



Case report

Synchronous tumors of gastric carcinoma combined gallbladder cancer and pseudotumor chronic pancreatitis

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ABSTRACT

Introduction and importance: Synchronous primary cancers in the stomach and gallbladder were not previously reported in the medical literature. Pseudotumor pancreatitis was also described many years ago. It was misdiagnosed and required surgery for pancreatic head neoplasms.**Presentation of case:** A 57-year-old male patient went to our hospital for abdominal pain. He was indicated for gastroduodenal endoscopy, and the result was adenocarcinoma. Abdominal ultrasound and Ctsan detected the gallbladder fundus's localized thickening structure and the pancreatic head's hyperechoic structure. The endoscopic ultrasound and MRI showed a gallbladder + pancreatic head tumor with chronic pancreatitis with pancreatic stones. The patient underwent distal gastrectomy, cholecystectomy, and pancreaticoduodenectomy. **Clinical discussion:** The detection of gastric cancer is often based on upper gastrointestinal endoscopy and biopsy results. Gallbladder cancer is often diagnosed at an advanced stage, and only very few patients are diagnosed early. Pancreatic cancer often occurs in the head of the pancreas. Symptoms may include obstruction of the common bile and Wirsung duct, often in advanced stages. Surgery for the gallbladder, distal stomach, and head of pancreatic tumors are related to each other located in a neighboring location in the anatomy, so surgery to remove all three tumors is relatively similar to a pancreaticoduodenectomy procedure.**Conclusion:** Synchronous tumors of gastric carcinoma combined with gallbladder cancer and pseudotumor chronic pancreatitis are rare. The attitude of treating these three diseases at the same time requires a tumor board. Simultaneous surgery for gallbladder, stomach, and pancreatic head tumors can be performed if the tumors are still in the resectable stage.

1. Introduction and importance

Synchronous primary cancers in the stomach and gallbladder have not previously been reported in the medical literature. Stomach cancer is a common malignancy, ranking sixth among diagnosed cancers worldwide, accounting for 5.6 % of all prevalent cancers, as reported in GLOBOCAN 2020 [1]. Gallbladder cancer ranks 25th among cancers according to GLOBOCAN 2020, accounting for 0.6 % of cancers in both genders [1]. Some cases are diagnosed with gallbladder metastasis from gastric cancer [2,3]. Gastric cancer associations worldwide, such as the

Japanese Gastric Cancer Association and the National Comprehensive Cancer Network, have provided many guidelines for diagnosing and treating gastric cancer [4,5]. The treatment of gallbladder cancer also has many guidelines from associations such as the Japanese Society of Hepato-Biliary-pancreatic Surgery and the European Society of Medical Oncology [6–8]. Pseudotumor pancreatitis was also described many years ago. It was misdiagnosed and required surgery as with a procedure for pancreatic head tumors [9]. There are many guidelines from different associations worldwide on diagnosis and management for each type of cancer [5,6,10]. However, combining treatment with multiple

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surgical techniques on the same patient makes surgeons ask many questions: Are these diseases and surgeries related, or can they be performed simultaneously? Can a patient endure so many procedures at the same time? It is a matter of individualized patient treatment and flexible application of guidelines in treating these cancers.

Starting from a rare case, without previous reports in the medical literature, with three primary pathologies discovered simultaneously, deciding on treatment requires a combination of many factors. Therefore, we report the case with concurrent gastric cancer, gallbladder cancer, and pseudotumor pancreatitis. This case report followed SCARE guidelines [11].

2. Presentation of case

A 57-year-old male patient had a history of epigastric pain six months before hospitalization with intermittent abdominal pain, no vomiting, and normal defecation. He was treated by medication without gastric endoscopy. He went to our hospital because of abdominal pain that had not responded to previous treatment. The general examination did not detect any abnormalities, such as jaundice or any medical equipment attached to the patient, and the abdominal examination found no tenderness or distention. The patient's ECOG performance status was grade 0. He was indicated for gastroduodenal endoscopy, which detected an ulcerative lesion in the lesser curvature (Fig. 1A). The ulcer biopsy showed invasive adenocarcinoma (Fig. 1C). The patient underwent an abdominal ultrasound, which detected the localized thickening structure of the gallbladder fundus and the hyperechoic structure of the pancreatic head parenchyma with scattered calcified nodules, suspected of chronic pancreatitis. The patient was assigned to a thoracoabdominal CT scan that detected enlargement of the solid portions and increased enhancement in the lumen of the gallbladder (arterial phase) and suspected images of the distal common bile duct stenosis causing dilation of the internal and extrahepatic biliary tract and chronic pancreatitis.

