediatrician also found the examination to be normal, but Lucy's weight had fallen slightly to 22.1 kg. She requested a FBC, U&E and LFT and arranged to see

her in the clinic in one month's time with a repeat weight. Advice was given to Lucy's parents to seek further medical advice via the GP or A&E should she deteriorate significantly in the interim.

Comment

At this stage it was unclear whether the alarm symptoms of blood in the stools and weight loss were significant or simply caused by a presumed viral gastroenteritis. Hence, it was reasonable to avoid rushing into a full set of investigations and to re-assess her following a short time period.

Lucy's blood tests were normal, but at follow-up her weight had fallen further to 21.2 kg. Her pain had persisted at the same severity and frequency and she had experienced two further episodes of blood in the stool associated with some mucus. Hence, the paediatrician referred Lucy to a paediatric gastroenterologist for further investigation.

Comment

Weight loss and bloody stools are two of the alarm symptoms associated with a higher prevalence of organic disease and hence require further investigation and in certain circumstances such as this, specialist referral.¹ See figure 1 for guidance on investigation and specialist referral.

Organic causes of CAP in children are highlighted in table 4.

Lucy was seen by a paediatric gastroenterologist 1 month later. Her abdominal pain had persisted and she was still having occasional episodes of blood and mucus in her stool. Her abdominal examination was again normal; her weight was now 20.9 kg. Hence, he organised for upper and lower gastrointestinal endoscopies.

Comment

There is little evidence on the diagnostic yield or cost-effectiveness of colonoscopy in children; however, the American Society of Gastroenterology has recommended the following indications:¹⁵

- Abdominal pain (clinically significant).
- Diarrhoea (chronic, clinically significant with weight loss, fevers, anaemia).
- Malaena/haematochezia.
- Anaemia (unexplained).
- Failure to thrive/weight loss.
- Polyposis syndrome, lesion on imaging, stricture management.

Clearly, Lucy fulfilled these criteria for a colonoscopy.

The use of oesophagogastroduodenoscopy and *H pylori* testing in children with CAP remains controversial.

A retrospective study of 1191 children with CAP identified abnormalities in 38% of oesophagogastroduodenoscopies.¹⁶ In a recent prospective study, 6% of children

undergoing endoscopy for CAP had organic pathology (excluding isolated *H pylori* infection); 33% of the children with alarm symptoms and signs had organic pathology, compared with just 2.8% without ($p < 0.01$).¹⁷

Even when endoscopic or histopathological abnormalities are identified, it does not necessarily affect prognosis in children with CAP.¹ A recent meta-analysis showed no association between *H pylori* and CAP in children, but some evidence for an association with epigastric pain; however, this was not confirmed in children seen in primary care.¹⁸

The American Academy of Paediatrics, the North American Society for Paediatric Gastroenterology, Hepatology and Nutrition and the American Society for Gastrointestinal Endoscopy all agree that endoscopy is only indicated for children with CAP associated with alarm symptoms and signs.^{1 15}

Due to the complexity of current evidence, invasive nature of the procedure and cost of endoscopy, we recommend referral to a paediatric gastroenterologist for consideration of this investigation when alarm symptoms and signs are present.

At endoscopy, Lucy's upper and lower gastrointestinal tracts looked grossly normal. A Campylobacter-like organism test undertaken for *H pylori* was negative. Biopsies were taken and sent for histology. The paediatric gastroenterologist organised for a faecal calprotectin test to be undertaken while waiting for the biopsy results and out-patient follow-up in 6 weeks.

Comment

Faecal calprotectin testing has a high sensitivity for Crohn's disease and ulcerative colitis. A positive faecal calprotectin result in children corresponds to a probability of IBD of 86% and a negative result a probability of 15%.¹⁹

Before Lucy's 6 week follow-up appointment she presented acutely to the accident and emergency department with an episode of abdominal pain. The pain was more severe than it had been previously and was now predominately in the right iliac fossa (RIF). She had associated bilious vomiting and a small amount of fresh blood per rectum.

On examination she looked unwell. She was afebrile, had normal oxygen saturation, respiratory rate and blood pressure, but a tachycardia of 130 bpm. Her abdomen was soft, but with tenderness and a palpable mass in the RIF. An ultrasound scan confirmed a RIF mass. Diagnostic laparoscopy (proceeding to mini-laparotomy) demonstrated a chronic/recurrent ileo-caecal intussusception which was resected and primary anastomosis performed. Histology confirmed a B-cell lymphoma within the chronic intussusception with clear resection margins. Following management co-ordinated by the paediatric oncologists she made a full recovery.

