International Journal of Surgery Case Reports 83 (2021) 105976

Contents lists available at ScienceDirect

International Journal of Surgery Case Reports

journal homepage: www.elsevier.com/locate/ijscr

Case report

Post-pregnancy recurrent biliary colic with intraoperative diagnosis of limy bile syndrome

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ARTICLE INFO

Keywords:
Limy bile syndrome
Cholelithiasis
Laparoscopic cholecystectomy
Incidental finding
Pregnancy
Case report

ABSTRACT

Introduction: Limy bile syndrome (LBS) is an unusual condition in which gallbladder and/or bile ducts are filled with paste-like radiopaque material with a high calcium carbonate content. It can be rarely associated with PTH disorder and hypercalcemia.

Presentation of case: A 35-year-old woman presented with epigastric and right hypochondrium pain since a few hours. Similar attacks occurred in the past months soon after a pregnancy with vaginal delivery. Laboratory findings were not significant. The abdominal ultrasound highlighted a micro-lithiasis of gallbladder without complications. Considering the recurrent biliary attacks, laparoscopic cholecystectomy was performed with intraoperative diagnosis of LBS. A subsequent endocrinological screening highlighted a normocalcemic hyperparathyroidism associated with Vitamin D deficiency, likely related to the recent pregnancy and not to LBS.

Discussion: LBS is a rare condition with not clear etiology, frequently associated with cholelithiasis, of which it shares clinical presentation and potential complications. Diagnosis of LBS is based on abdominal X-ray/computed tomography scan, or it could be an intraoperative finding. The gold standard treatment is represented by laparoscopic cholecystectomy. The pregnancy with its related cholestatic phenotype could facilitate the LBS manifestation. An endocrinological screening should be performed to rule out a concomitant calcium metabolism disorder.

Conclusion: Knowledge of this rare condition could help general surgeons handle it properly.

1. Introduction

Limy bile (also known as milk of calcium bile) syndrome (LBS) is an unusual condition in which gallbladder and/or bile ducts are filled with paste-like radiopaque material with a high calcium carbonate content. It could be diagnosed by abdominal X-ray/computed tomography (CT) scan or it could represent an incidental finding after cholecystectomy. It can be rarely associated with PTH disorder and hypercalcemia. We report the clinical case of LBS in a young women who underwent cholecystectomy for recurrent biliary colic appeared soon after pregnancy. The case report was realized according to international SCARE checklist [1].

2. Presentation of case

A 36-year-old woman with no comorbidities and no drug history presented at our Emergency Department with an important epigastric and right hypochondrium pain since a few hours, without vomit and fever. In the past months, soon after pregnancy, she already experienced several similar pain attacks and therefore she had an abdominal ultrasound which demonstrated a micro-lithiasis of gallbladder. Since this finding, she has been prescribed ursodeoxycholic acid with no benefit. At the examination, she presented with mild tenderness in the right hypochondrium with negative Murphy's sign and no jaundice. Laboratory findings are listed in Table 1 and were not significant. Because of patient's age and the high clinical diagnostic suspicion of biliary colic, we didn't perform abdominal X-ray or abdominal CT scan. We only repeated an abdominal ultrasound which confirmed the presence of millimetric stones in the gallbladder without inflammation figures and with no common bile duct dilatation (Fig. 1).

Considering the recurrent biliary attacks resulting in impairment of quality of life, even if in absence of acute cholecystitis, laparoscopic cholecystectomy was performed during the same recovery. Surgery was done by a well versed surgeon experienced in minimally invasive

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https://doi.org/10.1016/j.ijscr.2021.105976
Received 18 April 2021; Received in revised form 7 May 2021; Accepted 9 May 2021
Available online 13 May 2021

Table 1
Laboratory findings at the Emergency Department access.

Laboratory test	Finding	Normal range
WBC count	6.03 K/µl	4.00–10.80
Hemoglobin	13.20 g/dL	12.00–16.00
PLT count	192 K/µl	130–424
INR	0.93	0.80–1.20
CRP	0.50 mg/L	<5.00
ALT	11 U/L	<49
AST	25 U/L	<34
Bilirubin	0.5 mg/dL	0.3–1.2
ALP	77 U/L	33–98
GGT	9 U/L	<38

WBC: White Blood Cells; PLT: platelet; INR: International Normalized Ratio; CRP: C-reactive protein; ALT: Alanine Amonotransferase; AST: Aspartate Transaminase; ALP: Alkaline Phosphatase; GGT: Gamma-glutamyltransferase.

surgery. At the gallbladder check at the end of surgery we noticed a gallbladder filled with a white unusual paste-like material with interposed micro-stones (<5 mm) and therefore the LBS diagnosis was made (Fig. 2). Histological examination of the gallbladder showed a chronic cholecystitis with acute exacerbation.