The endoscopic ultrasound and MRI showed a gallbladder + pancreatic head tumor with size 14×30 mm and 23×21 mm, respectively, chronic pancreatitis with pancreatic stones (MRI gallbladder tumor, mild dilatation of common bile duct, chronic pancreatitis) (Fig. 2A, 3A). CEA and CA19-9 tests were within normal range. The Total bilirubin blood test was $10.5 \mu\text{mol/L}$, and the direct bilirubin was $4 \mu\text{mol/L}$. The protein and albumin blood test were 69.5 g/L and 36.1 g/L , respectively. The patient was well-nourished with the Subjective Global Assessment (SGA) score-A. We discussed treatment options with radiologists, sonographers, endoscopists, and oncologists. The patient was diagnosed with three primary tumors without distant and peritoneal metastases. We consulted and discussed the treatment method with the patient and family, and the result was decided to deal with stomach cancer, gallbladder tumor, and pancreatic head tumor simultaneously.

The patient underwent distal gastrectomy, cholecystectomy, and

pancreaticoduodenectomy (Figs. 1B, 2B, 3B). Since this surgery involved three tumors at three different sites, we systematically calculated lymphadenectomies separately for each tumor to avoid missing regional lymph nodes. This procedure included groups of nodes No. 1, 3, 4, 5, 6, 7, 8a, 9, 11p, and 12a for gastric carcinoma. A standard lymphadenectomy in pancreatic cancer (additional groups 13, 17, 14a, 14b, 12b, 12c; groups 5, 6, and 8a were included in the gastric regional lymph nodes) was performed. Regional gallbladder lymph nodes were located in regional lymph nodes of the stomach, and pancrea were described and removed above. We performed a lateral pancreaticojejunal anastomosis (the duct-to-mucosa anastomosis) with drainage in the lumen of the Wirsung duct, an end-to-end biliary anastomosis behind the lateral pancreaticojejunostomy, and a final gastrojejunostomy (Fig. 4A). Open the feeding jejunostomy after the gastrointestinal anastomosis.

Postoperatively, the patient appeared to have a pancreatic-enteric fistula on postoperative day 3 with amylase of 296 U/L of fluid from the peripancreatic drain. Prolonged pancreatic fistula, infection, and malnutrition were treated medically. However, on postoperative day 13, we evaluated the patient with Clavien-Dindo classification grade IIIA (requiring ultrasound-guided percutaneous drainage to the fluid collection near the pancreatic anastomosis) (Fig. 4B, C). The patient did not recover for long because of the anastomosis leakage and the surgical site infection. The drainage was culture-positive for *Acinetobacter baumannii* and *Enterobacter* spp. We continued antibiotic treatment with an anaerobic antibiotic, metronidazole, and additional meropenem sensitive to the *Acinetobacter* culture result. After about 36 days of treatment, the patient's fluid collection in the drain was gradually reduced, the incision dried gradually, the patient's condition was stable, and he could be discharged from the hospital. Usually, there is mild abdominal pain that is not noticeable. Pathological tumor-node-metastasis (pTNM) staging with Gastric cancer was pT2 adenocarcinoma, Gallbladder cancer was pT3, and the 30 harvested lymph nodes were negative (Figs. 1C, 2C, D). The pancreatic pathological result was a benign cyst and chronic pancreatitis with calculi inside the pancreatic parenchyma (Fig. 3C). In the gallbladder specimen, the immunohistochemistry stain showed CK7, CEA, CK19-9 positivity, and CK20, CDX-2 negativity (Fig. 5C, D). Whereas, the gastric tumor cells were positive for CK7, CEA, CK19-9, CK20, and CDX-2 (Fig. 5A, B). This result excluded a metastasis situation and confirmed that the lesions in the stomach and gallbladder were two different tumors. He didn't accept postoperative chemotherapy and continued follow-up after surgery at 3rd month, 6th month, and one year of disease-free survival.

