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Original Articles

Inflammatory Bowel Disease in Hong Kong Chinese Children: A 10-year Experience in a University Hospital

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Abstract Crohn's disease (CD) and ulcerative colitis (UC), that are collectively known as inflammatory bowel disease (IBD), are uncommonly seen in Asian paediatric population. We have retrospectively reviewed paediatric IBD patients managed in our hospital in the last 10 years. ***Methods:*** Retrospective review of patients diagnosed to have IBD before the age of 15 with focus on clinical presentations and outcomes. ***Results:*** 7 CD and 2 UC patients were identified. Mean age of onset of symptoms for CD was 10.7 years while the 2 UC patients presented at 33 months and 10 years old respectively. Mean time interval between onset of symptoms and diagnosis made was 20.4 months. Two CD patients were misdiagnosed to have TB colitis initially. Pathology patterns for CD were isolated small bowel disease in 2/7, isolated colonic disease in 1/7 and 4/7 with both terminal ileum and colon involvement. Two UC patients had proximal extent of involvement to descending and transverse colon respectively. Anaemia, thrombocytosis, high ESR and hypoalbuminaemia were the most consistently abnormal biochemical results at presentation. 8/9 patients had remission of symptoms at 3 months after medical therapy. One CD patient underwent surgical intervention because of failure of medical treatment and growth failure. In majority of patients the disease ran a chronic intermittent course. Two patients were complicated with psychiatric disorders requiring specific therapy. ***Conclusions:*** IBD is an uncommon disease in our paediatric population and delay in diagnosis has been significant. Accumulation of experience and high index of suspicion improve the diagnosis. Management strategy should include medical, surgical and psychosocial aspects.

Key words Children; Chinese; Inflammatory bowel disease

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Introduction

Crohn's disease (CD) and ulcerative colitis (UC) are collectively known as inflammatory bowel diseases (IBD). The unique features of chronic relapsing inflammation of the gastrointestinal tract and its extraintestinal manifestations characterise the disease for which the etiology remains unknown despite enormous amount of research in past decades. Of note, the question whether UC and CD are two different disease entities or are different manifestations of a single disease process remains unanswered.[1,2] Epidemiological studies and clinical experience have unequivocally shown that IBD affects white populations much more commonly than non-whites. In those countries like United States, Norway and Canada where IBD is

prevalent, CD and UC each has a prevalence of around 100 per 100,000 populations.[3-5] As IBD primarily affects young adults, the incidence of paediatric IBD is low. In Hong Kong, paediatric patients with IBD are very infrequently encountered even in well-established paediatric centres. Very scanty data exists regarding the presentations and clinical outcomes of IBD in our Chinese paediatric patients. To share our limited experience with our colleagues, we have retrospectively reviewed the paediatric patients with IBD managed in our hospital over the last 10 years.

Methods

We conducted a retrospective review of case records of patients diagnosed to have IBD before the age of 15 and had been jointly managed by paediatricians and paediatric surgeons. Focus was put on age of onset of symptoms, clinical features, delay in diagnosis, disease pathology and clinical outcomes. Analysis on clinical outcomes only included those patients who had received treatment in our hospital and had been followed up for over 1 year after treatment. Endoscopy was the principal tool for investigation. Diagnosis of either CD or UC was based on the endoscopic findings, histological features and exclusion of enteric infections (Figure 1). Standard medical treatment included 5-aminosalicylate agents and steroids. Immunomodulatory agents were reserved for patients dependent on high dosages of steroids in maintaining remission. Surgical intervention was considered for failure of medical treatment, growth retardation, surgical complications such as obstruction, perforation, haemorrhage and fistula formation.

Results

Nine subjects were identified in our study (male=4, female=5) (Table 1). Two patients suffered from UC while the remaining seven had CD. The mean age of onset of symptoms for CD was 10.7 years (range from 5 to 14 years). The two UC patients started to have symptoms at the age of 33 months and 10 years respectively. None of our patients

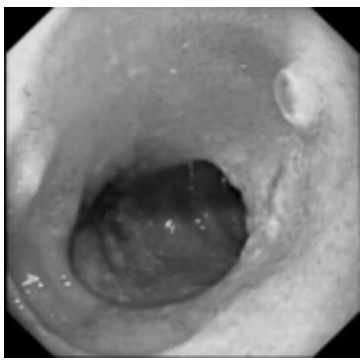

Figure 1 Endoscopic view of Crohn's disease in duodenum.

