 doi:10.20944/preprints202008.0217.v1

SpyGlass DS -Directed Radiofrequency Ablation with Double Biliary Metal Stent Placement for Managing Recurrent Obstructive Jaundice Secondary to Castleman Disease: A Case Report of a Rare Disease (with videos)

Li-Jia Wen[1], Jun-Hong Chen[2], Liang Guo[3], Kai Liu[2]

[1] Department of Hepatopancreatobiliary Surgery, The First Hospital of Jilin University, Changchun 130021, Jilin Province, China

[2] College of Clinical Medicine, Jilin University

[3] Department of Pathology, The First Hospital of Jilin University, Changchun 130021, Jilin Province, China

Corresponding author: Kai Liu, PhD, Chief Doctor, Department of Hepatopancreatobiliary Surgery, The First Hospital of Jilin University, No. 71, Xinmin Street, Changchun 130021, Jilin Province, China. 6kai@163.com

 doi:10.20944/preprints202008.0217.v1

Abstract

Castleman disease (CD) rarely presents with obstructive jaundice, which poses a diagnostic and therapeutic challenge to the management of the disease. A 40-year-old man was referred to our hospital for emergent management of upper abdominal pain. An abdominal mass was removed, and the postoperative pathology showed retroperitoneum CD, which was subsequently managed by adjuvant therapy of combination chemotherapy and steroids. One month later, a biliary metal stent was placed due to the presentation of obstructive jaundice. After approximately 3 months, the patient experienced another episode of obstructive jaundice, and SpyGlass DS cholangioscopy (Boston Scientific, Natick, Mass, USA) was performed via the biliary track for biopsy, which pathologically showed biliary malignancies. Radiofrequency ablation was performed with a probe (EMcision, Montreal, Canada), and another uncovered metal stent was placed within the existing metal stent. No stent occlusion occurred during a 6-month follow-up period. In conclusion, CD rarely presents with obstructive jaundice, and a combination of radiofrequency ablation with metal stent implantation under cholangioscopy can prolong the stent patency time and the survival time of patients.

Key words: Castleman disease; radiofrequency ablation; cholangioscopy; SpyGlass DS; biliary tract; obstructive jaundice

 doi:10.20944/preprints202008.0217.v1

1. Introduction

Castleman disease (CD) is a rare lymphoproliferative disorder that was first described by Benjamin Castleman [1]. Clinically, CD can be divided into unicentric and multicentric subtypes, which lead to different prognoses [2]. Radical surgical resection with adjuvant chemoradiotherapy is the treatment of choice. In cases of multiple metastasis, palliative care may be the only option.

CD rarely presents with obstructive jaundice. At present, only 12 relevant case reports can be found in the literature, and most of the patients in these reports received radical operations [3]. Radiofrequency ablation (RFA) has been proven to be a safe and effective method for the treatment of biliary malignancies [4]. In 2015, the novel digital single-operator cholangioscopy system (SpyGlass DS) was introduced and provides high-resolution images for visualization of the biliary tract and biopsy biliary stricture for establishing a definitive diagnosis [5]. Here, we report the first case of multicentric CD that involved the biliary tract and presented with obstructive jaundice, which was further treated by RFA and metal stent placement under SpyGlass DS cholangioscopy, and finally achieved complete and durable remission.

2. Case report

The study was approved by the institutional research ethics committee of the First Hospital of Jilin University, the project identification code 19K041-001, June 2019. and written informed consent was obtained from each subject. A 40-year-old man presented to our hospital with yellow skin, sclera, and dark urine lasting for 5 days. The patient had undergone celiac tumor resection in our hospital 4 months previously with a postoperative pathological diagnosis of retroperitoneum CD with positive hilar

