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Cholangiocarcinoma and Gallbladder Cases: An Expert Panel Case-Based Discussion

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Cholangiocarcinoma and gallbladder malignancies are aggressive gastrointestinal malignancies with management dependent on resectability, comorbidities, and location. A multidisciplinary discussion with medical oncologists, radiation oncologists, and surgeons is necessary to determine the optimal treatment approach for each patient. Surgical resection offers the best chance for a long-term cure. Recent studies, such as the phase II SWOG S0809 and the phase III BILCAP study have highlighted the importance of adjuvant treatment with radiation therapy and chemotherapy, respectively, in resected disease. In patients with unresectable disease chemotherapy and chemoradiation therapy to a high dose can improve overall survival and locoregional control. In this expert panel we have brought together radiation oncologists and a medical oncologist to provide case-based feedback on their institutional practices.
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Case 1: Extrahepatic Cholangiocarcinoma (Resectable)

A 71-year-old male with a past medical history of hypercholesterolemia presented with right upper quadrant discomfort and dark urine to his primary care physician. A complete history and physical exam was significant for clay colored stools, pruritis, and jaundice without any evidence of ascites, hepatomegaly, or encephalopathy. His ECOG performance status was 0. Laboratory values at the time of diagnosis were the following: a serum total bilirubin of 1.8 mg/dL with a direct bilirubin of 1.5 mg/dL; alkaline phosphatase of 259 U/L; elevated transaminases 2-3 times the reference value. A contrast enhanced computed tomography (CT) scan of the abdomen and pelvis showed intrahepatic biliary dilation with an ill-defined lesion identified at the hilum of the liver at the confluence of the right and left hepatic bile ducts, measuring 15 mm. The rest of the common bile duct was normal in caliber, no intraparenchymal extension or lesions were identified in the liver, and there was no associated lymphadenopathy. A complete radiologic work-up was negative for metastatic disease (Fig. 1).

1. What is your treatment recommendation?
2. If radiation treatment is recommended, what dose, fractionation and treatment volumes would you propose?
3. If the patient underwent resection, cholecystectomy with Roux-en-Y hepaticojejunostomy, and the tumor was noted to be present < 1 mm from the hepatic parenchymal margin (R1), would you boost the close/positive margin? If so, to what dose?

Expert Opinion No. 1 (University of Pennsylvania-Radiation Oncology)

This patient presented with a perihilar or "Klatskin" tumor, at the confluence of the left and right hepatic bile ducts and an otherwise normal common bile duct (Bismuth II). Given his good performance status, elevated transaminases, dilation of the intrahepatic biliary ducts with a normal common bile duct, and lack of metastatic disease, he is an appropriate surgical candidate, and we would recommend a radical surgical