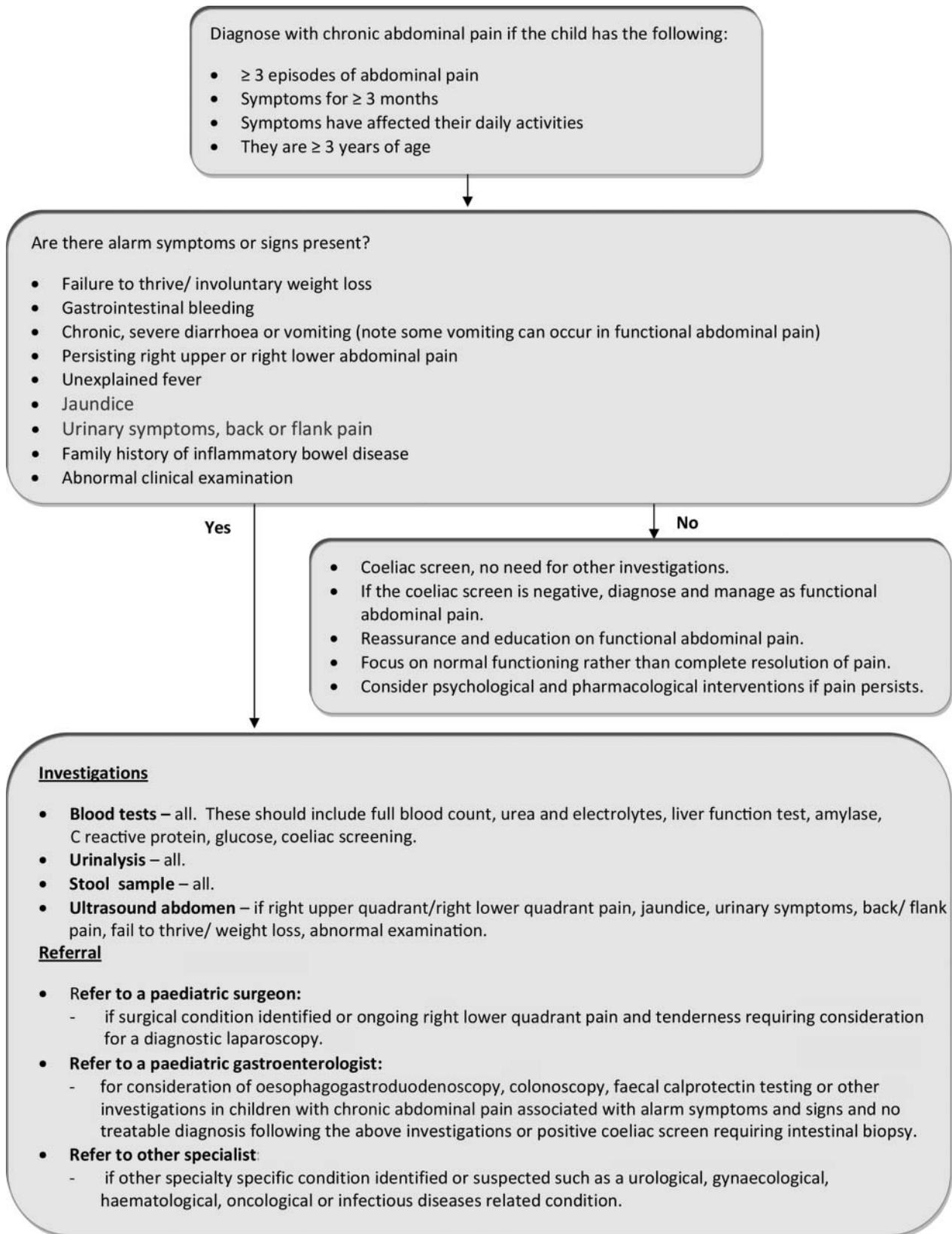


Figure 1 Pathway for the investigation, management and referral of children with chronic abdominal pain.

Comment

It could be argued that an earlier ultrasound scan may have identified the mass sooner, prompting further investigation (with CT or MRI±biopsy), diagnosis and

appropriate management with chemotherapy rather than surgery. However, with Lucy's initial symptoms of per rectal bleeding and mucus, gastrointestinal endoscopies were an appropriate investigation choice at that stage.

