



# Cholecystoduodenal fistula caused by aggressive mucinous gallbladder carcinoma with a porcelain gallbladder

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## Abstract

Cholecystoduodenal fistula secondary to gallbladder carcinoma (GBC) is extremely rare and develops when the tumor penetrates into the adjacent duodenum. A porcelain gallbladder is also a very rare entity that involves the calcification of the gallbladder wall and can be associated with the development of GBC. Herein, we report an unusual case of a patient with cholecystoduodenal fistula, which has been caused by aggressive mucinous gallbladder carcinoma with a porcelain gallbladder. A 68-year-old man was referred to our department due to significant accumulation near the neck of the gallbladder detected by FDG positron emission tomography/computed tomography (PET/CT), which was performed as a check-up of postpneumectomy for lung cancer. Abdominal contrast CT and magnetic resonance imaging revealed porcelain-like circumferential calcification of the gallbladder wall and a mass in the region detected by FDG PET/CT. Furthermore, upper endoscopy revealed a submucosal tumor with apical ulceration in the posterior wall of the duodenal bulb. Histopathological examination of its biopsy specimen rendered a diagnosis of adenocarcinoma. The patient was preoperatively diagnosed with either gallbladder cancer or duodenal cancer, and subtotal stomach-preserving pancreatoduodenectomy and radical cholecystectomy with gallbladder bed resection were performed. The resected gallbladder revealed a porcelain gallbladder, which formed the cholecystoduodenal fistula. These specimens were histopathologically diagnosed as mucinous adenocarcinoma of the gallbladder with an abundant mucin production.

**Keywords** Cholecystoduodenal fistula · Mucinous adenocarcinoma · Porcelain gallbladder

## Introduction

Gallbladder carcinoma (GBC) is rare and characterized by a lack of symptoms in the initial stage, leading to difficulties in treatment [1]. Histopathologically, the majority of GBCs are adenocarcinomas. Among the adenocarcinomas, mucinous adenocarcinoma is a rare variant that comprises approximately 2.5% of all of the GBCs. It is characterized by extracellular mucin, which comprises more than 50% of the tumor volume [2]. A porcelain gallbladder is also a very rare

entity that involves the calcification of the gallbladder wall and can be associated with the development of GBC [3].

Cholecystoduodenal fistula (CDF) has been reported with an incidence of 0.15–5% in biliary diseases [4]. Although most CDFs occur as late complications of gallstone disease, they can develop following GBC when the tumor penetrates into the adjacent duodenum.

Herein, we report an unusual case of a patient with CDF caused by aggressive mucinous gallbladder carcinoma with a porcelain gallbladder.

## Case report

A 68-year-old man presented to our department because FDG PET/CT demonstrated an intense uptake near the neck of the gallbladder. His medical history included lower lobectomy of the right lung 4 years ago and upper lobectomy of the right lung for lung cancer 2 years ago. FDG PET/CT

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had been performed during follow-up care for lung cancer every 6 months, and this time, it revealed porcelain-like circumferential calcification of the gallbladder wall (Fig. 1a). Furthermore, it also revealed an abnormal accumulation of FDG near the neck of the gallbladder (Fig. 1b). Physical examinations revealed no abnormal findings. Blood tests showed that serum CEA and CA19-9 were slightly elevated at 12.4 ng/ml and 778 U/ml, respectively. Meanwhile, a liver function test analysis, including the assessment of aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, and lactate dehydrogenase, was normal. However, gamma-glutamyltransferase was slightly elevated at 88 U/L. On ultrasound sonography (US), the gallbladder lumen could not be observed as US showed acoustic shadowing caused by the calcification of the gallbladder.

