Clinical Characteristics of Idiopathic Ulcerative Colitis in Children

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INTRODUCTION

Idiopathic ulcerative colitis (IUC), beside Crohn’s disease, represents the most frequent clinical entity among chronic inflammatory bowel diseases [1, 2, 3]. It is characterized by diffuse mucosal inflammation most prominent in the distal parts of the colon, and in a smaller number of cases also in the region of the terminal ileum (“backwash ileitis”) [2, 4]. However, the increased usage of gastroscopy at the time of initial colonoscopy was followed by the understanding that histological lesions can be also seen on the gastric mucosa [5]. Depending on the extent of the inflammation of the colon, IUC is classified as proctitis, proctosigmoiditis, left-sided colitis and pancolitis [1, 2, 3]. In children the pancolic form is most frequent, occasionally occurring under the feature of “toxic colon” [3]. In addition, in a significant number of cases the disease is also followed by hepatobiliary and systemic manifestations [1, 2, 3].

According to the results of different regional studies, today 41.1-150:100,000 persons suffer from IUC, while the annual incidence ranges from 1.4-7.3:100,000 persons [1, 3]. Although the data for children are considerably fewer, it is estimated that both the prevalence and the annual incidence are almost identical to those in adults [1]. Also, it is known that the white race has a higher predisposition for the disease, particularly Ashkenazi Jews, as well as the population living in the developed countries, urban areas and regions with cold climate [6-9]. The difference in gender predisposition for the disease has not been proved [8, 9].

Although being recognized as a clinical entity 135 years ago, the pathogenesis of IUC has not been fully clarified until today [1, 2, 10]. It is considered that beside polygenic predisposition different environmental factors also play the basic role in the development of the disease [2, 6, 9-12]. The autoimmune hypothesis, based on the activation of macrophages in the large bowel mucosa by still unidentified antigens, is considered as most acceptable [2, 10]. According to this hypothesis the activated macrophages secrete proinflammatory cytokines which, by binding to the cell receptors of the immune system, lead to different autoimmune and paracrine effects resulting in an uncontrolled inflammatory process, i.e. bowel mucosa damage, as well as other manifestations of the disease. The most significant proinflammatory cytokines are interleukin-1 and -6, tumour necrosis factor alpha and chemokine IL-8 [10].

SUMMARY

Introduction Idiopathic ulcerative colitis (IUC) represents a rare disease of childhood. It usually occurs at age over 10 years, and below that exceptionally rarely.

Objective The aim of the paper was to analyze the clinical signs, symptoms and therapeutic procedures in children with IUC.

Methods The aims of the paper were based on a sample of 17 children (11 male and 6 female, mean age 11.90±3.50 years; range 3.8-17.5 years) with IUC. The disease diagnosis was based on characteristic endoscopic and pathohistological findings.

Results The basic signs of the disease involved chronic mucosal haemorrhagic diarrhoea which was confirmed in 16 of 17 patients, with body weight deficiency (10), recurrent abdominal pain (6), fever (5), slowed-down maturation (5), marked anorexia (4), and tenesmus (3). Two patients had recurrent aphthous stomatitis, 2 anal fissures, 2 arthralgia, one autoimmune hepatitis and one pyoderma gangrenosum. None of the children had longitudinal growth retardation. Elevated sedimentation rate and C-reactive protein levels were registered in 11, sideropenia in 10, anaemia in 6 and hypoalbuminemia in 3 patients. The remission of proctosigmoiditis and left-sided colitis was achieved with aminosalicylates, and of pancolitis with the combination of aminosalicylates and glucocorticoids, except in cases of steroid-dependent colitis, which additionally required azathioprine.

Conclusion The main signs of IUC in children are chronic mucous haemorrhagic diarrhoea, body weight loss and sideropenic anaemia, while the basic therapy consists of aminosalicylates, and in more severe cases the initial use of glucocorticoids and later azathioprine.

Keywords: idiopathic ulcerative colitis; clinical signs; children
OBJECTIVE

The study aim was to analyze symptoms, clinical and laboratory findings in children with IUC. In addition, therapeutic procedures, by which a complete clinical and laboratory disease remission was achieved, were also taken into consideration.