Table 1 Results of IBD patients

Patient no.	Sex	Pathology	Initial treatment	Long-term outcome (mean follow-up 5.4 years)
1	F	CD, t+c	Anti-TB drugs, oral steroid + 5-ASA	Failed medical treatment and complicated with growth failure. Underwent surgical resection recently.
2	F	CD, t+c	Anti-TB drugs, oral steroid + 5-ASA	Died of unrelated cardiomyopathy.
3	F	UC	5-ASA, oral + enema	Chronic intermittent disease. 5-ASA enema as maintenance.
4	M	CD, j	Surgical resection followed by 5-ASA	Completely asymptomatic. Oral 5-ASA as maintenance.
5	M	CD, t+c	Oral steroid + 5-ASA	Chronic intermittent disease. Immunosuppresants + oral 5-ASA as maintenance.
6	F	UC	5-ASA, oral + enema	Chronic intermittent disease. 5-ASA enema as maintenance.
7	F	CD, c	Oral steroid + 5-ASA	Defaulted follow-up.
8	M	CD, t+c	Oral steroid + 5-ASA	Chronic intermittent disease. Oral 5-ASA as maintenance.
9	M	CD, d	Oral steroid + 5-ASA	Pending follow-up result. Oral 5-ASA as maintenance.

CD=Crohn's disease; UC=Ulcerative colitis; t=terminal ileum; c=colon; j=jejunum; d=duodenum; 5-ASA=5-aminosalicylate agents.

had family history of IBD. Recurrent abdominal pain and episodic diarrhoea were the main presenting symptoms in CD patients. One patient just presented with recurrent perianal abscesses and fistula-in-ano, without any complaint of other gastrointestinal symptoms. Two CD patients also complained of blood in the stools. Perianal skin tag, aphthous stomatitis and significant weight loss at presentation were each noted in 3 out of 7 CD patients. Recurrent unexplained fever was reported in 2 out of 7 CD patients. Both UC patients presented with stools mixed with blood and mucus without any abdominal pain or diarrhoea or other systemic symptoms.

The most consistent abnormal blood results in our series were anaemia, thrombocytosis, hypoalbuminaemia and raised ESR, each of which occurred in over 85% of cases at their first presentation to our hospital. Diagnosis was made by endoscopy with biopsies in all but one patient who underwent laparotomy for suspected small bowel lymphoma and intra-operatively found to have IBD of jejunum. Histology confirmed CD from the resected jejunum. The other six CD patients included four with both terminal ileum and colon involvement, one with isolated colonic disease and one with isolated duodenal disease. The two UC patients showed proximal extent to descending and transverse colon respectively on colonoscopy. The mean time interval between onset of symptoms and the diagnosis of IBD made was 20.5 months (range from 6 weeks to 3 years). Two CD patients were wrongly diagnosed to suffer from TB colitis initially and received anti-TB treatment. The initial positive stool culture of salmonella in one of the UC patients also misled the clinicians and delayed the final diagnosis. The CD patient who presented with recurrent perianal disease had undergone multiple surgical interventions before the correct diagnosis was made.

All CD patients received oral steroids and 5-ASA agents to induce remission except the one who had undergone resection of affected jejunum at diagnosis and was put on 5-ASA agent only after surgery. 5-ASA agents in both oral and enema preparations were given to the two UC patients as initial treatment. Complete remission of symptoms was achieved at 3 months after commencement of treatment in all but one patient with CD. Among the nine patients in this series, one defaulted follow-up in our hospital soon after diagnosis was made and another was too recently diagnosed to allow any meaningful study of the disease course. The remaining seven patients had a mean follow-up of 5.4 years after initial treatment. One patient died a year after the diagnosis because of unrelated cardiomyopathy. One patient had remained completely asymptomatic since commencement of treatment. Four patients had chronic intermittent disease with exacerbation and remission of symptoms. One of these four patients required immunosuppressive drugs in the maintenance therapy while the other three were on 5-ASA agents only. One CD patient developed continuous disease refractory to medical treatment including immunosuppressive drugs and anti-TNF antibody and was further complicated with growth failure and delayed sexual maturation. She subsequently underwent surgical resection of affected bowel. Two patients in our series had received psychiatric therapy for mood disorder and paranoid schizophrenia respectively.

