CASE REPORT

Extrahepatic cholangiocarcinoma with poor prognosis: A case report

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Abstract

Cholangiocarcinoma is the second most common primary hepatic malignancy arising from biliary epithelium. Hilar Cholangiocarcinoma is the most common type. As there are no early symptoms in this disease, patients often present at an advanced stage of disease, which makes their prognosis extremely poor. Resection is the only curative option, but fewer than 20% of patients are eligible for surgery after staging, usually because of advanced disease.

We are reporting a case of a 50 year old female who presented to us with obstructive jaundice, she underwent investigations and found to have extrahepatic cholangiocarcinoma she underwent laparotomy and found to be inoperable due to advances local growth of the tumor.

Keywords: cholangiocarcinoma, malignancy arising from biliary epithelium, obstructive jaundice, inoperable cholangiocarcinoma

Introduction:

Obstructive jaundice is a complex complication in patients with advanced tumors.[1] The causes of obstructive jaundice are variable, but it is most commonly due to choledocholithiasis; benign strictures of the biliary tract; pancreaticobiliary malignancies; and metastatic disease. Pathophysiology caused by obstructive jaundice involving coagulopathies, infection, renal dysfunction, and other adverse events. Patients are inclined to develop nutritional, infectious and systemic complications. Appropriate pre-operative evaluation and optimization can greatly contribute to a favorable outcome for per-operative jaundiced patients.[2] Biliary Stenting is the method of palliation in patients with biliary obstruction.[1] Most malignant tumors causing obstructive jaundice have poor prognosis such as pancreatic cancer, cholangiocarcinoma, gall bladder cancer, and etc. Majority of these tumors usually present with distant metastasis. Mortality depends on the cause of obstruction. Several mortality related factors are age and gender, sepsis, bilirubin levels, CA 19-9, albumin levels, drainage procedures and comorbid diseases.[3]

Case Report:

50 year old Asian female presented to the hospital with a one and half month history of painles progressive jaundice, pain in epigastrium, vomiting and fever. Jaundice was gradually progressive along with yellow discoloration of skin, sclera, nails and mucous membranes, dark yellow urine and pale stools and with recurrent episodes of itching. Her pain in epigastrium was gradual in onset, continuous, dull aching in nature, non-radiating, aggravates on vomiting and has no relieving factor. Vomiting was sudden in onset, non-projectile, 3-4 times per day, yellowish–greenish in color, watery in consistency, about half a cup in quantity. Fever was low grade, intermittent, not associated with rigors or chills, has no specific time of occurrence, no aggravating

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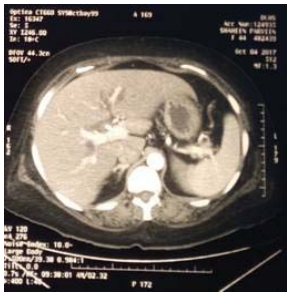

Figure 1: CT findings of extrahepatic cholangiocarcinoma

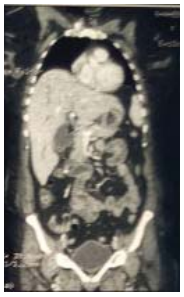

Figure 2: saggital view of CT scan showing cholangiocarcinoma

factor, relieves on medication. Along with these complains she was having generalized weakness & fatigability, on and off constipation, undocumented slight weight loss, reduced appetite and disturbed sleep. She had a past medical history of Diabetes Mellitus (diagnosed 6 months back) controlled by combination therapy of sitagliptin & metformin and hypertension (for last 4 years) controlled by Amlodipine. She had a past surgical history of 1 LSCS 19 years back and hernia repair 2 years back. Her past Ob/Gyn history was not significant. Her family history was positive for Asthma, Diabetes and Hypertension. There was no history of TB contact or any malignancy in family.

Initially patient was being treated on OPD basis at public sector hospital. On investigations initial diagnosis of choledocolithiasis was made. Her ERCP was planned and done on 26/09/2017 which failed. Sphincterotomy was done with stent placement. Stone could not be retrieved. CBD was moderately dilated with a large filling defect in proximal CBD. Despite stent placement jaundice was not relieved. After that Pt was re-admitted on 29/09/2017 in the same Hospital and treated with the diagnosis of Cholangitis. She was discharged on 04/10/2017, CT abdomen was done and she was called for follow-up.

After 1 week on 11/10/2017 she presented in OPD and was admitted to in patient facility. At presentation she was febrile with a fever of 100F, rest of the vitals were WNL. On physical examination she was ill looking, obese, icteric female who was well oriented to time place and person, having yellow discoloration of the skin of whole body, nails, sclera and mucous membranes. There was no edema. Her thyroid gland and lymph nodes were not palpable. On per abdominal examination her abdomen was distended, stretch and scratch marks were present all over abdomen, there was lower midline operative scar of previous surgery. On palpation her abdomen was soft and non-tender with Courvoisier's sign positive, liver was palpable but was smooth, firm and non-tender. Liver and gall bladder were dull to percussion, fluid thrill was present and her gut sounds were audible on auscultation. Rest of the systemic examination was unremarkable.

