

## VALIDITY OF DIAGNOSTIC CRITERIA OF CHRONIC CHOLECYSTITIS

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### Abstract

The clinical diagnosis of chronic cholecystitis (CCH) is generally verified by biopsy. It involves numerous and variable morphological findings, ranging from minimal to gross alterations in the gallbladder structure. Many surgeons have misused the term cholecystitis as a synonym for cholecystolithiasis. The controversial category of “minimal CCH” includes the presence of slight mononuclear infiltration of the gallbladder mucous membrane, regardless of whether lithiasis is present or not.

We examined histological findings in gallbladder mucous membranes from autopsy materials of 10 persons unaffected by hepatobiliary disease. Histological findings from five subjects, in whom post mortem changes were absent, revealed “minimal CCH”, which is easy to misdiagnose and confuse with the appearance of a normal immunological barrier.

In a series of 20 gallbladders harvested from the explanted livers of transplanted patients with unaffected extrahepatal biliary tracts, “minimal CCH” was observed in all cases. We conclude that the diagnosis of CCH based on the presence of “minimal changes” is not valid and cannot support the indication for cholecystectomy, if this is evaluated *ex post*.

We revised biopsy specimens evaluated as CCH by various pathologists. Out of 100 biopsic samples analysed and classified on the basis of a scheme designed by us, “minimal CCH” findings were present in the “atrophic cholecystitis” and “miscellaneous” categories.

We assessed the validity of CCH diagnosis by analysing the biopsy records of 100 patients with cholecystectomy, in whom the diagnosis was based on both clinical and morphological findings. Most of the records (63) had the term “chronic cholecystitis” as a concluding diagnosis and, only in 37 records, more or less detailed descriptions of pathological alterations in gallbladder walls were provided.

It is concluded that further studies are needed to elucidate the pathological basis of “minimal CCH” and its relation to the natural immunological barrier protecting the mucous membrane of the gallbladder.

### Key words

gallbladder, mucous membrane, chronic cholecystitis, minimal chronic cholecystitis, immunological barrier

### INTRODUCTION

The diagnosis of chronic cholecystitis (CCH) is generally established by cooperation of two specialists, i.e., clinician and pathologist. The latter is usually regarded as superior (often regardless of the quantity of tissue he had examined). Nevertheless, it is the histology that remains indicative. The validity of histological findings may be doubtful in cases where there is a disagreement between the

diagnosis of a surgeon and that of a pathologist. Moreover, the authors of a modern textbook on surgical diagnosis and therapy have recently suggested that CCH can be diagnosed in patients with gallstones even without the histological examination of removed gallbladders. They believe that evident cholecystolithiasis is a sign sufficient for the diagnosis of CCH, even in patients whose gallbladders may be inconspicuous, normal or with a moderately altered mucous membrane, while the wall is without scars. Current morphological criteria of CCH are, of course, acceptable (1). Similar attitudes of surgeons towards the diagnosis of CCH gave an impetus to the investigations described in this paper.

Cholecystectomy is a routine and common intervention with various modifications. According to our estimation, patients undergoing this operation have a high risk of postoperative disorders due to objective as well as subjective reasons. The accurate CCH diagnosis is based on histomorphology. This is a leading fact in complicated and fatal cases of cholecystectomy, when the urgency of such an intervention is assessed by experts and both clinical and morphological data are analysed, especially in cases when surgeons insist on an operation.

This paper is a contribution to this sophisticated problem based on various brief and incomplete descriptions of bioptic diagnoses. By analysing our own material (both bioptic and necroptic) as well as the wordings of diagnostic records written by skilled pathologists, we tried to determine the hallmark of this study, i.e., the validity of the presence of mononuclear cells in the mucous membrane of gallbladders for the diagnosis of CCH.

