Crohn's disease of the small intestine: clinical course variants and problems of differential diagnostics

Leonid B. Lazebnik, Asfold I. Parfenov, Eleonora S. Sivash
Central Research Institute of Gastroenterology (CRIG),
Moscow, Russia

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In 2009 we shall notice 75-year of the first describing natural history of this disease by B. Crohn, L. Oppenheimer and G. Ginsberg in 1932.
Crohn's disease (CD) of small intestine (local granulomatous enteritis) is one of the most difficult one for diagnostics.

The problems are possible long-term non-signs natural history, often significances with the extraintestinal manifestations and complexity of visualization characteristic of the most part of the intestine.
For 1991-2005 in Department of Small Intestine Diseases of CRIG ys (Asfold I. Parfenov) 120 patients with small intestine Crohn’s disease (66 male and 54 female with age 23-77 ys) were observed.

- It was 1.2% of whole other patients with diseases of bowel.
- The first symptoms, that could be associated with CD at 53% of them where fixed with age of 20-30.
- With 82.5% of them the CD was diagnosed within 2-7 years after the appearance of the first clinical symptoms.
Affecting factors of the clinical picture:

- localization of injury,
- acuteness of the disease development,
- severity and extension of local inflammation,
- complications,
- extraintestinal manifestations.
Localization of inflammation

- With 77 pts (61.7%) process was localized in the terminal part of the ileum (terminal ileitis), in 32 pts in the caecum, in 8 pts in the ascending colon, and in 3 pts into the duodenum.

- So, 97.5% of pts suffering from CD of the small intestine had an affected distal part of the ileum, and 33.3% had a concomitant inflammation of the colon (mostly caecum)
Clinical forms of the small intestine
crohn’s disease (of the incoming for CRIG)

- Acute start
- Chronical recurrent
- Stenosing of intestine
Acute start
(n=36, 30.0%)

- Were hospitalized into the Surgery Department of CRIG because of heavy pain at right hypogastrium,
- Were operated on due to emergency indications,
- Terminal part of the ileum was resected with 17,
- Terminal part of the ileum plus segment of the small intestine was resected with 9,
- Resection of the ileum plus right hemicolectomy was made with 4.
Chronical recurrent (n=38, 31,6%)

- In the half of them inflammation restricted mainly to the submucous layer of the intestine.
- The initial clinical manifestations were fever, accelerated ESR, hyperleukocytosis and other signs of inflammation.
- A few months or years later the signs of a transmural lesion of intestinal wall and lumen constriction (chronical diarrhea, bleeding a. cramping pain) were appeared.
- So symptoms of malabsorption (anemia, loss of proteins, oedemas and less of body weight) were accrued.
Stenosis of intestine (n=46, 38.4%)

- Chronical abdominal pain and extraintestinal manifestations for a long time (episodes of unmotivated fever, pains in the joints, erythema nodosum, etc.).
- The disease can remain undiagnosed for many years. If it breaks out in the childhood, the patient can become physically disabled.
- Sometimes it is possible to reveal an infiltrate in the abdomen with the palpitation. Symptoms of intestinal obstruction can accrue later: cramping pains mostly in the right iliac region accompanied by vomiting, abdominal swelling, loud borborygmus, and stool and flatus retention.
- Visible peristaltics with occasional rising swells appears.
- The diagnosis is confirmed by an X-ray examination or laparotomy.
The mucous coat had an uneven relief. Cicatricial alterations of the wall resulted in the constriction of the intestinal lumen and development of partial and even complete intestinal occlusion.

