# **OPISTHORCHIASIS AND VIRAL HEPATITIS B: CLINICAL CASES**

OPISTORCHOZA I WIRUSOWE ZAPALENIE WĄTROBY TYPU B: PRZYPADKI KLINICZNE

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#### ABSTRACT

Introduction: Among the cases of biohelminthosis, which are registered in Ukraine, opisthorchiasis is the most common and constitutes the second largest centre in Europe. Due to the growth of migration processes and global tourism, opisthorchiasis is becoming increasingly relevant for the countries of the European Union and the United States. Under modern conditions, the clinical course of many infectious and parasitic diseases has changed.

The aim: The present paper discusses and analyzes the cases of opisthorchiasis and hepatitis B virus which are challenging in terms of diagnostics and choice of treatment tactics. Conclusion: The course of acute infections, the formation of results and the effectiveness of treatment are influenced by a number of factors, among which mixed infections are of particular interest.

KEY WORDS: opisthorchiasis, hepatitis B, diagnostics, treatment tactics.

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#### INTRODUCTION

Opisthorchiasis is a natural and focal biohelminthosis caused by trematode parasites (Opistorchis felineus and Opistorchis viverrini). It is characterized by the predominant lesion of the liver, gallbladder, pancreas and has a systemic effect on health, increases susceptibility to other infections, modifies the course of concomitant diseases, and possesses a carcinogenic effect [1,2,3].

The cases of opisthorchiasis caused by Opistorchis felineus are registered at the territory of Ukraine and the European Union (EU). The area of its prevalence extends from the Yenisei river basin to the western borders of Europe, however, the disease is focal in nature. The largest focus of opisthorchiasis in the world has been formed in the Ob-Irtysh river basin, where the infection rate reaches 65-95% [1,3,4,5]. In Ukraine, opisthorchiasis is recorded in virtually all regions, but the level of contamination of population by opisthorches, according to different authors, varies from 0.2% to 60.0% depending on the region. The largest endemic focus of opisthorchiasis is the Dnieper river basin – Sumy and Poltava regions [6,7].

Due to the growth of migration processes and global tourism in the world, opisthorchiasis is increasingly registered in the countries where the disease is not endemic [8,9]. As a rule, the contamination with Opistorchis felineus occurs due to consumption of infected raw or pickled fish of the carp family during visits to endemic areas or as a result of illicit traffic of this fish from endemic regions [3,9,10]. In addition, the emigration of population from the endemic regions of Ukraine and Russia to the countries of North America, Western Europe and Israel over the past decades has led to the influx of people with latent chronic opisthorchiasis [3,9,10]. However, health workers from non-endemic regions lack any alertness about this disease, which impedes the timely diagnosis. In addition, the expansion of opisthorchiasis habitat is possible. Interesting is the fact that in Italy from 2003 to 2011 there were 8 outbreaks of acute opisthorchiasis, in which 211 people died. Contamination occurred due to the consumption of raw fish from two lakes in central Italy [11,12,13]. Moreover, the scientific literature of recent years with increasing frequency reports the detection of Opistorchis felineus among animals (red fox, ferrets, dogs, cats, fish and mollusks) in Germany, Italy, Poland, Portugal and Spain [3,10,13,14]. The present data indicate the likelihood of circulation of Opistorchis felineus in the EU countries in a latent form for many years.

It is generally accepted that clinical manifestations of opisthorchiasis are characterized by non-specificity and polymorphism of symptoms, which complicates the diagnosis [11,12,15]. Meanwhile, the timely detection of the acute phase of the disease is extremely important in terms of prescribing the adequate specific treatment, prevention of chronic process and adverse effects. Certain difficulties also arise in doctor's practice at the stage of verifying the diagnosis of acute opisthorchiasis. This is due to frequent absence of Opistorchis felineus eggs in the duodenal content and feces for a long time after contamination. Existing serological diagnostic methods are also insufficiently sensitive and specific, therefore, the detection or absence of specific



Figure 1. Dynamics of biochemical parameters

antibodies to Opisthorchis in the blood is not a valid basis for the diagnosis or its exclusion [10,11,15]. Therefore, the epidemiological history and a set of clinical and laboratory data are crucial in the diagnosis of opisthorchiasis.

Despite the fact that acute opisthorchiasis currently retains typical features [6,7], the presence of concomitant pathology in patients, as well as combined (mixed) infection with the predominant lesion of the hepatobiliary tract complicates the diagnostic search, leads to errors in differential diagnosis and raises difficulties in the choice of treatment tactics. It is known that the presence of opisthorchiasis invasion masks and / or aggravates the course of other pathological processes, and in its turn, the infection that runs with the liver damage, irrespective of their clinical form (manifested or latent), affects the course of opisthorchiasis [2,3,4, 5].