At presentation her Hb was 8.4, TLC was 28.2, creatinine of 1.39, total bilirubin of 30.06, direct bilirubin of 20.47, SGPT of 75, alkaline posphatase of 2057, GGT of 1092, SGOT of 156, INR of 1.4. Hepatitis A, B and C profile was non-reactive. CT scan of Abdomen shows Stent in CBD. Moderate intra-hepatic biliary ductal dilatation. Enhancing peri-ductal thickening seen extending along the intra- & extra-hepatic duct predominantly along the CBD. Multiple peripherally enhancing hypodense lesions are seen in both lobes of liver. Overall appearance raising the possibility of cholangitic abscesses, portal vein shows normal opacification. There was no evidence of portal venous thrombosis. Gall bladder appears normal with internal hyperdensity representing calculi.

Pre-op diagnosis was Choledocholithiasis with Cholangitis. IV fluids and IV antibiotics were started. Her TLC count started to decrease gradually. Rest of the symptomatic management was started. Cholecystectomy plus choledochotomy with T-tube insertion was planned. Patient was prepared for surgery. Her Hb was optimized. FFPs were transfused due to deranged coagulation profile. High risk consent was taken. Patients and attendants were fully councelled about the risks. Written and informed consent was taken.

Surgery was done on 17/10/2017. Abdominal cavity was explored by giving Kocher's incision, Hemorrhagic moderate amount of ascitic fluid drained. Large distended gall bladder filled with multiple calculi. Solid mass at the confluence of

cystic duct, common hepatic duct & CBD engulfing the portal vein (cholangiocarcinoma) with metastasis. Lymph nodes were enlarged. Nodes were palpable in the right lobe of the liver. There was nutmeg appearance of liver. Stent was placed above the mass, mass was fixed and unable to remove, hence, tumor was inoperable. Cholecystectomy was done. Stent was manipulated proximally towards the CBD.

In her post-operative investigations her TLC count kept on raising, her coagulation profile was deteriorating, her LFTs initially improved then kept on worsening.

Biopsy of the gall bladder and cystic duct shows full thickness of wall showing an invasive neoplastic lesion composed of atypical glands lined by cells showing moderate pleomorphism, also infiltrating into the attached liver tissue. Features were consistent with moderately differentiated adenocarcinoma. As per histopathology report she was T3. According to TNM staging. Her tumor was stage 4 tumor.

Discussion:

Cholangiocarcinoma is the most common primary biliary malignancy arising from the cholangiocytes that line the biliary tree, is an adenocarcinoma of bile duct epithelium. CCAs is classified based on their anatomic location, as follows: intrahepatic CCA (iCCA), perihilar CCA (pCCA), or distal CCA (dCCA). pCCA is the most common type of CCA also known as hilar or Klatskin tumors.[4, 5, 9,10] Prevalence of CCA is highest in Asia.[4] The mean age of diagnosis of CCA is 50 y. Incidence rate for pCCA plus dCCA is around 0.97/100,000.[10] Male are affected more from the disease than females (1.9 and 1.5 per 100,000, respectively).[9] Most CCAs are sporadic and have no identifiable risk factors.[9] Hepatolithiasis is the major risk factor for CCA in Asian countries.[4] Chronic biliary inflammation secondary to calculi has been proposed to increase the risk of malignancy.[10] Definite risk factors of CCA are; primary sclerosing cholangitis, liver fluke infection (Opistorchisviverrini), hepatolithiasis and biliary malformation (choledochal cysts, Caroli's diease).[5]

It is challenging to diagnose CCA because of its paucicellular nature, anatomic location, and silent clinical character. Diagnosis requires a multidisciplinary approach that involves clinical, laboratory, endoscopic, and radiographic analyses.[10]

The most common cause of perihilar biliary obstruction is Perihilar Cholangiocarcinoma.[7] pCCA can develop anywhere from the second-order biliary ducts to above the site of cystic duct origin. 90% of patients with pCCAs have painless jaundice, 10% have cholangitis, and 56% have systemic symptoms such as malaise, abdominal discomfort, nausea, anorexia, or weight loss. Weight loss with jaundice is common which regains after biliary stenting. Depending on the presence or absence of liver disease patient can have cutaneous manifestations.[9]

A new surgical staging system known as Bismuth–Corlette classification for pCCA has been introduced to improve and standardize determination of prognosis. It includes; assessment of biliary tree involvement (common bile duct, confluence, right and/or left hepatic ducts, and both ducts involvement), tumor size (>1 cm, 1–3 cm, or ≥3 cm), tumor morphology (sclerosing, mass-forming, mixed, or polypoid), degree and specific location of hepatic artery and portal vein encasement (vessel involvement >180° indicates encasement), volume of the potential liver remnant, other liver diseases (fibrosis, non-alcoholic steatohepatitis, or PSC), status of lymph node groups (hilar and along the hepatic artery vs celiac and periaortic), and presence of distant metastases.[9]