Discussion

Recent reports from United Kingdom suggested that there has been an increase in new cases of paediatric IBD over the last two decades, with an estimated incidence of 5.3 per 100,000 children under the age of 16.[6-8] No similar epidemiological study has ever been done in Hong Kong although our local experience tells us that the figure here should be lower. We identified only nine subjects in the last 10 years by searching through the Clinical Management System, personal databases of concerned pathologist and clinicians. It is still possible that we may have missed some patients in this study, particularly if they were diagnosed in early years and had defaulted follow-up for long enough to be forgotten. However, this number is not expected to be high. As our overall patient number is small, it is impossible to draw any conclusion whether we are now seeing more paediatric IBD than before as in other western countries. But the fact that CD has been more frequently encountered than UC in our paediatric population seems to correspond well to western data.[7] The first two CD patients in our series were misdiagnosed as TB colitis, thus significantly delaying the correct diagnoses and appropriate treatment. This signified the difficulty of recognising this uncommon disease during the time when our experience of managing paediatric IBD was so scarce. Making a distinction between CD and colonic tuberculosis has been a diagnostic challenge, especially in places where mycobacterial infection is still prevalent. Granulomas in CD may not be seen in mucosal biopsies. In our series, in only around 50% of specimens were granulomas seen. In TB colitis, when granulomas are detected in biopsies, classical caseous necrosis may not be present. Instead, "naked granuloma" reminiscent of CD may be seen. The sensitivity of histochemical stain and culture for TB is low to make a definite exclusion of TB colitis

sometimes difficult. However, with the recent advance in molecular biology, the sensitivity of detecting mycobacterium in tissue has been greatly enhanced by molecular diagnostic test of TB PCR. Today, with a careful correlation of the biopsy findings, clinical and endoscopic features, a correct diagnosis can often be made as in our more recent patients in the series.

Another factor that contributes to delay of making the diagnosis is false reassurance that symptoms are infective or functional in origin. Index of suspicion is understandably low for uncommon disease like IBD in children. Recurrent abdominal pain and diarrhea were the chief presenting symptoms in our CD patients. Functional disorder such as irritable bowel syndrome and infective gastroenteritis are far more common in children than IBD. Moreover, other systemic manifestations like fever and weight loss happened in less than half of our patients. Patients with full-blown diseases should raise enough suspicion. However, patients just presenting with abdominal pain and diarrhoea without obvious per rectal bleeding and other extraintestinal features pose most of the diagnostic difficulties. The severity of the symptoms, particularly the abdominal pain, should alert the clinicians to the possibility of IBD. Useful screening tests should be ordered without delay. Anaemia, thrombocytosis, high ESR and hypoalbuminaemia have been shown to have high sensitivity for IBD in both of our series and the literature.[2,9] Positive culture of bacterial pathogens in stools may not exclude IBD especially when symptoms persist or recur after treatment as in one of our UC patients. It has been shown that bacterial gastroenteritis can be associated with or trigger the first episode of IBD.[10,11]

The pathology patterns in our CD patients (isolated small bowel disease in 2/7, small and large bowel disease in 4/7 and isolated colonic disease in 1/7) are similar to the western counterparts, as are their clinical courses.[9] Data in the literature suggests that majority of paediatric CD patients run a course of remission interspersed with exacerbation of symptoms. Patients with continuous disease refractory to all medical treatments are candidates for early surgery to improve the quality of life by alleviating the symptoms and more importantly to prevent the undesirable outcome of growth retardation which can result from both the disease itself and the medical therapies.[12] Surgery should be done before the pubertal growth spurt is complete. It is still too early to conclude on the percentage of our patients requiring surgery eventually although western data suggests that up to 86% of paediatric CD patients and 26% of paediatric UC patients will have had surgery within 15 years after presentation of disease.[13,14] Two of our nine patients were complicated with mood disorder and paranoid schizophrenia requiring psychiatric treatment. Management of paediatric patients with IBD would never be complete without looking into the psychosocial impact of the disease on both the patients and their families. Studies have shown that IBD significantly affects the quality of life in paediatric patients.[15,16] Low self esteem, anxiety, depression, antisocial behaviour, schooling problems are common to children with IBD. Clinicians looking after paediatric IBD patients should be sensitive to early signs of psychosocial problems. Giving advice to improve communication between parents and patients, helping patients to develop coping skills specific for the disease, and providing adequate information in regards to the medical aspects of the disease have been increasingly emphasised in the management of paediatric IBD.

In summary, IBD is an uncommon disease in our paediatric population. Accumulation of experience has improved the diagnostic accuracy. The possibility of IBD should always be born in mind by paediatricians and any clinician who looks after paediatric patients everyday, as a prompt diagnosis is of key importance for early treatment and the prevention of serious complications.

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