Contrast-enhanced CT revealed circumferential thickening and calcification of the gallbladder wall. It also revealed a 33- × 25-mm-diameter low-density mass between the posterior wall of the duodenum bulb and gallbladder neck, which was thought to be the region of FDG uptake by FDG PET/CT (Fig. 2a, b). T2-weighted magnetic resonance imaging (MRI) showed a lobulated mass with high signal intensity (Fig. 2c). MR cholangiopancreatography revealed no findings in the bile ducts (Fig. 2d). On the other hand, as the mass was in contact with the duodenum, an upper endoscopy was performed. The endoscopy revealed a submucosal tumor (SMT) with apical ulceration in the posterior wall of the duodenal bulb, measuring approximately 20 mm (Fig. 3). A biopsy specimen obtained from the apical ulceration of the SMT showed an adenocarcinoma by histopathological examination. Finally, the patient was preoperatively diagnosed with either gallbladder cancer originated from its neck or duodenal cancer.

We performed subtotal stomach-preserving pancreatoduodenectomy and radical cholecystectomy including lymph node dissection with gallbladder bed resection. Part of the neck or body of the gallbladder was adherent to the posterior wall of the duodenal bulb and formed a fistula. The resected gallbladder revealed a porcelain gallbladder, which had formed the CDF (Fig. 4a–c). The gallbladder wall diffusely

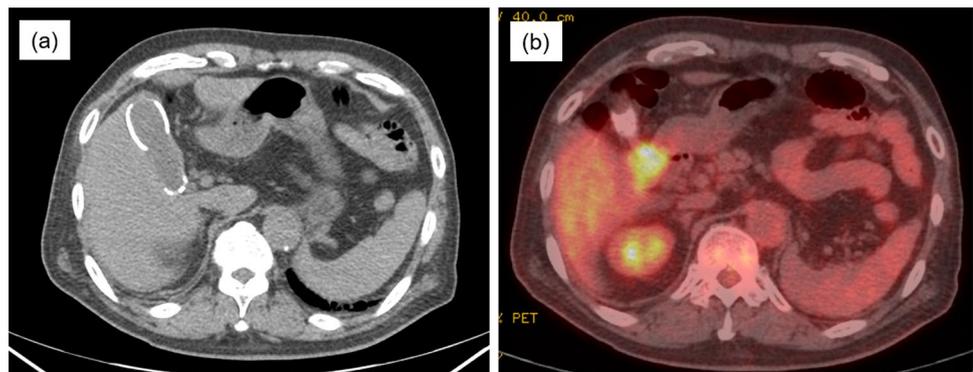
thickened and its lumen was filled by necrosis and calculi. A histopathological study revealed cancer cells in the extensive gallbladder wall, and fistula to the duodenum and invasion of the liver (Figs. 5, 6a, b, 7). The increase in tubulovillous adenocarcinoma with abundant mucin production was the main constituent, and mucinous nodules were extensively present. Moderately or poorly differentiated adenocarcinoma cells were also observed at the site of invasion, as well as lymphatic vessel invasions. The final diagnosis was mucinous adenocarcinoma of the porcelain gallbladder with invasions to the duodenum and liver.

## Discussion

Gallbladder carcinoma is one of the most common biliary tract malignancies [5, 6]. Gallbladder carcinoma is difficult to diagnose because there are no prominent signs and symptoms in its early stage [7]. Although an increasing number of mucin-producing carcinomas have been observed in either pancreatic or biliary duct tumors, mucinous adenocarcinoma of the gallbladder is still rare and constitutes approximately 2.5% of these carcinomas [8–11]. The first case of mucinous adenocarcinoma of the gallbladder was described by Ishibashi et al. [9]. Mucinous adenocarcinoma produces high-viscosity fluid inside the gallbladder. US and MRI are useful for diagnosing it due to their ability to show the highly viscous character of the gallbladder's fluid content. In our case, the gallbladder lumen could not be identified by US because of acoustic shadowing of the porcelain gallbladder. Meanwhile, MRI was helpful in the qualitative diagnosis of the region of FDG uptake by FDG PET/CT. A T2-weighted MRI showed a lobulated mass with high signal intensity, which suggested mucinous adenocarcinoma. Importantly, mucinous adenocarcinoma is usually thought to be more aggressive and to spread more easily than non-mucinous adenocarcinoma [12]. Due to its rarity, however, the prognosis and optimal treatment remain unclear [7, 12].

