15-Year-Old Girl with Diarrhoea, Abdominal Pain and Fatigue: A Paediatric Case of Crohn's Disease.

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Clinical Points:

- Crohn's disease (CD) is an immune mediated inflammatory condition.
- Children suffering from CD may present with intestinal or extraintestinal symptoms.
- Useful indicators of CD in children presenting with abdominal pain are: a family history of inflammatory bowel disease, weight loss, growth failure, pallor fatigue, oral ulcers, erythema nodosum, digital clubbing, athralgia, and perianal fistulae or abscesses.
- Growth failure in particular is an important indicator of CD. As many as fifty percent of paediatric patients with CD have a decrease in height velocity before the onset of any other intestinal symptoms.
- Diagnosis of CD involves five steps: clinical suspicion of the illness from history and examination, exclusion of other illnesses that have similar presentation, differentiation between ulcerative colitis and CD, localisation of the diseased region and finally identifying any extraintestinal manifestations of the disease.
- Treatment of the ill patient with active CD typically involves the induction of remission by using potent therapy with a rapid mode of onset. Once remission is induced, the patient can be moved onto a maintenance drug regime.

PRESENTATION OF CASE

A.H., a 15 year old girl presented to casualty with a six week history of worsening diarrhoea, intermittent abdominal pain and fatigue. She described the diarrhoea as loose and mucous-like in consistency without any associated bleeding per rectum, nausea or vomiting. Her abdominal pain had sudden onset and occurred prior to bowel movements. She described it as "crampy" in nature, radiating all over her abdomen and was worst at the upper left quadrant. Pain was rated 8 out of 10 on a scale of 0-10 (with 10 representing the most severe pain) and was relieved by defecation. There were no aggravating or associated features with the pain. She had suffered weight loss of one stone in the six weeks prior to admission with accompanying anorexia. A.H. also had bilateral shoulder and elbow athralgia but did not complain of any rash or episodes of "red eye". She was seen by her general practitioner five weeks prior to presentation to casualty, who suggested that she was suffering from a viral "bug" and that her symptoms would subside. Her weight and height were plotted on a growth chart appropriate for her age and sex. At time of presentation she weighed 39.9 kilograms, which put her below the 3rd centile, and her height was 157cm which is on the 14th centile. There were no previous growth data available. She had pubertal delay and a family history of early menses was noted. A decision was made to admit her.

Upon admission, her vitals were found to be normal. She was apyrexic at 36.6 ^{0}C. Her heart rate was 72 beats per minute and her blood pressure was 115/78 mmHg. Upon inspection, pallor of the palmar creases and aphtous ulcerations in the mouth were noticed. Her abdomen was soft but tender, especially at the left iliac, supra pubic and right iliac area. There were no signs of peritonism or organomegaly and normal bowel sounds were present. Examination of her joints revealed a full range of movement and no tenderness, heat on palpation or signs of inflammation. Assessment of neurological, respiratory and cardiovascular systems were unremarkable. Rectal and peri-anal exams were deferred at this stage.

INVESTIGATIONS AND DIAGNOSIS

The differential diagnoses considered were Crohn's disease (CD), ulcerative colitis, irritable bowel syndrome, coeliac disease, infectious causes (e.g. *Salmonella*, *Campylobacter*, *Clostridium difficile*, *Escherichia coli* 0157:H7 or *Entamoeba histolytica*) and drug-induced colitis (e.g. non steroidal anti inflammatory medications). Rarer diagnoses would include amyloidosis, Whipple's disease and Behçet's disease.

Baseline investigations were performed in casualty and a consultation with the gastroenterology team was requested. Her full blood count was normal with the exception of a reduced haemoglobin level of 10.6 g/dL and an elevated platelet level of 532 X 10^9/L. C-reactive protein was elevated at 110.3 mg/L which was suggestive of active inflammation. Sodium and albumin levels were reduced to 134 mmol/L and 28 mg/L respectively. Infective causes mentioned in the differential diagnosis can mimic symptoms of inflammatory bowel disease and were ruled out by stool culture. A colonoscopy was carried out and biopsies of multiple areas of the colon were taken during the procedure. Abnormalities of the mucosa were noted on the descending and transverse colon and caecum. Aphthous ulcerations, discontinuous colitis with areas of normal mucosa (skip lesions) and a relative reduction of inflammation in the rectum (rectal sparing) were present which, were suggestive of CD. The histological findings were of non-caseating granulomas that were not

adjacent to ruptured crypts. An oesopha-gastro-duodenoscopy with biopsies found that the oesophagus, gastric body, antrum and duodenum had normal mucosa. These findings added weight to the diagnosis of CD. Other investigations that are useful in the diagnosis of CD but were not required in this case, include serological tests (*Saccharomyces cerevise* antibody is usually present in CD while perinuclear antineutrophil cytoplasmic antibodies are negative), barium follow through which can identify areas of narrowing of the intestine, spiral computed tomography scanning which can define the thickness of the bowel wall, mesentery, intra-abdominal and para-intestinal abscesses and pelvic magnetic resonance imaging which is useful if perianal disease is present.

