

Atypical Clinical Manifestations of Hepatobiliary Pathology

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Abstract

The traditional classification of hepatobiliary pathology can be presented [1], based on the etiological and pathogenetic factors of its occurrence, with a division into six groups of diseases:

1. Mainly functional disorders - dyskinesia, motor-tonic dysfunctions of the gallbladder (GI), bile ducts and sphincters. Regardless of the etiology, they are usually divided into hyper- and hypokinetic dysfunction of the gastrointestinal tract and dysfunction of the sphincter of Oddi. Primary dyskinesia is formed on unchanged structures of the biliary tract. Secondary dyskinesia develops against the background of abnormalities of the gastrointestinal tract and ducts, chronic cholecystitis and cholelithiasis (GI).
2. Inflammatory diseases are cholecystitis, cholangitis and cholangiohepatitis.
3. Metabolic diseases - GI, hemosiderosis, Konovalov-Wilson's disease, Gaucher's disease and others.
4. Parasitic - giardiasis, opisthorchiasis and other infestations.
5. Benign and malignant tumors.
6. Structural anomalies (congenital malformations) - absence of the gastrointestinal tract, bifurcation, constriction, diverticula, hypoplasia, aplasia of the bile ducts.

Keywords: Gallbladder (GI); Hepatobiliary Pathology; Hypoplasia; Aplasia

Hepatobiliary pathology has always been and remains one of the most difficult to diagnose, although numerous instrumental and laboratory methods of examination of patients are used in modern clinics to verify the diagnosis. They should be listed with some reservations. So, endoscopic methods are well developed, but they always have a variety of technical difficulties, are not always applicable in each specific case due to the high cost of the equipment used. Radiological methods are widely available, but they are characterized by low sensitivity and specificity only with an irrefutable clinical picture. The method of endoscopic retrograde cholangiopancreatography has many side effects and is contraindicated in cholestasis in the gastrointestinal tract and bile ducts. Magnetic resonance cholangiopancreatography reduces the risk of possible complications due to noninvasiveness, but has significant drawbacks, since it is impossible to identify stones smaller than 2 mm and obtain information about the degree of narrowing of the duct when using it. The data of modern ultrasound diagnostic devices significantly depend on the technical skills of the operator, pronounced flatulence and obesity of the patient, the degree of

adhesions in the abdominal cavity. These disadvantages are practically devoid of endoscopic ultrasound and magnetic resonance imaging techniques, but they are limited due to the cost of procedures. Dynamic cholescintigraphy and staged chromatic duodenal probing significantly expand the possibility of verifying the diagnosis, but they are also not used in all clinics. Morphological examination after puncture liver biopsy is considered the gold standard of diagnosis, but it is not always applicable. The possibilities of diagnostic search are significantly expanded by laboratory methods, since in various cases of hepatobiliary pathology, clinical syndromes are almost simultaneously present. These are: the phenomena of cytolysis, cholestasis and jaundice, immune inflammation, liver failure and portal hypertension of varying degrees. Nevertheless, all of these various combinations of disease variants and their leading pathogenetic mechanisms lead to clinical masks of pathology of the hepatobiliary zone, which lead to incorrect diagnoses and inadequate medical care.

Cardiological mask of biliary pathology: The classical description of this suffering was first presented back in 1883 [2] by Professor of the Imperial Medical and Surgical Academy of Russia Sergey Petrovich Botkin: "... Often cholelithiasis is expressed in phenomena focusing mainly in the heart area... The patient will complain of attacks of pain in the side of the heart, coming with a clear change in its function, arrhythmia, difficulty breathing and T. D., in a word, with a clear picture of angina... Such an attack lasts 8 - 10 hours instead of several minutes, and after several such attacks, the patient suddenly turns yellow...". Such situations allowed us to identify several clinical variants of diseases: cholecystocardial, cholecystocoronary, hemodynamic and arrhythmic. We observed the occurrence of atypical chest pains with signs of ischemia on the ECG, respectively, of the posterior wall of the left ventricle and the blood pressure level of 180/90 mmHg, which occurred in the morning after a hearty dinner in a 40-year-old man. The absolute absence of any previous complaints of the patient was noted. After sublingual administration of kapoten at a dose of 25 mg, the blood pressure level changed by 160/110 mmHg, and an urgent ultrasound examination of the liver made it possible to make an accurate diagnosis of a valve stone at the mouth of the LC. Cardiological symptoms in patients with biliary pathology were noted in 24.5% of cases of chronic stone-free cholecystitis and may occur without abdominal pain. Nevertheless, if a pathology of the hepatobiliary zone is suspected, the characteristic pain points should be carefully palpated. They are well known and are divided into anatomical and topographic zones:

1. Bubble point;
2. Epigastric region;
3. Choledocho-pancreatic zone;
4. Soreness in the area of the right proc. Acromion;
5. Pain zones near 8 - 11 thoracic vertebrae;
6. Blade point;
7. The point of the diaphragmatic nerve at the point of departure of the right sternocleidomastoid muscle from the clavicle.

