

# **PERSPECTIVES OF WORLD SCIENCE AND EDUCATION**

Abstracts of XIII International Scientific and Practical Conference

Osaka, Japan

9-11 September 2020

**Osaka, Japan**

**2020**

**UDC 001.1**

The 13<sup>th</sup> International scientific and practical conference “Perspectives of world science and education” (September 9-11, 2020) CPN Publishing Group, Osaka, Japan. 2020. 256 p.

**ISBN 978-4-9783419-8-3**

The recommended citation for this publication is:

*Ivanov I. Analysis of the phaunistic composition of Ukraine // Perspectives of world science and education. Abstracts of the 13th International scientific and practical conference. CPN Publishing Group. Osaka, Japan. 2020. Pp. 21-27. URL: <https://sci-conf.com.ua/xiii-mezhdunarodnaya-nauchno-prakticheskaya-konferentsiya-perspectives-of-world-science-and-education-9-11-sentyabrya-2020-goda-osaka-yaponiya-arhiv/>.*

**Editor**

**Komarytskyy M.L.**

*Ph.D. in Economics, Associate Professor*

Collection of scientific articles published is the scientific and practical publication, which contains scientific articles of students, graduate students, Candidates and Doctors of Sciences, research workers and practitioners from Europe, Ukraine, Russia and from neighbouring countries and beyond. The articles contain the study, reflecting the processes and changes in the structure of modern science. The collection of scientific articles is for students, postgraduate students, doctoral candidates, teachers, researchers, practitioners and people interested in the trends of modern science development.

**e-mail:** [osaka@sci-conf.com.ua](mailto:osaka@sci-conf.com.ua)

**homepage:** <https://sci-conf.com.ua>

©2020 Scientific Publishing Center “Sci-conf.com.ua” ®

©2020 CPN Publishing Group ®

©2020 Authors of the articles

**TO THE QUESTION OF THE COMPLEXITY OF DIFFERENTIAL  
DIAGNOSIS OF ILEOCEAL TUBERCULOSIS  
AND CROWN DISEASES**

**Yevstihnieiev Ihor Volodymyrovych**

c.m.s., assistant

State Institution “Dnipropetrovsk Medical  
Academy of Health Ministry of Ukraine”

**Abstract.** The article discusses the problems of diagnosis and differential diagnosis of Crohn's disease (CD) and tuberculosis ileocecalis (TI). Endoscopic and radiation research methods, histological diagnostics, bacterioscopy, culture on nutrient media, molecular genetic methods, unfortunately, do not always make it possible to reliably differentiate these two diseases. The incidence of diagnostic errors for CD and TI can reach 30-40%. TI is the most common lesion of the gastrointestinal tract. The predisposition of the terminal ileum to tuberculosis infection is due to several factors: stasis in this part of the intestine, closer contact of the pathogen with the mucous membrane, accumulation of lymphoid tissue [1, p. 14831]. Clinical manifestations range from acute lesions to chronic and subclinical. Abdominal tuberculosis (AT) has been called the “great mystifier,” although this expression can be applied to all manifestations of extrapulmonary tuberculosis (TB).

**Key words:** abdominal tuberculosis, Crohn's disease, ileocecal tuberculosis, differential diagnosis, diagnostic methods.

The concomitant lesion of the jejunum in TI can be manifested by the presence of single or multiple strictures of varying length. Although jejunal lesions are rare in non-TI TB, differential diagnosis with CD is done in the presence of strictures. One of the complications of small intestine TB can be intestinal obstruction with the

progression of hyperplastic thickening of the intestinal wall, narrowing of the lumen and adhesions.

With intestinal TB, ulcerative and ulcerative-hyperplastic lesions are distinguished. These two types of morphological changes can occur simultaneously. Morphological manifestations in small intestine TB are manifested in a wide range, there are often difficult situations in the differential diagnosis of CD.

Genetic disorders in these diseases are observed to a certain extent at the same chromosome loci, and there are also some general developmental mechanisms in pathogenesis. First of all, the development of a chronic granulomatous inflammatory process should be noted. These two diseases occur on the background of a congenital defect in the immune system and infection with the formation of granulomas.