METHODS

The study goals were achieved on a sample of 17 children, 11 male and 6 female, aged 3.8 to 17.5 years (11.90±3.50 years), hospitalized due to IUC and treated from 2000 to 2007. Beside taking a detailed medical history involving the onset, type, character of the problems, and a complete clinical examination, including a precise measurement of body height (BH) and body weight (BW) compared to standard values, each patient also underwent corresponding laboratory analyses: erythrocyte sedimentation rate, C-reactive protein, a complete blood count with leucocyte formula, serum iron, total protein and albumin concentration in blood, ionogram, blood acid-base, hepatogram, prothrombin time, partial thromboplastin time, as well as three consecutive examinations of stool for pathogenic bacteria and Entamoeba histolytica [13]. In addition to the clinical examination, to define precisely the degree of the patient’s maturation, X-ray en-face images of the left hand were compared to the corresponding standard. After the required preparation, all patients underwent a video-gastroduodenoscopy and a total colonoscopy with multiple biopsies of the gastric mucosa, duodenum and colon. The obtained endoscopic findings, as well as biopsy locations were recorded in detail. Immediately after collection, the samples of gastric mucosa, duodenum and colon were immersed in a 4% puferized formalin solution and sent for a pathological analysis. IUC diagnosis was based on characteristic endoscopic and pathohistological findings. The exclusion of amebiasis and bacterial infections was of additional diagnostic and therapeutic significance.

The undertaken therapeutic measures that depended on the severity of the disease and achieved effect were recorded and analyzed in detail.

The frequency of symptoms, clinical signs and laboratory findings of IUC, as well as the effect of therapeutic procedures were presented in absolute numbers, while non-compliant BW related to the ideal for the corresponding age, gender and height is expressed in percentages.

RESULTS

Mean time from the onset of the disease symptoms to IUC diagnosis in our patients was 4.67±8.65 months. The predominant clinical sign of the disease was chronic mucosal haemorrhagic diarrhoea revealed in 16 of 17 patients, BW deficiency, recurrent abdominal pain, fever and anorexia (Table 1). Five patients had BW deficiency of over 20% compared to age- and gender-related standards, while BH was normal in all. Skeletal maturity retardation (range -0.33 to -2.33 years, mean value -0.75±0.79 years) was recorded in five patients; three with pancolitis and two with left-sided colitis. Two patients had aphthous stomatitis, 2 anal fissures and arthralgia, 2 aphthous stomatitis, one pyoderma gangrenosum and another one autoimmune hepatitis. The most frequent laboratory abnormalities were elevated sedimentation rate and increased C-reactive protein in blood recorded in 11 patients, sideropenia, anaemia and hypoalbuminemia (Table 2).

Of 17 patients, eight had left-sided colitis, six pancolitis and three proctosigmoiditis. None of the patients had either extraintestinal manifestations or microscopic changes of the gastric mucosa. The frequency of the extraintestinal manifestations and their association with the extent of bowel mucosa inflammation is presented on Table 3.

In children with rectosigmoiditis and left-sided colitis disease remission was achieved by application of aminosalicylates (40-60 mg/kg/day), and in pancolitis patients by aminosalicylates combined with prednisone (1-2 mg/kg/day, maximally 40 mg/kg/day) for 14 days. Fifteen patients were kept in remission by aminosalicylates (30-50 mg/kg/day), and two with steroid-dependent pancolitis by aminosalicylates combined with azathioprine (1.5-2 mg/kg/day). The therapeutic measures were not followed by any side-effects. None of the patients required specific diet or blood transfusion. Having in mind the probiotic characteristics of yoghurt, this dairy product was suggested to...

Table 1. Symptoms and clinical signs of idiopathic ulcerative colitis in 17 patients

<table>
<thead>
<tr>
<th>Symptoms/clinical signs</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic mucosal haemorrhagic diarrhoea</td>
<td>16</td>
</tr>
<tr>
<td>Body weight deficiency more than 10%</td>
<td>10</td>
</tr>
<tr>
<td>Recurrent abdominal pain</td>
<td>6</td>
</tr>
<tr>
<td>Fever</td>
<td>5</td>
</tr>
<tr>
<td>Anorexia</td>
<td>4</td>
</tr>
<tr>
<td>Tenesmus</td>
<td>3</td>
</tr>
</tbody>
</table>

Table 2. Basic laboratory findings in 17 patients

<table>
<thead>
<tr>
<th>Laboratory parameters</th>
<th>Number of patients</th>
<th>Range (X±SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elevated sedimentation rate</td>
<td>11</td>
<td>27-110 (41.67±33.51)</td>
</tr>
<tr>
<td>C-reactive protein &gt;5 mg/l</td>
<td>11</td>
<td>6-103 (29.93±32.37)</td>
</tr>
<tr>
<td>Serum iron &lt;10.7 μmol/l</td>
<td>10</td>
<td>2.7-9.9 (6.78±4.58)</td>
</tr>
<tr>
<td>Anaemia (Hb&lt;115 g/l)</td>
<td>6</td>
<td>60-109 (92.16±18.06)</td>
</tr>
<tr>
<td>Albumin level in blood &lt;37 g/l</td>
<td>3</td>
<td>26-28 (27.00±1.00)</td>
</tr>
</tbody>
</table>

X – mean value; SD – standard deviation
all. Iron deficiency recorded in 10 patients was corrected orally over a 2-4 month period. Also, the intake of multivitamin preparations during the first 2-3 months of recovery was suggested to all the patients.