From this point of view, the combination of opisthorchiasis with diffuse liver lesions of viral etiology is particularly relevant, since viral hepatitis B and C constitute an important, socially significant infection both in Ukraine and throughout the world. According to the degree of negative influence on the health of population and the level of morbidity, viral hepatites in Ukraine occupy a dominant place in the structure of infectious pathology and account for about 30% of all infectious diseases [1].

In connection with the aforesaid, particular attention is given to examples of clinical cases with combination of opisthorchiasis and hepatitis B virus (HBV).

# THE AIM

The present paper discusses and analyzes the cases of opisthorchiasis and hepatitis B virus which are challenging in terms of diagnostics and choice of treatment tactics.

## **RESULTS AND DISCUSSION**

**CLINICAL CASE 1** 

A patient, aged 26, a shop assistant at the grocery super-

market, was hospitalized on September 14, 2012 at the infectious diseases clinic for 7 days with the diagnosis of «acute hepatitis A?». At hospitalization: complaints of icterus of the skin and sclera, darkening of the urine, feces discoloration, discomfort in the epigastrium, nausea, repeated vomiting, lack of appetite, general weakness, itching of the skin, temperature rise up to 37.4°C. From the epidemiological history, it was found out that in July 2012, she had rest in Crimea, where during the excursions drank water from mountain sources; 3 weeks before the disease, she ate pickled fish (carp) which was cooked at home. The patient lives in the Orzhytsya district of the Poltava region, which is endemic in opisthorchiasis. Three years ago, the patient underwent a long-term treatment at the dentist's office with teeth extraction and prosthetic care. Physical changes: low-grade fever, jaundice, moderate hepatomegaly. At the additional examination in the clinical blood analysis – leukocytosis (11.3x10<sup>9</sup>/l), expressed eosinophilia (62%); in the biochemical blood assay – increased bilirubin level (96 µmol/l) and transaminases (ALT - 178 U/l, AST - 149 U/l, ALP - 791 U/l); in the ultrasound study of the abdominal cavity – hepatomegaly. In multiple coproovoscopy using formalin-ethereal mixture - no eggs of helminths and protozoa were found. In the screening for viral hepatitis A, B and C, as well as HIV – negative results. We diagnosed acute opisthorchiasis and prescribed symptomatic treatment.

Against the background of the conducted treatment (antibiotics, detoxification agents, sorbents, hepatoprotectors), there was a wave-like character of jaundice with repeated clinical and biochemical exacerbations, characterized by the increase in temperature to subfebrile numbers, the increase in dyspeptic and intoxication syndromes, increased level of total bilirubin due to direct fraction, ALT and alkaline phosphatase (Fig. 1).

The hemogram retained leukocytosis (10.5-12.6x10<sup>9</sup>/l), eosinophilia (44-67%), in the ultrasound study of the abdominal cavity, the dynamics revealed the signs of

cholecystocholangitis, splenomegaly joined to hepatomegaly. In connection with the wave-like course of jaundice, prolonged increase in transaminases and preservation of low-grade fever, re-examination for viral, autoimmune hepatites, helminth invasions was conducted, as well as examination for the exclusion of mechanical jaundice and verifying the diagnosis of acute opisthorchiasis. Examination in the dynamics: on the 58th day of the disease, the eggs of Opistorchis felineus were found in coproovoscopy; in the PCR study of blood, HBV DNA was detected (1.74x10<sup>4</sup> IU/ml), by ELISA method, serological markers of HBV were found (HBsAg, anti-HBe, anti-HBcor (total) with negative - anti-HBs and HBeAg) and autoimmune (ANA – 1:3200 with negative AMA-2). Final diagnosis: Acute opisthorchiasis against the background of chronic hepatitis B (HBeAg-negative), the replicative phase of moderate activity with autoimmune syndrome.

In view of the prolonged course of the disease, the remitting character of jaundice, preservation of leukocytosis, eosinophilia, high levels of total bilirubin (149.1 mmol/l), ALT (284.7 U/l), alkaline phosphatase (341 U/l), and the presence of autoimmune syndrome, we decided to carry out dehelminthization with praziquantel at a daily dose of 10 mg/ kg of the body weight, in combination with detoxification and desensitizing therapy (including glucocorticosteroids). After dehelminthization, the patient's condition improved, within 2 weeks jaundice disappeared, dyspeptic phenomena diminished, body temperature and hemogram rates normalized; however, the increased ALT level remained at 238 U/l, AST – up to 99.6 U/l, ALP – up to 187 U/l.

In January 2013, 3 months after the episode of acute opisthorchiasis, the patient repeatedly presented with complaints of periodic pain in the right hypochondrium, nausea in the morning, itching of the skin. Physical data: subicteric sclera, hepatosplenomegaly. At the additional examination: eosinophilia - 14%, total bilirubin - 34 µmol/l, ALT – 45 U/l, AST – 32 U/l, ALP – 120 U/l; in the ultrasound study of the abdominal cavity – diffuse changes of the liver, signs of cholecystopancreatitis; the fibroscan data - F0-1 according to METAVIR; in coproovoscopy, the eggs of Opistorchis felineus were found. Blood analysis using PCR method revealed HBV DNA (2.5x10<sup>4</sup> IU/ml) in the absence of autoimmune markers (ANA, AMA-2 negative). The patient was prescribed a repeated course of dehelminthization with praziquantel. After re-treatment within a month, the hemogram and biochemical parameters were completely normalized.