The similarity of abnormalities in the genome is to some extent confirmed by the similarity of phenotypic manifestations with the absence of pathognomonic symptoms. Not only clinical symptoms are similar, but also changes in the intestine during colonoscopy with ileoscopy, as well as the results of histological examination. Caseous necrosis as a morphological criterion of the tuberculous process is not always easy to identify, especially in the treatment of concomitant diseases, the appointment of antibacterial drugs, in particular, fluoroquinolones and amikacin.

One of the “masquerade” manifestations of TB complications in the distal ileum, which is especially common in children, is the occurrence of vitamin B12 deficiency. Against the background of macrocytic anemia with the development of dystrophic and atrophic changes in the cerebral cortex, the child becomes irritable, tearful, problems with schooling arise. The main clinical symptoms are represented by severe weakness, decreased performance, fever, bedwetting, dysarthria may occur.

With progressive damage to the central nervous system, convulsions, ataxia, paraplegia occur. At TI, the demyelination process develops in the nervous system with clinical manifestations of polyneuropathy.

Late diagnosis of TI also leads to progressive bowel stenosis, and bowel perforation may occur. In both CD and TI, the ileocecal region is more commonly affected. By the nature of the ulcers during endoscopic examination, TI can be

assumed, however, with the destruction of the ileocecal valve, the diagnosis becomes more complicated. Ulcers can also be on the mucous membrane of the cecum with indistinct endoscopic criteria and the absence of pathognomonic symptoms.

The optimal choice of lesion sites for taking multiple biopsies is important. The presence of granulomas with caseous necrosis, detection of *Mycobacterium tuberculosis* (MBT) during bacterioscopy of a biopsy specimen, obtaining a culture after sowing on nutrient media make it possible to confirm the diagnosis of TI. According to the authors, the sensitivity of the culture method in the study of biopsies at TI is about 70% [2, p. 495].

Material after surgical interventions and autopsies is also being examined. In certain situations, the presence of DNA MBT in biopsy specimens confirms the diagnosis, taking into account clinical symptoms, radiation and laboratory research methods.

ELISA and other immunological methods are used to detect anti-neutrophil cytoplasmic antibodies and anti-*Saccharomyces cerevisiae*. These antibodies are considered specific for CD, however, sometimes high titers of these antibodies in the blood can be detected at TI. When conducting differential diagnosis of TI, T-SPOT based on serum antibodies and immunohistochemical methods with antibodies to MBT antigens in biopsies are also used.

A positive response to anti-tuberculosis therapy with no recurrence of TI is also important. In the diagnosis, cases are difficult in the treatment of confirmed CD and development against the background of drug-induced immunosuppression of TI, or a combination of specific and nonspecific processes with lesions of the ileocecal region.

Only the data of colonoscopy with ileoscopy based on endoscopic conclusion about the presence of TI are inconclusive without histological confirmation of caseous necrosis in granulomas, detection of MBT or DNA MBT.

**The data below on the possibility of verifying tuberculous intestinal lesions confirm the problems of diagnosing these two diseases [3, p.2]:**

- On histological examination of intestinal biopsies, caseous necrosis in granulomas is determined in 66-86% of patients with TI [4, p. 473];
- Detection of MVT in preparations by microscopy with Ziehl-Nielsen staining is possible in 30% of patients with TI;
- The growth of MBT in tissue culture biopsies is less than 20%;
- The ability of the polymerase chain reaction (PCR) to detect MBT DNA in biopsies varies widely from 22% to 75%.

The presence of certain common mechanisms in the development of CD and TI is accompanied by a phenotypic similarity in clinical symptoms with the possibility of developing TI during treatment with CD. With inflammatory bowel diseases, it can be difficult to answer the question: there is an exacerbation of the underlying disease or the addition of a tuberculous inflammatory process.

This problem is especially relevant for developing countries, where the prevalence of both CD and TI is about 2%. So when an ulcerative lesion is detected for the first time in the ileocecal section by an endoscopist, the probability of CD and TI is 50% to 50%. It is important to select the most informative areas of the intestine for biopsy as possible.

