REVISTA ESPAÑOLA DE
ENFERMEDADES DIGESTIVAS
The Spanish Journal of Gastroenterology

Title:
Klatskin tumors and "Klatskin-mimicking lesions": our 22-year experience.

Authors:
Konstantinos Tsalis, Styliani Parpoudi, Dimitrios Kyziridis, Orestis Ioannidis, Natalia Antigoni Savvala, Nikolaos Antoniou, Savvas Symeonidis, Dimitrios Konstantaras, Ioannis Mantzoros, Manousos-Georgios Pramateftakis, Efstathios Kotidis, Stamatios Angelopoulos

DOI: 10.17235/reed.2018.5749/2018
Link: PubMed (Epub ahead of print)

Please cite this article as:
Tsalis Konstantinos, Parpoudi Styliani, Kyziridis Dimitrios, Ioannidis Orestis, Savvala Natalia Antigoni , Antoniou Nikolaos , Symeonidis Savvas, Konstantaras Dimitrios , Mantzoros Ioannis, Pramateftakis Manousos-Georgios, Kotidis Efstathios, Angelopoulos Stamatios. Klatskin tumors and "Klatskin-mimicking lesions": our 22-year experience. . Rev Esp Enferm Dig 2018. doi: 10.17235/reed.2018.5749/2018.

REVISTA ESPAÑOLA DE
ENFERMEDADES DIGESTIVAS
The Spanish Journal of Gastroenterology

OR 5749

Klatskin tumors and "Klatskin-mimicking lesions": our 22-year experience

Konstantinos Tsalis, Styliani Parpoudi, Dimitrios Kyziridis, Orestis Ioannidis, Natalia Antigoni-Savvala, Nikolaos Antoniou, Savvas Symeonidis, Dimitrios Konstantaras, Ioannis Mantzoros, Pramateftakis Manousos-George, Kotidis Efstathios and Stamatios Angelopoulos

Fourth Surgical Department. Medical School. Aristotle University of Thessaloniki. Thessaloniki, Greece. General Hospital "George Papanikoalou". Thessaloniki, Greece

Received: 04/06/2018

Accepted: 04/09/2018

Correspondence: Orestis Ioannidis. Fourth Surgical Department. Medical School. Aristotle University of Thessaloniki. Thessaloniki, Greece. General Hospital "G. Papanikoaloau". Alexandrou Mihailidi, 13. 54640 Thessaloniki, Greece

e-mail: iorestis@auth.gr

ABSTRACT

Background and study purpose: hilar cholangiocarcinoma, also known as Altemeier-Klatskin tumor, is a rare malignancy that arises in the confluence of the hepatic ducts of the porta hepatis. The prognosis is rather poor. Several lesions mimic these tumors and lead to a misdiagnosis, resulting in radical hepatic resections. These lesions are known as Klatskin-mimicking lesions. We present our experience with the diagnosis and treatment of pathological lesions that can mimic a perihilar cholangiocarcinoma and establish an algorithm of treatment.

Methods: for the current retrospective study, a prospectively established bile-duct tumor database was analyzed by selecting patients with a preoperative diagnosis of perihilar cholangiocarcinoma.

Results: in the last 22 years (from January 1st, 1996, to December 31st, 2017), 73 patients who were referred to our tertiary center with a primary diagnosis of a

Klatskin tumor were treated. All patients underwent a thorough evaluation before deciding upon the treatment. However, only 58 cases had a confirmed preoperative diagnosis of hilar cholangiocarcinoma in the final histopathological examination. The final diagnosis in 15 patients differed from the primary cause for referral and the lesions were regarded as Klatskin-mimicking lesions.

Conclusions: clinicians should always highly suspect Klatskin-mimicking lesions when they evaluate a patient for a possible hilar cholangiocarcinoma in order to avoid a misdiagnosis and propose a proper treatment.

INTRODUCTION

Cholangiocarcinoma consists of a rare entity of malignancies that arise from the biliary tree. The location of the carcinoma defines the three different subtypes: intrahepatic cholangiocarcinoma, hilar cholangiocarcinoma and distal cholangiocarcinoma. It is the second most common primary hepatic malignancy after hepatocellular carcinoma (1). Hilar cholangiocarcinoma was first reported by Altemeier et al. in 1957 (2) and then subsequently described by Klatskin et al. in 1965 (3). The Altemeier-Klatskin tumor occurs within 2 cm of the confluence of the right and left hepatic duct at the hepatic hilum and accounts for 50-70% of all cholangiocarcinomas (4).

The diagnosis of this tumor can be technically challenging and requires a high suspicion in order to detect lesions that mimic a Klatskin tumor but are not malignant and do not require a wide resection. Ultrasound (US), computed tomography (CT) and magnetic resonance imaging (MRI) scans are used for this purpose. The use of endoscopic retrograde cholangiopancreatography (ERCP) has also offered great advantages for the identification of these lesions and to assess their extension into the liver, as well as allowing the collection of cytology samples or biopsies (5). However, a high proportion of patients (up to 15%) undergo surgery and extensive resections of what is thought to be a Klatskin tumor. However, the final histopathological examination reveals a benign lesion (6-8), which is widely known as a Klatskin-mimicking lesion. Hence, such an aggressive surgical treatment may not have been necessary. Unfortunately, the diagnostic tools used nowadays do not

always provide an accurate diagnosis and distinction between the benign and malignant nature of a lesion at the hepatic hilum (9).