- The inflammation extended to the serous coat and adjacent tissues and organs, which was confirmed by revealed fistulas and commissures as well as typical alterations of vessels.
Signs of the transmural lesion of the intestinal wall at CD

- The inflammation extended to the serous coat and and adjacent tissues and organs, which was confirmed by revealed fistulas and commissures as well as typical alterations of vessels.
- Arterioles thickened and were surrounded with conjunctive and tissue “couplers” constricting the lumen.
Extraintestinal manifestations of Crohn’s disease in observed 120 patients (CRIG)

<table>
<thead>
<tr>
<th>Localization</th>
<th>n</th>
<th>(%)</th>
</tr>
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<tbody>
<tr>
<td>Myoarthricular (arthritis, spondylitis, sacroileitis)</td>
<td>14</td>
<td>(11.7%)</td>
</tr>
<tr>
<td>Skin and mucousa (erythema nodosum, stomatitis)</td>
<td>8</td>
<td>(6.7%)</td>
</tr>
<tr>
<td>Eyes (iridocyclitis, keratoconjunctivitis)</td>
<td>5</td>
<td>(4.1%)</td>
</tr>
<tr>
<td>Total</td>
<td>27</td>
<td>(22.5%)</td>
</tr>
</tbody>
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**Extraintestinal manifestations of Crohn’s disease (collected literature database)**

<table>
<thead>
<tr>
<th>Localization</th>
<th>Characteristics</th>
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<tbody>
<tr>
<td>Skin</td>
<td>Sweet syndrome (acute dermatosis, pyoderma). Vesiculo-ulcerous and granulomatous lesions</td>
</tr>
<tr>
<td>Mucous coats</td>
<td>Granulomatous cheilitis, saliva glandulitis, stomatitis</td>
</tr>
<tr>
<td>Muscles</td>
<td>Myopathy</td>
</tr>
<tr>
<td>Eyes</td>
<td>Orbital myositis</td>
</tr>
<tr>
<td>Vessels</td>
<td>Aortitis, Takayasu's disease, Schönlein-Henoch vasculitis</td>
</tr>
<tr>
<td>Lungs</td>
<td>Granulomatous tracheobronchitis, sarcoidosis</td>
</tr>
<tr>
<td>Liver</td>
<td>Granulomatous hepatitis, sclerosing cholangitis.</td>
</tr>
<tr>
<td>Kidneys</td>
<td>Amyloidosis</td>
</tr>
<tr>
<td>Nervous,</td>
<td>Neuropathy. Epilepsy, depression</td>
</tr>
</tbody>
</table>
Diagnostics
In CRIG

the diagnosis of acute form of Crohn’s disease was confirmed within laparoscopy or laparotomy.
Sarcoid granulomas with Pirogov-Langhans cells located in the submucous layer and marked infiltration of the intestinal wall with lymphoid cells (A) and ulcers extending to the serous coat (B) were revealed in the surgery material in the intestinal walls in 40% of patients.
Clinical diagnostics of the primary chronic and stenosing forms of CD

- The diagnosis for the stenosing in primary chronic forms of CD was usually made 3-5 years after the appearance of clinical symptoms.
- A loss of body weight.
- An asymmetry of the stomach in some patients due to the infiltrates.
- Fe-a. or B₁₂-deficiency anemia in some patients.
- Stable hypoproteinemia.
Videoimage endoscopy
(small intestine of patient 45 ys with severe myopathy of uncertain genesis (CRIG)).

- Multiple erosions of the small intestine.
- The intestinoscopy in the middle parts of the small intestine revealed signs of granulomatous inflammation characteristic of CD.
- The treatment with Metypred and Pentasa arrested pains in the muscles and resulted in the morphological remission of CD.
Ileoscopy of terminal part of the ileum

- Oedema, uneven hyperemia, aphthosis (initial morphological alterations)
- Ulcers
According to the classification suggested by H. Herlingtr and D. Medlinte and based on X-ray morphological alterations, three stages of CD are distinguished:

- **Stage I – early alterations** (7.5%). Typical characteristics: thickening and straightening of folds, presence of multiple superficial ulcers being 0.1-0.2 cm in the diameter. The intestinal wall is still elastic.

- **Stage II – intermediate alterations** (22.5%). Nodular relief, ulcerations, rigidity of the mesenteric edge and bulging of the opposite edge in the form of pseudodiverticulums. The intestinal wall is thickened, and the width of the intestinal lumen is within the limits of the norm.