Right-sided (irritative) vegetative syndrome was described during palpation of the spine as a consequence of dystrophic and degenerative changes of reflex genesis in the intervertebral discs. In such cases, due to prolonged excitation of the receptors of the autonomic nervous system in the underlying tissues, focal soreness can be determined, completely unrelated to the pathology of the liver and biliary tract.

The epidemic review [3] presents the data of many researchers (Table 1) that the leading signs of the underlying pathology in the form of cholecystitis can lead to serious complications of existing comorbid cardiovascular diseases.

The cumulative risk coefficient was 1.23 (95% confidence interval 1.16 - 1.30) for fatal and non-fatal events without gender differences. When analyzing the relationship of the consequences of cholecystectomy for the occurrence of cardiovascular complications, the

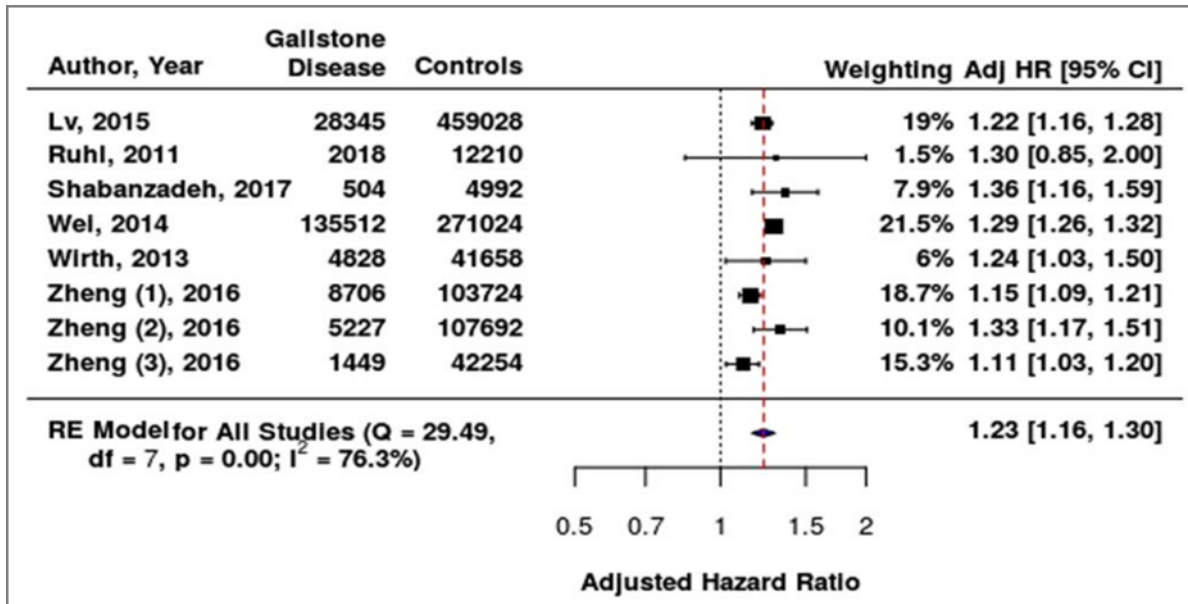


Table 1: Cumulative risk factor for fatal and non-fatal events of cardiovascular diseases in cholecystitis.

risk coefficient was 1.41 (95% with a confidence interval of 1.21 - 1.64). The exact mechanisms of association of these pathologies are unknown. The authors suggested a possible role of the intestinal microbiota and outlined further research in this direction [4].