This study aimed to present the experience within our clinic during the last 22 years with regard to the management of patients with Altemeier-Klatskin tumors and Klatskin-mimicking lesions. Furthermore, a review of the literature on this subject was performed and the key points for an accurate diagnosis are highlighted.

MATERIALS AND METHODS

Our institution is a tertiary referral center for hepatobiliary disease and all imaging modalities for the management of the disease are available, which include CT and MRI scans. The interventional Radiology Department also performs percutaneous biliary interventions (drainage and stenting), angioplasties and transarterial chemoembolization (TACE). Furthermore, the endoscopic team is considered as well qualified and performs many ERCPs a year. Furthermore, the endoscopic ultrasound scan (EUS) has been introduced into the clinical practice during the last five years. Finally, the intraoperative ultrasound scan (IOUS) has also been available since 2010.

Our clinical database from the last 22 years (1996-2017) was analyzed in order to collect information of all patients diagnosed with a Klatskin tumor who were referred to our tertiary center. All patients were thoroughly evaluated, including a physical examination, complete medical and surgical history, hematological and serological examinations and radiological imaging. Most patients had already undergone US and CT scans at the time of referral. Since an accurate diagnosis of hilar cholangiocarcinoma may be challenging and Klatskin-mimicking lesions should always be considered, all the patients underwent a contrast-enhanced triple-phase helical CT scan, MRI scan and a magnetic resonance cholangiopancreatography (MRCP). Moreover, these radiological studies were thought to be necessary as detailed information is crucial in order to plan the surgical procedure. In some cases, a percutaneous transhepatic cholangiography (PTC) or an ERCP was performed to collect more information with regard to the extension of the tumor and to obtain specimens for cytological examination. Endoscopic or percutaneous drainage of the biliary tree was performed when the bilirubin level was more than 10 mg/dl. We

aimed to achieve a preoperative bilirubin level of less than 3 mg/dl as recommended by Makuuchi et al. (10) and Nimura et al. (11). The preoperative evaluation also included serum tumor markers, such as CA 19-9 and CEA, which contributed to the final diagnosis.

RESULTS

All 73 patients (51 male and 22 female) who were referred to our tertiary center were diagnosed with Altemeier-Klatskin tumors. Seventy patients were treated surgically. The final histopathological examination showed Klatskin tumors in 58 patients (Table 1). Thirty-eight were male and 20 were female, with a median age of 62.6 years. The surgical approach differed and was based on the preoperative findings.

A tumor resection was performed in 33 patients. An excision of the extrahepatic biliary tree was performed in 21 cases and an extensive hepatectomy and excision of the extrahepatic biliary tree was performed in the remaining 12 cases. However, 25 patients had unresectable tumors and palliative surgery was performed. The postoperative mortality was 6.06% (two patients). The first patient died due to a myocardial infarction and the second died from sepsis.

In 15 patients (13 males and two females), the final histopathological examination did not show a hilar cholangiocarcinoma. Nine of these patients were treated in the first decade of our experience. The preoperative investigations performed for these patients and the year in which the investigations were performed, the management and outcome are shown in table 2.

Five patients (four males and one female) were proved to have intrahepatic lithiasis (Fig. 1). These patients were treated with a left-hepatic lobectomy and Roux-en-Y hepaticojejunal anastomosis. Four males were diagnosed with Mirizzi syndrome. The underlying pathology was recognized during the operation in three cases and an open cholecystectomy was performed. A right hepatectomy and the excision of the extrahepatic biliary tree were performed in the fourth patient. This patient developed postoperative liver insufficiency and despite the bioartificial liver support (MARS), he died on the 32nd postoperative day.

The presence of metastatic lymph nodes in the porta hepatis secondary to rectal cancer that obstructed the biliary tree was found in a female patient. After ten days of percutaneous biliary drainage, the patient underwent an exploratory laparotomy to remove the tumor. The invasion of the main portal vein trunk by the tumor was observed during surgery and she was treated with an intubation technique, as stent placing via ERCP or PTC was not available during that time. The final diagnosis was made on the 14th postoperative day due to rectal bleeding. The morbidity was minor and she passed away seven months after the operation.

Recently, the presence of metastatic lymph nodes in the porta hepatis secondary to right-colon cancer that obstructed the biliary tree was discovered in a male patient. Following the initial investigation via US, CT and MRI-MRCP scans which revealed enlarged lymph nodes in the porta hepatis, the possibility of a metastatic gastrointestinal neoplasm was considered. This was further investigated with gastroscopy and colonoscopy. The colonoscopy revealed a right-colon adenocarcinoma and following chemotherapy, the patient underwent a right hemicolectomy.

