ORIGINAL ARTICLE

CONTENTS

Clinical and diagnostic features of Crohn's disease in young children

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ABSTRACT

Aim: To highlight the distinctive features of CD in young children, based on personal clinical experience in observation and treatment, with the objective of improving the accuracy of diagnosis and the effectiveness of treatment.

Materials and Methods: The study involves the results of treatment 11 young children with CD. The diagnosis was based on the combination of the following data: clinical manifestations of the disease and its course, as well as the results of laboratory, instrumental, and step biopsy with morphological studies.

Results: In young patients with CD, combined lesions of the small and large intestines predominate, manifesting as gastrointestinal disorders against the background of a severe general condition, intoxication, and extraintestinal complications. Young children with CD often show signs of asthenic syndrome, developmental delay, and high inflammatory activity. All the children in the study showed low serum iron levels, dysproteinemia, and high calprotectin levels.

Conclusions: 1. CD in young children has such clinical features as combined lesions of the small and large intestines (45.45% of cases), high activity of the disease. frequent extraintestinal manifestations of the disease, and developmental delay. All young children with CD upon admission to the hospital were in severe condition, exhibiting signs of intoxication, diarrhea, and blood in their stools. 2. Laboratory findings are characterized by serum iron deficiency, dysproteinemia, and high levels of calprotectin. 3. Knowledge of the clinical and diagnostic features of CD is essential for specialists to provide appropriate medical care.

KEY WORDS: Crohn's disease (CD), children, early age, clinical picture, diagnosis

Wiad Lek. 2024;77(9):2015-2019. doi: 10.36740/WLek/195170 DOI

INTRODUCTION

Crohn's disease (CD) in young children poses a substantial problem for these vulnerable patients. It is a gastrointestinal disease of unclear etiology, characterized by transmural (affecting all layers of the intestinal wall) segmental granulomatous inflammation, leading to intestinal (local) complications and extraintestinal (systemic) manifestations [1, 2]. Currently, the approaches to diagnosing and treating CD remain a topic of ongoing discussion among experts globally. CD is among the conditions that present significant challenges for practicing physicians. The increasing mortality rate among children with CD, including infants, is concerning and has attracted significant attention from both international and domestic researchers [3]. In recent years, there has been a noted increase in the incidence of CD in European countries. The early-onset incidence (new cases per year) in children is 4.37 per 100,000, and the prevalence is 14 per 100,000 [4]. According to a population-based Scottish study, over the past four decades, the incidence of early-onset CD and ulcerative colitis has tripled – in children under 5, the frequency increased from 0.7 (1981–1985) to 2.0 per 100,000 per year (2008–2013) [5]. Experts estimate that the approximate number of patients with CD in Ukraine is 30.33 per 100,000 of the population, with 48% experiencing moderate to severe inflammatory activity, though the exact number of patients is unknown due to the absence of a registry [6]. In the last decade, there has been a trend toward an increase in early-onset cases, with the incidence of CD in childhood having tripled [7, 8]. However, to this day, CD in young children remains one of the least studied pathologies. Global research offers only incomplete and controversial data on the clinical presentation, diagnostic potential, and treatment strategies for CD in young children.

AIM

Aim was to highlight the distinctive features of CD in young children, based on personal clinical experience in observation and treatment, with the objective of improving the accuracy of diagnosis and the effectiveness of treatment.

MATERIALS AND METHODS

The study included the results of examination, treatment, and observation of 11 children with CD aged from 11 months to 3 years. Patient data were collected from medical history, review of outpatient case records, hospital discharge reports, and other relevant sources. The diagnosis was based on a combination of the following data: assessment of clinical manifestations of the disease and its course, and the results of laboratory, instrumental, and morphological studies. The instrumental methods of examination in children included: endoscopic examination with biopsy (fibrogastroduodenoscopy, fibrocolonoscopy, sigmoidoscopy), barium X-ray examinations of the gastrointestinal tract, double-contrast CT scan of the abdomen, MRI of the abdomen and pelvis, and morphological examination of clinical biopsy material. Biopsies should be multiple (or stepped), which involves taking samples from 5 areas along the large intestine, including the rectum and ileum. The gold standard for examining children with perianal lesions is rectal examination under anesthesia. When symptoms of CD appear at an early age, it is necessary to exclude the presence of primary immunodeficiency [9]. Thus, an immunological marker for suspected CD is antibodies to Saccharomyces cerevisiae. CD is verified by the morphological examination of clinical biopsy material [10, 11].

The activity of CD was assessed using the PCDAI (Pediatric Crohn's Disease Activity Index), as presented in Table 1 [12].

The study applied commonly accepted methods for statistical data processing in medical and biological research. Non-parametric methods were used due to the non-representative sample and the preference for analyzing qualitative rather than quantitative characteristics. Numerical indicators are presented in absolute values and in percentage ratios.

Compliance with bioethical principles was ensured.

