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Case Report

Bronchobiliary Fistula: A Challenging Opponent to Treat in Stage IV intrahepatic Cholangiocarcinoma (iCC) Patients

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Abstract

A 57-year-old female underwent a left hemihepatectomy due to intrahepatic cholangiocarcinoma (iCC) in 2017. Asymptomatic for two and a half years, in 2020, the patient was admitted to the department due to cholangitis and tumor recurrence. The patient underwent four Endoscopic Retrograde Cholangiopancreatography (ERCP) procedures in total and Percutaneous Transhepatic Biliary Drainage (PTCD). As for palliative oncological treatment she underwent radio-chemotherapy. Six months following PTCD, another ERCP was performed exchanging external biliary drainage to internal. Seven months following the last radiotherapy, a Bronchobiliary Fistula (BBF) was identified. Quality of life remained hugely impaired, with associating dyspnoea, fatigue and a persistent chronic cough with biliary sputum. The patient was treated symptomatically. BBF was treated throughout the next two years through consecutive ERCP's with biliary stenting as well as continuous PTCD implementation until the patient's death in 2022. Curative treatment of bronchobiliary fistulas in stage IV iCC is challenging and associated with major mortality risk. The most reasonable strategies available in treating such patients are through ERCP with biliary stenting and PTCD, thus, surgery and other treatment options remain limited.

Keywords: Bronchobiliary Fistula; Intrahepatic Cholangiocarcinoma; Percutaneous Drainage

Introduction

Bronchobiliary fistula (BBF) is a rare complication which causes bile to extravasate from the biliary tree into the bronchial tree. Its high mortality and morbidity rates pertain to the patients' symptoms of chronic cough with massive bile expectorate [1]. Biles corrosive properties leads to inflammation, infection and significant tissue damage. First described by Peacock in 1850, BBF requires an early diagnosis and urgent treatment consisting of invasive surgical resection in order to close the fistula, however this is often challenging and not always possible [2]. Many metastatic cancers contradict the possibility of surgery. For example, liver and biliary cancer, pancreatic cancer and gastric cancer [3]. To the best of our knowledge from 1981 there have been merely 68 cases of BBF following liver resection reported in PubMed. Treatment strategies remain extremely challenging and questions whether a disease-free status in oncological liver patients is feasible.

Bronchobiliary Fistula (BBF) constitutes a rare and clinically significant complication characterized by the aberrant flow of bile from the biliary tree into the bronchial tree. The associated elevated rates of mortality and morbidity are primarily attributed to the distressing symptomatology experienced by patients, marked by chronic cough accompanied by copious bile expectoration [1]. The corrosive nature of bile gives rise to a cascade of deleterious effects, encompassing inflammation, infection and substantial tissue injury. Initially delineated by Peacock in 1850, the management of BBF necessitates expeditious recognition and intervention, typically entailing invasive surgical resection to effectuate fistula closure; however, this endeavor is frequently met with formidable challenges and is not universally feasible [2]. The presence of metastatic cancers, such as those originating

in the liver, biliary tract, pancreas and stomach, often contraindicates the pursuit of surgical intervention [3]. Notably, our comprehensive review of the literature since 1981 has yielded a scant 68 reported cases of BBF subsequent to liver resection documented in PubMed. This scarcity of cases underscores the rarity and complexity of this clinical entity. The intricate landscape of treatment modalities prompts a critical inquiry into the attainability of a disease-free state in oncologic liver patients grappling with this formidable complication.

Case Description

A 57-year-old female underwent a left hemihepatectomy for the treatment of intrahepatic Cholangiocarcinoma (iCC) in June 2017. The patient began radio-chemotherapy post-operatively. Asymptomatic for two and a half years, in March 2020, the patient was then referred back to our centre following the first symptoms of cholangitis.

In March 2020, an Endoscopic Retrograde Cholangiopancreatography (ERCP) was carried out showing no strictures of the biliary tree (ERCP1). Three weeks later, a second ERCP was performed, revealing a stricture at the bifurcation of the hepatic duct (posterior sector) with distended segmentation. The patient underwent Percutaneous Transhepatic Bile Duct Drainage (PTCD) which drained on average 800ml of bile per day, reducing symptoms of cholestasis. Two months later, May 2020, a third ERCP (ERCP3) was performed with biliary stenting. The right hepatic duct was stenotic; however, biopsy results showed no characteristic signs of neoplasia. A second PTCD was placed post endoscopic stenting and remained throughout the next 4 months.