The histological examination revealed a primary nonfunctioning neuroendocrine tumor of the extrahepatic biliary tree in a male patient who had undergone a left hepatectomy and the excision of the extrahepatic biliary tree. The patient had undergone surgery for colonic cancer 12 years previously and a mass in the hepatic hilum was discovered on the abdominal CT scan during his regular follow-up. MRI and a MRCP were performed which showed the dilation of the intrahepatic biliary system of the left liver, even though the patient was asymptomatic. An FNA biopsy was not performed as the lesion was not safely accessible. Therefore, the preoperative diagnosis was hilar cholangiocarcinoma based mainly on the imaging findings. Thus, a left hepatectomy, a resection of the extrahepatic biliary tree and a reconstruction with Roux-en-Y hepaticojejunostomy was performed. Complementary diagnostic tests were performed when the final histological examination results were received. This included an octreotide scintigraphy using 111In-pentetreotide (octreotide scan), upper- and lower-gastrointestinal endoscopies and a small bowel series to rule out the possibility of being a metastatic

lesion.

Another interesting case included the evaluation of a 56-year-old male patient with increased levels of serum gastrin and recurrent episodes of upper-gastrointestinal bleeding. According to his medical history, he had a truncal vagotomy and gastrojejunostomy ten years before admission. He presented the first episode of upper GI bleeding four years before admission and three years later, the level of serum gastrin was 1.688 pg/ml. Conventional imaging studies did not reveal any apparent lesion, only a dilated left-lobe of the biliary tree. The patient had a somatostatin receptor scintigraphy (octreoscan/SRS) due to a high suspicion, which revealed an increased uptake of the radiotracer at the left hepatic lobe. The patient underwent a laparotomy and a small lesion was found on the left hepatic lobe using the IOUS. Thus, a left hepatectomy was performed. The histological examination identified a neuroendocrine tumor that was classified as a primary hepatic gastrinoma. Finally, the preoperative evaluation of two male patients identified IgG4-related cholangiopathy and they were treated conservatively with prednisolone at a dose of 0.6 mg/kg/day for six months. The postoperative mortality in this group of patients was 6.67%.

DISCUSSION

Hepatobiliary malignancies account for 3% of the 560,000 annual cancer-related deaths in the USA and cholangiocarcinoma accounts for a small portion of these cases (10-20%) (12). The Altemeier-Klatskin cholangiocarcinoma is a rare primary tumor (yearly incidence of 2-4 cases per 100,000 patients) that occurs at the confluence of the right and left hepatic duct and the proximal common hepatic duct (1,13). The detection and the diagnosis of the tumor are rather difficult, and it has a poor prognosis with five-year survival rates of less than 5% (14). An extensive R0 resection of the tumor offers the best chances of a curative treatment and the five-year survival rate rises to 28-40%. The surgical approach for the treatment of Klatskin tumors is quite difficult and requires expertise. The associated mortality rate is 7.5-18% and the complication rate is 19-85% (15-18). The peak prevalence of the disease occurs during the seventh decade of life and there is a slight male

predominance (1.5:1) (12). In our case series, the median age of the patients was 62.6 years and a male predominance was observed (38 males:20 females). The postoperative mortality was slightly lower (6.06%).

Hilar cholangiocarcinoma generally occurs sporadically, although several identified risk factors have been linked to its development. There is a distinct geographic variation and a higher incidence is seen in Southeast Asia. This observation reflects a regional difference in risk factors and epidemiology (19). Histopathologically, most tumors are adenocarcinomas (95%), with a grade ranging from well-differentiated to undifferentiated types (20).

Serum tumor markers such as CA 19-9 and CEA are widely used in the routine clinic and they are helpful tools to diagnose certain malignancies and to monitor the efficacy of the therapy. CA 19-9 alone plays an important role in the management of hepatobiliary and pancreatic malignancies, although its validity remains controversial. CEA is another important tumor marker for colorectal, gastric, gallbladder, breast, urinary tract and lung carcinoma and is routinely used in patients with suspected malignancies. Both tumor markers have a threshold that can predict malignancy. CA 19-9 serum concentrations of more than 1,000 U/ml and CEA serum levels four times higher than the reference serum value of 3.6 ng/ml most likely indicate malignancy (21). Specifically in serum, CA 19-9 can be helpful in those patients with indeterminate biliary strictures. In cases of primary sclerosing cholangitis (PSC), a CA 19-9 concentration less than 129 U/ml has a sensitivity and specificity of 79% and 98%, respectively. In cases with no PSC, a CA 19-9 serum concentration of less than 100 U/ml has a sensitivity of 76% and a negative predictive value of 92% compared to that in patients with benign strictures (22).

In our everyday practice, both tumor markers are used preoperatively as an important aid in the final diagnosis, especially in ambiguous cases. Moreover, the preoperative levels of the markers are a useful reference during the postoperative follow-up of these patients. Hence, early diagnosis and proper surgical management are thought to be essential in the management of hilar cholangiocarcinoma and may prolong the survival of patients. Systemic chemotherapy with cisplatin plus gemcitabine in patients with locally advanced or metastatic biliary cancer was

associated with a significant survival advantage as compared with gemcitabine alone, without an additional substantial toxicity (23).