Psychosomatic disorders in biliary pathology can be detected in 86% of patients versus 22 - 33% of cases in somatic pathology. The initial violations of the psychological status of the patient significantly aggravate the course and outcome of the liver diseases that have arisen [5]. Depression is especially important as a provoking factor of unbearable pain and subsequent complications [6]. Perhaps these conditions potentiate the general suffering of the patient. Study participants reported feeling anxious (9%), real depression (8%), past sexual trauma (18%) or physical abuse (10%). Women have a higher risk of depression. Half of the patients were diagnosed with other functional disorders against this background, and first of all (34%) irritable bowel syndrome. The psychological portrait of a patient with biliary pathology most accurately reflects the long-standing psychological characteristics: Greek. “Chole” → “choleric”, “Bile” → “bile character”. A bilious person is usually irritable, angry. Patients are picky, conflicted, quarrelsome, suspicious. Experts note their hypochondria, depression, psychotic reactions, phobias, asthenic states. Premenstrual tension syndrome is often associated with young women with biliary pathology. They tend to demand unnecessary diagnostic procedures from the doctor; prescribing certain treatment, which they perform with reluctance or do not perform at all, but at the same time they are dissatisfied with both the doctor and the results of treatment. Therefore, it is necessary to take into account the peculiarities of communication between the doctor and patients with functional biliary pathology. During the consultation, it is necessary to take into account that the success of treatment is increased due to a good relationship between the doctor and the patient. The quality of consultation and patient satisfaction are determined by:

- Empathy (empathy);
- Avoiding professional jargon;
- The honesty of the forecast and all advice;
- Acknowledging that you don't have all the answers.

The doctor will not have enough 10 - 15 minutes to receive such a patient and should count on a longer contact [7]. But if you take the time to consider all these factors during the first visit when making a diagnosis of a functional disorder, a competent and psychologically trained doctor “will save time (your own) and money (of the patient) on future visits...”. The following useful questions are recommended (Table 2) during the consultation:

Questions	The purpose of the question posed
Can you tell me your story from the beginning?	It may have psychotherapeutic significance for the patient.
What (in your opinion) is it happening to your health?	It helps to identify the Patient’s distorted ideas about their health.
If we could change one thing in your well-being, what would it be?	This helps you focus on the main factor for the patient.
What would you do in your life if these symptoms decreased?	This helps to determine the incentive for recovery.
Is there anything else in your life that is bothering you?	This helps to identify psychosocial problems that contribute to the onset of symptoms and which may need to be addressed by a psychotherapist.

Table 2: Suggested questions of the doctor when collecting the anamnesis of a patient with hepatobiliary pathology.

During the subsequent examination of the patient, unexpected diagnoses and clinical findings may be revealed that do not correspond to the initial presentation of the doctor after the physical examination.

Giant stones of the ZHP: Rarely, but gallstones larger than 5 centimeters can be diagnosed as unexpected findings. They can be localized in the gastrointestinal tract, biliary tree, intestines. They are more often mixed in composition (cholesterol and bilirubin). More often (2:1 compared to men) they are determined in women, usually this condition is associated with diabetes mellitus and in 60 - 80% the formation of gallstones is asymptomatic. However, with a thorough study of the anamnesis, it is possible to identify very moderate previous symptoms in the form of recurrent biliary pain, exacerbations of chronic cholecystitis with minor obstruction, stretched over time. Such cases require surgical treatment even in the absence of a clinical picture [8]. The operation of choice is laparoscopic cholecystectomy, since when migrating through the fistula between the gallbladder and the duodenum 12 or small/large intestine, they can cause gallstone ileus. According to the same authors, gallstones over 3 cm have a relative risk of gallbladder cancer.

Accidental” gallbladder cancer: According to statistics, they make up from 0.19% to 5.5% of all cholecystectomies with a ratio of women to men of 14:1. At the time of diagnosis, usually [9] such findings are asymptomatic and in 80% it is detected accidentally during routine histological evaluation. Cases of aggressive cancer with a poor prognosis should be clarified. This is determined by the following risk factors: “porcelain” LC, polyps over 1.5 cm, the presence of a long-term GI, age over 50 years, the occurrence of empyema, genetic predisposition, geographical and ethnic factors. Women are also the most predisposed to such options.

Currently, there is a tendency among pathologists to move from the current practice of routine histopathological evaluation of all LC samples to a more selective approach [10]. With a thorough microscopic and histological examination of 14,731 patients with macroscopically abnormal-looking LC (abnormal samples), the incidence of malignant pathology was 0.14%. Based on the results of such a study, a selective histological assessment can be recommended when analyzing samples in patients older than 50 years, after emergency surgery or surgery with a difficult dissection, leading to a transition from laparoscopy to open surgery.