Cholecystoenteric fistula was first described by Courvoisier in 1890 [13]. The fistula can form anywhere in the

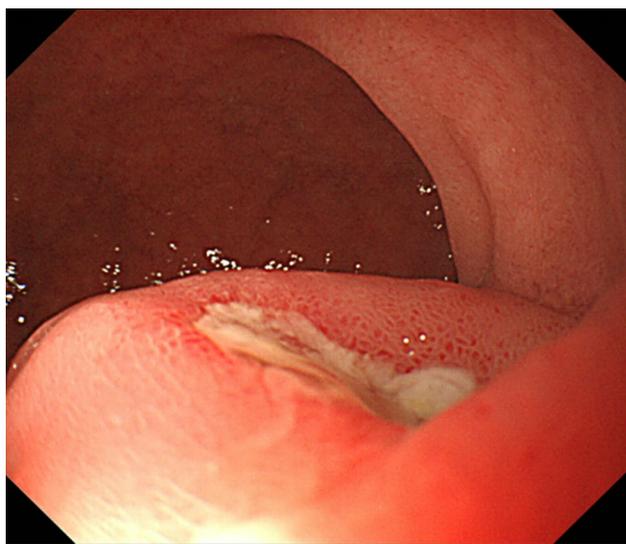
**Fig. 1** **a** PET-CT image showing a porcelain gallbladder with a circumferential calcification of the gallbladder wall. **b** PET-CT image revealed a high FDG uptake adjacent to the neck of the gallbladder





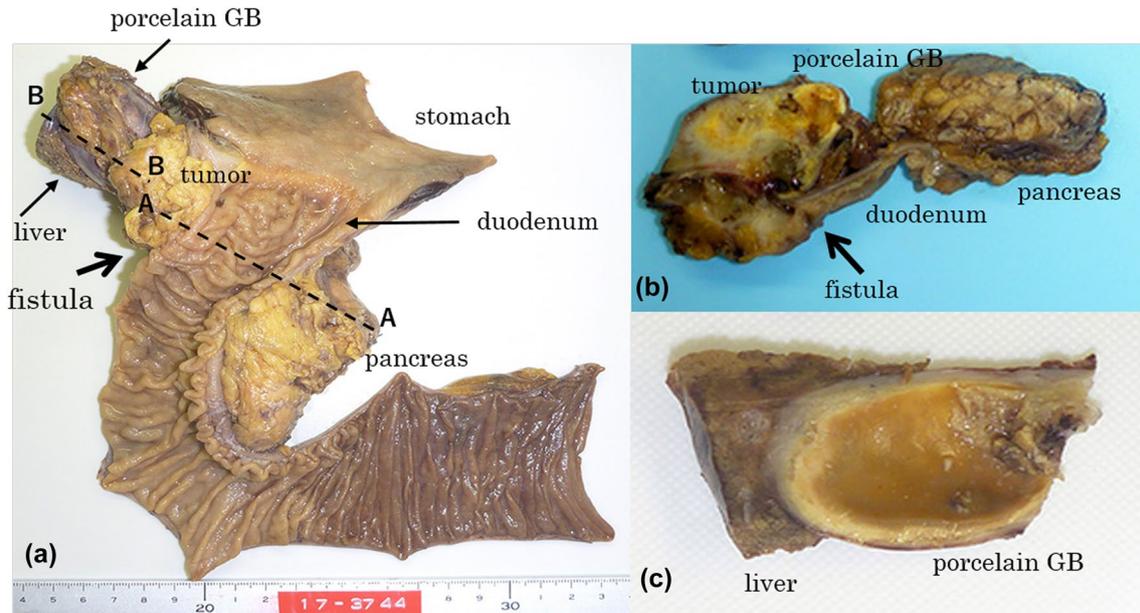
**Fig. 2** **a** CT revealed that the mass lesion was primarily enhanced at the circumference. **b** Coronal image of CT revealed that the mass contacted the duodenal wall firmly, which was suspicious of the exist-

ence of CDF. **c** T2-weighted MRI revealed a high signal intensity lobulated mass. **d** MRCP revealed no significant findings in the bile ducts