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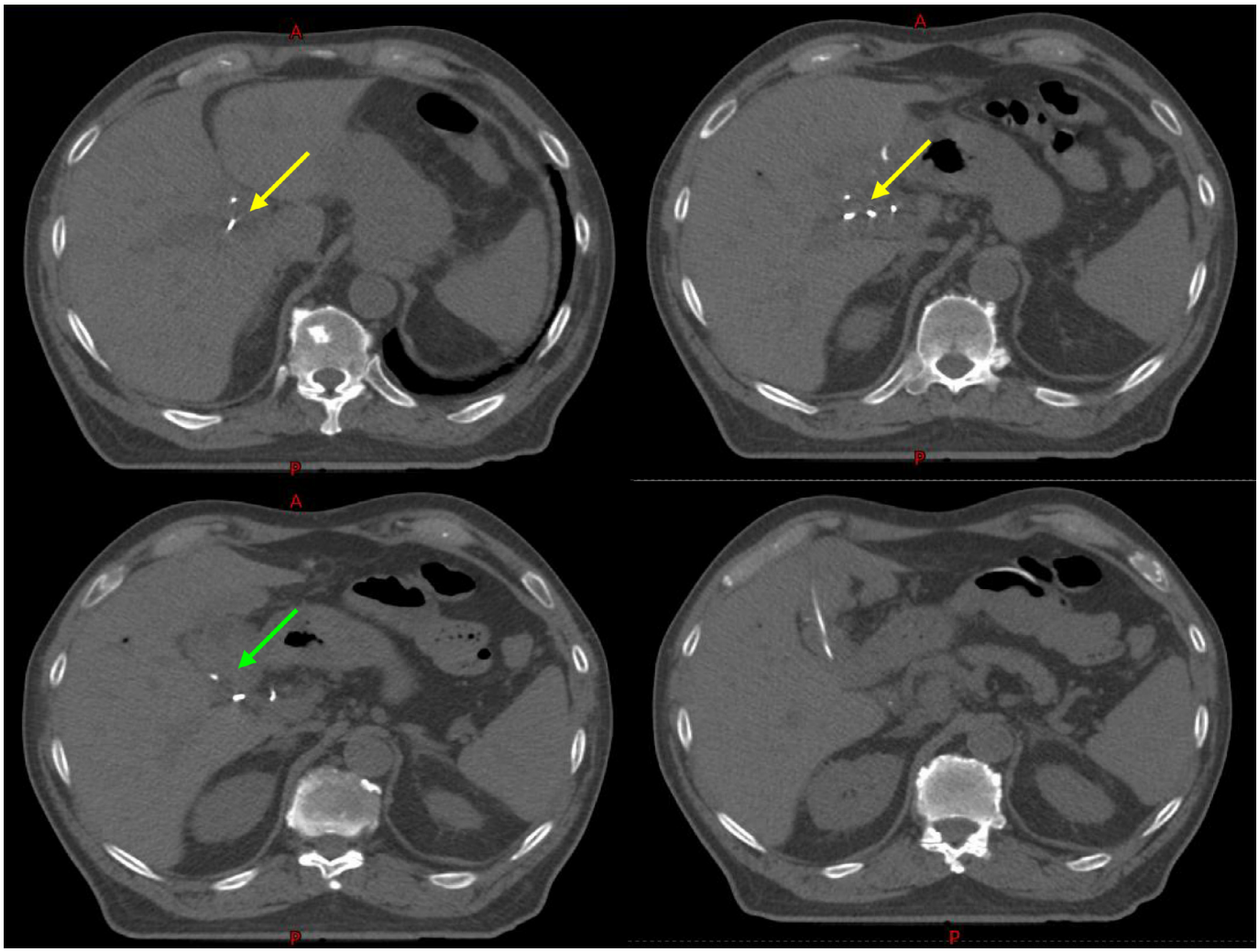

Figure 1 (A) Preoperative computed tomography (CT) axial images of the abdomen (upper panel) with contrast from a patient diagnosed with extrahepatic cholangiocarcinoma showing dilated intrahepatic biliary ducts (blue arrows) and a hilar cholangiocarcinoma (yellow arrows). (B) Postoperative CT axial slices without contrast through the abdomen (lower panel) s/p tumor and extrahepatic bile duct resection, cholecystectomy (green arrows pointed at operative bed) and a Roux-en-Y hepaticojejunostomy (white arrow). (Color version of figure is available online.)

resection: en bloc hepatectomy, resection of the extrahepatic bile ducts, cholecystectomy, a Roux-en-Y hepaticojejunostomy, and a regional lymphadenectomy,[1] with adjuvant chemotherapy and chemoradiation based on the recent phase II SWOG S0809 study.[2] Survival for patients with unresectable disease is poor and typically only 6-9 months, whereas surgical resection offers the only curative treatment option. In a large retrospective series of patients with extrahepatic cholangiocarcinoma (EHCC), treated with external beam radiation, those patients who underwent an R0 resection had a statistically significant longer median survival (24 months vs 13 months) compared to those who had an R2 resection.[3]

These tumors typically recur locally, and numerous retrospective series have indicated that adjuvant radiation treatment increases median survival and increases local-regional control.[4-7] The only prospective study, SWOG S0809, is a phase II trial which treated patients with an R0 or R1 resection with adjuvant gemcitabine and capecitabine followed by external beam radiation with concurrent capecitabine with a median overall survival (OS) of 35 months for patients with R0/R1 disease.[2] We would therefore recommend treatment per the SWOG regimen with postoperative gemcitabine followed by adjuvant radiation with concurrent capecitabine for this patient.

We would treat with intensity-modulated radiotherapy (IMRT) and would contour the elective nodal volume including the retropancreaticoduodenal nodes, celiac, and portal vein lymph nodes. We would then contour the resection bed (preop volume and postop), including all surgical clips and treat this and the elective lymph node volume to 45 Gy (in 1.8 Gy fractions). We would deliver a concurrent boost to the tumor bed to a total of 55 Gy in 25 fractions given the R1 resection, per SWOG S0809.[2] We would follow the IMRT constraints in the SWOG study, limiting the mean liver dose to < 30 Gy, small bowel maximum < 54 Gy, and no more than 50% of the combined kidney volume > 18 Gy.[2]