

Cholecystitis Xanthogranulomatous Clinical Pathological an Analysis of 20 Cases

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Received: 31 Mar 2021

Accepted: 19 Apr 2021

Published: 24 Apr 2021

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Keywords:

Cholecystitis; Xanthogranulomatous; Foamy Macrophages

Citation:

Salinas JCV, Cholecystitis Xanthogranulomatous Clinical Pathological an Analysis of 20 Cases. The New American J Med. 2021; V1(4):1-4

1. Abstract

The XGC is a rare variant of chronic cholecystitis, is considered a non-neoplastic reactive process, however, is an entity that confuses macroscopically and image for gallbladder cancer. It is characterized by the presence of chronic inflammatory infiltration, granuloma formation with fibrosis, histiocytic reaction with foamy macrophages (rich in lipids broad vacuolated cytoplasm). This study aims to describe pathological findings in 20 cases identified in a review in 5 years compared to 1671 cases of cholecystectomy in patients IGBJ. The review of cases ranging from 1 September 2011 to 1 September 2016.

2. Introduction

Xanthogranulomatous cholecystitis is a chronic inflammatory condition, first described by Christensen and Ishak in 1970 as a “fibroxanthogranulomatous inflammation” and later as “xanthogranulomatous cholecystitis” by McCoy et al [8-9].

Various terms have been used to describe this process including ceroid granuloma, histiocytic granuloma type ceroid, fibroxanthogranulomatous inflammation, biliary granulomatous cholecystitis [1-2].

Generally, this entity is seen in adult women with classic symptoms in favor of chronic cholecystitis, although it is uncommon, its prevalence ranges from 0.7 to 1.8% of all cholecystectomy specimens in the United States, 1.2 to 10% in Japan. 10-13% in India [7].

Its etiology is unknown; however, most researchers postulate that

extravasation of bile in the gallbladder wall is an important pathogenic factor. Bile leakage occurs both by the rupture of the Rokitsky-Aschoff sinuses or by the ulceration of the mucosa, which initiates a chronic inflammatory reaction in the interstitial tissue composed of fibroblasts and macrophages, which in the inescapable process of cholesterol and bile phospholipids, secondary condition a destructive enzymatic discharge of the microenvironment of the gallbladder wall and its surroundings. Stone obstruction and chronic infection have been implicated as risk factors that contribute to the pathogenesis [3-5].

At the pathological examination; macroscopically, it is characterized by yellowish intramural nodular areas. Microscopically, it can present data of chronic cholecystitis that also shows proliferative fibrosis secondary to chronic destructive inflammation and the presence of foamy macrophages (a key finding for dx), this produces thickening of the gallbladder wall with extension to other adjacent structures or fistula formation due to ulceration. of the mucosa [10] (Figure 1).

3. Material and Methods

The reports of surgical specimens obtained by cholecystectomy and sent to the Department of Pathological Anatomy of the Bolivian-Japanese Gastroenterological Institute Cochabamba (IGBJ) between September 1, 2011 and September 1, 2016 were reviewed. Out of a total of 1671 cholecystectomies performed in this during this period, 20 cases with histopathological diagnosis of xanthogranulomatous cholecystitis were identified, which constitute the study sample. The slides of these reports were reviewed (Figure 2).