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 9 August 2020 doi:10.20944/preprints202008.0217.v1

and periportal lymph nodes (Figures 1–3). Adjuvant therapy of combination chemotherapy and steroids had been administered. Moreover, the patient underwent endoscopic retrograde cholangiopancreatography (ERCP) with metal stent placement 1 month after the initial resection for unknown origin obstructive jaundice. Examination after admission revealed a total bilirubin concentration of 180.7 μmol/L (normal range <26.0 μmol), direct bilirubin concentration of 157.3 μmol/L (normal range <26.0 μmol), CA19-9 concentration of 72.3 U/mL, CA-125 concentration of 21.6 U/mL, alpha fetoprotein concentration of 2.37 ng/mL, carcinoembryonic antigen concentration of 5.59 ng/mL, and C-reactive protein concentration of 21.3 mg/L. Enhanced computed tomography (CT) scanning revealed a high-density shadow in the initially placed biliary metal stent, suggesting lumen obstruction (Figure 4). ERCP was repeated, and multiple tumor-like areas of hyperplasia could be seen in the lumen of the metal stent, and SpyBite biopsies was collected via SpyGlass DS (Figure 5, Video 1). The final diagnosis was CD with bile duct metastasis. RFA (10 W, 2 min) was performed (Figure 6). SpyGlass DS imaging showed changes after RFA (Figure 7). A second biliary uncovered metal stent was inserted, and X-ray imaging showed the double stent (Figure 8). Finally, no occlusion of the stent occurred during 6 months of follow-up.

3. Discussion

CD is a rare disease entity in which the causes of reactive lymphadenopathy are unknown. Pathologically, CD features obvious proliferation of lymphoid follicles, blood vessels as well as plasma cells to varying degrees [2], and further can be divided into hyaline-vascular type and plasma cell type. Clinically, it is characterized by

 doi:10.20944/preprints202008.0217.v1

significant enlargement of deep or superficial lymph nodes and, in some patients, systemic symptoms and/or multiple system damage.

The disease is classified as unicentric CD (UCD) or multicentric CD (MCD) subtypes. UCD is more common in young people; pathologically, 90% of UCD cases are the hyaline-vascular type, and surgical resection of enlarged lymph nodes offers a good prognosis. In comparison, MCD is less common than UCD, and patients with MCD always present with enlargement of multiple lymph nodes in combination with systemic symptoms. In some cases, these symptoms include only fever or liver splenomegaly. However, in 20%–30% of patients, MCD manifests as nephrotic syndrome, amyloidosis, myasthenia gravis, Kaposi's sarcoma, or B-cell lymphoma. MCD is usually invasive and associated with infection, and the prognosis is poor when it is associated with malignant transformation or lymphoma [6].

To date, 13 cases of CD with jaundice, including the present case, have been reported in the English literature [3], including 7 MCD and 6 UCD cases. Histopathologically, 7 cases were diagnosed as hyaline vascular type, 3 cases as plasma cell type, and 3 cases as the mixed type. In all UCD cases, resection was success, and symptoms disappeared completely during follow-up. In contrast, cases of MCD were partially controlled or relapsed.

The involvement of the biliary tract poses diagnostic and therapeutic challenges in the management of CD. A systematic review of nine studies with 505 patients[7] found that RFA combined with biliary stent placement offered a pooled mean difference of 50.6 days in stent patency (95% confidence interval [CI], 32.83–68.48) and had a longer over survival (hazard ratio, 1.395; 95% CI, 1.145–1.7; P<.001) in comparison with stent placement alone. Thus, the efficacy and safety of RFA for managing unresectable extrahepatic cholangiocarcinoma have been demonstrated.

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 9 August 2020 doi:10.20944/preprints202008.0217.v1

Digital single-operator cholangioscopy (SpyGlass DS) with direct visualization and biopsy for diagnosis of biliary tract diseases has been shown to be safe and to offer a high success rate[8]. RFA for malignant biliary stricture using SpyGlass DS not only retains the safety but also increases the success rate of the treatment. In addition, SpyBite can easily execute biopsies under SpyGlass DS, leading to improved diagnostic accuracy [9-11].