Patients presenting with the above signs and symptoms and with known risk factors should be evaluated for cholangiocarcinoma. Laboratory analysis is mostly non-specific and reflects the associated cholestasis and cholangitis.[5]

Radiologic evaluation is critical for detection and evaluation of tumor extent, as well as for preoperative planning.[5] MRI, CT, endoscopic retrograde cholangiography (ERCP), and endoscopic ultrasound (EUS) are used most frequently to

diagnose and stage pCCA.[9] Of these, MRI plus MRCP is the imaging modality of choice as it can assess resectability and tumor extent with an accuracy of up to 95%.[10] ERCP, percutaneous transhepatic cholangiography (PTC) and EUS, are diagnostic as well as therapeutic.[5] EUS aids in evaluation of regional lymphadenopathy and omental metastasis.[10] ERCP and PTC allow assessment of strictures, sampling of biliary epithelial cells and therapeutic dilatation and placement of stent. The accuracy of CT in the assessment of resectability has been reported as 60–88% and has a high negative predictive value for advanced disease 85-100%.[5]

Surgical resection is the only curative treatment of choice for pCCA, if feasible[4, 9,10] although only 10-15% are resectable at presentation. Resection should only be done with curative intent, because non-curative or debulking resection has no significant survival benefit compared with patients not treated surgically.[4] Recommendations concerning the perioperative management of the patients with obstructive jaundice including preoperative biliary drainage, anti-infection, nutrition support, coagulation reversal, cardiovascular evaluation, perioperative fluid therapy, and hemodynamic optimization should be taken.[2] It is challenging to stage pCCA accurately which is required to make a management plan.[9] Bismuth-Corlette staging classification which is based on the anatomic location of the CCA helps in decision making.[10] Contraindications to surgical resection of hilar CCA are: (i)bilateral hepatic duct spread, (ii)extensive involvement of main trunk of portal vein, (iii)bilateral involvement of hepatic, arterial or portal venous branches, (iv)combination of vascular involvement with evidence of contralateral ductal spread, (v)lymphnodeinvovement of ductal spread, (vi)significant comorbidities.[4]

Surgical resection entails lobar hepatic and bile duct resection, regional lymphadenectomy, and Roux-en-Y hepaticojejunostomy.[10] Five-year survival rates after R0 resection for hilar CCA are 11% to 41%. Perioperative morbidity following resection of hilar CCA is 31% to 85%, and postoperative mortality is 5% to 10% at major referral centers.[4]

With the emergence of new liver transplantation protocols, neoadjuvantchemoradiation followed by transplantation has become an appealing option for highly selected patients.[10] Patients who are not eligible for surgical resection or liver transplantation, systemic chemotherapy with gemcitabine and cisplatin is recommended. Adequate biliary drainage is essential in case of biliary obstruction to relieve cholestasis and to increase the tolerance for chemotherapy.[9,10]

Obstructive jaundice is a cumbursome complication in patients with advanced solid malignancies, therefore, palliative therapies are quite important in the management of this disease. Biliary drainage via endoscopic stenting is as successful as surgical choledochojejunostomy or hepaticojejunostomy for relief of cholestasis and restoration of biliary drainage and is the only method of relieving biliary obstruction in patients as most of the patients have lost the chance of operability.[4] Palliation not only reduces bilirubin level, it can also improve the patient's quality of life and prolong survival, and may also provide the possibility for subsequent treatment. Obstructive jaundice caused by hilarcholangiocarcinoma not only affects the patient's liver function, but also influence the patient's survival time. Infection is one of the most common complications in patients with obstructive jaundice, which could lead to death peroperatively.[1] In cases where endoscopic stent placement is not feasible, PTC can be employed for biliary drainage.[4]

Prognosis is highly dependent on resectability. Median survival with unresectable CCA is 3-6 months and following a curative resection is 24 months.

Our patient was a female with cholelithiasis presented with symptoms which were present for a short duration. Her malignancy was undiagnosed despite mutiple investigations, although a diagnostic and a therapeutic procedure of ERCP was done as well. She was not the candidate of surgical resection and palliation was the

only thing that was being provided to her. She recovered well and was allowed to go home she remained alright and re-admitted after 3 months with history of loss of appetite, vomiting and abdominal pain. Conservative management given to her inspite of all efforts she died after 3 months.

Conclusion:

Cholangiocarcinoma is a fatal disease, as patients tend to present late with unresectable disease. Many patient-related and disease-related factors may alter survival.

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Role and contribution of authors:

Dr. Hajrah Hilal Ahmed, collected the references and did initial writeup.

Prof. Dr. M. Jamaluddin critically review the article and madew the final changes.

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