

Calcified Carcinoma of the Gallbladder with Calcified Nodal Metastasis Presenting as a Porcelain Gallbladder: A Case Report

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Porcelain gallbladder is regarded as a risk factor of gallbladder cancer. A porcelain gallbladder with calcified regional lymph nodes was found using computed tomography (CT) and magnetic resonance imaging (MRI) in a 43-year-old man who presented with nausea, vomiting, and abdominal pain. His cholecystectomy specimen showed diffuse wall thickening and contained small gallstones. Histological examination revealed diffuse infiltrative adenocarcinoma with extensive intratumoral calcification (calcified carcinoma). The majority of the calcified material was located within or replaced the tumor glands, and was not found in the stroma. A lymph node was totally replaced with a calcified metastatic adenocarcinoma. To the best of our knowledge, only one case of calcified lymph node metastasis from a calcified carcinoma of the gallbladder has been previously reported in the literature. We herein add a case of calcified carcinoma of the gallbladder with calcified lymph node metastasis, presenting as a porcelain gallbladder on CT and MRI.

Key words

Gallbladder, Carcinoma, Metastasis, Lymph node, Calcification, Computed tomography, Magnetic resonance imaging

Introduction

Porcelain gallbladder, or calcified gallbladder, is an uncommon finding of chronic cholecystitis characterized by extensive calcification in the wall of the gallbladder [1]. The term "porcelain gallbladder" has been used to describe the bluish discoloration and brittle consistency of the gallbladder wall, but is more generally used as a description for all types of gallbladder wall calcification [1]. The prevalence of porcelain gallbladder in cholecystectomy specimens ranges from 0.06-0.80% [2]. The incidence of gallbladder cancer from porcelain gallbladder has not been clearly delineated and was estimated to range from 12.5-61% in a study dating back to the 1960s [3], however two more recent studies

reported a much lower incidence of gallbladder cancer in porcelain gallbladder (0-5%) [4,5]. The association between porcelain gallbladder and carcinoma remains unclear with controversial results depends on the calcification patterns [5]. To the best of our knowledge, only one case of calcified lymph node metastasis from calcified carcinoma of the gallbladder has been previously reported in the literature.

In the present study, we introduce a case of calcified carcinoma of the gallbladder with calcified lymph node metastasis, presenting as a porcelain gallbladder using computed tomography (CT) and magnetic resonance imaging (MRI) along with a review of literature.

Case Report

A 43-year-old man presented with a 1-week history of nausea, vomiting, and abdominal pain. There were no palpable abdominal masses, and the rest of the abdominal examination was unremarkable. Laboratory data showed leukocytosis (white blood cell count, 16,790/mm³) and hyperbilirubinemia (total bilirubin, 3.7 mg/dL; direct bilirubin, 2.7 mg/dL) but a normal serum calcium level. Abdominal CT revealed circumferential calcification in the thickened gallbladder wall, cystic

duct lymph nodes with dense calcification and portocaval lymph nodes with partial calcification, and punctuated calcifications inside the gallbladder lumen (Fig. 1A). MRI of the abdomen demonstrated signal voids in the gallbladder and lymph nodes consistent with calcifications seen on CT (Fig. 1B). Surgery was initiated using a laparoscopic approach with an impression of cholecystitis and gallstones, but was converted to an open cholecystectomy. Numerous hard lymph nodes were seen under the common bile duct and one lymph node was biopsied. Palliative cholecystectomy was performed, and there was no evidence of peritoneal seeding. The resected gallbladder measured 6 × 3 × 2.5 cm