In summary, we report the first case of multicentric CD presenting with jaundice due to biliary tract re-occlusion, which was treated by SpyGlass DS-directed RFA and double metal stent insertion, subsequently leading to complete and durable remission of the disease.

4. Conclusions

CD rarely presents as jaundice due to obstruction of the biliary track. However, such cases can be feasibly and effectively managed by SpyGlass DS-directed RFA with metal stent insertion, which may improve stent patency time and survival time.

Funding: Supported by the Jilin Science and Technology Development Program (CN), No. 20191102031YY.

Author contributions: W.- L.J. and L.K were involved in the patient's treatment and edited and wrote the paper; C.-J.H. gathered detailed clinical information; G.L. conducted pathological examination and make pictures. All authors approved the final manuscript.

REFERENCES

1 Castleman, B.; Iverson, L.; Menendez, V.P. Localized mediastinal lymphnode hyperplasia resembling thymoma. *Cancer* **1956**, 9, 822-30 [PMID: 13356266]

2 Talat, N.; Belgaumkar, A.P.; Schulte, K.M. Surgery in Castleman's disease: a systematic review of 404 published cases. *Ann. Surg.* **2012**, 255, 677-84 [PMID: 22367441 DOI: 10.1097/SLA.0b013e318249dcdc]

3 Zhai, B.; Ren, H. Y.; Li, W. D.; Reddy, S.; Zhang, S.J.; Sun, X.Y. Castleman disease presenting with jaundice: A case report and review of literature. *World. J. Clin. Cases.* **2019**, 7, 373-381 [PMID: 30746379 DOI: 10.12998/wjcc.v7.i3.373]

4 Yang, J.; Wang, J.; Zhou, H.; Zhou, Y.; Wang, Y.; Jin, H.; Lou, Q.; Zhang, X. Efficacy and safety of endoscopic radiofrequency ablation for unresectable extrahepatic cholangiocarcinoma: a randomized trial. *Endoscopy* **2018**, 50, 751-760 [PMID: 29342492 DOI: 10.1055/s-0043-124870]

5 Navaneethan, U.; Hasan, M. K. Kommaraju, K.; Zhu,X.; Hebert-Magee, S.; Hawes, R.H.; Vargo, J.J.; Varadarajulu, S.; Parsi, M. A. Digital, single-operator cholangiopancreatoscopy in the diagnosis and management of pancreatobiliary disorders: a multicenter clinical experience (with video). *Gastrointest. Endosc* .**2016**, 84, 649-55 [PMID: 26995690 DOI: 10.1016/j.gie.2016.03.789]

6 **Fujimoto, S**.; Koga, T.; Kawakami, A.; Kawabata, H.; Tokumine, Y.; Nishimoto, N.; Fujiwara, H.; Nakatsuka, S. I.; Shiozawa, K.; Iwaki, N.; Masaki, Y.; Yoshizaki, K. Tentative diagnostic criteria and disease severity classification for Castleman disease: A report of the research group on Castleman disease in Japan. *Mod. Rheumatol.* **2018**, 28, 161-167 [PMID: 28880697 DOI: 10.1080/14397595.2017.1366093]

7 Sofi, A. A.; Khan, M. A.; Das, A.; Sachdev, M.; Khuder, S.; Nawras, A.; Lee, W. Radiofrequency ablation combined with biliary stent placement versus stent placement alone for malignant biliary strictures: a systematic review and meta-analysis. *Gastrointest. Endosc.* **2018**, 87, 944-951.e1 [PMID: 29108980 DOI: 10.1016/j.gie.2017.10.029]

8 Kurihara, T.; Yasuda, I.; Isayama, H.; Tsuyuguchi, T.; Yamaguchi, T.; Kawabe, K.; Okabe, Y.; Hanada, K.; Hayashi, T.; Ohtsuka, T.; Oana, S.; Kawakami, H.; Igarashi, Y.; Matsumoto, K.; Tamada, K.; Ryozawa, S.; Kawashima, H.; Okamoto, Y.; Maetani, I.; Inoue, H.; Itoi, T. Diagnostic and therapeutic single-operator cholangiopancreatoscopy in biliopancreatic diseases: Prospective

multicenter study in Japan. *World. J. Gastroenterol*. **2016**, 22, 1891-901 [PMID: 26855549 DOI: 10.3748/wjg.v22.i5.1891]