**DISCUSSION**

At the time of diagnosis, the age of our patients was about 12 years, same as reported by other authors [7, 8, 10]. Some of them have indicated that the average age of the disease onset can be even considerably lower, which may be explained by a more expressed predisposition and/or higher influence of external factors, as well as by a better paediatric healthcare [20]. In our sample of patients the number of boys compared to those of girls was higher but without significance, as detected by other authors [7, 18, 19].

In our patients the average time elapsed from the onset of first symptoms to IUC diagnosis was rather long (about 4.5 months), but without any significant difference in comparison to other authors [7, 18, 19, 20]. Having in mind the fact that IUC is rare in children, the main reason for this occurrence is parents’ and/or the physician’s belief that the child is affected by infective disease which feature similar clinical presentation, such as amebiasis or relapsing bacterial diarrhoea. Initially, in several patients the disease had a mild course or their clinical symptoms predominantly consisted of extraintestinal manifestations. Two children were the victims of inadequate care; in one due to a premature death of both parents and in another due to parent’s low educational level.

The basic clinical signs of IUC in children are mucosal haemorrhagic diarrhoea, followed by abdominal pains, fever, anorexia, BW deficiency and tenesmus, which was also revealed in our group of patients [1, 2, 3, 7, 14, 21]. Other disease manifestations, such as aphthous stomatitis, anal fissures, autoimmune stomatitis, fever, retardation of longitudinal growth and maturity, arthralgia or arthritis, pyoderma gangrenosum and other were considerably rarer or rare [15-22]. In our group of patients fever and slowed-down maturation were recorded in less than one-third, while aphthous stomatitis, anal fissures and arthralgia in 4. Only one patient had pyoderma gangrenosum, another one autoimmune hepatitis, while a slowed-down longitudinal growth was not disclosed in any of the patients.

Increased erythrocyte sedimentation rate and C-reactive protein in blood, iron deficiency and sideropenic anaemia represent the basic laboratory findings in IUC patients [1, 2, 3, 6-10]. Increased erythrocyte sedimentation rate and C-reactive protein in blood, the non-specific indicators of inflammation, are in correlation with the severity of the disease and its extent. In IUC sideropenia and sideropenic anaemia are multifactorial disorders. In their pathogenesis, beside rectorrhagia and anorexia, the significant participant is a hepatic polypeptide hepcidin which, as a reactant of acute phase of inflammation, blocks the intestinal iron absorption, as well as its mobilization from the depot [23-26]. In the most severe forms of the disease, hypoalbuminemia develops as a consequent occurrence of exudative enteropathy and negative protein caloric outcome [1, 2, 3]. In our three patients with pancolitis and severe malnutrition serum albumin level was subnormal.

Left-sided colitis was recorded in half of our patients, pancolitis in one-third and rectosigmoiditis in three. In the initial phase of childhood IUC other authors also report similar findings [18, 19, 20]. Sharif et al. indicate at the possibility of focal gastritis, not only in children with Chron’s disease, but also in those with IUC [5]. In all our patients, concurrently with colonoscopy, we also performed esophagogastroduodenoscopy with multiple biopsies and pathohistological analyses of gastric and duodenal mucosa, and none showed pathological findings.

Aminosalicylates form the basic therapy of IUC, which, in the severe forms of the disease must be initially combined with glucocorticoids [1, 2, 3, 27]. In slightly lower dosages, these preparations are most often sufficient for sustaining disease remission, except in its resistant forms when they are combined with cytostatics or other immunosuppressive medications [1, 2, 3, 28, 29, 30]. In our patients with rectosigmoiditis and left-sided colitis, the remission was achieved with aminosalicylates only, while in those with pancolitis glucocorticotherapy was also necessary. In 15/17 of our patients aminosalicylates were sufficient for sustaining remission, except for two cases of steroid-dependent colitis in whose therapy azathioprine was added.

**CONCLUSION**

The predominant signs of IUC in children are chronic mucosal haemorrhagic diarrhoea, loss of body weight and sideropenic anaemia, recurrent abdominal pain, slowed-down maturation and anorexia. In the phase of disease diagnostics in almost half of the children we verified left-sided colitis, in one-third pancolitis and in one-fifth proctosigmoiditis. In children with rectosigmoiditis and left-sided colitis disease remission was achieved with aminosalicylates and in those with pancolitis by the combination of aminosalicylates and glucocorticoids. Sustained remission of the disease can be achieved with aminosalicylates, except in resistant cases when the application of azathioprine is also necessary.

**REFERENCES**