Despite the wide access to imaging modalities and serum tumor markers, the established diagnosis of hilar cholangiocarcinoma remains difficult and is not always feasible. Although it is thought to be ideal, establishing a definite preoperative diagnosis is not always possible and most of the patients undergo major resections based on a strong probability for malignancy. Klatskin tumors need to be differentiated from other benign and malignant lesions that mimic their clinical presentation and the radiological findings. These lesions are widely known as Klatskin-mimicking lesions and pose a diagnostic dilemma (24). Many authors have presented a large series of patients who underwent major liver resection for what was then a benign lesion. The rate of Klatskin-mimicking lesions ranges from 5% to 15%, reaching up to 31% in some reports (6-8,25,26). In the case series presented here, the rate of Klatskin-like tumors was 18.3% during a 22-year period. Nine of the 13 misdiagnosed cases occurred during the first decade of our clinical practice when imaging modalities were not so reliable, the experience was limited and the suspicion was weaker. Since newer diagnostic modalities have been available, only one patient with biliary lithiasis (with Mirizzi syndrome) was managed as a Klatskin tumor. Unfortunately, the outcome was fatal.

Many lesions, such as tuberculosis, sarcoidosis, lymphoma and metastasis are complicated with prominent lymph nodes around the liver hilum. These may mislead the radiologist and thus be considered as advanced Klatskin tumors. Moreover, lesions such as primary sclerosing cholangitis, intrahepatic stones and oriental cholangiohepatitis may mimic a Klatskin tumor and harbor signs of an early-stage cholangiocarcinoma. Therefore, all the patients suspected of having hilar cholangiocarcinoma must be evaluated to identify and exclude the patients with certain disorders that do not require surgical intervention, but require an alternative management (24).

Five patients (7%) were treated in our case series for a suspected hilar cholangiocarcinoma. However, the lesion was proved to be intrahepatic lithiasis during the surgery. Intrahepatic lithiasis is the classical feature of a syndrome known

as recurrent pyogenic cholangitis (RPC). On average, presentation occurs between the third and fifth decade of life with no gender predominance (27). The diagnosis of hepatolithiasis is mainly achieved based on radiological examinations. Contrast-enhanced CT scans detect dilated bile ducts, strictures and stones (28,29).

MRI and MRCP can provide realistic images of the bile ducts and are the best modalities to delineate stones, the extent of the stricture and the lobar atrophy (30). However, there are many limitations and difficulties in the differential diagnoses of intrahepatic lithiasis and Klatskin tumors due to the changes made in the porta hepatis due to chronic inflammation (31). Modern imaging modalities have contributed the most in the avoidance of a misdiagnosis and both the CT and MRI scans provide important information. Based on our experience, the combination of CT and MRI/MRCP is necessary to guide an accurate diagnosis.

Another Klatskin-mimicking lesion involves the so-called Mirizzi syndrome and there were four such cases in our clinic. One of the four patients with Mirizzi syndrome underwent a major resection for a hilar cholangiocarcinoma and the final histological examination revealed the actual diagnosis. Although this patient had a thorough preoperative evaluation with a CT scan and MRI/MRCP, the inflammation and fibrosis at the porta hepatis was so extended that an intraoperative accurate diagnosis was not even possible. Subsequently, a right hepatectomy and extrahepatic bile-duct resection was performed, which is a major operation. Unfortunately, the patient died a month later due to liver insufficiency. The correct identification of Mirizzi syndrome is crucial as the chosen treatment is a cholecystectomy, which has significantly lower morbidity and mortality rates compared to more radical resections performed for Klatskin tumors (24).

A female patient who, at first, was thought to have a Klatskin tumor was managed with an operative intubation of the hilar mass using silastic tubes and Roux-en-Y hepaticojejunostomy. She suffered a metastatic hilar lymphadenopathy secondary to rectal cancer two weeks after the operation. The diagnosis was made due to an episode of lower gastrointestinal bleeding during the same hospitalization and a rectal cancer was found by colonoscopy. Recently, a male patient with a possible diagnosis of a Klatskin tumor was shown to have enlarged lymph nodes in the porta

hepatis. This led to the investigation of another primary gastrointestinal malignancy prior to surgical intervention, which revealed a right-colon cancer.

Many malignancies involve the lymph nodes of the porta hepatis and mimic hilar cholangiocarcinoma. Metastatic lymphadenopathy that occurs in the hepatic hilum is quite difficult to differentiate from a Klatskin tumor on radiological imaging. The key points that may help to avoid a misdiagnosis are usually the absence of ductal dilatation and the involvement of both sides of the confluence in the lesion. Moreover, evaluating the patient thoroughly and obtaining their detailed medical and surgical history, including the evaluation of current symptoms, is crucial (24). This was probably the reason for our misdiagnosis in the female patient.

Neuroendocrine tumors (NETs) of the bile duct are derived from the neuroendocrine system and represent 0.2-2% of all gastrointestinal NETs. They usually occur in the common bile duct (58%) and the most common symptom is obstructive jaundice (32). Preoperative diagnosis is quite difficult, even in the era of modern radiological imaging. A surgical resection was used to treat neuroendocrine tumors. However, differentiating them from non-neuroendocrine tumors is crucial to plan a proper therapeutic strategy (33). In our institution, we saw a male case who was misdiagnosed with a Klatskin tumor, whereas the final histological examination showed a nonfunctioning neuroendocrine tumor. Hepatic gastrinomas are very rare and surgical resection is the treatment of choice (34). A patient was referred for further evaluation and treatment after a left biliary tree dilatation was found on the CT scan. Meticulous medical history revealed the presence of Zollinger-Ellison syndrome.