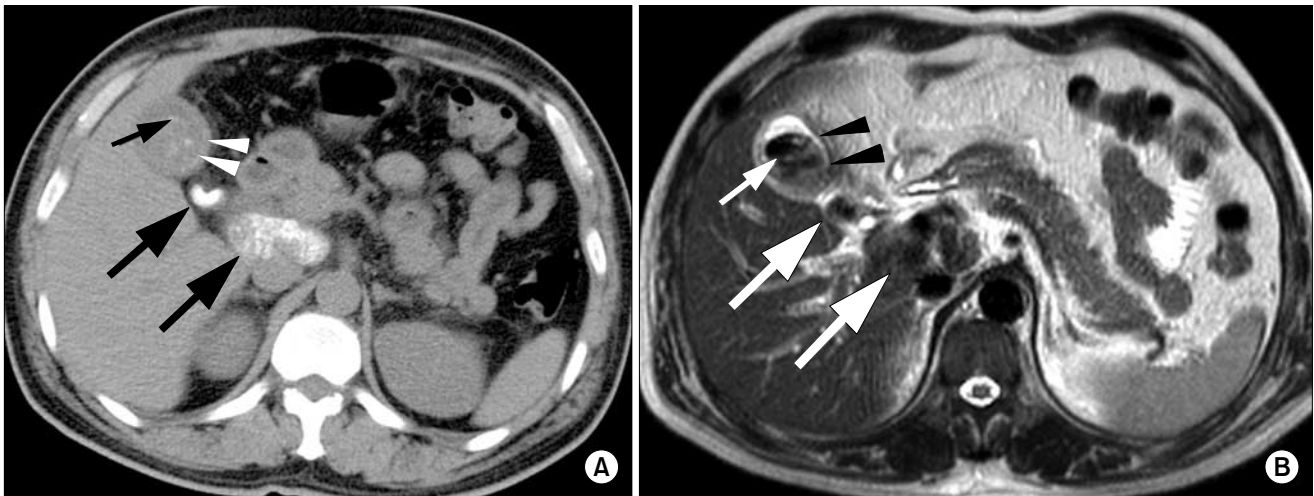


Fig. 1. (A) Unenhanced computed tomography scan showed circumferential calcification in the thickened wall of the gallbladder (arrowheads) and extensive calcified regional lymph nodes (arrows). Multiple punctuated hyperdense lesions, which were found to be gallstones, were also noted inside the gallbladder lumen (small arrow). (B) T2-weighted magnetic resonance image at 9000/1200 (TR/TE) demonstrated areas of signal void in the gallbladder wall (arrowheads), within enlarged lymph nodes (arrows), and inside the gallbladder lumen (small arrow).

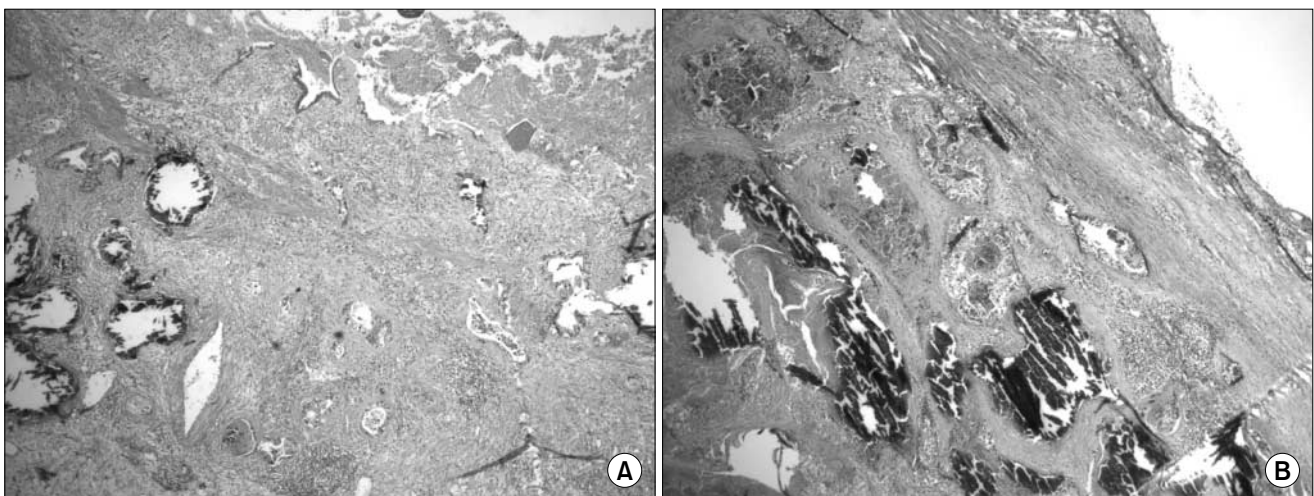


Fig. 2. (A) Histological examination of the resected gallbladder revealed denuded mucosa and infiltrative, well-differentiated adenocarcinoma with numerous fine to coarse calcifications. The majority of the calcified material was located within or replaced the tumor glands, and not found in the stroma (H&E, ×40). (B) Histological examination of the regional lymph node revealed metastatic adenocarcinoma with calcification (H&E, ×40).

with diffuse wall thickening up to 1 cm. Mucosal nodularity of the gallbladder was observed, and the gallbladder contained small gallstones. Histological examination of the resected gallbladder revealed denuded mucosa and infiltrating well-differentiated adenocarcinoma with numerous fine to coarse calcifications on entire lateral wall (Fig. 2A). The majority of the calcified material was located within or replaced the tumor glands, and was not found in the stroma. The tumor had invaded through the gallbladder wall and pericholecystic fat with frequent lymphatic and perineural invasions. A 1.5 cm sized lymph node was totally replaced with a metastatic adenocarcinoma with calcifications (Fig. 2B). As well, a resected margin of the cystic duct was involved with cancer. The cancer was measured to be stage IIB (T2N1M0).