#### MATERIALS AND METHODS

1. In 100 patients with cholecystectomy, the bioptic material was examined with regard to the general criteria of CCH used by various pathologists who had examined the sections and concluded (briefly or widely) their diagnosis with the term "CCH". The clinical diagnoses were generally designated as "chronic cholecystitis" and/or "cholecystolithiasis". Each gallbladder was first examined macroscopically and altered tissue was excised, fixed with 10% formalin, embedded in paraffin, and stained with haematoxylin-eosin. Two to three sections were made from each sample.

2. In 100 biopsy records, the description of CCH diagnosis was checked in order to find out whether it was accurate and corresponded to the chronic cholecystitis diagnosis. These records were divided into two groups: group 1 contained records with a concise, brief and simple description, i.e., „chronic cholecystitis“. In group 2, there were records with more or less detailed descriptions of histological findings.

3. Samples were collected and histologically examined as follows:

a) 10 autopsy gallbladders from randomly selected persons unaffected with hepatobiliary diseases were processed generally in the same way as the bioptic

material, with the exception of the topical and quantity abnormalities: in each gallbladder, samples were taken from the fundus, the corpus (generally with a fragment of adhering liver tissue) and one piece was excised from the collum. Our attention was focused on the cellulisation of mucous membranes, especially in their upper parts.

b) 20 gallbladders were harvested from the explanted livers of patients whose extrahepatal biliary tracts were not affected. In each case, the material was reduced to 1 section from each liver. There were 13 men and 7 women in this group.

## RESULTS

1. The bioptic material was classified and the following CCH categories were found:

(i) atrophy of the mucous membrane with mononuclear infiltrate, 15 cases; atrophy of all layers with mononuclear infiltrate, 7 cases;

(ii) hyperplastic inflammation of the mucous membrane, 27 cases; chronic disperse inflammation of the wall, 4 cases;

(iii) chronic interstitial inflammation without fibrosis in 12 cases and with fibrosis in 4 cases;

(iv) combined or mixed processes, 15 cases;

(v) miscellaneous, 16 cases.

2. Evaluation of the biopsy records.

The clinical diagnoses found on the biopsy records were generally described as “chronic cholecystitis“ and/or “cholecystolithiasis“. The diagnoses based on biopsy findings were divided as follows:

(i) CCH diagnosis without further histological details, 63 cases.

(ii) CCH diagnosis with a more or less detailed description of structural and inflammatory changes in the gallbladder wall, 37 cases.

3a. Necropsy specimens showed positive results only in 5 cases; the rest of the material had significant autolytic changes, bile imbibition etc. All the well-preserved sections (5 cases) revealed focal accumulation of mononuclears (lymphocytes, plasmocytes and macrophages) in the lamina propria of the gallbladder mucous membrane. As for the distribution of mononuclear cell types, no differences were found in the regions investigated, i.e., cellulisation in the fundal, corporal and collic areas appeared similar.

3b. In all 20 biopsy specimens excised from gallbladders harvested during liver transplantation, the histological findings were similar to those found in the necropsy specimens. In some cases, single neutrophils and eosinophils were observed. Cellulisation was, as a rule, located to the upper part of the mucous membrane.

## DISCUSSION

The results of the first part of this study confirmed that the CCH diagnosis covered a wide range of morphological changes, as shown by our classification scheme. Nevertheless, doubts persist as for the representative value of individual samples, although uncertainty might have been minimised by performing a macroscopic examination of each gallbladder before sampling.

The first category in our classification may be a topic for discussion due to the fact that similar histological features are observed in a variety of CCH conditions known as “minimal CCH“ as well as in normal gallbladders and can be regarded as a manifestation of cellular immunological barriers analogical to the barriers developed in the mucous membranes of the respiratory, gastrointestinal, and urogenital tracts of healthy persons (2,3,4). Moreover, similar mononuclear cells have recently been also found in alveolar spaces in the lungs of normal persons (5.). Our results confirm the view that an immunological barrier may exist in the mucous membrane of healthy gallbladders and that it is continuous with the barrier in the interlobular portal tract of the liver (6.). On the other hand, some authors consider the mononuclear infiltration of portal tracts to be an “interstitial hepatitis“ caused by viral or bacterial infection (7.).