In September, the patients' symptoms of cholangitis exacerbated. Ultrasonography revealed PTCD displacement from the biliary tree, which was subjected to PTCD removal. A fourth ERCP (ERCP4) with stenting was carried out the following day. ERCP4 revealed cell proliferation projecting from the duodenal papilla, encircling the distal end of the prosthesis (Fig. 1). The main stem of the right hepatic duct was also constricted along its whole length. It was during this fourth ERCP did the tissue histopathology reveal fibrosis of the epithelium stroma, without characteristics of cell dysplasia. Onco-pathology examination was still negative, though clinical presentation suggested iCC recurrence. For further palliative oncology treatment, A Magnetic Resonance Cholangiopancreatography (MRCP), Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) were done, which displayed characteristics of recurrent iCC with infiltration along the walls of the biliary ducts with significant stricture of the biliary hilum, thickening of the biliary tract wall and cellular proliferation surrounding stricture and prosthesis was evident.

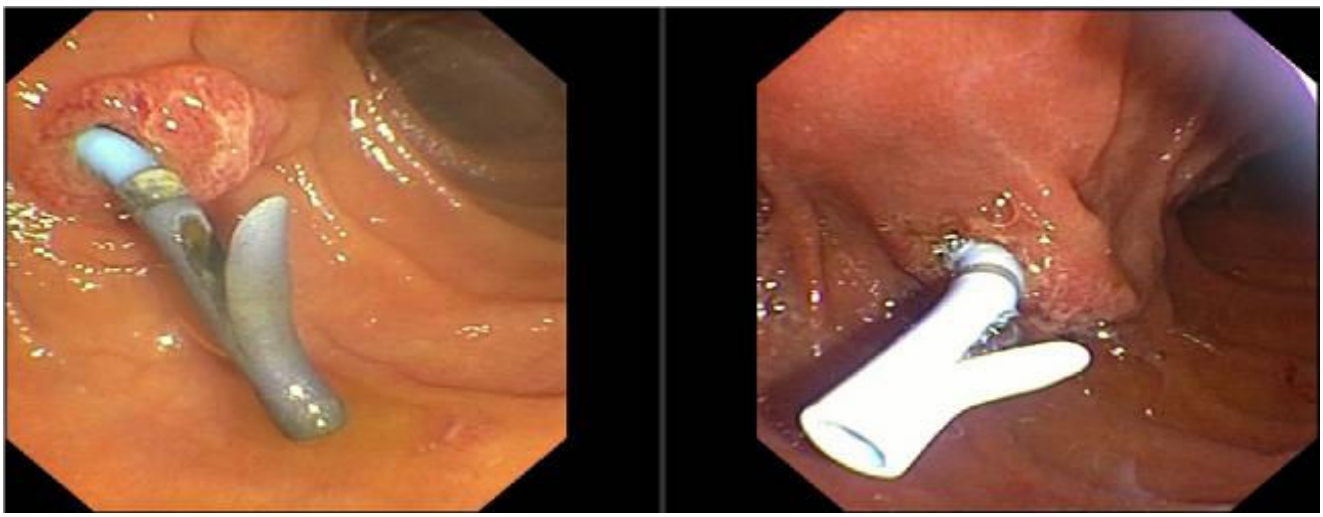

Figure 1: Shows displacement of plastic prosthesis from cellular proliferation protruding from the duodenal papilla.

Ten-days post to ERCP4, the third PTCD was placed into the patient's right hepatic duct, reducing daily biliary drainage to 200 ml and total bilirubin levels decrease from 2.02 mg/dL to 0.85 mg/dl. The patient was discharged following a month-long hospitalization and referred for further oncological treatment. Following three months of radiotherapy, the patient was readmitted to our department due to another episode of cholangitis. The third PTCD was then replaced. The patient reported symptoms of a dry cough, present several weeks. At that point adverse effects of radiotherapy were assumed and high-dose codeine was administered. Chemotherapy was initiated the following week.

Four months later, June 2021, the patient was admitted to an external pulmonary disease centre. CT scans proved radiotherapy induced-lung damage, pulmonary embolism and pneumonia. The patient was treated with ceftriaxone and enoxaparin. Two weeks later, the patient was readmitted to our centre for elective PTCD replacement, however upon admission she was already jaundiced. After a successful procedure the patient was discharged in good general condition.