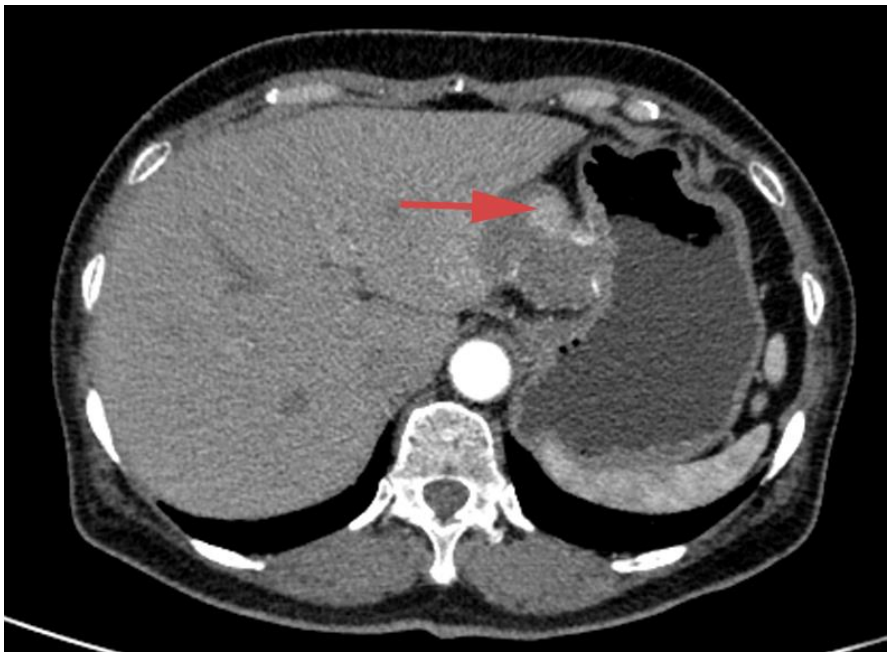
9 Gunasingam, N.; Craig, P. I. Cholangioscopy-directed radiofrequency ablation of complex biliary cholangiocarcinoma. *VideoGIE*. **2019**, 4, 211-213 [PMID: 31061941 DOI: 10.1016/j.vgie.2018.12.017]

10 Mavrogenis, G.; Deprez, P. H.; Wallon, J.; Warzee, P. Bile duct adenoma causing recurrent cholangitis: diagnosis and management with targeted Spyglass access and radiofrequency ablation. *Endoscopy* **2012**, 44 Suppl 2 UCTN, E290-1 [PMID: 22933260 DOI: 10.1055/s-0032-1310036]

11 Ogura, T.; Onda, S.; Sano, T.; Takagi, W.; Okuda, A.; Miyano, A.; Nishioka, N.; Imanishi, M.; Amano, M.; Masuda, D.; Higuchi, K. Evaluation of the safety of endoscopic radiofrequency ablation for malignant biliary stricture using a digital peroral cholangioscope (with videos). *Dig. Endosc.* **2017**, 29, 712-717 [PMID: 28181704 DOI: 10.1111/den.12837]