The impact of gallstones on the integrity of the gallbladder wall, particularly on the mucous membrane, seems to be overestimated. In our experience, a single stone, especially one composed of cholesterol, need not injure the gallbladder layers. Moreover, pathologists receive gallbladders (ectomised by surgeons) open and without content. That is why, as a rule, they are not able to evaluate the potential impact of gallstones.

Czech histologists in their textbooks do not report on the existence of an immunological barrier in the mucous membrane of gallbladders (8. 4.) and neither do others (2. 10. 9.). In contrast, some authors have described numerous lymphocytes and plasma cells scattered in the lamina propria of the gallbladder mucous membrane (3. 11.) while others have observed them in relation to the Aschoff-Rokitansky sinuses (12.).

It is logical to assume that the view held by some authors that the absence of mononuclears in the mucous membranes of normal gallbladders (4, 8, 9) may have originated within this organ is based on limited personal experience, and that the lack of experience can also account for an opinion that such mucus membrane cellulisation is a pathological feature. Moreover, in our gallbladder materials, the infiltrates in question were not found diffusely distributed and there were regions of the mucous membrane where they were missing completely.

The results of our study show that, in the majority of cases (63%), the brief surgical diagnosis of “chronic cholecystitis“ (with or without stones) was in accord with the diagnosis made by a pathologist.

Questionable cases, in which CCH may have been misinterpreted as an “immunological barrier“, occurred only in the first and the last category of our classification scheme. We were not able to quantify them precisely due to technical difficulties. We believe that mononuclears sparsely distributed in the upper layer of the gallbladder mucous membrane in otherwise intact tissue represent an immunological barrier (analogous to the barriers in other mucous membranes) and that this finding may be easily misinterpreted and evaluated as “mild“ or “minimal“ chronic cholecystitis. The diagnosis of CCH alone should not serve as a basis for the surgeon’ decision to perform cholecystectomy, particularly if the patients hesitates to undergo the operation, on should not justify this decision in the case of a fatal postoperative course with the possibility of a later litigation.

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## VALIDITA DIAGNOSTICKÝCH KRITÉRIÍ CHRONICKÉ CHOLECYSTITIDY

### S o u h r n

Klinicky diagnostikovaná chronická cholecystitis (CCH) je potvrzována biopticky ze vzorku makroskopicky ohodnoceného odňatého žlučníku. Rozsah změn typických pro cch je značný a bývají zahrnovány i problematické varianty “minimální cch“ či “lehká CCH“ a pod., kde jsou pouze řídké mononukleární infiltráty v horní vrstvě sliznice, jež patrně mají význam imunitní bariéry, analogické sliznicím gastrointestinálního či respiračního traktu. Někteří klinici a chirurgové označují každý žlučník s kameny vedle termínu “cholelitiáza“ i ne dosti správně jako “CCH“.

Na základě analýzy preparátů ze 100 žlučníků odňatých z indikace CCH (ev. cholelithiasis) bylo stanoveno morfologické zastoupení typických změn při CCH, kde problematické “minimální“ varianty jsou v první a poslední podskupině.

Ve druhé části studie jsme zhodnotili formulace bioptických nálezů u vzorků žlučníků s klinickou a morfologickou diagnosou CCH. Text bioptického nálezu redukováný na dvě slova “cholecystitis chronica“ obsahovalo 63 průvodek. Zbytek měl formulaci s více-méně méně širším popisem patologických změn. Máme za to, že klinickou diagnózu CCH mohou podpořit pouze formulace širší neboť se vyloučí možná záměna s projevem imunitní bariéry.

Ve třetí části studie jsme zjišťovali přítomnost řídké mononukleární infiltrace sliznice normálních žlučníků jak z pitevních odběrů tak z explantovaných jater. V obou případech jsme v jinak intaktních žlučnicích našli “minimální CCH“ či správněji normální imunitní bariéru.

Bylo by vhodné tuto problematiku dále ujasnit, neboť v literatuře nejsou názory na imunobariéru žlučníku jednotné.

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