IgG4-related sclerosing cholangiopathy mainly affects the large bile ducts and appears with concentric bile duct thickening, smooth strictures, multifocal involvement, minimal proximal dilatation and the absence of ectasia and pruning (35). It has a benign progression and responds well to oral corticosteroids. The associated pancreatitis can resolve spontaneously (24). A level of IgG4 over 300 mg/l has a high specificity for diagnosis (36). A male patient was referred to our clinic with obstructive jaundice and diagnosis of hilar cholangiocarcinoma. Imaging studies identified multiple strictures, stenosis of the biliary tree and diffuse enlargement of

the pancreas. The presence of IgG4-related cholangiopathy was suspected due to these findings, which was confirmed by the high levels of IgG4 (778 mg/l). The patient was treated with prednisolone at 0.6 mg/kg/day for six months and achieved a complete remission. The accurate interpretation of radiological findings is crucial to avoid unnecessary surgical intervention, as in this case. Recently, we successfully managed a similar case of IgG4 cholangiopathy.

Our 22-year experience has led us to develop an algorithm for the management of patients with a primary diagnosis of hilar cholangiocarcinoma. This algorithm is based on a thorough evaluation of the patient, guiding us to the indicative treatment. In the beginning, when confronting a patient with obstructive jaundice, we would perform an US as a first step. If the US revealed a hilar stricture or intrahepatic bile duct dilatation but no CBD dilatation, it would be investigated further. This included the measurement of CA 19-9 and CEA levels and an MRI-MRCP. If the CA 19-9 level was high (more than 129 U/ml) and MRI-MRCP indicated malignancy, histological confirmation was essential. Thus, ERCP, PTC, or EUS plus FNA would be performed. When the cytological results were positive, we would proceed to standard surgical management. Conversely, if the CA 19-9 level was low (less than 129 U/ml), primary imaging modalities were not suggestive of malignancy and were of minimal concern and the cytological examination was negative, the patient would be under a close follow-up schedule. Moreover, when the imaging findings were suggestive of IgG4 cholangiopathy, IgG4 levels were measured and the patient would be treated conservatively if the diagnosis was confirmed. In addition, IgG4 can be considered for all patients with studies that do not indicate malignancy, not only those with imaging data, but also as a matter of cost and availability. A diagnostic dilemma would occur when the results of all previous studies were indeterminate. If there was a minimal suspicion of malignancy, a close follow-up is mandatory. On the contrary, a PET scan would be performed if there was significant suspicion and the proper treatment, either surgical or conservative, would be decided upon according to the results. As there are no surgical means for obtaining tumor tissue, either by laparoscopy or by open surgery, follow up is considered to be safe in cases with a minimal suspicion due to the related morbidity and mortality of a

surgical intervention (Fig. 2).

CONCLUSIONS

The accurate preoperative diagnosis of an Altemeier-Klatskin tumor is challenging and must consider all the information collected from the medical history, physical examination, hematological examinations and radiographic imaging. However, the clinician should highly suspect other entities that may mimic a Klatskin tumor when interpreting the radiological and pathological data. A thorough diagnostic evaluation should be performed before any endoscopic or radiologic intervention. Modern radiologic imaging modalities, such as MRI-MRCP, would probably be helpful for the differential diagnoses of entities such as Mirizzi syndrome, intrahepatic lithiasis and IgG4-related cholangiopathy. These may be helpful in identifying a small proportion of the Klatskin-mimicking lesions and any unnecessary morbidity and perhaps mortality associated with a radical resection. Many of these lesions could be treated with more conventional methods. However, in many circumstances such as in hilar strictures, resection would probably continue to be the only means of achieving a definitive diagnosis.

REFERENCES

1. Hennedige TP, Neo WT, Venkatesh SK. Imaging of malignancies of the biliary tract - An update. Cancer Imaging 2014;14:14. PMID: 25608662. DOI: 10.1186/1470-7330-14-14

2. Altemeier WA, Gall EA, Zinninger MM, et al. Sclerosing carcinoma of the major intra hepatic bile ducts. AMA Arch Surg 1957;75:450-61. PMID: 13457619. DOI: 10.1001/archsurg.1957.01280150140015

3. Klatskin G. Adenocarcinoma of the hepatic duct at its bifurcation within the porta hepatis. An unusual tumor with distinctive clinical and pathological features. Am J Med 1965;38:241-56. PMID: 14256720. DOI: 10.1016/0002-9343(65)90178-6

4. Khan SA, Thomas HC, Davidson BR, et al. Cholangiocarcinoma. Lancet 2005;366:1303-14. PMID: 16214602. DOI: 10.1016/S0140-6736(05)67530-7

5. Li J, Kuehl H, Grabellus F, et al. Preoperative assessment of hilar cholangiocarcinoma by dual-modality PET/CT. J Surg Oncol 2008;98:438-43. PMID: 18767120. DOI: 10.1002/jso.21136