The postoperative course was uneventful and she was discharged on the first postoperative day. Through a literature search, we became aware of the rare but possible association between LBS and primary hyperparathyroidism [2,3] and therefore an endocrine-metabolic screening was performed with biochemical evidence of normocalcemic hyperparathyroidism and Vitamin D deficiency (Table 2). A neck ultrasound was negative for parathyroid hyperplasia or adenomas.

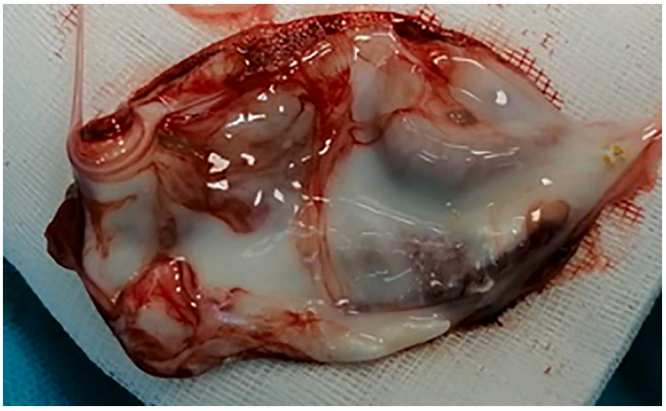

Fig. 2. The gallbladder check at the end of intervention showed a gallbladder filled with a white unusual paste-like material with interposed micro-stones (<5 mm).

Table 2
Laboratory findings of endocrine-metabolic screening.

Laboratory test	Finding	Normal range
Serum calcium	9.1 mg/dL	8.7–10.4
Serum phosphorus	3.8 mg/dL	2.4–5.1
Urinary calcium excretion	150 mg/24 h	50–150
Vitamin D (25OHD)	21.1 ng/mL	25–80
Parathormone	40.2 pg/mL	6.5–36.8

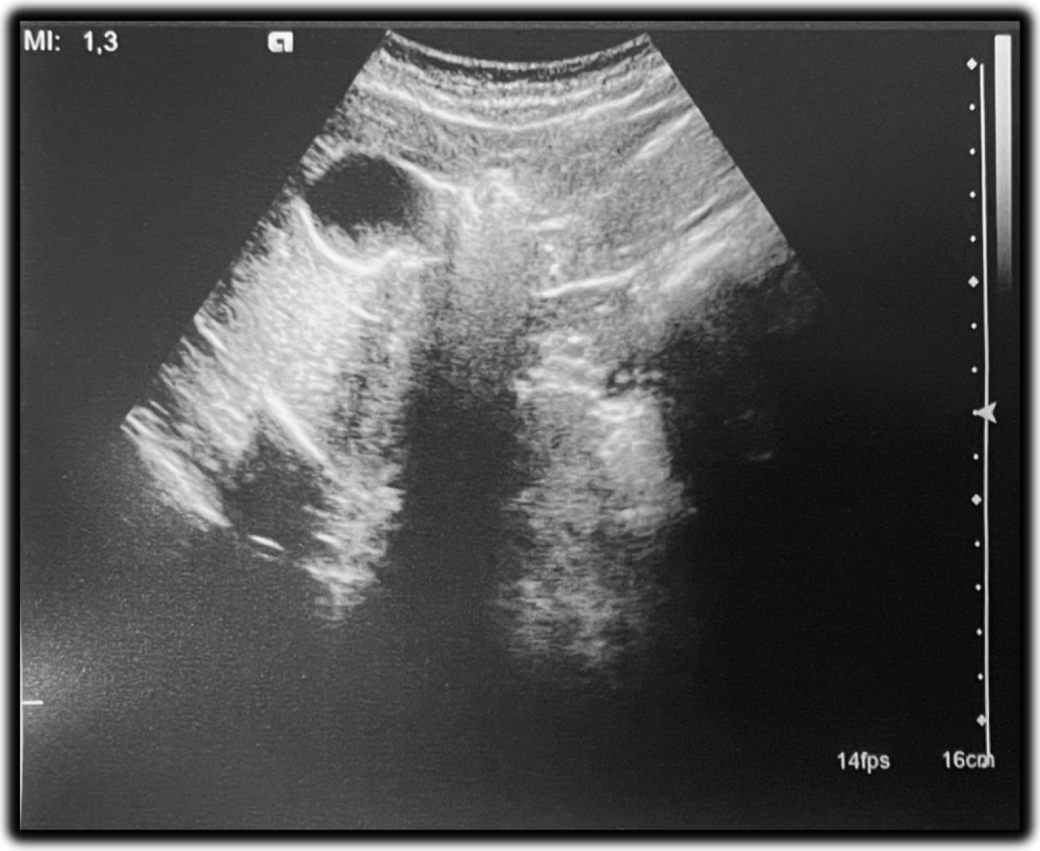

Fig. 1. An ultrasound picture which shows the presence of millimetric stones in the gallbladder without inflammation figures.

