Case report

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

Marco Migliore a,1, Giorgio Giraudo a, Laura Gianotti b, Valentina Testa a, Felice Borghi a

a Department of Surgery, General and Oncologic Surgery Unit, Santa Croce e Carle Hospital, Cuneo, Italy
b Division of Endocrinology Diabetology and Metabolism, S. Croce and Carle Hospital, Cuneo, Italy

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.
surgery. At the gallbladder check at the end of surgery we noticed a
gallbladder filled with a white unusual paste-like material with inter-
posed 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 ul-
trasound was negative for parathyroid hyperplasia or adenomas.

| 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 Aminotransferase; AST: Aspartate
Transaminase; ALP: Alkaline Phosphatase; GGT: Gamma-glutamyltransferase.

| 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.

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).
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 epigastrum 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 cholelithiasis, 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.

References

[1] R. Agha, T. Franchi, C. Sohrabi, M. Ginimol, A. Kerwan, SCARE Group, The SCARE 2020 guideline: updating consensus surgical Case Report (SCARE) guidelines, Int. J. Surg. 84 (2020) 226–230.
[2] Y.S. Koca, T. Koca, I. Barut, Limy bile syndrome complicated with primary hyperparathyroidism, Case Rep. Surg. 2015 (2015) 928217.
[3] Y. Takatori, K. Yamauchi, Y. Negoro, K. Noro, A. Yoshida, W. Nanamiya, M. Tamai, T. Kobayashi, Y. Yamane, S. Akamoto, N. Suzuki, A. Sasaki, Limy bile syndrome complicated with primary hyperparathyroidism, Intern. Med. 42 (1) (2003) 44–47.
[4] M.M. Suddhakar Krishnan, K.H. Lim, Limy bile: case report and review of literature, Singap. Med. J. 24 (1983) 374–376.
[5] Y. Masuda, Y. Mizuguchi, T. Kanda, H. Furuki, Y. Mamada, N. Tanai, Y. Nakamura, M. Yoshioka, A. Matsushita, Y. Kawano, T. Shimizu, E. Uchida, Successful treatment of limy bile syndrome extending to the common bile duct by laparoscopic cholecystectomy and common bile duct exploration: a case report and literature review, Asian J. Endosc. Surg. 10 (1) (2017) 59–62.
[6] S. Narayshkin, B.W. Trotman, E.C. Raffensperger, Milk of calcium bile: evidence that gallbladder stasis is a key factor, Dig. Dis. Sci. 32 (9) (1987) 1051–1055.
[7] P.H. Dixon, C. Williamson, The pathophysiology of intrahepatic cholestasis of pregnancy, Clin. Res. Hepatol. Gastroenterol. 40 (2) (2016) 141–153.
[8] E. Peroux, Y. Geoffroy, J. Potet, Unenhanced computed tomography to identify intrahepatic and extrahepatic limy bile, Clin. Gastroenterol. Hepatol. 10 (3) (2012) e27–e28.