6. Verbeek PCM, Van Leeuwen DJ, De Wit LT, et al. Benign fibrosing disease at the hepatic confluence mimicking Klatskin tumors. Surgery 1992;112:866-71. PMID: 1332203

7. Gerhards MF, Vos P, Van Gulik TM, et al. Incidence of benign lesions in patients resected for suspicious hilar obstruction. Br J Surg 2001;88:48-51. PMID: 11136309. DOI: 10.1046/j.1365-2168.2001.01607.x

8. Knoefel WT, Prenzel KL, Peiper M, et al. Klatskin tumors and Klatskin mimicking lesions of the biliary tree. Eur J Surg Oncol 2003;29:658-61. PMID: 14511613. DOI: 10.1016/S0748-7983(03)00148-3

9. Juntermanns B, Kaiser GM, Reis H, et al. Klatskin-mimicking lesions: still a diagnostical and therapeutical dilemma? Hepatogastroenterology 2011;58:265-9. PMID: 21661379. DOI: 10.1055/s-0031-1289085

10. Makuuchi M, Thai BL, Takayasu K, et al. Preoperative portal embolization to increase safety of major hepatectomy for hilar bile duct carcinoma: a preliminary report. Surgery 1990;107:521-7. PMID: 2333592

11. Nimura Y, Hayakawa N, Kamiya J, et al. Hepatic segmentectomy with caudate lobe resection for bile duct carcinoma of the hepatic hilus. World J Surg 1990;14:535-45. PMID: 2166381. DOI: 10.1007/BF01658686

12. Zani S Jr, Pappas TN. Management of cholangiocarcinoma. In: Cameron JL, Cameron AM. Current surgical therapy. 11th ed. Philadelphia: Elsevier Inc.; 2014. pp. 414-9.

13. Lang H, Kaiser GM, Zöpf T, et al. Surgical therapy of hilar cholangiocarcinoma. (Article in German) Chirurg 2006;77:325-34. PMID: 16568258. DOI: 10.1007/s00104-006-1177-4

14. Mosconi S, Beretta GD, Labianca R, et al. Cholangiocarcinoma. Crit Rev Oncol Hematol 2009;69:259-70. PMID: 18977670. DOI: 10.1016/j.critrevonc.2008.09.008

15. Kawasaki S, Imamura H, Kobayashi A, et al. Results of surgical resection for patients with hilar bile duct cancer: application of extended hepatectomy after

biliary drainage and hemihepatic portal vein embolization. Ann Surg 2003;238:84-92. PMID: 12832969. DOI: 10.1097/01.SLA.0000074984.83031.02

16. Pichlmayr R, Weimann A, Klempnauer J, et al. Surgical treatment in proximal bile duct cancer. A single center experience. Ann Surg 1996;224:628-38. PMID: 8916878. DOI: 10.1097/00000658-199611000-00007

17. Neuhaus P, Jonas S, Bechstein WO, et al. Extended resections for hilar cholangiocarcinoma. Ann Surg 1999;230:808-18. PMID: 10615936. DOI: 10.1097/00000658-199912000-00010

18. Jarnagin WR, Fong Y, DeMatteo RP, et al. Staging, resectability, and outcome in 184 patients with hilar cholangicarcinoma. Ann Surg 2001;234:507-17. PMID: 11573044. DOI: 10.1097/00000658-200110000-00010

19. Shaib Y, El-Serag HB. The epidemiology of cholangiocarcinoma. Semin Liver Dis 2004;24:115-25. PMID: 15192785. DOI: 10.1055/s-2004-828889

20. Khan SA, Davidson BR, Goldin R, et al; British Society of Gastroenterology. Guidelines for the diagnosis and treatment of cholangiocarcinoma: consensus document. Gut 2002;51:VI1-VI9. PMID: 12376491. DOI: 10.1136/gut.51.suppl_6.vi1

21. Juntermanns B, Radunz S, Heuer M, et al. Tumor markers as a diagnostic key for hilar cholangiocarcinoma. Eur J Med Res 2010;15:357-61. PMID: 20947473. DOI: 10.1186/2047-783X-15-8-357

22. Blechacz B, Komuta M, Roskams T, et al. Clinical diagnosis and staging of cholangiocarcinoma. Nat Rev Gastroenterol Hepatol 2011;8:512-22. PMID: 21808282. DOI: 10.1038/nrgastro.2011.131

23. Valle J, Wasan H, Palmer DH, et al; ABC-02 Trial Investigators. Cisplatin plus gemcitabine versus gemcitabine for biliary tract cancer. N Engl J Med 2010;362:1273- 81. PMID: 20375404. DOI: 10.1056/NEJMoa0908721

24. Senthil Kumar MP, Marudanayagam R. Klatskin-like lesions. HPB Surg 2012;2012:107519. PMID: 22811587. DOI: 10.1155/2012/107519

25. Wetter LA, Ring EJ, Pellegrini CA, et al. Differential diagnosis of sclerosing cholangiocarcinomas of the common hepatic duct (Klatskin tumors). Am J Surg 1991;161:57-63. PMID: 1846276. DOI: 10.1016/0002-9610(91)90361-G