Table 4 Organic causes for chronic abdominal pain in children

Medical	Surgical
Infective: urinary tract infections*, helicobacter pylori related gastritis/ ulcer, tuberculosis, giardiasis, rheumatic fever, brucellosis, typhoid, other parasitic infection	Urological: urolithiasis, obstructive uropathy/hydronephrosis, polycystic kidneys
Inflammatory: inflammatory bowel disease, gastro-oesophageal reflux disease, non-steroidal anti-inflammatory drug related gastritis/ ulcer	Gastrointestinal: Meckel's diverticulum, duplication cyst, malrotation with or without volvulus, post-surgical adhesions, recurrent intussusception, bezoar, appendicular colic
Metabolic: lactose intolerance, diabetes mellitus, porphyria, sickle cell, lead poisoning.	Hepatobiliary: gallstones, choledochal cyst, other congenital malformations, chronic pancreatitis
Autoimmune: coeliac disease*	Other: small bowel lymphoma, other neoplastic disease, ovarian pathology, referred pain from testes
Gynaecological: pelvic inflammatory disease, endometriosis, polycystic ovaries, simple ovarian cyst	
Psychological: school phobia/ bullying, child abuse.	
Other: constipation*, splenic disease, leukaemia	

*The most common organic causes are highlighted. A detailed history and examination is paramount to help identify rarer causes and guide investigations appropriately.

In this case an acute admission prompted further investigation using diagnostic laparoscopy. However, there is also some evidence to support the use of elective diagnostic laparoscopy±appendectomy in children with chronic RLQ pain. A study of 44 children undergoing diagnostic laparoscopy and appendectomy for chronic RLQ pain identified intra-operative pathologies in 45% including: six Meckel's diverticulum, three inflamed appendix, four with adhesions to the caecum, four mesenteric adenitis, two hernia and one ovarian cyst.²⁰ On histology, 73% had abnormalities of the appendix, including signs of acute/chronic appendicitis or faecolith, one carcinoid tumour and one Crohn's disease. Despite these positive findings, only 57% had complete resolution of their pain at 2 years and 14% partial resolution. Other similar studies have reported pain amelioration rates of 70–100% at postoperative follow-up.²⁰

Although diagnostic laparoscopy±appendectomy may benefit some patients, others will undergo an invasive surgical procedure and continue to have pain. Hence, this investigation/ intervention should be reserved for select patients who have persisting RLQ pain that is affecting their quality of life despite thorough investigation and conservative management. In these circumstances, referral should be made to a paediatric surgeon (see figure 1).

DISCUSSION

In UK studies, 10–14% of children from school populations have been diagnosed with CAP. Sixty-nine per cent of children with CAP visit a doctor at least once. Only 5–10% of these will have an underlying identifiable organic cause and with nearly 12 million children in the UK this poses a great challenge to GPs and paediatricians. The difficulty is deciding which children require further investigation to ensure potentially serious organic causes are not overlooked whilst avoiding over-investigation which can be detrimental to children and their families and result in significant cost to the National Health Service.

We have produced a pathway summarising the current evidence for how to investigate, manage and refer children with CAP (figure 1). The hope is that this along with the advice above will help GPs and paediatricians manage this difficult condition more easily and effectively in their daily practice. No clinical pathway on this subject can lead to an accurate early diagnosis for 100% of children, but it aims to cover the majority of cases using the best evidence available. Any organic causes that are not initially identified are likely to trigger alarm symptoms and signs as the case evolves resulting in further investigation and management at that stage. This may result in a delayed diagnosis in a minority of cases but will avoid inappropriate investigation for the majority of children.

Key points

- CAP in children is common affecting 10–14% children in the UK.
- Only 5–10% of children with CAP have an underlying organic cause.
- Investigations do not help distinguish between organic and functional abdominal pain in the absence of alarm symptoms and signs and should ideally be avoided.
- Functional abdominal pain is managed optimally by making a positive diagnosis, providing reassurance and education, avoiding extensive investigations and focussing on a return to normal function rather than resolution of pain.
- Alarm symptoms and signs should prompt further investigation and where appropriate referral to a paediatric gastroenterologist or surgeon as outlined in the evidence-based pathway provided.

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Competing interests None.

Provenance and peer review Commissioned; externally peer reviewed.

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