3. Clinical discussion

3.1. Diagnosis

The detection of gastric cancer is often based on upper gastrointestinal endoscopy and biopsy results [4]. The patient was admitted to the



Fig. 1. A. The endoscopy showed a 1x1cm ulcerated lesion in the lesser curvature of the stomach (blue arrow), B. The ulcerated lesion of the gastric specimen in the scissor's nose. C. HE $\times 100$. The histopathology shows an image of irregular-shaped and dilated neoplastic glands invading the muscle layer with intraluminal mucus and debris. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

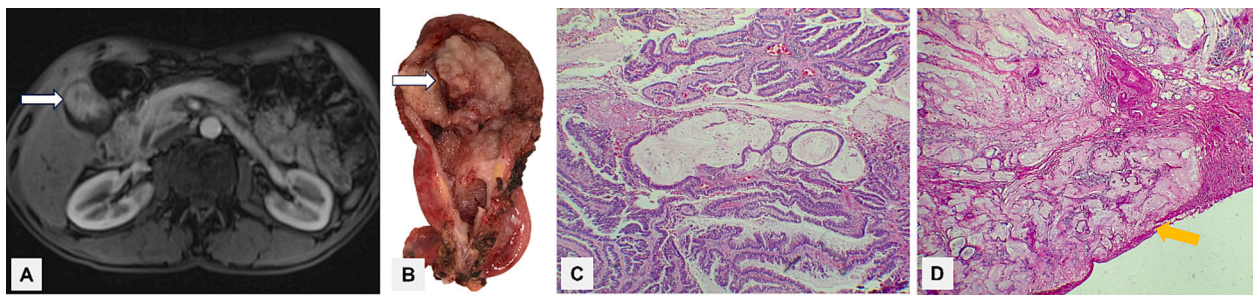


Fig. 2. A. The T1-weighted abdominal contrast MRI showed a mass within the gallbladder lumen (white arrow), B. The gallbladder specimen, C. HE $\times 100$. Neoplastic tubules of various sizes are lined by columnar cells with hyperchromatic nuclei. The tumor cells are arranged in a tubular pattern with intraluminal mucus and papillary pattern, spreading into connective tissue and serosa. D. HE $\times 40$. Histopathological image shows tumor cells floating in large extracellular mucin lakes with serosal invasion (yellow arrow). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

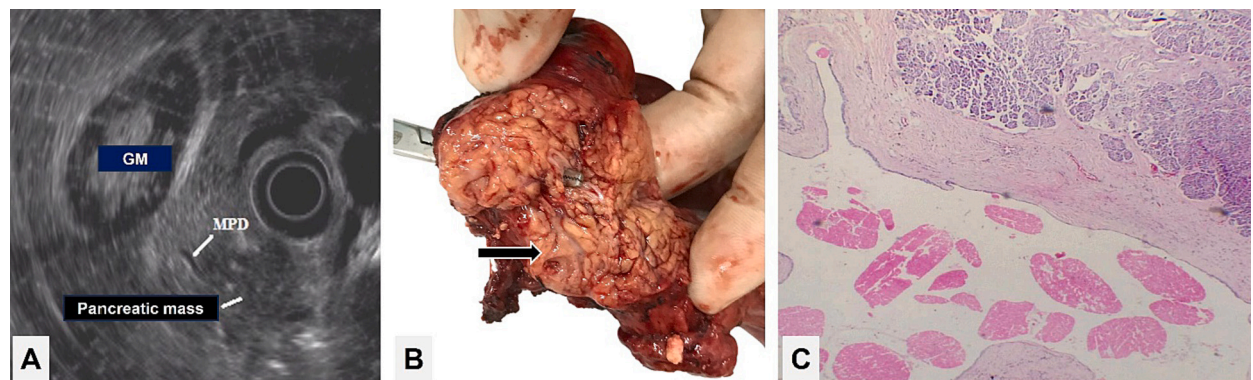


Fig. 3. A. The *endo*-ultrasonography (EUS) showed the gallbladder and pancreatic mass. GM: Gallbladder Mass, MPD: Main Pancreatic Duct, B. Pancreatic specimen with the tumor image (black arrow). C. HE $\times 40$. Dilated cysts are lined by small cuboidal cells, surrounded by normal pancreatic tissue.