Upon readmission, August 2021, the patient's symptoms of cough exacerbated, fluctuating in severity and causing insomnia. Bile in the sputum was confirmed in biochemistry tests. A MRCP imaging concluded a Bronchobiliary Fistula (BBF). A fifth ERCP (ERCP5) was carried out with repositioning of the biliary stents. This proved successful easing the patients symptoms of the BBF. The patients general state improved greatly and the cough almost completely terminated.

Furthermore, in October 2021, the patient was admitted to our centre in stable general condition for a scheduled ERCP and PTCD removal. The sixth ERCP (ERCP6) showed bile duct cancer recurrence via neoplastic invasion of the right hepatic duct. Diagnostic imaging concluded infiltration of the right branch of the portal vein with secondary portal hypertension. The patients' persistent cough returned two days after ERCP6, with massive bile expectorate. Bronchoscopy revealed bile in the pharynx, larynx and bronchi. The patient was consulted by thoracic surgeons who disqualified her from surgery due to high risk of middle and lower lobe lung injury with a doubtful chance of a permanent BBF closure. A minimal procedure was performed by percutaneous drainage to the subphrenic area, to drain the bile that entered the pleural cavity. Long-acting steroids and codeine was administered.

Over the next two months, the patient's symptoms of cholangitis remained dormant due to three consecutive ERCP's with stenting. The direct visualization of the fistula appeared in the seventh ERCP (ERCP7), November 2021. Neoplastic cells were seen protruding from the newly placed double 8.5F9 cm plastic prosthesis, from the Papilla of Vater. Histopathology confirmed cell dysplasia and atypia. We continued to manage the patient's bile-producing cough as well as suppress the symptoms of cholangitis, while she resumed radio-chemotherapy treatment (Fig. 2).

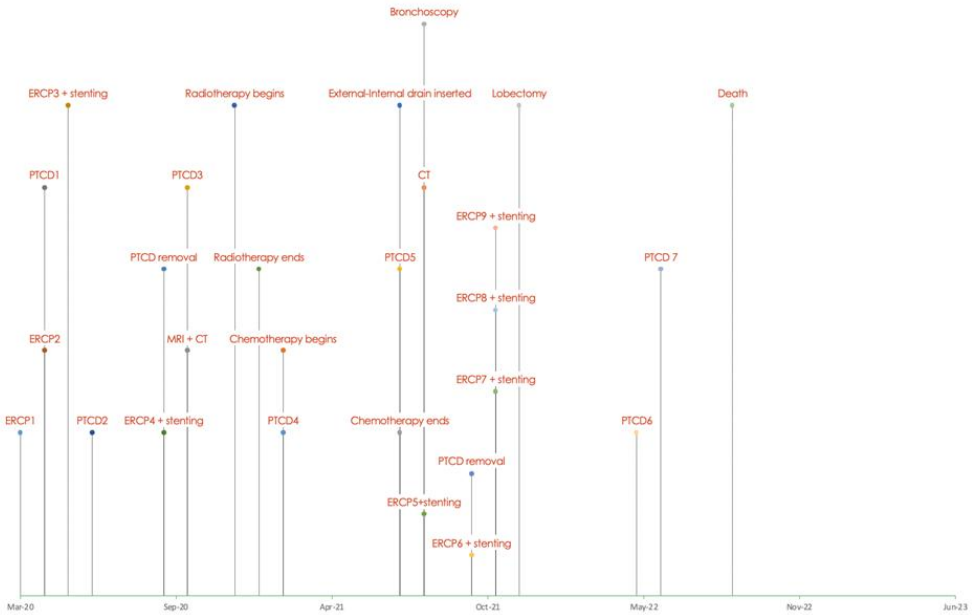

Figure 2: The above diagram shows management and treatment initiated within the course of a 21-month period.

As a follow up, December 2021, the patient sought additional treatment for further management of chronic biliptysis. Against our medical advice, the patient underwent a lobectomy of the lower lobe of the right lung, at an external thoraco-surgery clinic near the patients home. Post-surgery, the chronic cough with massive bile expectorate was suppressed for two-months, however returned at a much larger frequency and quantity. The patients level of bilirubin elevated to 11 mg/dL shortly post-lobectomy. Following several hospitalizations until September of 2022, where her overall health deteriorated and diagnostic imaging revealed iCC peritoneal dissemination, with a persistent BBF, she eventually succumbed on the 17th September 2022.