The follow-up study of the patient lasted for three years. During this period, no episode of clinical and biochemical exacerbation of opisthorchiasis was registered. No complaints. At the physical examination – nothing abnormal detected. In the screening for HBV: in blood tests by PCR (12.04.16.) – HBV DNA less than 75 IU/ml, by ELISA method, ANA – not detected, HBsAg, anti-HBe, anti-HBcor (total) are preserved at negative HBeAg and anti-HBsAg; in the ultrasound study of the abdominal cavity – no pathology detected; in the fibroscan data – F0 according to METAVIR.

The given case is of interest because the patient had a mixed pathology of the hepatobiliary system, which determined the peculiarities of the clinical course and laboratory diagnosis of both acute (opisthorchiasis) and chronic (CHB) infectious processes. Thus, acute opisthorchiasis had an atypical wave-like course with increased clinical and laboratory signs of the liver damage, which can be explained by the polyetiologic lesion of the hepatobiliary tract. Attention was attracted by the late verification of the diagnosis of acute opisthorchiasis, as well as the absence of markers of hepatitis B in the acute period of helminthic invasion, due to immunosuppressive action of pathogens. For a practitioner, the issue of the timing of dehelminthization in the context of constantly high rates of cytolysis, cholestasis and autoimmune markers turned out to be a challenge. The prescription of praziquantel against the background of detoxification and desensitizing agents with the inclusion of glucocorticosteroids fully justified itself and led to the normalization of clinical and biochemical indicators.

# **CLINICAL CASE 2**

Patient K., aged 26, a manipulation nurse at the ophthalmologic clinic, was hospitalized in June 2016 at the infectious diseases clinic on the 5th day of the disease with complaints of nausea, bitter taste in the mouth, icterus of the skin and sclera, darkening of the urine, weakness. From epidemiological anamnesis: the patient was not vaccinated against hepatitis B; 2 months ago, there was an episode of injury with an injection needle during the intravenous manipulation; the patient regularly undergoes medical examinations for the markers of viral hepatitis B and C, which were identified as negative in January 2016; 3 months ago the patient underwent tooth extraction at the dentist's office. During the last 2 years, she consumes pickled fish from the carp family (home-cooked). Physical data: jaundice, hepatomegaly. At the additional examination: in the complete blood count – neutrophilosis 15%, in biochemical study: total bilirubin 104.1 mmol/l, ALT 736.6 U/ml, AST 1398.1 U/ml, fibrinogen 1.78 g/l, in the ultrasound study of the abdominal organs: moderate hepatosplenomegaly. In the blood test by PCR: HBV DNA - detected, HCV RNA - not detected; serological markers of HBV (HBsAg, anti-HVcor IgM) were detected by the ELISA method.

In coproovoscopy with the use of formalin-ethereal mixture – no eggs of helminths and protozoa were found. Clinical diagnosis: Acute hepatitis B, icteric form. Symptomatic treatment (diet, detoxification agents, sorbents) was prescribed. During the week, jaundice intensified, low-grade fever joined, hepatomegaly remained at the same level. At the additional examination: in the complete blood count appeared monocytosis – 21% and eosinophilia – 7%; in the biochemical study – the increased level of general bilirubin up to 181.4  $\mu$ mol/l, ALT up to 1791 U/l, AST up to 1001 U/l, ALP up to 242.5 U/l, LDH up to 531 U/l, GGT up to 278.1 U/l. In coproovoscopy, the eggs of Opistorchis felineus were found. Final diagnosis: Acute hepatitis B, icteric form against

the background of chronic opisthorchiasis, exacerbation stage. The patient continued the symptomatic treatment until complete normalization of the parameters of cytolysis and cholestasis, after which dehelminthization with praziquantel at a daily dose of 10 mg/kg of the body weight was conducted. At the examination of the patient in 6 months, normalization of clinical and laboratory parameters was observed, HBV DNA was not detected by PCR method, seroconversion of HBeAg into anti-HBe, HBsAg into anti-HBs occurred. In the control coproovoscopy (3-times) and analysis of duodenal contents, no eggs of opisthorchis were found. The follow-up continues.

In this clinical case, attention was attracted by the manifestation of chronic opisthorchiasis against the background of developed clinical presentation of acute hepatitis B. The chronic invasion was detected in a timely manner and dehelminthization in the reconvalescence period of acute hepatitis B contributed to self-elimination of hepatitis B virus and promoted the patient's recovery.

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