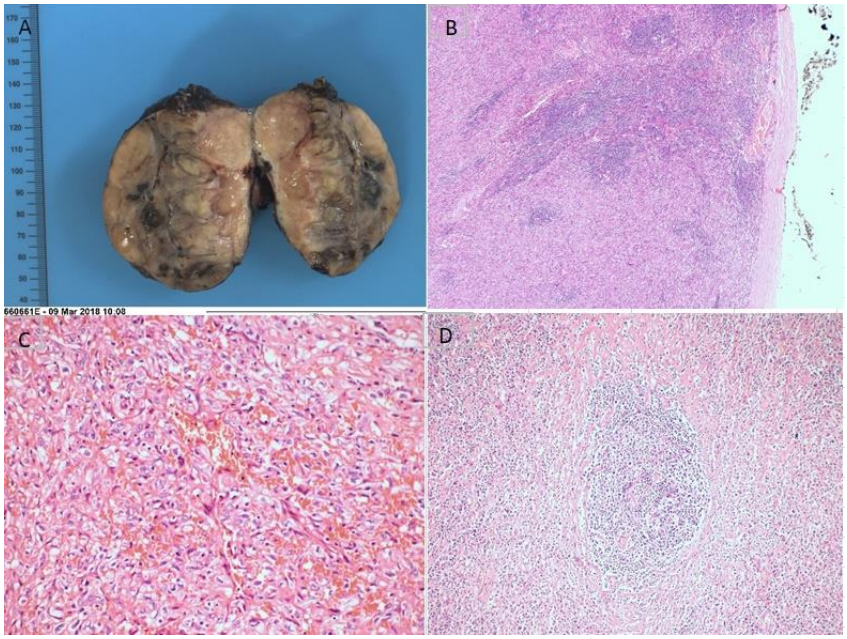
 doi:10.20944/preprints202008.0217.v1

Figure 1. Space occupying lesion, measuring about 6×5 cm, in the patient's abdomen.



Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 9 August 2020 doi:10.20944/preprints202008.0217.v1

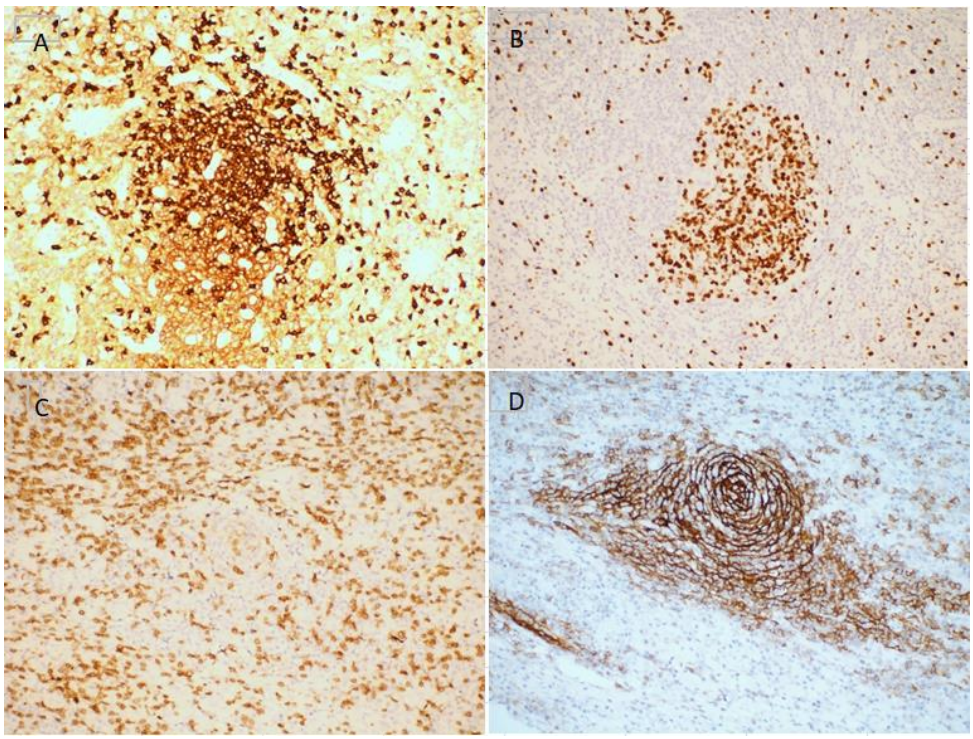
Figure 2. Pathohistological features of mixed type Castleman disease.