Discussion

Cholangiocarcinoma is a highly invasive tumor; it is frequently multifocal and unresponsive to treatment. Due to the lack of specific symptoms and late diagnosis, most patients are unsuitable for resection and thus, palliative treatment options are sought. These are chemotherapy, radiotherapy and loco-regional treatment such as radiofrequency ablation, trans-arterial chemoembolization and radioembolization [4]. The best possible treatment in the management of iCC is surgical resection. Despite the astonishing 80% recurrence rate, a major hepatectomy resection is the mainstay of surgery intervention, with the aim to achieve a margin negative, R0, resection [4,5].

Management of bronchobiliary fistula is primarily conservative, with biliary and abscess drainage [4-12]. Conservative treatment includes Endoscopic Retrograde Biliary Drainage (ERBD), sphincterotomy, Endoscopic Nasobiliary Drainage (ENBD), endoscopic stone extraction, Percutaneous Transhepatic Cholangial Drainage (PTCD) and cyanoacrylate glue seal [12-32]. Only after these methods have failed, surgical intervention such as thoracotomy and liver resection are considered as outcome is often unsuccessful [4,12]. In the case of our patient, BBF treatment was comprised of biliary drainage using PTCD and ERCP with biliary stenting.

ERCP guided biliary stenting and PTCD works to release biliary obstruction rapidly and efficiently. It is the preferred palliative treatment option for patients with malignant biliary obstruction.8 These interventions aim to: (a) minimize the pressure and stress on the biliary tree, (b) to drain the bile from the dilated hepatic ducts to prevent cholangiostasis and subsequent cholangiosepsis and (c) to minimize the flow of bile through the fistula [13]. Undeterred by our recommendations, the patient underwent an open lobectomy in an external facility, three-months after the first symptoms of biliptysis. However, the symptoms of biliptysis were only suppressed for three-months and chronic cough with massive bile expectorate returned, in larger quantities. We feel that invasive procedures such as lobectomy are of extremely high risk of further complications and provide little to no benefits in onco-advanced patients. Most thoracic surgeons will refrain from thoracotomy in this type of patient.

Some authors believe thoracotomy is a necessity for successful fistula closure. Joh, et al., and Eryogit, et al., aim to prove this argument using lobectomy in a Hepatocellular Carcinoma (HCC) patient and in a hydatid disease patient. [1,16] Moreover, Eryogit, et al., argued that a persistent fistula with a patent biliary channel is indictive for thoracotomy and such delay in surgical treatment could result in 'further damage' to the lung [1]. However, this statement does not consider the heavy risk burden in palliative patients. As Hanna, et al., suggests, T3 or T4 tumors and N2 or N3 disease stand as absolute contraindications for thoracoscopic surgery [8]. Literature also states, thoraco-surgery is not viable due to risk of post-lobectomy, de novo fistula formation. Although extremely rare, this usually appears in patients with risk factors for fistula formation [14,15].

The etiology of BBF in our patient remains unclear. However, based on existing literature we hypothesize an iatrogenic origin. BBF can occur as a complication of conservative treatment such as PTCD, surgical treatment such as liver resection and oncological treatment such as radiotherapy [10,13]. After 30-cycles of radiotherapy in one month, our patient was then hospitalized for radiotherapy-induced lung damage, pulmonary embolism and pneumonia. Three weeks post-hospitalization, the patient developed the first symptoms of biliptysis. BBF was then diagnosed via MRCP.

The prognosis of cholangiocarcinoma is dramatically poor, with 95% of patients dying within five years from initial diagnosis. [9,29]. As patients undergo palliative treatment, mainly systemic chemotherapy, the median survival time is 2-6 months [10,30]. Patients with a concurrent fistula orifice possess a major probability of developing pulmonology complications, including pneumonia, bronchiectasis, respiratory failure and death [17-19]. Our treatment strategy aims to improve the quality of life and minimize the risk of these complications for the patient, while undergoing palliative treatment for iCC. We have chosen the less invasive options of treatment for patients with a generally low survival rate i.e., ERCP with stenting and PTCD. With this mindset, our decision was justified by an acceptable survival period of over 5 years from liver resection and over 1 year survival with a persistent BBF. Major complications of Percutaneous Transhepatic Cholangiography (PTC) have been reported to be 4% and Percutaneous Biliary Drainage (PTBD), 7-10% [20-23]. Low-risk complication rates make these invasive procedures optimal for managing patients with iCC malignancy.