Considering all the options for unexpected diagnoses, it is necessary to list the main clinical pain masks. These are: chronic pain in the anterior abdominal wall; myofascial pain syndrome; chronic pelvic pain, all of them account for 10 to 30% in the clinic of atypical hepatology. The usual cause of pain is a combination of stress and insufficient motor activity. By the nature of the pain, it can be determined that it is not very intense, but persistent, often long-term, which seriously violates the quality of life of the patient. More often it is not associated with defecation and is not accompanied by bloating and other elements of dyspepsia, there is a weakening of pain in the supine position or, conversely, at the time of physical exertion. It is possible to identify areas of local hypertonicity (trigger points) in the muscles, palpation of which is accompanied by soreness and can provoke a painful attack. The recommended therapeutic approach in such cases is a combination of physical therapy, thermal procedures, work with a psychotherapist and taking medications, usually antidepressants and anticonvulsants [11].

The practitioner should take into account that complaints of bitterness in the mouth do not always determine the mood to detect hepatobiliary pathology in a patient [12]. The causes of bitterness in the mouth are numerous and this must be taken into account in each case. Such a symptom is determined by the general condition and habits:

- Breathing through the mouth,
- Dehydration of the body,
- Dry mouth,
- Pregnancy,
- Smoking tobacco and vapes,
- Taking herbal remedies (infusion and decoction of St. John's wort, sea buckthorn oil),
- Products (cedar and almonds).

The basis of disturbing sensations may be diseases and conditions not associated with damage to the gastrointestinal tract, namely:

- Allergies and stuffy nose,
- Upper respiratory tract infection (sinusitis, acute respiratory infections, flu, pharyngitis),
- Nasal polyps,
- Salivary gland infection,
- Sjogren's syndrome, vitamin B12 and zinc deficiency,
- Gingivitis, glossitis,
- Intoxication with mercury, lead, copper.

Many medications can change perception to a feeling of bitterness in the mouth:

- Acetylcholinesterase inhibitors in the treatment of Alzheimer's disease,
- Bronchodilators and bronchospasmolytics in the treatment of bronchial asthma and chronic nonspecific lung diseases,
- Captopril in the treatment of hypertension,
- Individual antibiotics, for example clarithromycin,
- Chemotherapy and drugs such as vinblastine, vincristine and procarbazine,
- Griseofulvin used in fungal skin infection,

- Lithium preparations in the treatment of manic psychoses,
- Penicillamine (cuprin) in the treatment of rheumatoid arthritis and Wilson-Konovalov’s disease,
- Rifampicin in the treatment of tuberculosis or prevention of bacterial meningitis,
- Drugs for the treatment of thyroid diseases.

Other causes are also possible: surgical dental procedures, the consequences of injuries or damage to the upper respiratory tract, operations on the ears, nose or throat, radiation therapy of the head and neck, dental or orthodontic devices, such as braces.

Taking into account all of the above, an algorithm for diagnosing hepatobiliary pathology is proposed, based on the analysis of the last three months of all signs of the disease and provided the first appearance of symptoms is at least six months before diagnosis [13]. They begin with an analysis of possible functional diseases (Table 3) in the absence of organic changes that explain the pain.

Roman criteria III	Roman criteria IV
E1. Functional disorder of the gallbladder	E1. Biliary pain
E2. Functional disorder of the sphincter of the Oddi biliary type	E1 a. Functional disorder of the gallbladder
	E1b. Functional disorder of the Oddi biliary sphincter
E3. Functional disorder of the Oddi sphincter of pancreatic type	E2. Functional disorder of the sphincter of the pancreatic type Oddi

Table 3: Functional diseases of the biliary zone.

The clinic of spasm of the Oddi sphincter (K 83.4) is determined according to the Roman criteria IV (biliary pain) by clear functional signs:

- Localization in the right hypochondrium and epigastrium;
- More than 30 minutes, persistent;
- Not daily;
- Quite intense;
- Does not decrease after defecation;
- Decreases insignificantly (less than 20%) after taking antacids, suppression of hydrochloric acid secretion, after eating or changing the position of the body;
- May be combined with nausea and/or vomiting;
- Radiates into the back and/or right scapular area;
- Causes sleep disturbances (may lead to waking up at night).

To facilitate the medical interpretation of biliary pain, a certain [14] logical formula is proposed: biliary pain + absence of changes in bile ducts according to ultrasound data ± low contractility of the gastrointestinal tract, normal level of liver enzymes, bilirubin, amylase/ lipase = functional disorder of the gastrointestinal tract. At the same time, the primary etiopathogenetic factors of functional disorders of the biliary tract (FRBT) should be taken into account:

- Hereditary predisposition;
- Congenital pathology of the biliary system (weakness of the smooth muscles of the gastrointestinal tract, abnormalities of the structure of the gastrointestinal tract or biliary tract);
- Constitutional predisposition (asthenic body type or obesity);
- Old age;
- Violation of the regulation of the autonomic nervous system (discoordination of the gastrointestinal tract and sphincters of the biliary system).