(A): The cutting surface; (B): the intact tumor envelope (C): infiltrating neoplastic cells with marked pleomorphism (D): rod-shaped glassy changes were seen in the germinal center.

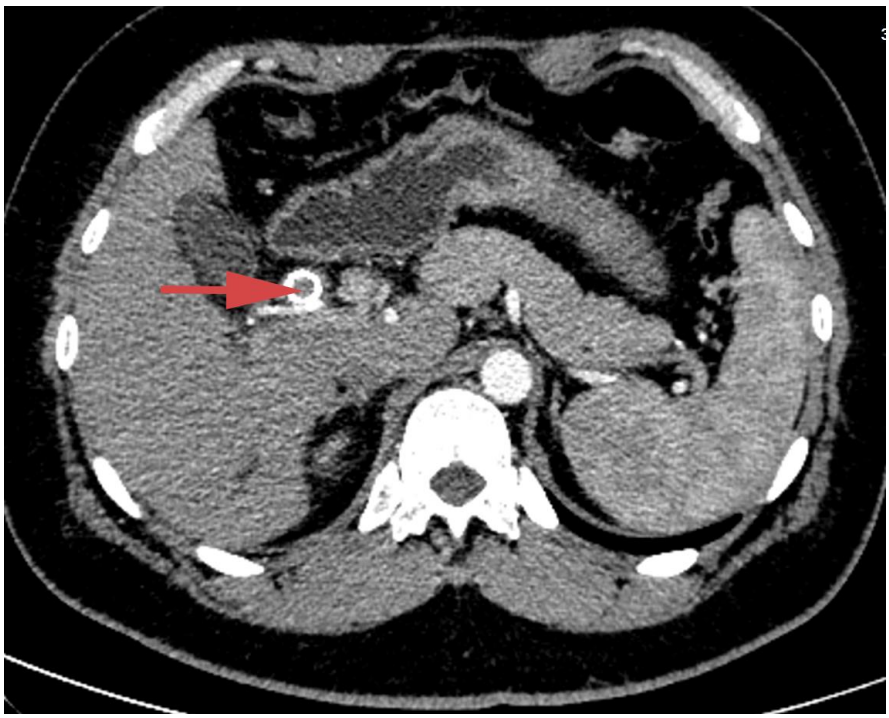
Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 9 August 2020 doi:10.20944/preprints202008.0217.v1

Figure 3. Immunohistochemistry features of mixed type Castleman's disease. Hematoxylin staining. Magnification, ×200. A, CD3; B, CD20; C, CD21; D, Ki-67.