Fig. 4. A. The image during the operation showed the proper hepatic artery (red arrow), the portal vein (blue arrow), the common hepatic duct, and the pancreatojejunostomy (white arrow). B. the axial plane. C. the coronal plane. The postoperative Ct scan showed the abscess next to the pancreatojejunal anastomosis (black arrows). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

hospital with abdominal pain and had a 1x1cm ulcerated lesion in the lesser curvature of the stomach endoscopy, and the biopsy resulted in invasive carcinoma. For staging of gastric cancer, the patient performed an abdominal ultrasound and CT scan and found several regional lymph nodes <6 mm surrounding the stomach. The diagnosis of gastric cancer was clinically staged as T1-2 N0 M0 (Stage I –AJCC 8th). Another detection was a tumorous lesion in the gallbladder, along with the image of stenosis of the common bile duct causing dilation of the intrahepatic bile duct and the common bile duct measuring 10 mm and chronic pancreatitis. Gallbladder cancer is often diagnosed at an advanced stage, and only very few patients are diagnosed early. In advanced cases, overall survival was only 12–14 months [12]. This case representation was discovered accidentally through abdominal ultrasound, and the abdominal and chest CT scan found the cT<4 N0 stage (AJCC 8th). Abdominal and chest contrast CT assessed no distant metastatic lesions. For gallbladder tumors, stage diagnosis is very important to have a

simple or radical cholecystectomy approach. Gallbladder cancer can be discovered incidentally after a simple cholecystectomy, but when T-stage above T1a, a radical cholecystectomy with a segment IVb/V liver resection and ligamentary lymphadenectomy is required [7].

Pancreatic cancer often occurs in the head of the pancreas. Symptoms may include obstruction of the common bile and Wirsung duct, often in advanced stages. Clinical symptoms of pancreatic cancer include jaundice, abdominal pain, weight loss, diarrhea, and steatorrhea [10]. Abdominal MRI could be used when a CT scan was inconclusive or cystic pancreatic lesions (Levels of Evidence IV, Recommendation grade C) [10]. Magnetic Resonance Cholangiopancreatography and endoscopic ultrasonography (EUS) were performed to examine the pancreas and pancreaticobiliary junction. The MRI showed images of chronic pancreatitis and 9 mm dilation of the common bile duct with 1x2cm hyperintense structures in the head of the pancreas. However, people found chronic pancreatitis with a hyperechoic lesion as a pancreatic