The most common reasons for the development of BBF apart from congenital malformation, is based on the exposure of well-known risk factors. These are liver diseases such hepatic hydatid cyst or amebic liver abscess, biliary tract obstruction such as

stenosis, cysts and stones; inflammatory conditions such as liver cirrhosis, hepatitis B, hepatitis C and primary sclerosing cholangitis; blunt or penetrant injury and iatrogenic fistulas that result due to liver resection and radiofrequency ablation [4,13,23-25,29].

In our presenting case, our patient was diagnosed with cholelithiasis. These stones remained dormant for a period of 15-years. The patient was asymptomatic with no further evaluation or treatment of the stones. Until 2017, the patient presented to the hospital with acute abdominal pain and fever and was eventually diagnosed with cholangiocarcinoma. It is in the patient's best interest to carry out routine checkups, especially with a long-term cholelithiasis diagnosis. A critical feature of cholelithiasis is the migration of stone formation to the cystic duct, causing cholecystitis [28]. Literature suggests unpredictable attacks of gallstones lead to an increased risk of cancer such as gallbladder cancer and bile duct cancer [27,28]. Nordenstedt, et al., report on a population-cohort study with complete follow up of up to 43 years indicating that gallstones increase the risk of both intra and extrahepatic cholangiocarcinoma. However, this risk is said to decrease over time after cholecystectomy [26,30-32].

Conclusion

In summary, managing a broncho-biliary fistula in patients with advanced stage IV cholangiocarcinoma poses a formidable challenge. The emergence of this complication during intrahepatic Cholangiocarcinoma (iCC) treatment is influenced by a multitude of factors, making it difficult to attribute to a single cause. Our extensive experience underscores the importance of prioritizing ERCP and PTCD as primary treatment modalities, while advocating caution with regard to thoracic surgery in these oncologicaly advanced cases. It is crucial to recognize that the presence of a broncho-biliary fistula in malignantly afflicted patients serves as a significant adverse prognostic indicator. While achieving definitive success in treatment may be elusive, it remains imperative to steadfastly focus on optimizing the quality of life for these patients.

Conflict of Interest

The authors have no conflict of interest to declare.

References

1. Eryigit H, Oztas S, Urek S, Olgac G, Kurutepe M, Kutlu CA. Management of acquired bronchobiliary fistula: 3 case reports and a literature review. J Cardiothorac Surg. 2007 Dec;2:1-4.
2. Liao GQ, Wang H, Zhu GY, Zhu KB, Lv FX, Tai S. Management of acquired bronchobiliary fistula: A systematic literature review of 68 cases published in 30 years. World J Gastroenterol. 2011;17(33):3842-9.
3. Kim HB, Na YS, Lee HJ, Park SG. Bronchobiliary fistula after ramucirumab treatment for advanced gastric cancer: A case report. World J Clin Cases. 2019;7(19):3039-46.
4. Bartolini I, Risaliti M, Fortuna L, Agostini C, Ringressi MN, Taddei A, et al. Current management of intrahepatic cholangiocarcinoma: from resection to palliative treatments. Radiol Oncol. 2020;54(3):263-71.
5. Akateh C, Ejaz AM, Pawlik TM, Cloyd JM. Neoadjuvant treatment strategies for intrahepatic cholangiocarcinoma. World J Hepatol. 2020;12(10):693-708.
6. Gao F, Pan T, Wang Y. Biliopleural fistula following percutaneous transhepatic cholangiodrainage and irradiation biliary stent insertion successfully treated with coil embolization: a case description. Quant Imaging Med Surg. 2022;12(2):1636-40.
7. Wu JM, Ho TW, Yen HH, Wu CH, Kuo TC, Yang CY, et al. Endoscopic retrograde biliary drainage causes intra-abdominal abscess in pancreaticoduodenectomy patients: an important but neglected risk factor. Ann Surg Oncol. 2019;26(4):1086-92.
8. Hanna JM, Berry MF, D'Amico TA. Contraindications of video-assisted thoracoscopic surgical lobectomy and determinants of conversion to open. J Thorac Dis. 2013;5(Suppl 3):S182-9.
9. Xi XJ, Zhang Y, Yin YH, Li H, Ma DD, Qu YQ. Bronchobiliary fistula following radiofrequency ablation for liver metastases from breast cancer: A case report and literature review. Medicine (Baltimore). 2018;97(43):e12760.
10. Ni Q., Shen W., Zhang M., Yang C., Cai W., Wu M., et al. Prognostic analysis of radical resection for intrahepatic cholangiocarcinoma: a retrospective cohort study. Oncotarget. 2017;8:75627-37.
11. Chua HK, Allen MS, Deschamps C, Miller DL, Pairolero PC. Bronchobiliary fistula: principles of management. Ann Thorac Surg. 2000;70(4):1392-4.
12. Kuo YS, Lee SC, Chang H, Hsieh CB, Huang TW. Thoracoscopic surgery for bronchobiliary fistula: a case report. J Cardiothorac Surg. 2015;10:102.
13. Crnjac A, Pivec V, Ivanecz A. Thoracobiliary fistulas: literature review and a case report of fistula closure with omentum majus. Radiol Oncol. 2013;47(1):77-85.
14. Naranjo Gómez JM, Carbajo Carbajo M, Valdivia Concha D, Campo-Cañaveral de la Cruz JL. Conservative treatment of post-lobectomy