The patient received concurrent chemoradiation (5580cGY, 31 fractions) for palliation, and 5-fluorouracil (400 mg/m²) was given for 3 days at the beginning and end of the therapy. The patient relapsed after 3 months with peritoneal seeding, and he received 6 cycles of combination chemotherapy with 5-fluorouracil, adriamycin (doxorubicin hydrochloride) and mitomycin C. The patient was still alive without recurrence at the 4-year follow-up.

Discussion

Porcelain gallbladder is rare and has been found in only 0.06-0.80% of cholecystectomy specimens [2]. It is more common in women than men, and is most commonly diagnosed in people between 50-70 years of age [3]. Although porcelain gallbladder has been regarded as a precancerous lesion, the relationship between gallbladder cancer and the porcelain gallbladder remains unclear. The reported frequency of carcinoma found in porcelain gallbladder specimens in 1960s ranged from 12.5-61% [3]. It is unclear whether the above data included cases of calcified carcinoma of the gallbladder. All current surgical treatment recommendations for porcelain gallbladder are based on these data; however two studies in 2001 reported a much lower incidence of gallbladder cancer in porcelain gallbladder (0 to 5%) [4,5]. Towfigh et al. [4] identified no carcinoma among 15 cases of porcelain gallbladder from 10,741 cholecystectomy specimens. Stephen and Berger [5] reported 44 porcelain gallbladders among 25,900 gallbladder specimens. Porcelain gallbladder is classified on the basis of the calcification pattern as complete (broad, continuous bands of calcification in the muscularis) or incomplete type (multiple, punctuate calcifications) [1,4-6]. The overall incidence of gallbladder cancer in porcelain gallbladder was 5% (2/44) and no cancer was found in the complete type [5]; therefore, it has been suggested that the two types of calcification are associated with different cancer risks [4-6]. A prophylactic simple cholecystectomy is the treatment of choice for porcelain gallbladder [7]. If a malignancy is detected postoperatively, a re-wedge resection of liver with dissection of the lymph nodes of hepato-duodenal ligament for T1 tumors and hepatic IVb/V resection combined with lymph node dissection for T2 tumors is recommended. More radical procedures are needed for advan-

ced tumors infiltrating the serosa or beyond [8]. Recently, laparoscopic cholecystectomy is even suggested for the complete type of porcelain gallbladder [7]. Due to the relatively low incidence of cancer in the completely calcified gallbladder, non-operative management is proposed for such gallbladder cases if the operation risk is high. More accurate criteria according to the calcification pattern may be needed to define porcelain gallbladder. On the basis of CT findings, our case appeared as the complete type; however, microscopically, the calcification was of the extensive intramural multiple punctuate form in the tumor glands. It may be difficult to pathologically differentiate a primary calcified carcinoma of the gallbladder from a carcinoma arising in a porcelain gallbladder because there are no pathological findings or descriptions for the calcifications observed in the previously reported cases of carcinoma arising in the porcelain gallbladder [2,3,9,10]. Calcification patterns with a broad continuous form along the fibrous stroma and no association with tumor glands or the metastatic lymph nodes in the carcinoma arising in porcelain gallbladder may be useful for the differential diagnosis.

The pathogenesis of intratumoral calcification may be explained by dystrophic calcification in the areas of tumor necrosis, likely resulting from a localized metabolic disturbance, i.e., lower metabolic rate and lower CO₂ concentrations, leading to a localized alkaline environment [11], or by the behavior of mucin glycoproteins as ion-exchange resins, a factor which may contribute to the deposition of calcium [12]. The majority of the reported cases of calcified carcinoma of the visceral organs and gallbladder were mucinous type of adenocarcinoma with multiple granular, punctuate calcifications on radiologic findings [13-15]. This type of calcification was usually located in the mucin pools. However, our case was not a mucinous type and the calcification may be more related to dystrophic calcification associated with tumoral necrosis. If intratumoral calcification is extensive in diffuse infiltrating carcinoma as observed in our case, the radiologic findings may appear as a complete-type of porcelain gallbladder. Thus, calcified carcinoma may have been included in the cases of so-called "cancer arising in porcelain gallbladder." Parker and Joffe [14] commented that his patient with calcified carcinoma of the gallbladder was relatively young, (a 44-year-old female), and most of the previously reported calcified carcinomas of visceral organ also tended to be young. Our case was also relatively young (43-year-old male); however the clinical characteristics of calcified carcinoma of the gallbladder could not be speculated on due to its rareness.