**Fig. 3** Endoscopy images revealed an SMT with a central ulceration

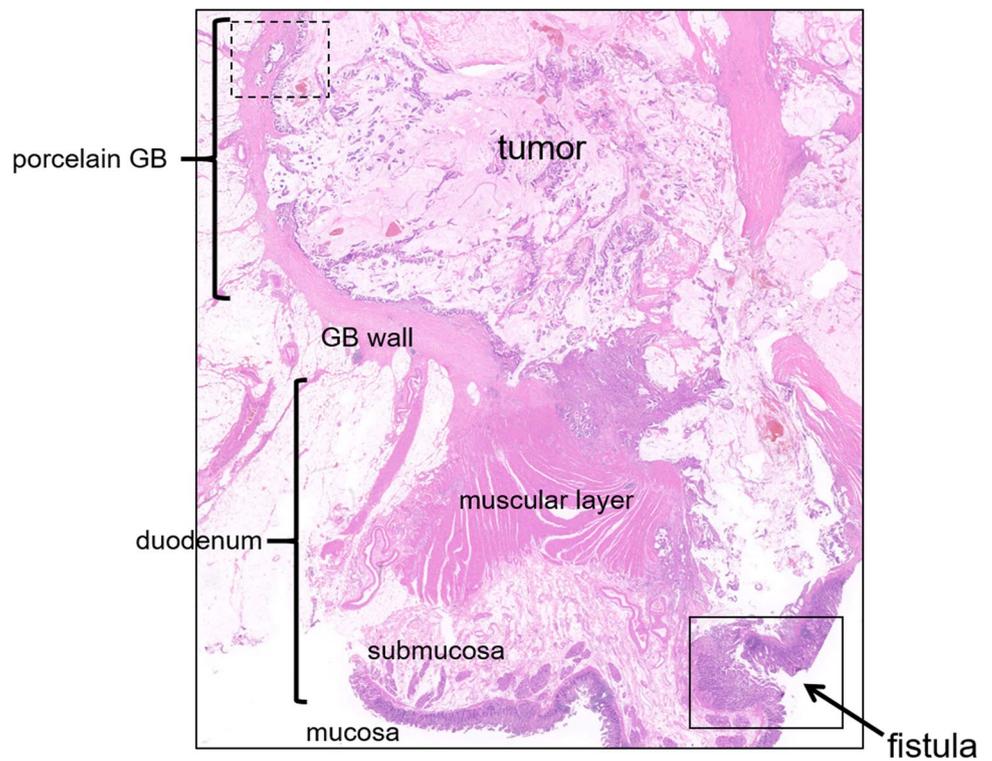
gastrointestinal tract, with the most common location being cholecystoduodenal (~60%), cholecystocolic (17%), cholecystogastric, and choledochoduodenal fistulas (5%) [14]. Cholecystoduodenal fistula is the most common type of cholecystoenteric fistula, and it is often accompanied by complications of acute or chronic cholecystitis in noncalcified gallbladder. Delpierre et al. reported a case of acute cholecystitis in a porcelain gallbladder, resulting in a CDF [15]. Cholecystoduodenal fistula in our case occurred in a porcelain gallbladder with gallbladder carcinoma, which had no acute inflammation. It is still unclear whether a porcelain gallbladder without acute inflammation has a direct relationship with CDF. Meanwhile, a small percentage of cholecystoenteric fistula accompanied by malignancy has been reported [16]. Fukunaga et al. investigated the causes of 187 cases of cholecystoenteric and reported that 91% of the cases had calculous cholecystitis, 4% duodenal ulcer penetration, and 4% had duodenal infiltration of gallbladder carcinoma [17]. They presumed the mechanism of the formation of cholecystoenteric by infiltration of gallbladder carcinoma