Of all the primary factors presented, the most difficult is the differential diagnosis of acquired and congenital deformities, which ultrasound diagnostics doctors most often verify as a “Bend of the gallbladder”. These features of the structure of the LC in the population are determined with a frequency of 15 to 30 percent and its form is described in terms of: “hook-shaped, Phrygian cap, bull horn, mouth-shaped, S-shaped, kinks, constrictions, partitions...”. The listed variants of the features of the ultrasound form of the LC do not have a characteristic clinical picture. Similar “defects” or anomalies of the structure of the digestive tract are found accidentally in children or adults without complaints about digestion. Abdominal pain caused by biliary dyskinesia is equally often observed both in persons with deformities of the gastrointestinal tract and in patients with its typical appearance. Therefore, with the revealed deformations of the LC, special therapeutic and preventive measures do not need to be taken! In such cases, it is necessary to focus diagnostic attention and confirm the possible dysfunction of the gastrointestinal tract by applying an instrumental examination algorithm. Ultrasound cholecystography is usually used. The volume of the LC is determined on an empty stomach and after ingestion of a contraction stimulator. This approach allows us to evaluate the contractility (emptying fraction) of the LC. The method is accessible and safe, but... not standardized! It is possible to use bilioscintigraphy with preparations of imidodiacetylic acid labeled ^{99m}Tc . The parameters of accumulation and excretion of bile are evaluated. The procedure is safe, informative comparable to the manometry of the Oddi sphincter, but... also not standardized!

Significant abnormalities of the gastrointestinal tract can lead to a violation of the passage of bile and become a risk factor for the development of inflammation and GI. These include LC with multiple/multiple partitions, when its dimensions do not exceed normal values and the cameras communicate with each other. The same meaning should be given to the term “Phrygian cap”, which is verified in 1 - 6% of the population.

Secondary etiopathogenetic factors of FRBT should also be listed:

- Chronic gastrointestinal diseases (gastritis, duodenitis, colitis, YAB, hepatitis);
- Chronic inflammatory processes of the abdominal cavity and pelvic organs;
- Infections (bacterial, viral, helminthic, giardiasis, parasitic);
- Endocrine disorders (diabetes mellitus, obesity, hyper- and hypothyroidism, hyperestrogenemia (including during pregnancy));
- Postoperative conditions (cholecystectomy, resection of the stomach, intestines);
- Allergic diseases;
- Psychoemotional overload;
- Physical inactivity;
- Alimentary disorders (food poor in plant fibers, as well as with an excess of carbohydrates and animal proteins, irregular diet, over-eating, fast food, fasting with a sharp reduction in body weight, prolonged parenteral nutrition);
- The use of medications (oral contraceptives, drugs for normalization of lipid metabolism, ceftriaxone, sandostatin derivatives), leading to a violation of the rheological properties of bile.

The SARS-Cov-19 pandemic in the period 2020-2022 aggravated nutritional problems, but did not lead to a sharp change in the symptoms of liver and biliary tract diseases [15]. Against the background of a marked increase in inflammatory diseases of the upper respiratory tract in general medical practice, diagnoses of “dyskinesia of the gallbladder and bile ducts” or K82.8.0 (syn.: dysfunction, functional disorders) of the gastrointestinal tract still dominate. The criteria for its diagnosis remain the same. These are: characteristic biliary pain, absence of stones/sludge and other structural changes of the gastrointestinal tract according to ultrasound data. Additional confirmatory signs during in-depth examination are: a decrease in the fraction of emptying of the gastrointestinal tract (< 40%) according to the results of ultrasound cholecystography or bilioscintigraphy; normal indicators of the activity of liver enzymes, amylase/lipase and the level of direct bilirubin in the blood.

Conclusion

In conclusion, it should be clarified that functional diseases of the hepatobiliary zone and the biliary system are justified by the phenomena of dyskinesia and inflammation, which (quite logically) should be considered a key link in the pathogenesis of subsequent organic diseases. When verifying hepatobiliary diseases, atypical clinical masks of manifestations of functional and structural disorders in the liver and biliary tract should be taken into account.

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