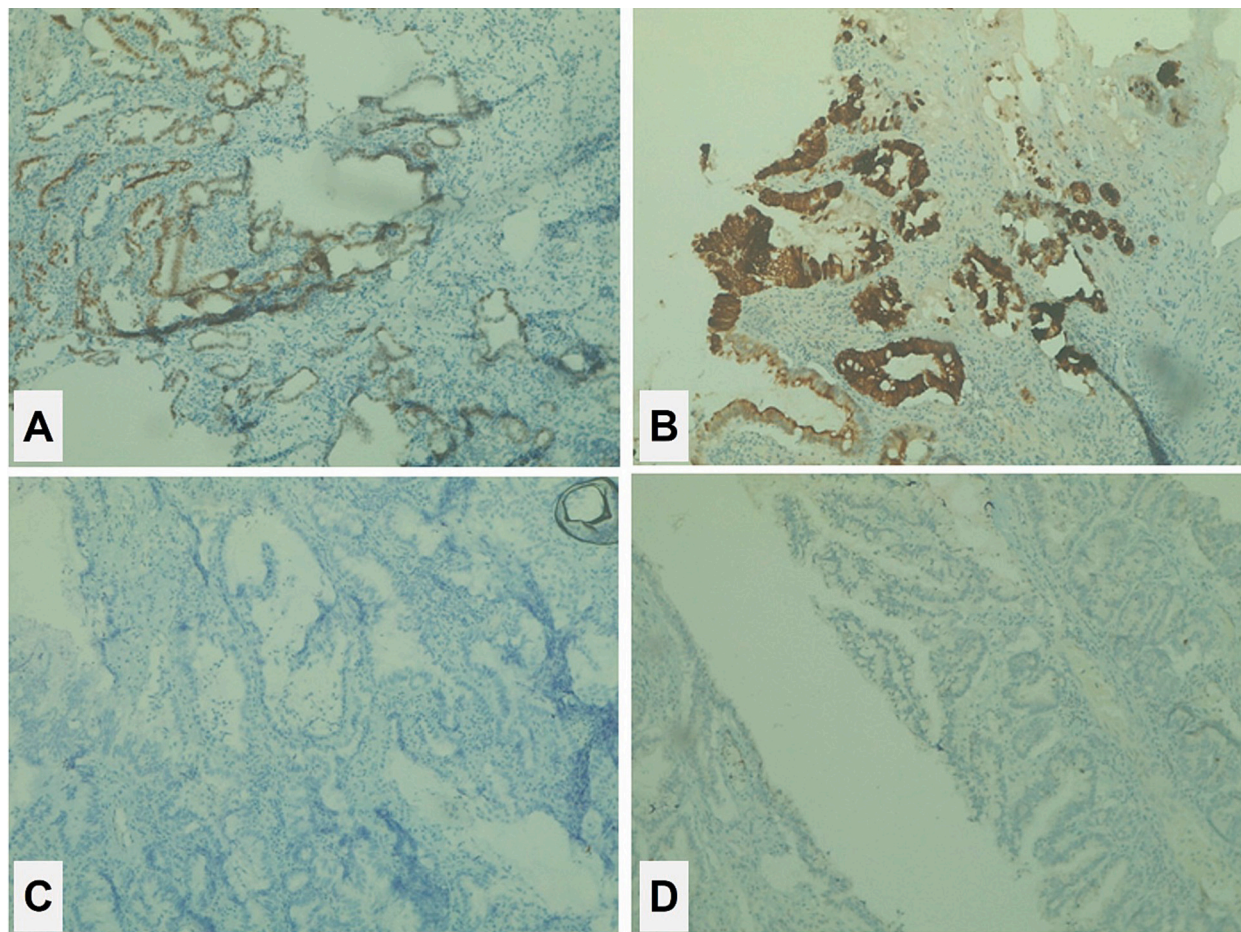


Fig. 5. Immunohistochemical assessment of gastric and gallbladder specimens in patients. IHC of the gastric specimen ($\times 100$). A. CDX-2 (+), B. CK20 (+). IHC of gallbladder specimen ($\times 100$). C. CDX-2 (–), D. CK20 (–).

head tumor in EUS, with many radiopaque structures of pancreatic stones interspersed with pancreatic cysts.

Some chronic pancreatitis abnormalities may resemble pancreatic ductal adenocarcinoma on imaging, which makes accurate preoperative diagnosis difficult and may lead to unnecessary surgery [9]. Ultrasound-guided fine needle (EUS-FNA) aspiration is required for this patient. A preoperative, accurate pathological diagnosis of pancreatic cancer is necessary before surgery. The routine performance of EUS-FNA was at level B evidence and grade 2 recommendation in the 2019 and 2023 Japan Pancreas Society guidelines [13,14]. The European Society of Medical Oncology recommended that EUS find-needle was preferred over cytology or CTscan-guided biopsy. If the EUS-guided fine needle is still negative for cancer cells after two attempts, treatment can proceed without histological evidence [6]. Provided a multidisciplinary tumor board discussion exists, and carbohydrate antigen (CA) 19-9 was consistent with malignant pancreatic neoplasms [10]. In this case, was it necessary to perform EUS-FNA routinely? If the results are negative, was it necessary to have surgery to treat malignant pancreatic tumors? We have discussed the issue of prolonging the diagnosis time in patients with multiple cancer lesions (stomach and gallbladder) and the typical images on imaging and endoscopic ultrasound of the pancreatic head. We discussed and agreed and decided to perform surgery on this patient without EUS-FNA, mainly because a negative result may require subsequent monitoring of tumor progression if suspected it is a benign lesion. This was not possible in this case when other malignant lesions were diagnosed. Diagnosing rare multiple neoplasms requires coordination between clinical departments and radiologists, interventional

endoscopists, oncologists, and surgical oncologists. After consulting with the experts on the tumor board, we agreed on a diagnosis of a synchronous tumor of stomach cancer, gallbladder tumor, and pancreatic head tumor. We decided on radical surgical treatment first, then based on pathology to determine the subsequent management. The role of the tumor board is crucial in diagnosis and treatment, especially in situations requiring multidisciplinary coordination.