**Fig. 4** a The resected specimen including gallbladder, duodenum, pancreas head and part of liver. b The cut surface of line A shown in a. The arrow represents the cholecystoduodenal fistula. c The cut sur-

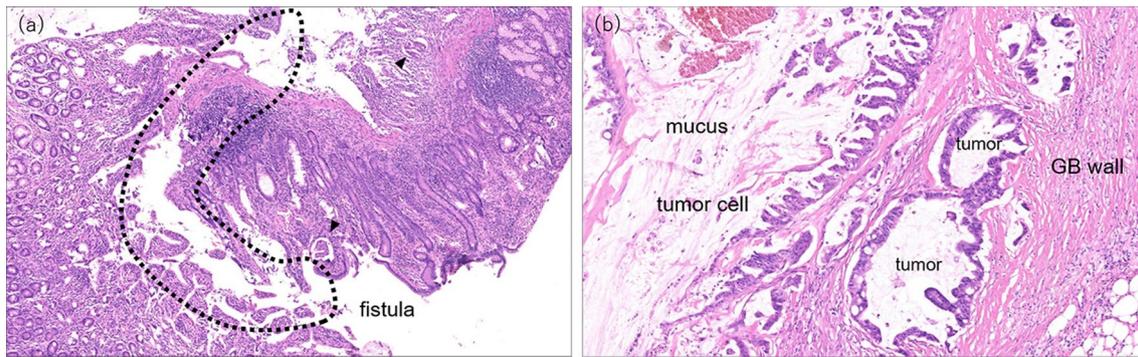
face of line B shown in a. Porcelain gallbladder and gallbladder bed of the resected liver are represented

**Fig. 5** A microscopic image of cholecystoduodenal fistula. Gallbladder cancer invades in the wall of the duodenal and form cholecystoduodenal fistula (arrow)



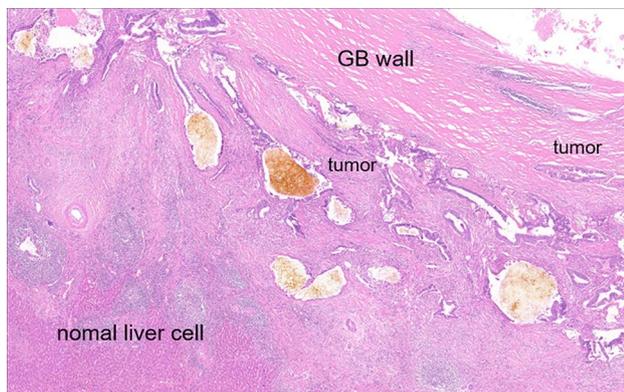
as follows. Collapse of cancer tissue might induce tissue necrosis and penetration to duodenal wall, resulting in internal fistula formation between gallbladder and duodenal wall. On the other hand, Bochus advocated that primary cause of

fistula formation was not so much the duodenal invasion of the gallbladder carcinoma but the existence of gallstones and chronic cholecystitis that preceded cancer invasion [18]. Although, in our case, it was difficult to clarify how the



**Fig. 6** **a** The orifice of the fistula at higher magnification (square in Fig. 5). The dotted lines show the fistula. Importantly, tumor cells are shown in the duodenal mucosa along the fistula (arrowheads). **b**

Tumor cells in the wall of the gallbladder (dotted square in Fig. 5). Adenocarcinoma cells grow within the wall of gallbladder and retention of mucous is seen inside of the gallbladder



**Fig. 7** Hepatic invasion of the tumor. Gallbladder wall is replaced with fibrous connective tissues and invaded by tumor cells. Furthermore, tumor cells invade liver bed

existence of porcelain gallbladder had a role in causing the gallbladder carcinoma and CDF, we speculated the mechanism that gallbladder carcinoma directly invaded to the wall of the duodenum and formed CDF as tumor cells were seen in the duodenal mucosa along the fistula in histopathology.