OUTCOME AND FOLLOW UP

A.H. was put on oral prednisolone for three months (1mg/kg/day). After three weeks, the dose was tapered as she was in remission. She was also prescribed a polymeric diet to take once daily. Information regarding long-term complications of CD were discussed with A.H. and her family. Reassurance was given that most complications of the condition can be successfully treated. Four months following admission she was seen as an out-patient and is currently well.

DISCUSSION

Overview of management of CD in a child

The incidence of CD in childhood and adolescence has been estimated to be 3 per 100,000 and has increased during the last decade (1). This has resulted in an increase in the number of clinical trials performed in this area, as current treatment is largely based on data extrapolated from adult trials (2). A multidisciplinary approach is taken in the management of paediatric CD that involves input form paediatricians, gastroentologists, ophthalmologists, general practitioners, nurses, dieticians and psychologists. There are four principle components of a treatment program for a child with CD: i) medical therapy, ii) surgical management, iii) nutritional rehabilitation and iv) psychological support.

Medical therapy administered depends either on the region and severity of the disease or on the type of complication the patient is experiencing (2). Corticosteroids are used to induce remission in moderate to severe CD. Studies have shown that budesonide has a lower toxicity, but lower efficacy compared to prednisolone (2). However long term budesonide use has been associated with growth failure and therefore is only used for short term therapy (not more than four months) (3). Aminosalicylates are indicated for mild mucosal disease in the small bowel and colon. Sulfasalazine is strongly indicated for disease that is limited to the colon whereas mesalamine is best indicated for patients without colonic involvement (2). Azathioprine and 6-Mercaptopurine (6-MP) are thiopurine drugs, and are used for corticosteroid resistant CD. 6-MP is best suited for maintenance of remission and is indicated in refractory CD, fistulating CD or growth failure. Azathioprine is metabolised into 6-MP, therefore these drugs are the same in terms of effectiveness and differ only in their dosing. Side effects include suppression of the immune system which renders patients more prone to infections, pancreatitis, and hepatotoxicity. There is also a very small risk of developing lymphoma (4). Monoclonal antibodies that block tumour necrosis factor α can be used in treatment resistant patients. Infliximab is particularly effective in fistulating CD and its use has been associated with infusion reactions, and infections such as re activation of tuberculosis. A few cases of T-cell lymphoma have been reported (5,6). Methotrexate is indicated, but not often used in refractory CD. Side effects include myelosupression, oral ulcers, infection, hepatitis and pulmonary dysfunction. Antibiotics such as ciprofloxacin and metronidazole are used to treat infectious complications of the disease, such as abdominal or peri-anal abscesses. Intravenous cyclosporin can be used to induce remission in some cases.

Surgical management is reserved for patients that do not respond to medical treatment or develop complications (e.g. fistulas). Surgery is particularly beneficial for patients with limited disease. In severe cases full colonic resection and ileostomy may not be avoidable. Studies have also shown that 6-MP may be the most effective prophylactic agent (7,8).

Nutritional rehabilitation includes primary therapy. This is total enteral nutritional therapy that suppresses inflammation and therefore induces remission of CD (9,10). Partial enteral nutrition is used in patients with growth failure for two reasons; to increase calorie intake and to maintain remission. Supplementation therapy may be given to children with CD who are at risk of micronutrient deficiencies such as vitamins A, D and E, and of zinc, selenium, and folic acid (9,10).

Psychological management may be required in paediatric CD given the chronic and relapsing nature of the disease. It may cause depression (13) or school absenteeism due to increased fatigue or teasing from classmates (14).

Complications

Peri-anal complications such as fissures, ulceration, fistulas, abscesses, and stenosis are often a distressing feature of CD. The majority will heal without treatment, but others may require antibiotics, steroid suppositories, immunomodulators or even surgery. Inflammation of the stomach and duodenum can occur in severe cases of CD which may be treated with oral steroids and immunomodulators (15). Oral lesions such as mucogingivitis, mucosal tags, deep ulceration, cobblestoning and lip swelling occur commonly in children with CD (16,17). A high percentage of patients develop malnutrition, which have undesirable consequences such as delayed growth and puberty in children, decreased ability to tolerate surgery, and psychosocial problems. Osteopenia has been reported (18) and oesteoporosis occurs in up to 30% of children which is due to a combination of factors such as vitamin D deficiency, calcium malabsorption and corticosteroid therapy (19, 20). Other less common complications include uveitis, episcleritis, erythema nodosum and pyoderma gangrenosum.

Prognosis

Unfortunately to date no large-scale multi-centre study has been conducted into the prognosis of children with CD and so we are reliant on data taken from adult trials. CD patients exhibit a widely varying prognosis. Relapsing episodes of varying severity can be a feature. Others may undergo complete remission. Mortality and morbidity is directly related to the complications experienced by the patient. Severe cases may require multiple surgeries that could require lifelong parenteral nutrition dependence.

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