RESULTS

While CD primarily affects the terminal ileum (a synonym for the disease is terminal ileitis), in young children, combined involvement of the small and large intestines predominates. Among the studied patients, 5 children exhibited combined involvement of the small and large intestines, which accounted for 45.45% of cases. In 2 (18.18%) young children, there was involvement of the ileum, in 3 (27.27%) patients only the large intestine was affected, and in 1 (9.09%) patient, there was involvement of the jejunum, which corresponded to the data presented by Aloi M et al. [13]. Perianal complications, known as 'perianal Crohn's disease', were observed in 3 children in the study group: in 2 children with involvement of the large intestine and in 1 child with involvement of the ileum, accounting for 27.27%.

Upon admission to the hospital, the main manifestations of CD in young children were abdominal pain, vomiting, abdominal distension, the presence of purulent-hemorrhagic and mucous discharge from the rectum, fistulas in the buttock and perineal areas, rectal erosion, perianal dermatitis, loose stools, fever, and more. All young children with CD admitted to the hospital were in serious condition with signs of intoxication. Common symptoms in young children with CD included anemia, weakness, fever of unknown origin, fatigue, weight loss, loss of muscle mass, developmental delay, stunted growth, and more. More than half of the patients, namely 6 children (54.54%), had extraintestinal manifestations of CD: lesions of the oral mucosa in the form of canker sore, eye involvement such as iridocyclitis, and erythema nodosum. The analysis of the disease history data revealed that patients had previous complaints and changes in their general condition ranging from 1 month to 2 years.

Based on the nature of bowel movements, weight, height, the presence of perianal and extraintestinal manifestations, as well as laboratory changes (levels of Ht, ESR, and albumin), CD in the majority of young children in the study group was active. The high activity of CD in these young children, as assessed by the PCDAI (Pediatric Crohn's Disease Activity Index) scores, corresponded to moderate and severe forms of the disease.

All patients had inflammatory changes in their blood tests, including elevated ESR, leukocytosis, and high levels of C-reactive protein. It is noteworthy that all young children with CD in the study group had iron deficiency (low serum iron levels) and dysproteinemia. The level of fecal calprotectin, an inflammatory protein that indicates the degree of intestinal inflammation, was also elevated. The method of measuring fecal calprotectin has been implemented in practical healthcare as a screening tool to differentiate between inflammatory and non-inflammatory bowel diseases. In patients with CD, the level of calprotectin increased by 3-4 times or more (the normal range is 50 mcg/g) [14].

Upon admission to the hospital, the studied group of patients had elevated average values of the leukocyte intoxication index (LII) and the hematological index of intoxication (HII).

Antibodies to Saccharomyces cerevisiae, which serve as an immunological marker when CD is suspected, were detected in 6 young children, accounting for 54.54%.

Symptoms such as abdominal pain, weight loss, diarrhea, and asthenic syndrome were predominant

Table 1. Pediatric Crohn's Disease Activity Index (PCDAI)

Criteria	Presence	Scores
Abdominal Pain	None	0
	Mild intensity	5
	Severe	10
Bowel Movements, Frequency, Consistency	0-1 time/day, liquid, no blood present	0
	2-5 times/day, with minor blood presence	5
	≥ 6 times/day	10
Weight	No weight loss	0
	Weight loss of 1-9%	5
	Weight loss ≥ 10%	10
Height	Below 1st percentile	0
	From 1st to 2nd percentiles	5
	Below 2nd percentile	10
Abdominal Tenderness	No tenderness	0
	Tenderness or palpable mass	5
	Severe tenderness	10
Perirectal Manifestations	None	0
	Fistula, inflammation	5
	Abscess	10
Extraintestinal Manifestations	None	0
	One manifestation	5
	More than 2 manifestations	10
Hematocrit (children under 10 years)	≥33%	0
	28-32%	2.5
	≤28%	5
Hematocrit (girls 11-18 years)	≥34%	0
	29-34%	2.5
	≤29%	5
Hematocrit (boys 11-14 years)	≥35%	0
	30-34%	2.5
	≤30%	5
Hematocrit (boys 15-18 years)	≥37%	0
	32-36%	2.5
	≤32%	5
ESR (mm/hr)≤	≤ 20	0
	20-50	2.5
	≥50	5
Albumin (g/dl)	≥3.5	0
	3.1-34	5
	≤3	10
PCDAI Interpretation	No activity (remission)	≤ 10 scores
	Mild to moderate	11-30 scores
	Severe	30-100 scores

in young children. Among patients under one year of age, low body weight was present in 100% of cases, and growth delay occurred in 50% or more of the children. In children aged 1-3 years, disturbances in weight and height indicators were observed in 82.82% of cases (9 patients), and diarrhea in 63.64% (7 children). Blood in the stool was noted in 72.73% of the young children.