Nishi et al. examined the histopathology of gallbladder carcinoma with cholecystoenteric fistula. They reported that the proportion of squamous cell carcinoma and adenocarcinoma was higher than it of adenocarcinoma [19]. This might demonstrate that the difference of histologic features plays a role in causing direct infiltration to duodenal wall and fistula formation. Histopathology of the carcinoma in our case was mucinous adenocarcinoma, which is thought to be more aggressive than non-mucinous adenocarcinoma.

A porcelain gallbladder is also a rare entity and has been shown in less than 1% of cholecystectomy specimens [3, 20]. Interestingly, several authors have reported that the gallbladder is frequently accompanied by gallbladder carcinoma [21]. Etala reported that the incidence of gallbladder carcinoma associated with a porcelain gallbladder was

62% [22]. In general, cholecystectomy has been performed to prevent its further progression to carcinoma when diagnosed to be a porcelain gallbladder, as it might be thought as a premalignant condition. However, several studies have recently shown that the potential risk of developing carcinoma in a porcelain gallbladder might be much lower than previously described [23, 24]. In a subgroup analysis of 13 studies, the rate of gallbladder malignancy was noted to be only 6% (ranging from 0 to 33%) in patients with gallbladder calcification including a porcelain gallbladder [23]. Moreover, Machado et al. advocate that based on evidence in the current literature, a prophylactic cholecystectomy is not routinely recommended for all patients with a porcelain gallbladder and should be restricted to those with conventional indications, such as young patients [24]. On the other hand, Joo et al. recently reported a case of mucinous adenocarcinoma with a porcelain gallbladder [25]. In our case, mucinous adenocarcinoma was also accompanied with a porcelain gallbladder, resulting in a CDF. Further investigations about the relationship between porcelain gallbladder and malignancy are necessary.

In conclusion, we have reported an unusual case of CDF caused by aggressive mucinous gallbladder carcinoma with a porcelain gallbladder. Attention should be paid to porcelain gallbladders, given that it might be accompanied by cancer, and gallbladder mucinous adenocarcinoma might be more aggressive and prone to more easily forming CDF.

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## Compliance with ethical standards