3.2. Management

The treatment of this disease is unique, requiring a coordinated approach to treating many different tumor locations. Surgery for the gallbladder, distal stomach, and head of pancreatic tumors are related to each other located in a neighboring location in the anatomy, so surgery to remove all three tumors is relatively similar to a Whipple procedure. Pancreatic head resection with R0 resection margin and a minimum lymph node dissection of 16 lymph nodes is necessary [10]. After pancreatic cancer resection, completion of chemotherapy for six months is recommended at grade IA. The choice of CRT (40Gy and 5-FU) was interim analyzed, showing a significant difference in postoperative survival [10]. Gastrectomy with lymph node dissection of at least 16 lymph nodes is also recommended in gastric bypass surgery [15]. Guidelines for the treatment of stomach cancer and gallbladder cancer are also clearly described in the guidelines of the European Society of Medical Oncology and the Japanese Association of Gastric Cancer [5,7]. In our case, the clinical stage of the stomach and gallbladder was locally advanced. Therefore, we prescribed gastrectomy and cholecystectomy

with regional lymph node dissection. Gastrectomy with lymphadenectomy is common in the treatment of stomach cancer. However, gallbladder cancer is relatively rare, so the correct choice is still difficult. Especially in this case, the T-stage diagnosis of gallbladder tumor during surgery did not extend beyond the serosa, the tumor located in the viscera side (T-stage 1–2), and no invasion into the liver, so we chose the cholecystectomy with lymphadenectomy without segment IVb/V hepatectomy.

Regarding the laparoscopic or open surgical approach, no difference was shown in the hospital stay or oncological efficacies of these surgical methods for gastric cancer in Western countries [16]. However, studies in the East have the same oncological results, but laparoscopic surgery has a low rate of complications [17,18]. Although most studies were retrospective in gallbladder cancer, oncological outcomes were similar for laparoscopic and open surgery. Surgeons with sufficient laparoscopic experience may opt for laparoscopic surgery as an alternative surgical strategy [19]. Similar to cholecystectomy due to cancer, the choice of laparoscopic or open surgical treatment in pancreaticoduodenectomy is still debated. Despite its longer operating time, several studies show that laparoscopic duodenectomy remains a safe, viable alternative to open surgery. Additionally, short-term oncological outcomes were non-inferior in the laparoscopic group. In our case, we chose a laparotomy to treat the multiple tumors of this patient.

Serious complications are rare for gastric, with the rate <1 % [17,18]. Postoperative complications of gallbladder surgery were also rarely described, and the overall complication rate is not high [19]. However, according to different studies, pancreaticoduodenectomy is a surgery with a high rate of pancreaticojejunostomy leakage of 21.4 % [20]. In our case, the complication of pancreaticojejunostomy fistula appeared, seriously affecting the patient's postoperative condition and requiring percutaneous drainage under ultrasound guidance. This severe complication requires intervention to be evaluated as Clavien-Dindo grade IIIA. Pancreatic duodenectomy surgery needs to be performed in large centers with adequate facilities. According to author Karim S. et al., the mortality rate after this surgery is 4 %, a high rate and a challenge for surgeons [20].

4. Conclusion

Primary stomach cancer, concurrent with gallbladder cancer, is rare. Pseudotumor chronic pancreatitis is also rare. The attitude of treating these three diseases at the same time requires a tumor board. Simultaneous surgery for gallbladder, stomach, and pancreatic head tumors can be performed if the tumors are still in the resectable stage.

Human and animal rights

The authors' institutions do not require Ethics committee approval or a case report or case series containing information on fewer than three patients.

Consent

Written informed consent was obtained from the patient to publish 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.

Ethical approval

There is no ethical approval was obtained as it's a case report but a written consent was taken from the patient.

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Author contribution

Minh Thao Nguyen: concept and design of the manuscript, data collection, data analysis, and writing the paper.

Anh Vu Pham: concept and design of the manuscript, data collection, drafting, revision.

All authors participated in the approval of the final version.

Guarantor

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Conflict of interest statement

None declared. The authors have no financial, consultative, institutional, and other relationships that might lead to bias or conflict of interest.

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