26. Koea J, Holden A, Chau K, et al. Differential diagnosis of stenosing lesions at the hepatic hilus. World J Surg 2004;28:466-70. PMID: 15085401. DOI: 10.1007/s00268-004-7034-z

27. Digby KH. Common-duct stones of liver origin. Br J Surg 1930;17:578-91. DOI: 10.1002/bjs.1800176804

28. Tsui WM, Chan YK, Wong CT, et al. Hepatolithiasis and the syndrome of recurrent pyogenic cholangitis: clinical, radiologic, and pathologic features. Semin Liver Dis 2011;31:33-48. PMID: 21344349. DOI: 10.1055/s-0031-1272833

29. Lee JW, Han JK, Kim T, et al. CT features of intraductal intrahepatic cholangiocarcinoma. Am J Roentgenol 2000;175:721-5. PMID: 10954456. DOI: 10.2214/ajr.175.3.1750721

30. Wani NA, Robbani I, Kosar T. MRI of oriental cholangiohepatitis. Clin Radiol 2011;66:158-63. PMID: 21216332. DOI: 10.1016/j.crad.2010.06.017

31. Kim HJ, Kim JS, Joo MK, et al. Hepatolithiasis and intrahepatic cholangiocarcinoma: a review. World J Gastroenterol 2015;21:13418-31. PMID: 26730152. DOI: 10.3748/wjg.v21.i48.13418

32. Maggard MA, O'Connell JB, Ko CY. Updated population based review of carcinoid tumors. Ann Surg 2004;240:117-22. PMID: 15213627. DOI: 10.1097/01.sla.0000129342.67174.67

33. Tsalis K, Vrakas G, Geroukis T, et al. Primary neuroendocrine tumor of the extrahepatic biliary tree mimicking Klatskin tumor. J Gastrointestin Liver Dis 2010;19:341-2. PMID: 20922208

34. Tsalis K, Vrakas G, Vradelis S, et al. Primary hepatic gastrinoma: report of a case and review of literature. World J Gastrointest Pathophysiol 2011;2:26-30. PMID: 21607163. DOI: 10.4291/wjgp.v2.i2.26

35. Oh HC, Kim MH, Lee KT, et al. Clinical clues to suspicion of IgG4-associated sclerosing cholangitis disguised as primary sclerosing cholangitis or hilar cholangiocarcinoma. J Gastroenterol Hepatol 2010;25:1831-7. PMID: 21091993. DOI: 10.1111/j.1440-1746.2010.06411.x

36. Zen Y, Nakanuma Y. IgG4 cholangiopathy. Int J Hepatol 2012;2012:472376. PMID: 21994885. DOI: 10.1155/2012/472376

REVISTA ESPAÑOLA DE
ENFERMEDADES DIGESTIVAS
The Spanish Journal of Gastroenterology

REVISTA ESPAÑOLA DE
ENFERMEDADES DIGESTIVAS
The Spanish Journal of Gastroenterology

Table 1. Patients referred to our clinic due to the suspicion of a Klatskin tumor and their underlying condition

Underlying condition	*No. of patients*	*Sex*	*Age*
Altemeier-Klatskin tumor	58	38 male/20 female	m = 62.6 y
Intrahepatic lithiasis	5	4 male/1 female	m = 66.5 y
Mirizzi syndrome	4	4 male	m = 56 y
Portal lymphadenopathy secondary to colorectal cancer	2	1 female 1 male	m = 57 y
Nonfunctioning NET	1	1 male	75 y
Intrahepatic gastrinoma	1	1 male	55 y
IgG4 cholangiopathy	2	2 male	61 y

Table 2. Underlying conditions and investigation studies performed, management and outcome of 15 patients who presented with a pathology that mimics a Klatskin tumor

Underlying condition/No.	*US*	*CT*	*MRI-MRCP*	*ERCP*	*PTC*	*CEA*	*CA19-9*	*Other*	*Management*	*Outcome*	*Year the patients were managed*
Intrahepatic lithiasis											
1	+	+		+		+	+				1996
1	+	+		+		+	+		Left lobectomy + Roux-en-Y hepaticojejunal anastomosis	Good	1998
1	+	+		+		+	+				1999
2	+	+	+	+		+	+				2005
Mirizzi syndrome									Open cholecystectomy	Good	
1	+	+		+		+	+				1997
1	+	+				+	+				1999

1	+	+	+	+		+	+		Right hepatectomy + extrahepatic bile duct resection + Roux-en-Y hepaticojejunal anastomosis	Liver failure-death on the 32 nd postoperative day	2000
1	+	+				+	+		Open cholecystectomy	Good	2007
Portal lymphadenopathy due to rectal cancer								Colonoscopy after rectal bleeding	Intubation + Roux-en-Y hepaticojejunostomy	Death after 7 months	
Portal lymphadenopathy due to colon cancer 1								Colonoscopy	Chemotherapy + right hemicolectomy	Good	
Primary nonfunctioning NET 1		+	+			+	+		Left hepatectomy + extrahepatic bile duct resection + Roux-en-Y hepaticojejunal anastomosis	Good	2009
Primary i ntrahepatic gastrinoma 1								Serum gastrin, octreoscan	Left hepatectomy	Good	

IgG4 cholangiopathy 1 1	 + +	 + +	 + +	 +	 	 + +	 + +	Serum IgG4	Prednisolone 0.6 mg/kg/day for 6 months	Good	 2015 2016

The + symbol means that the examination was performed.