**Conflict of interest** We state that there is none to declare.

**Human/animal rights** All procedures followed have been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

**Informed consent** Informed consent was obtained from all patients for being included in the study.

## References

- Sharma A, Sharma KL, Gupta A, et al. Gallbladder cancer epidemiology, pathogenesis and molecular genetics: recent update. *World J Gastroenterol*. 2017;23:3978–98. <https://doi.org/10.3748/wjg.V23.i22.3978>.
- Albores-Saavedra J, et al. Carcinoma of the gallbladder and extrahepatic bile ducts. In: Hamilton SR, Aaltonen LA, editors. WHO classification of tumors. Pathology and genetics of tumors of the digestive system. Lyon: IARC Press; 2000. pp. 206–12.
- Gómez-López JR, De Andrés-Asenjo B, Ortega-Loubon C. A porcelain gallbladder and a rapid tumor dissemination. *Ann Med Surg (Lond)*. 2014;3:119–22. <https://doi.org/10.1016/j.amsu.2014.09.002> (eCollection 2014 Dec).
- Angrisani L, Corcione F, Tartaglia A, et al. Cholecystoenteric fistula is not a contraindication for laparoscopic surgery. *Surg Endosc*. 2001;15:1038–41.
- Misra S, Chaturvedi A, Misra NC, et al. Carcinoma of the gallbladder. *Lancet Oncol*. 2003;4:167–76.
- Hundal R, Shaffer EA. Gallbladder cancer: epidemiology and outcome. *Clin Epidemiol*. 2014;6:99–109.
- Huang CP, Chiou YY, Chou YH, et al. Imaging findings in mucin-producing carcinoma of the gallbladder. *J Formos Med Assoc*. 2006;105:427–30.
- Tangde AR, Rathod SG, Joshi AR, et al. Mucinous adenocarcinoma of gallbladder: a case report. *Int J Res Med Sci*. 2017;5:5082–4.
- Ishibashi H, Minesuga K, Yamaguchi A, et al. A case of mucin-producing carcinoma of the gallbladder. *Tan to Sui*. 1986;7:1173–8 (in Japanese).
- Tian H, Matsumoto S, Takaki H, et al. Mucin-producing carcinoma of the gallbladder: imaging demonstration in four cases. *J Comput Assist Tomogr*. 2003;27:150–4.
- Nobusawa H, Hashimoto T, Munechika H, et al. US and CT findings of mucinous carcinomas of the gallbladder. *Nippon Act Radiol*. 1994;54:1359–67 (in Japanese).
- Dursun N, Escalona OT, Roa JC, et al. Mucinous carcinomas of the gallbladder: clinicopathologic analysis of 15 cases identified in 606 carcinomas. *Arch Pathol Lab Med*. 2012;136:1347–58.
- Ozkan A, Ozaydin I, Kaya M, et al. Malrotation-associated cholecystoduodenal fistula. *Am J Case Rep*. 2014;15:18–21.
- Mavroeidis VK, Matthioudakis DI, Economou NK, et al. Bouveret syndrome—the rarest variant of gallstone ileus: a case report and literature review. *Case Rep Surg*. 2013;2013:839370.
- DelPierre I, Tack D, Moisse R, et al. Cholecystoduodenal fistula in a porcelain gallbladder. *Eur Radiol*. 2002;12:2284–6 (Epub 2002 Feb 2).
- Hatakeyama K, Nagakawa T, Suga T, et al. Carcinoma of the gallbladder which progress on the mucosa of choledochocolonic fistula Nihon Shokakibyō Gakkai Zasshi. 2009;106:1063–9 (in Japanese).
- Fukunaga H, Aoki Y, Katsumi M, et al. Spontaneous internal biliary fistula. *J Jpn Pract Surg Soc*. 1982;43(2):173–82 (in Japanese).
- Bochus HL. *Gastroenterology*. 2nd ed. vol. 3. Philadelphia: Saunders; 1966. p. 852.
- Nishi T, Sogabe T, Shimizu T, et al. Tannoujuunishichourou wo Gappeishita Tannougan no Ichirei. (A case of gallbladder carcinoma with a cholecystoduodenal fistula. Tan to Sui. 1991;12:1009–15 (in Japanese).
- Gupta S, Misra S. Rare presentation of malignant porcelain gallbladder with intrahepatic ductal calcification and surgical obstructive jaundice. *Indian J Surg Oncol*. 2012;3(01):44–6.
- Polk HC Jr. Carcinoma and the calcified gall bladder. *Gastroenterology*. 1966;50:582–5.
- Etala E. Cancer de la vesicula biliar. *Prensa Med Argent*. 1967;54:1479–84.
- Schnelldorfer T. Porcelain gallbladder: a benign process or concern for malignancy? *J Gastrointest Surg*. 2013;17:1161–8.
- Machado NO. Porcelain gallbladder: decoding the malignant truth. *Sultan Qaboos Univ Med J*. 2016;16:e416–21.
- Joo YE, Kim HS, Choi SK, et al. Case of mucinous adenocarcinoma with porcelain gallbladder. *J Gastroenterol Hepatol*. 2003;18:995–8.

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