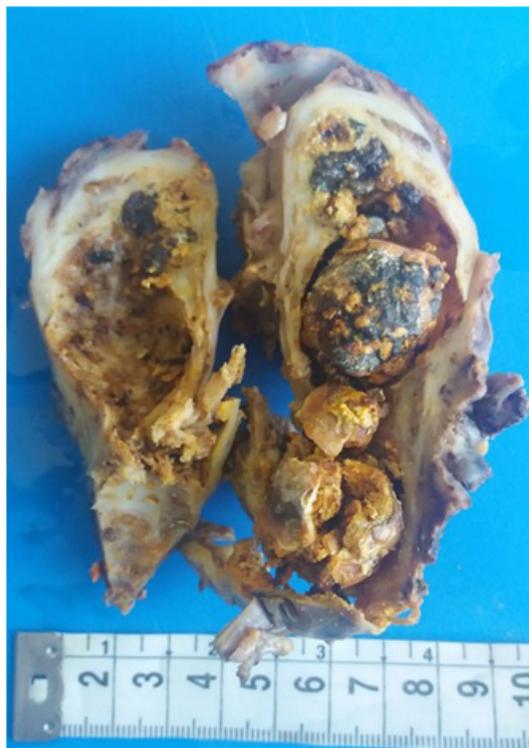


Figure 1: surgical specimen product of cholecystectomy, when cut with thickened walls of fibrous appearance with intramural yellowish areas associated with the presence of black-yellowish stones suggestive of cholesterol stones.

Histological section in H&E (4X), gallbladder wall, partially preserved mucosa, wall thickening, fibrosis, and groups of intramural foamy macrophages

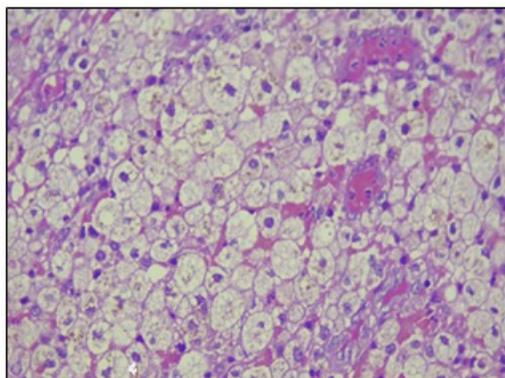


Figure2: Histological section H&E (40X) foamy macrophages or “foam cell” associated with acute and chronic inflammatory infiltrate

4. Results

In the period of time studied, 1671 cholecystectomies were performed in the Surgery Service of the Bolivian-Japanese Gastroenterological Institute Cochabamba, the review of slides shows that of this total, 20 cases correspond to the diagnosis of xanthogranulomatous cholecystitis by histopathological study. This corresponds to 1.19% of the total number of cholecystectomies in that period.

Of the 20 cases diagnosed with xanthogranulomatous cholecystitis, 55% [11] were male and 45% [9] were female. Age ranges from 20 to 63 years, with an average of 42.7 years (Figure 3).

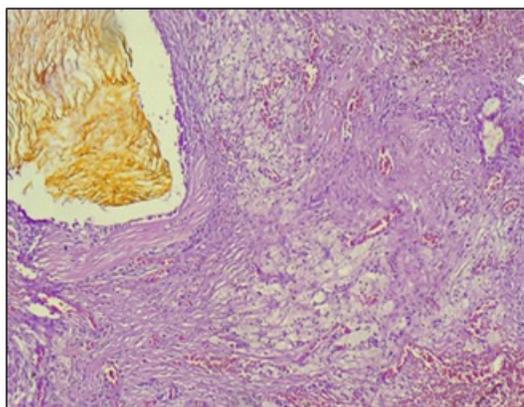


Figure 3: Histological section wall H and E (20X), bilirubin pigment compatible with intramural stone (red arrow), groups of foamy macrophages (blue arrow)

4.1. Pathological Characteristics

4.1.1. Macroscopic Findings: The review of reports shows as a common denominator specimens product of cholecystectomy with thickened walls, some of the reports report multifragmented tissues (difficulty in surgical approach due to suspicious appearance of malignant neoplastic), the cut wall reveals reticulated mucosa, others of erosive appearance, in wall thickness whitish areas associated with nodular foci of yellowish brown fibrotic intramural tissue; some cases showed hemorrhagic and necrotic areas. The reviewed reports show an association with lithiasis (stones that range from 0.5 to 3.5 cm long axis, most of them green-yellowish color suggestive of cholesterol stones) in 100% of the cases [12-15].