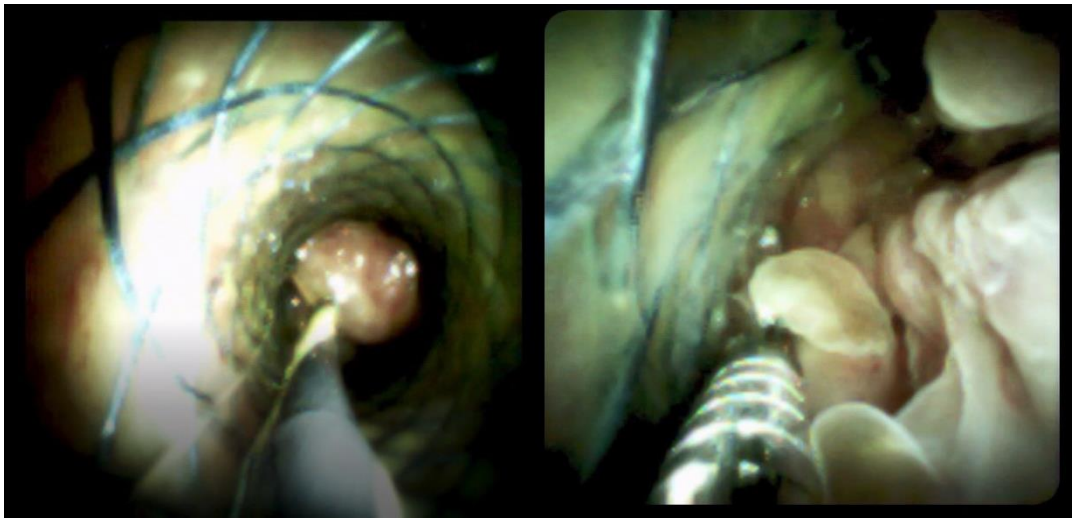
 doi:10.20944/preprints202008.0217.v1

Figure 4. Abdominal contrast-enhanced CT scan, showing high-density shadow in the initially placed biliary metal stent and lumen obstruction.



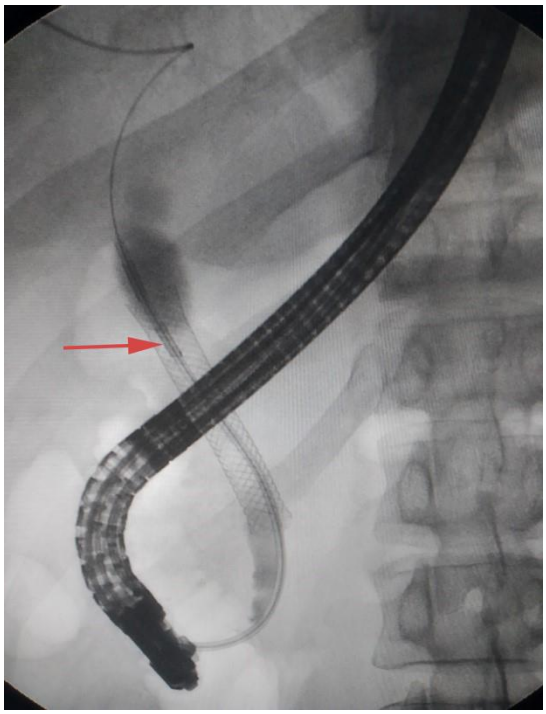
Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 9 August 2020 doi:10.20944/preprints202008.0217.v1

Figure 5. Images from the SpyGlass DS system show (A) multiple tumor-like areas of hyperplasia in the bile cavity, and (B) biopsies taken by SpyBite.



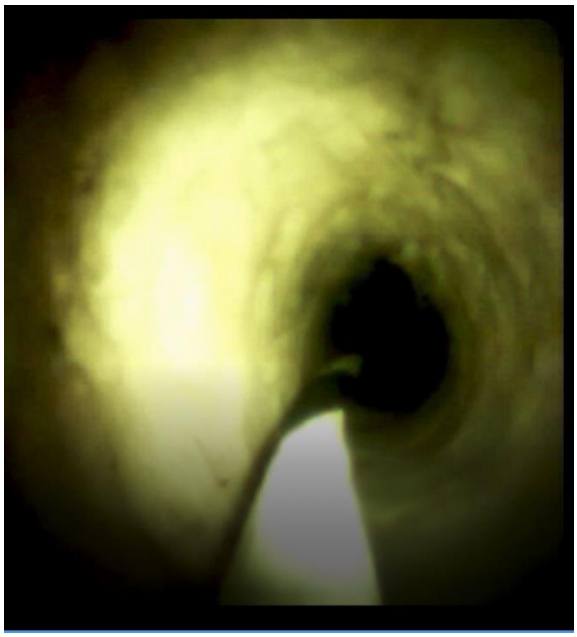
Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 9 August 2020 doi:10.20944/preprints202008.0217.v1

Figure 6. Radiofrequency ablation in the same plane with SpyGlass DS



 doi:10.20944/preprints202008.0217.v1

Figure 7. SpyGlass DS system image showing the change after radiofrequency ablation.



 doi:10.20944/preprints202008.0217.v1

Figure 8. X-ray image showing double stent after insertion of the second biliary uncovered metal stent (yellow arrow).