Key diagnostic methods for CD in children include endoscopic examinations. Children with CD exhibit aphthous lesions on a normal or inflamed intestinal mucosa, In one child, the jejunum was affected. During rectosigmoidoscopy and fibrocolonoscopy, there were signs of focal infiltration, swelling, hyperemia with the formation of a cobblestone appearance of mucosa in the affected segments of the colon, enhanced or absent vascular pattern, multiple ulcers with debris, and the presence of liquid hemorrhagic content and/or blood clots in the intestinal lumen [15].

Today, methods of MRI and CT with bowel filling using water, such as hydro-MRI and hydro-CT, have become widely used. They enable highly accurate assessment of bowel wall thickness, the presence of intestinal ab-

scesses, stenoses, and effusions. These methods have expanded the diagnostic capabilities for CD in young children and in the early stages of the disease [16].

In 2014, the Porto Criteria for diagnosing CD were published (by the European Society for Paediatric Gastroenterology, Hepatology and Nutrition). They emphasize that even among the methods of additional diagnosis for CD, there is none that can guarantee the detection of CD in a child with 100% certainty. Therefore, clinicians must be aware that the diagnosis of CD should be verified by morphological methods of investigation [17].

According to the results of the morphological examination of biopsies taken during diagnostic procedures, the characteristic changes in the small intestine were as follows: uneven lymphoplasmacytic infiltration, infiltration by segmented neutrophils, eosinophils, and focal lymphoproliferative changes in the lamina propria of the small intestine; lymphocytic infiltration, areas of fibrinoid necrosis of the vessel wall, ulcerative defects with proliferative inflammatory changes, and fibrosis of the muscle layer; lymphoproliferative changes in the serous membrane, and the presence of ulcers with smooth edges extending into the subserosal layer. The morphological changes in the biopsy material of the colon were as follows: infiltration and lymphoplasmacytic infiltration of the lamina propria of the mucous membrane, areas of mucosal fibrosis, follicle formation in the mucous membrane, focal angiomatosis, areas of hyperplasia of intramural ganglia, ulcerative and proliferative inflammatory defects of the mucosal and serosal layers; muscle layer fibrosis; thickening of the intestinal wall due to pronounced fibrotic changes, presence of ulcers with smooth edges extending to the subserosal layer.

The results of morphological examination of biopsy samples from the esophagus, stomach, and duodenum, taken during esophagogastroduodenoscopy (EGD), in some small children revealed chronic atrophic duodenitis and erosions of the gastric mucosa, changes characteristic of chronic gastroduodenitis, and the presence of gastropathy.

Diagnostic search for CD must include mandatory testing for yersiniosis, which should be excluded in patients with CD.

In the treatment of CD in young children, it is crucial to use a combined approach, integrating conservative and surgical treatments. Surgical and medical treatments for CD should complement each other. The key to effective treatment is timely diagnosis of the pathology and determining appropriate medical care for the child, which should be based on multidisciplinary approaches in both diagnostic and therapeutic strategies.

DISCUSSION

Clinical monitoring and diagnosis of CD in young children must be comprehensive and multidisciplinary, involving pediatricians, gastroenterologists, immunologists, pediatric surgeons, morphologists, and others in the diagnostic process.

Our own experience of observing children with CD aged 11 months to 3 years reveals differences in the clinical presentation and laboratory findings in this pathology. In young patients, combined lesions of the small and large intestines predominate, manifested by gastrointestinal disorders against the background of a generally severe condition, intoxication, and extraintestinal complications. Asthenic syndrome and developmental delay are typical for young children with CD. High activity of the inflammatory process is also common in young children [4].

Regarding laboratory features, all the children from the study had low serum iron levels, decreased albumin levels, elevated gamma globulin levels, and fecal calprotectin levels increased by 3-4 times or more. Antibodies to Saccharomyces cerevisiae, which serve as an immunological marker when CD is suspected, were detected in half of the patients (54.54% of cases). Yersiniosis was excluded in all children with CD, which we consider a mandatory step in the diagnostic search.

The primary diagnostic methods for this group of patients are endoscopic examinations with biopsy sampling and morphological verification of the diagnosis.

Given the high number of cases of late diagnosis and unsatisfactory treatment outcomes of CD in young children, the issue requires the development of a unified strategy and treatment approach.

CONCLUSIONS

1. CD in young children has such clinical features as combined lesions of the small and large intestines (45.45% of cases), high activity of the disease process according to the PCDAI index, frequent extraintestinal manifestations of the disease (54.54% of cases), and developmental delay (100% of cases). All young children with CD upon admission to the hospital were in severe condition, exhibiting signs of intoxication, diarrhea, and blood in their stools.
2. Laboratory findings in young children with CD are characterized by serum iron deficiency, dysproteinemia, and high levels of calprotectin.
3. Knowledge of the clinical and diagnostic features of CD in young children is essential for specialists involved in the treatment of such patients to provide appropriate medical care.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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RECEIVED: 27.05.2024
ACCEPTED: 18.09.2024