This case represents an unusual calcified metastatic lymph node from calcified carcinoma of the gall bladder and we could only identify one such previously reported case in the literature [14]. That report showed only a plain film of the abdomen, while our case revealed CT and MR findings of the abdomen. The abdominal CT presented here demonstrated circumferential calcifications in the thickened wall of the gallbladder, and the pathological examination showed numerous calcified tumor glands invading the gallbladder wall. There was also extensive calcification in the regional lymph nodes that were well defined with CT and MR. The lymph node was almost completely replaced by necrotic, calcified tumor glands with same pattern of calcification in the

gallbladder cancer and the metastatic lymph nodes.

Therefore, although no prior gallbladder image was available in our case, it is suggested that calcified carcinoma is a possible cause of porcelain gallbladder, i.e., porcelain gallbladder may result from the calcification of diffuse infiltrating tumor in the gallbladder wall. In addition to an uncommon occurrence, the detection of calcified lymph node metastasis on CT and MRI may be effective in differentiating a gallbladder carcinoma from porcelain gallbladder not harboring a carcinoma.

Conflicts of Interest

Conflict of interest relevant to this article was not reported.

References

1. Osler W. The principles and practice of medicine. 10th ed. New York: Appleton; 1925. p. 574.
2. Polk HC Jr. Carcinoma and the calcified gall bladder. *Gastroenterology*. 1966;50:582-5.
3. Ashur H, Siegal B, Oland Y, Adam YG. Calcified gallbladder (porcelain gallbladder). *Arch Surg*. 1978;113:594-6.
4. Towfigh S, McFadden DW, Cortina GR, Thompson JE Jr, Tompkins RK, Chandler C, et al. Porcelain gallbladder is not associated with gallbladder carcinoma. *Am Surg*. 2001;67:7-10.
5. Stephen AE, Berger DL. Carcinoma in the porcelain gallbladder: a relationship revisited. *Surgery*. 2001;129:699-703.
6. Shimizu M, Miura J, Tanaka T, Itoh H, Saitoh Y. Porcelain gallbladder: relation between its type by ultrasound and incidence of cancer. *J Clin Gastroenterol*. 1989;11:471-6.
7. Kwon AH, Inui H, Matsui Y, Uchida Y, Hukui J, Kamiyama Y. Laparoscopic cholecystectomy in patients with porcelain gallbladder based on the preoperative ultrasound findings. *Hepatogastroenterology*. 2004;51:950-3.
8. Goetze TO, Paolucci V. Adequate extent in radical re-resection of incidental gallbladder carcinoma: analysis of the German Registry. *Surg Endosc*. 2010;24:2156-64.
9. Berk RN, Armbuster TG, Saltzstein SL. Carcinoma in the porcelain gallbladder. *Radiology*. 1973;106:29-31.
10. Joo YE, Kim HS, Choi SK, Rew JS, Kim HJ, Kang HK, et al. Case of mucinous adenocarcinoma with porcelain gallbladder. *J Gastroenterol Hepatol*. 2003;18:995-8.
11. Sweeney DJ, Low VH, Robbins PD, Yu SF. Calcified lymph node metastases in adenocarcinoma of the colon. *Australas Radiol*. 1994;38:233-4.
12. Batlan LE. Calcification within the stomach wall in gastric malignancy: case report and review of literature. *Am J Roentgenol Radium Ther Nucl Med*. 1954;72:788-94.
13. Nagakura S, Shirai Y, Yamai K, Hatakeyama K. Calcification in mucinous cholangiocellular carcinoma. *Hepatogastroenterology*. 1999;46:465-6.
14. Parker GW, Joffe N. Calcifying primary mucus-producing adenocarcinoma of the gallbladder. *Br J Radiol*. 1972;45:468-9.
15. Rogers LF, Lastra MP, Lin KT, Bennett D. Calcifying mucinous adenocarcinoma of the gallbladder. *Am J Gastroenterol*. 1973;59:441-5.