4.1.2. Microscopic Findings: Histological slides stained with hematoxylin and eosins from patients with histopathological diagnosis of xanthogranulomatous cholecystitis were reviewed in the microscopic description. The cases that met the criteria of:

1. presence of abundant histiocytes with foamy cytoplasm (foam cell)
2. granulomatous reaction with foreign body-type multinucleated giant cells were selected
3. bile salts and cholesterol crystals in the inflammatory infiltrate
4. chronic and acute inflammatory infiltrate
5. fibrosis

Of the cases reviewed, it is striking that the diagnosis of remission in three of them was gallbladder cancer and the histopathological result showed only 1 positive but associated with xanthogranulomatous cholecystitis, the other two were diagnosed as negative for malignancy (Figure 4).

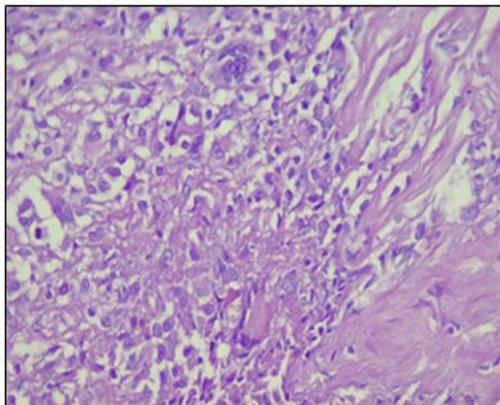


Figure 4: Histological section (40X) there is granuloma formation with the presence of a foreign body multinucleated giant cell (red arrow).

5. Discussion

Xanthogranulomatous cholecystitis is a rare entity, it was described as a variant of chronic cholecystitis, and it is considered a benign condition. Regarding the demographic characteristics in this study, I did not report a great difference by gender. The mean age of the patients was (42.7). With a wide range of variation of 20-64 years.

Clinically, it is difficult to distinguish CXG from other chronic diseases of the gallbladder since it can simulate a neoplastic lesion, the symptoms are not specific.

Only in three patients was gallbladder neoplasia suspected due to the macroscopic characteristics, which in one of the cases forced the surgeon to perform a rapid intraoperative biopsy, which was reported by the pathologist as "negative for neoplasia, compatible with a xanthomatous inflammatory process". In one of the cases, the diagnosis of neoplasia associated with xanthogranulomatous cholecystitis was confirmed, which reaffirms the fact that both entities are often confused, and it is only the definitive biopsy that clarifies the diagnosis. On the other hand, the fact that there is an over diagnosis of gallbladder cancer in CXG cases is reaffirmed, which can lead to erroneous therapeutic behaviors.

Some series have suggested the association between CXG and gallbladder cancer in 3 to 10% of cases. In this study this occurred in one case. On the other hand, no statistical difference was found in the incidence of cancer compared to the rest of chronic cholecystitis, for which we cannot affirm that CXG is associated with a higher risk of cancer.

The relationship between CXG and gallbladder carcinoma is unclear. It may simply be that CXG and adenocarcinoma are two complications of cholelithiasis and cholecystitis of certain duration. The association of CXG and carcinoma is important, because when both lesions are present in the same sample, the carcinoma may be missed completely or the extent of the tumor is either over or underestimated.

Several studies have shown the strong association between gallstones and CXG, as in this review all 20 cases had gallstones. Over time,

gallstones can lead to immobilization and rupture of the Rokitsky-Aschoff sinuses or mucosal ulceration leading to extravasation of bile into the gallbladder wall that incites a series of inflammatory cascade with the phagocytosis of bile lipids by macrophages and fibroblasts leading to the formation of xanthoma cells.

Only the histopathological study can definitively differentiate a CXG from a gallbladder carcinoma. The prognosis of this disease is very good compared to a gallbladder carcinoma that implies a high mortality.

6. Conclusion

In conclusion, although CXG is not considered a precursor lesion, it may be associated with a primary adenocarcinoma of the gallbladder, it is difficult to make a preoperative differentiation between the two lesions. It is important to take into account the possible coexistence to define the appropriate behavior.

There are no clinical findings or studies that reliably suspect this variety of chronic cholecystitis, so surgery, the macroscopic intraoperative appearance and subsequent histopathological study become the only weapon of diagnostic confirmation.

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