3. Discussion

Prevalence of LBS varies between 0.1 and 1.7% of cholecystectomy for benign gallbladder disease, being more frequent among young female [4,5]. Even if the exact etiopathogenetic mechanism is not known, calcium carbonate precipitation seems to be facilitated by the bile stasis [6]. Bile stasis can also be affected by gonadal steroids and their dramatic increase during pregnancy; a cholestatic effect of estrogen is known and in addition to estrogen, progesterone and its metabolites are of considerable importance in the modulation of bile acid signalling pathways, thus having an impact on the cholestatic phenotype [7]. In our patient, the recent pregnancy with its related bile stasis, have probably played a key role in the micro-stones formation and calcium carbonate accumulation with LBS manifestation. The chronic inflammatory changes at the histological examination could be either a contributing factor of calcium carbonate deposition or not specific and secondary.

In a few exceptional case reports [2,3], bile calcium deposition has been correlated to a primary hyperparathyroidism with parathyroid adenoma. However, in these exceptional reports characterized by high serum calcium levels related to hyperparathyroidism, obstruction of cystic duct and inflammation of the gallbladder seemed to be also present, facilitating calcium deposition. An endocrinological screening is therefore recommended in patients affected by LBS, also after surgery. In our case, the endocrinological laboratory tests highlighted a normocalcemic hyperparathyroidism secondary to Vitamin D deficiency probably not related to the LBS and therefore it could be considered an incidental finding probably related to the recent pregnancy. Note that vitamin D deficiency is quite common but underestimated in pregnancy leading to hyperparathyroidism, calcium bone mobilization and osteopenia.

The main symptoms of LBS (right hypochondrium and epigastrium pain) and its potential complications (cholecystitis, pancreatitis and obstructive jaundice) are the same of cholelithiasis. Actually, symptoms and complications are mainly caused by the frequent concomitant cholelitiasis, more than the calcium carbonate precipitation. Moreover, LBS is a rare condition. In view of this considerations, it's quite difficult to identify an algorithm for LBS diagnosis, even considering that the surgical treatment of symptomatic LBS is laparoscopic cholecystectomy, the same of symptomatic or complicated cholelithiasis.

The preoperative diagnosis of LBS could be done with abdominal X-ray/CT scan [8] while abdominal ultrasound is much less specific, but could reveal the concomitant cholelithiasis and its potential complications. Considering the higher frequency of LBS among young female, abdominal X-ray/CT scan are often avoided, leading to the possibility of an intraoperative diagnosis by checking the gallbladder content, as in our specific report. Note that abdominal X-ray and especially abdominal CT scan could help in the differential diagnosis from porcelain gallbladder in which the calcification is limited to the gallbladder wall instead of its entire content. Magnetic resonance cholangiopancreatography (MRCP) should be done in case of clinical and/or laboratory findings of cholestasis. In case of obstruction of common bile duct, laparoscopic cholecystectomy has to be associated to a concomitant endoscopic retrograde cholangiopancreatography (ERCP).

4. Conclusion

LBS is a rare condition. In our patient the recent pregnancy with its related bile stasis have probably played a key role on its etiopathogenesis. Abdominal X-ray/CT scan are the gold standard for preoperative diagnosis even if not pivotal. The treatment of choice of LBS is laparoscopic cholecystectomy, eventually associated to ERCP in case of common bile duct obstruction. A following endocrinological screening should be performed to rule out a concomitant calcium metabolism disorder. Knowledge of this rare condition could help general surgeons handle it properly.

Sources of funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Ethical approval

Ethical approval was not required for this case report.

Informed consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Registration of research studies

Not applicable.

Guarantor

Marco Migliore and Giorgio Giraudo act as guarantors for the report and accept responsibility for the work.

Provenance and peer review

Not commissioned, externally peer-reviewed.

CRediT authorship contribution statement

Marco Migliore, MD conceived, designed and drafted the article.

Giorgio Giraudo, MD, Laura Gianotti, MD, Valentina Testa, MD and Felice Borghi, MD contributed to conception of the work and contributed to critical revision of the manuscript for intellectual content.

All authors listed above gave final approval of the version to be published and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Declaration of competing interest

The authors report no declarations of interest.

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