Difficulties in diagnosis are caused not only by pathogenetic general mechanisms and phenotypic similarities, but also by the low predictive value of negative results of both histological and laboratory research methods. Thus, the inability to confirm the tuberculous process does not mean its absence. One of the important reasons for the problems of differential diagnosis of these diseases is TB pathomorphosis in modern conditions.

Endoscopic examination of the intestine. Ulcerative lesions in TI and CD are similar, more often isolated, superficial or deep ulcers. Areas of narrowing of the intestinal lumen with hypertrophic and nodular formations often alternate with ulcerative lesions with stenosis. Circular ulcerative lesion is determined in about half

of patients with TI, and in every fourth patient - ulcerative-proliferative or proliferative intestinal lesion.

To exclude erroneous diagnoses, taking into account the increase in the population of the number of cases with lesions of the ileum and the initial part of the cecum during colonoscopy, it is often necessary to conduct ileoscopy with examination of the terminal ileum. Longitudinal ulcers in most cases are identified with CD.

Ultrasound diagnosis (UD) CD of the small intestine. Among patients with inflammatory bowel disease, CD is about 40%, with more frequent small bowel involvement. The advantages of UD as a method for CD are: the absence of contraindications, the need for special training, non-invasiveness, accessibility, the ability to assess the condition of several parts of the abdominal cavity and pelvis.

**Indications for small bowel UD:**

- Pain syndrome in the right lower quadrant of the abdomen (both acute and chronic);
- Initial diagnosis in patients with suspected CD;
- Determination of the localization and degree of activity of the process;
- Diagnosis of CD complications;
- Observation of the patient in dynamics during treatment.

**The CD draws attention to:**

- Thickening of the wall of the small intestine from 4 to 10 mm, depending on the activity of the process;
- Thickening of the wall of the small intestine due to 3 layers (transmural lesion);
- Ulcers and erosions are accompanied by a lack of clear differentiation of the layers of the small intestine, hyperechoic inclusions in the submucosal layer;
- Enlargement of mesenteric lymph nodes, inflammatory infiltration of surrounding tissues;
- Complications (infiltrates, stenoses, fistulas, stenoses).

The results of treatment can also be assessed by the thickness of the wall of the small intestine. The UD method is sensitive in assessing the thickness of the intestinal wall with a decrease in infiltration during treatment. With the progression of sclerosis in the submucous layer of the ileum, the wall may be thickened up to 4-5 mm. With the progression of stenosis and narrowing of the intestinal lumen, the thickening may be somewhat larger. The method allows you to assess the localization of the pathological process and ulcerative defects.

UD of the small intestine is advisable to be carried out as a screening for the primary diagnosis of CD in the centers of medical and social care, as one of the methods of radiation diagnostics and to control the decrease in the infiltration of the intestinal wall in the lesions during treatment. Prevention of unnecessary appendectomies seems to be important in the use of UD.

With CD, the appendicular process and the cecum can be involved in the inflammatory process. Acute appendicitis with CD may also occur in the absence of an ileal lesion. The tactics when conducting screening using UD and an ileal wall thickness of 2-4 mm often consists in the appointment of laboratory examination methods to clarify the diagnosis. Endoscopic techniques and, in some cases, CT enterography (CTE) are more common if the ileal wall is  $\geq 4$  mm thick.

X-ray diagnostics. The manifestations of AT are nonspecific. This disease should be ruled out in patients with unexplained abdominal symptoms, risk factors, and differential diagnosis with CD.

X-ray with barium sulfate contrast is a laborious method, requires preparation of the patient, is used when endoscopy is impossible and expensive CTE. The inability to study biopsies and radiation exposure, insufficient information content compared to CTE reduce the capabilities of this method, although it is used in certain clinical situations (for example, control of the transit of contrast through various parts of the gastrointestinal tract).

In 70% of patients with TI, X-ray examination of the chest organs does not detect pathological changes [5, p. 278].

Several radiological symptoms have been described in TI, such as Stirlin's symptom. It occurs against the background of an exacerbation of a chronic inflammatory process involving the terminal ileum and cecum. There is a rapid advancement of contrast from the terminal ileum, the walls of the cecum in the region of the dome are rigid, and partial obliteration occurs in this segment of the large intestine.