bronchopleural fistula. Interactive Cardiovascular Thoracic Surg. 2012;15(1):152-4.
15. Cooper WA, Miller JI Jr. Management of bronchopleural fistula after lobectomy. Semin Thorac Cardiovasc Surg. 2001;13(1):8-12.
16. Joh HK, Park SY. Surgical Treatment of Bronchobiliary Fistula with Pulmonary Resection and Omentopexy. Korean J Thorac Cardiovasc Surg. 2020;53(1):38-40.
17. Nishimura S, Nakagawa Y, Sakata T, Suga M, Ando M. Bronchobiliary fistula. Nihon Kyobu Shikkan Gakkai Zasshi. 1996;34(6):689-93.
18. Chong CF, Chong VH, Jalihal A, Mathews L. Bronchobiliary fistula successfully treated surgically. Singapore Med J. 2008;49(8):e208-11.
19. Kirnák J, Vidiscák M, Cingel V, Smrek M, Horáková J. An unusual cause of respiratory failure. Bronchobiliary fistula. Cesk Pediatr. 1993;48(1):26-8.
20. Rosich-Medina A, Liau SS, Jah A. Cutaneous metastases from cholangiocarcinoma following percutaneous transhepatic biliary drainage: Case report and literature review. Int J Surg Case Rep. 2010;1:33-36.
21. Mueller PR, Van Sonnenberg E, Ferrucci JT. Percutaneous biliary drainage: technical and catheter related problems in 200 procedures. AJR 1982;138:17-23.
22. Harbin WP, Mueller PR, Ferrucci JT. Transhepatic cholangiography: complications and use patterns of the fine-needle technique: a multi-institutional survery. Radiology 1980;135:15-22.
23. Lazarou V, Moris D, Papalampros A, Tsilimigras DI, Karachaliou GS, Petrou A. Bronchobiliary fistula after hepatectomy: A case report and review of the literature. Mol Clin Oncol. 2019;11(6):602-6.
24. Kumar P, Mehta P, Ismail J. Brocho-biliary fistula: A rare complication after ruptured liver abscess in a 3½ year old child. Lung India. 2015;32(5):489-91.
25. Mandal A, Sen S, Baig SJ. Bronchobiliary fistula. J Minim Access Surg. 2008;4(4):111-3.
26. Nordenstedt H, Mattsson F, El-Serag H, Lagergren J. Gallstones and cholecystectomy in relation to risk of intra- and extrahepatic cholangiocarcinoma. Br J Cancer. 2012;106(5):1011-5.
27. Hsing AW, Gao YT, Han TQ. Gallstones and the risk of biliary tract cancer: a population-based study in China. Br J Cancer. 2007;97(11):1577-82.
28. Jones MW, Weir CB, Ghassemzadeh S. Gallstones (Cholelithiasis). 2022.
29. Turati F, Bertuccio P, Negri E, Vecchia CL. Epidemiology of cholangiocarcinoma. Hepatoma Res. 2022;8:19.
30. Chakunta HR, Sunderkrishnan R, Kaplan MA, Mostofi R. Cholangiocarcinoma: treatment with sorafenib extended life expectancy to greater than four years. J Gastrointest Oncol. 2013;4(4):E30-2.
31. Panda D, Aggarwal M, Yadav V, Kumar S, Mukund A, Baghmar S. Broncho-biliary fistula secondary to biliary obstruction and lung abscess in a patient with pancreatic neuro-endocrine tumor. J Egypt Natl Canc Inst. 2016;28(2):117-21.
32. Honrubia López R, Barbado Cano A, Ruiz Fernández G, Bustamante Robles KY. A bronchobiliary fistula treated with cyanoacrylate glue in a patient with liver cirrhosis. Rev Esp Enferm Dig. 2017;109(4):288.

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