- **Stage III – marked alterations** (70%). Ulcerative and nodular relief (the “cobblestone pavement” symptom), presence of deep slot-like ulcerations and formed constriction of the lumen in the form of a cord. The distance between the loops is enlarged, and the walls are thickened and rigid.
X-ray film of the ileum  CD stage I

(Eleonora S. Sivash)

The folds are enlarged, there are multiple filling defects in the relief, $d \sim 0.2$ cm with a point depot in the center – aphthous ulcers.
1. An enlargement X-ray film of the terminal part of the ileum – constriction of the terminal loop in the form of a “cord” for a great length. Two blind ducts, one of them being ~2.5 cm long – fistulas.

2. A fragment of the X-ray film of the ileum. Shortening of the mesenteric edge of the ileum with the bulging of the opposite edge and formation of pseudodiverticulum.
Ultrasonography makes it possible to record the thickening of the intestinal wall (1) and infiltrate of small intestine (2).
Differential diagnostics
DISEASES

- Acute appendicitis
- Yersinious ileitis
- Follicular ileitis
- Chronic ulcerous non-granulomatous ileitis (jejunoileitis)
- Eosinophilic enteritis
Acute appendicitis

- In contrast for acute appendicitis, CD has a longer anamnesis with preceding exacerbations.
- Videoimage endoscopy and laparoscopy facilitates the differential diagnostics greatly (a. sudden morphology exam!)
Yersinious ileitis

- Clinical and morphological manifestations of Yersinious ileitis and CD can be very similar.
- Serological and bacteriological markers (antibody) of the Yersinia infection are positive.
- Opposite to Crohn’s disease, the clinical and morphological remissions of Yersinious ileitis begin under of the antibacterial therapy (diagnosis ex juvantibus).
Follicular ileitis

- A typical endoscopy symptom: **nodular lymphoid hyperplasia** forming an uneven relief of the mucous coat in the distal part of the ileum.
- **Acute follicular ileitis** develops in childhood simultaneously with measles or other infections. Its clinical picture looks at acute appendicitis. Laparotomy reveals hyperemia a. edema of terminal part of ileum and even NLH 10-20 cm longinity, infiltration and enlargement of mesenterial lymphoid nodes.
**Follicular ileitis**

- **Subacute follicular ileitis** develops within several weeks and is characterized by pains, diarrhea, nausea, vomiting and high temperature. An infiltrate can form in the right iliac region. Reasons: tuberculosis, yersiniosis, viral or some other infection.

- **Chronical follicular ileitis** is characterized by moderate pains in the right iliac region. Marked NLH forms a relief resembling that at CD. Difference: absence of sclerosis of the intestinal wall.

- **Non-sclerosing ileitis.** Etiology is unknown, yet in some cases it can be chronic Yersinia ileitis.
Chronic ulcerous non-granulomatous ileitis (jejunoileitis)

- A rare disease of unknown etiology. Symptoms: chronic diarrhea, enteropathy with a hypoproteinemia, emaciation, pains in the stomach, fever, anemia, leukocytosis.

- A histologic study of biopsy: atrophy of the intestinal mucousa with ulcerations and mostly lymphoplasmocytic infiltration of the plate in the mucous coat of the small intestine.

- The treatment with an agluten diet has no effect. Corticosteroids promote the remission.

- The prognosis is uncertain, and spontaneous remissions are possible.
Eosinophilic enteritis

- Its clinical and macroscopic morphological picture resembles that of CD very much.
- Differential and diagnostic criteria are infiltration of the mucous coat with eosinophils and absence of sarcoid granulomas.
Conclusion

- Successful early diagnostics of Crohn’s disease of small intestine is stipulated by the knowledge of clinical manifestations of the disease and well-directed search for jointly brain storming with gastroenterologist, abdominal surgeon, roentgenologist, endoscopist a. morphologist.