Multispiral computed tomography (MCT) in the diagnosis of diseases of the small intestine is one of the leading methods in the diagnosis of diseases of this part of the intestine. The advantages of the method are objectivity, reproducibility, and the ability to record on digital media. Intravenous bolus administration of contrast agents makes it possible to clearly visualize pathological changes. The method provides a unique opportunity for 3D post-processing and scan reconstruction. MCT allows you to simultaneously assess the condition of all organs of the abdominal cavity.

The main areas of MCT use include the diagnosis of inflammatory diseases of the small intestine and tumors (including lymphomas) of this part of the intestine. CT enterography (CTE) includes 2 components: 1) filling the small intestine with a neutral medium for 1.5 hours before the study (2 liters of water); 2) intravenous bolus injection of contrast to visualize all layers of the small intestine.

#### **Tasks of CTE:**

1. Determination of the localization and prevalence of the inflammatory process;
2. Assessment of the degree of the inflammatory process after visualization of the thickness of the intestinal wall layers and their density;
3. Visualization of stenosis and pretenotic extensions;
4. Diagnosis of complications (interintestinal fistulas and adhesions, stenoses, abscesses);
5. The condition of the regional lymph nodes.

#### **MCT signs of the active stage of CD include:**

- Uniform diffuse thickening of the walls of the small intestine;
- Swelling of the submucosal layer;
- Increased accumulation of contrast by the mucous membrane;

– Stratification of the wall of the small intestine in the affected areas.

Postinflammatory changes in CD include fatty inclusions in the submucosa. When assessing the surrounding fatty tissue, attention is paid to the edema of the mesentery, its infiltration. Vascular arcades are determined, approaching the intestinal wall at a right angle (comb symptom). The condition of the mesenteric lymph nodes is also assessed.

SKE is also used as a method in the diagnosis of non-inflammatory bowel diseases such as celiac disease. In this disease, expansion of the loops of the small intestine with atrophy of the villi and a decrease in the height and number of folds are determined. Thus, CTE is a sensitive (90%) and specific (95%) method in the diagnosis of diseases of the small intestine.

MCT is also used in the diagnosis of tumors of the small intestine, in particular lymphomas and gastrointestinal stromal tumors. Ileal lymphoma is manifested by uneven thickening of the intestinal wall, accumulation of contrast and narrowing of the lumen.

Changes in TI and CD after MCT and CTE are often indistinguishable. It is necessary to take into account the possibility of developing a tuberculous process against the background of the appointment of immunosuppressants for CD.

One of the important tasks is the use of informative methods in the detection of MVT. The classic is the confirmation of the diagnosis of TB with the staining of sections with carbolic fuchsin according to the Ziehl-Nielsen method. The diagnosis is confirmed by identifying acid-fast bacteria. However, mycobacteria may be absent in biopsy sections if PCR is positive. It is informative to conduct an immunohistochemical reaction with serum to antigens of the mycobacterial complex, however, despite the high sensitivity and specificity, this method is not always available. When staining with hematoxylin-eosin, sections of necrosis, lumps, similar to those in karyorrhexis and disintegration of neutrophilic granulocytes, can be determined in sections [6, p. 34].

Also, these lumps were determined in the same sections when stained according to Ziehl-Nielsen. Acid-fast bacteria are either absent altogether, or are detected in

insignificant quantities. Epithelioid and giant cells are often determined in small numbers. Immunohistochemical study gives a positive reaction with specific serum with the identification of coccoid structures, predominantly extracellular. The identification of such structures requires additional evidence for the presence of morphologically altered acid-fast bacteria.

It is difficult to interpret morphological changes in biopsy specimens with pronounced alterative manifestations, which are more often observed in acute forms of TI and pronounced exacerbations of the chronic inflammatory process. The identification of the mycobacterium species and genotype is of clinical and epidemiological importance.

Currently, special attention is paid to the Beijing genotype B (I) strain. It is a drug-resistant W-strain with pronounced pathogenic properties. Often found in extrapulmonary TV, prone to dissemination and generalization. The Beijing strain expresses a large number of pro-inflammatory cytokines (IL-1 $\beta$ , IL-12, TNE- $\alpha$ ) [6, p. 36].