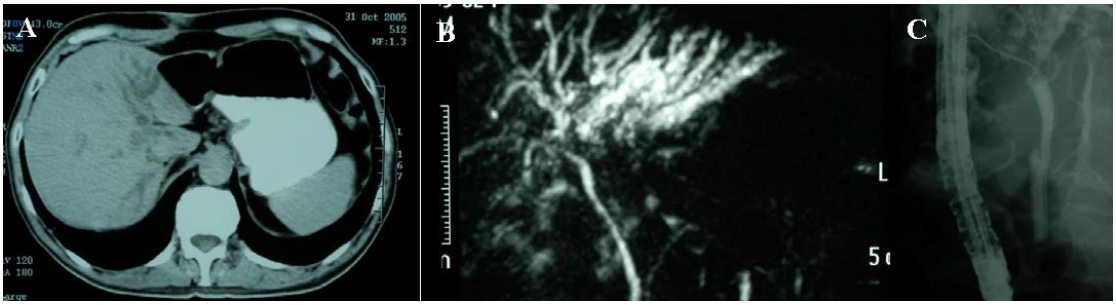

Fig. 1. A patient with intrahepatic lithiasis. A. CT scan that revealed dilated left intrahepatic ducts. B. MRCP showing a hilar stricture and dilated left intrahepatic ducts. C. ERCP showing a hilar stricture.

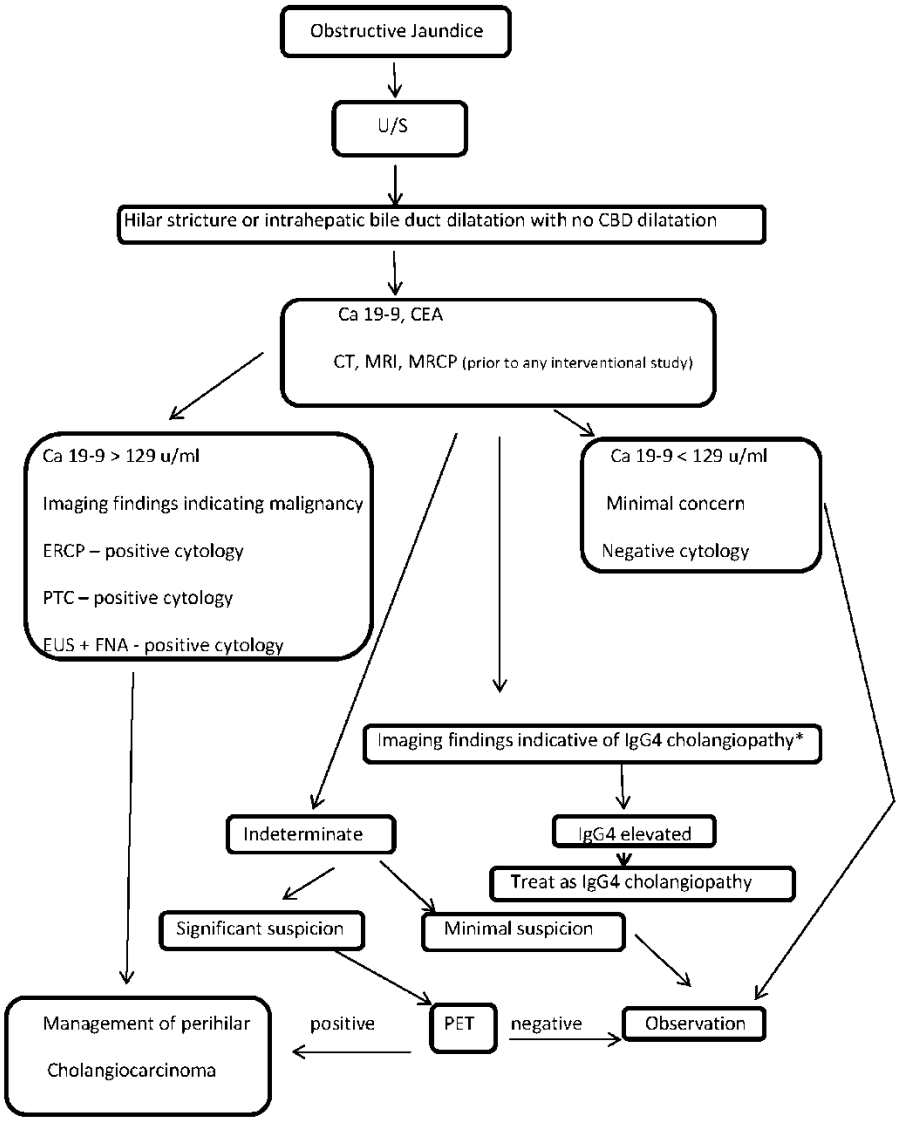

Fig. 2. Algorithm for the management of patients with a primary diagnosis of hilar cholangiocarcinoma. *IgG4 can be considered for all patients with studies that do not indicate malignancy, depending on the cost and availability.