The high level of expression of these proinflammatory cytokines, which does not depend on the level of the infectious pathogen, is important. Under conditions of non-sterile immunity after BCG vaccination and the action of local (abortive) strains, exposure to the Beijing strain leads to an immune conflict. The Beijing strain is able to cause an inflammatory process with a small number of microorganisms in the lesion [6, p. 36]. Reactivation of the old lesion or superinfection occurs.

Patients may be infected with mycobacteria of various strains and subtypes. Another problem is the combination of TB with other infections, it has been developed to a certain extent in the presence of HIV infection and TB; in many clinical situations, methods for identifying other pathogens are not used, mainly due to their high cost.

The presence of granulomas with caseous decay, specific mesenteric adenitis, transmural lesions of the intestinal wall suggests the presence of TI, not CD. At TI, minimal central necrosis in the granulomas of the submucosal layer can be determined. On the periphery are epithelioid cells and several giant cells of

Langhans. Thus, many issues of TB pathogenesis in modern conditions remain insufficiently studied.

TB pathomorphosis leads to the appearance of strains with pronounced expression of proinflammatory cytokines, when PCR with biopsy sections is positive, and microscopy and culture for acid-fast bacteria give a negative result, while the number of epithelioid and giant cells may be insignificant, caseous necrosis in granulomas is weak.

At the same time, it is often not possible to identify typical acid-fast mycobacteria in biopsy sections, and predominantly located extracellular polymorphic cocci are not stained according to Ziehl-Nielsen, but give positive results of the immunohistochemical method using specific antibodies to antigens of acid-fast mycobacteria.

Further study of the course of a specific inflammatory process in conditions of the simultaneous presence of a nonspecific inflammatory process, irrational treatment of concomitant diseases with antibacterial drugs, especially fluoroquinolones and amikacin, is also promising. An interesting problem is a comprehensive assessment of the possibility of developing TI in the treatment of CD and the optimal use of methods for early diagnosis of developing tuberculosis infection.

The most important task in the study of tissue biopsies is the optimization of methods for the detection of acid-fast mycobacteria and the improvement of morphological studies using immunohistochemical methods.

In patients with a probable diagnosis of TI, an examination is carried out to exclude bronchopulmonary TV, as well as damage to the lymph nodes in the mediastinum. In isolated terminal ileitis, TI is excluded (identification of *M. tuberculosis* or *M. bovis*, granulomas with caseous necrosis are determined), CD, sarcoidosis, nonspecific inflammatory bowel diseases (identification of *Yersinia* spp., *Salmonella* spp.). In the presence of ulcers in the ileum and cecum, amoebiasis and clostridial infection should be excluded.

## REFERENCES

1. U Debi, V Ravisancar, K Prasad et al. Abdominal tuberculosis of the gastrointestinal tract: Revisited. *World Journal of Gastroenterology*. 2014 Oct 18; 20 (40): 14831-14840. Published online 2014 Oct 28. Doi: 10.3748/wjg.v20.i40.14831.
2. Burke KA, Patel A, Jayaratnam A et al. Diagnosing abdominal tuberculosis in the acute abdomen. *Int J Surg*. 2014; 12: 494-499.
3. Ileo-Colonic Tuberculosis: Diagnostic Challenge /D. Epstein //Falk Foundation, Istanbul. 2007; <http://www.drfalkfarma.de/filadmin/media/praesentationen/fs159/s2p1.Pdf>.
4. Gan H, Mely M, Zhao J. Analysis of the clinical, endoscopic and pathologic features of intestinal tuberculosis. *J Clin Gastroenterol*. 2016; 50: 470-475.
5. Gurzy S, Molnar C, Contac A et al. Tuberculosis terminal ileitis: a forgotten entity mimicking Crohn's disease. *World J Clin Cases*. 2016; 4 (9): 273-280.
6. VA Zincerling, VV Svistunov, VE Karev et al. Morphological diagnosis of tuberculosis under present-day conditions. *Pathology archive*. 2015; 3: 33-39. Doi: 10.17116/patol20157733-9(p.3-9).