Tumor Boards in Interventional Oncology

A multidisciplinary discussion of the approach to treatment for four patients with cancers of varying origins and severities.

CASE 1

WITH DIMITRIS FILIPPIADIS, MD, PHD, EBIR; ALEXIS KELEKIS, MD, PHD, EBIR, FSIR; AND MAUREEN P. KOHI, MD, FSIR

A 35-year-old woman with a past medical history of ductal breast cancer (R0M0) resected 1 year ago followed by chemotherapy (12 cycles of paclitaxel) and initially disease-free on positron emission tomography (PET)/CT now presents with three new nodules in the right liver lobe segments 4A, 5, and 6. The largest lesion measures 1.7 cm on MRI.

Drs. Kelekis and Filippiadis: Our recommendation is percutaneous ablation using either radiofrequency or, even better, microwave energy. Advantages of microwave ablation over radiofrequency ablation include the ability to achieve temperatures over 100°C and the ability to produce larger ablation volumes in a shorter time that are less affected by the heat sink effect and any kind of impedance-driven performance. According to published data, oligometastatic breast cancer patients treated with curative intent may remain disease free for a long period of time. Percutaneous thermal ablation of breast cancer metastases is a safe, efficacious, and feasible treatment option. Negative prognostic factors include a tumor burden > 4 cm and triple-negative histologic subtypes. The survival rates in selected patients with breast cancer liver metastases treated with percutaneous thermal ablation are comparable to those achieved with surgery.[1]

Three metastatic lesions, all confined in the right liver lobe and each with a diameter < 2 cm, constitute an ideal oligometastatic candidate for percutaneous thermal ablation. Curative intent in terms of complete lesion ablation along with a safety margin of 1 cm should be the therapeutic goal. For oligometastatic breast cancer patients who present with fewer than five lesions, like the patient in this case, percutaneous thermal ablation combined with systemic chemotherapy and specific hormone therapy can play an important role in the management of patients with a limited number and sites of metastases.[2,3]

Another approach that has not been extensively studied is to combine percutaneous thermal ablation with transarterial chemoembolization (TACE). In a recent comparative study, Wang et al suggest combining percutaneous ablation with TACE for statistically significant better outcomes.[4]

Dr. Kohi: In the absence of randomized, comparative data, my recommendation is entirely based on my clinical experience. However, it should be noted

that my experience and the available data are almost exclusively in women with chemorefractory, progressive liver metastases from breast cancer. It would be very unusual to see such a patient in my practice, as she would likely be treated with another line of systemic chemotherapy or other targeted therapies. However, should she choose locoregional therapy, I would offer intra-arterial therapy as opposed to ablation. I would discuss with her the procedural steps, risks, and benefits of TACE using drug-eluting beads (DEB-TACE) and transarterial radioembolization (TARE). Ultimately, I would recommend TARE. Although there is no comparative data between DEB-TACE and TARE in women with liver metastases from breast cancer, in my experience, TARE has been associated with lower rates of toxicity and higher tolerability.

Several studies have evaluated the use of TARE in women with liver-dominant breast cancer metastases. Bangash et al treated 27 women with glass beads and reported an objective response rate of 39.1% and a median overall survival (OS) of 6.8 months. The authors reported 11% grade 3 toxicity.[5] Cianni et al treated 52 women with resin beads and reported a median OS of 11.5 months with a disease control rate of 91.4%. Toxicities occurred in < 4%.[6] Saxena et al treated 40 women with resin beads and demonstrated a median OS of 13.6 months with a disease control rate of 71.1%. Grade 1 and 2 toxicities were noted in 40% of the patients.[7] Additional studies exist that support the use of TARE for liver metastases from breast cancer.

If the patient does not desire TARE or is not a suitable candidate, I would proceed with DEB-TACE. Martin et al treated 40 women with doxorubicin-eluting beads (100–300 µm) and reported a median OS of 47 months with a tumor response rate of 57.5%. The authors also reported a 17% rate of grade 3 and higher toxicity.[8] Lin et al treated 23 women with doxorubicin-eluting beads (70–150 µm) and reported a median OS of 17 months and a disease control rate of 83%. Grade 3 or higher toxicity was observed in 45% of the patients.[9]

Overall, the data regarding TARE and DEB-TACE include heterogenous cohorts, varying techniques, and different response criteria, all reported in a retrospective manner without a control arm. In my practice, I have observed similar outcomes, with more women complaining of postembolization syndrome after DEB-TACE compared to TARE. Although thermal ablation is an alternative therapy for hepatic metastases from breast cancer, I would be inclined to use this approach in the setting of a solitary lesion.

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CASE 2

WITH GHASSAN K. ABOU-ALFA, MD, AND ROBERT J. LEWANDOWSKI, MD, FSIR

A 67-year-old man with a past medical history of compensated alcoholic cirrhosis and type 2 diabetes mellitus and no symptoms is diagnosed with three arterial hypervascular lesions of the right liver lobe on recent MRI. The largest lesion measures 6 cm and demonstrates segmental portal vein invasion. The patient's Eastern Cooperative Oncology Group performance score is 0, and his liver function status is Child-Pugh A.

Dr. Abou-Alfa: Considering the size of the lesions and the portal vein involvement, curative surgical resection and liver transplant are inappropriate options in this case.[1] Local therapy may be appropriate. Chemoembolization or embolization may be possible, although in view of the vascular involvement, certain experts may argue against this. Radioembolization could be considered as well. Unfortunately, the latest study of yttrium-90 (Y-90) radioembolization did not lead to any significant improvement in OS versus sorafenib in patients with hepatocellular carcinoma (HCC).[2] Thus, the use of systemic therapy would be appropriate and justified. The options include sorafenib and lenvatinib, pending the approval of the latter.[3,4]

Dr. Lewandowski: Recent prospective randomized trials on locoregional versus systemic therapy for patients with "advanced" HCC failed to meet their primary endpoint of an OS advantage of radioembolization over sorafenib.[2,5] Although not powered for noninferiority, these trials are consistent with current published literature revealing similar OS outcomes for these therapies in this patient population. Both published studies have significant limitations. In the SARAH trial,[2] 22% of patients who were randomized to radioembolization did not receive this therapy; 45% of patients had previous chemoembolization in which hepatic arteries were embolized, potentially limiting efficacy of future embolotherapies; 18 more days elapsed between randomization and initiation of therapy with radioembolization than with sorafenib; 34% had main portal vein tumor thrombosis (PVTT), which is a relative contraindication to radioembolization; and treatment centers had limited experience with radioembolization, an operator-dependent procedure. In the SIRVENIB trial,[5] 29% who were randomized to radioembolization did not receive this therapy and again there was limited experience with radioembolization at many centers, which included Myanmar and Mongolia. Both studies revealed better tumor response rates and higher quality of life with radioembolization versus sorafenib. Of note, neither study utilized higher-dose glass microsphere radioembolization.[6]

The question regarding optimal treatment for patients with locally advanced HCC should not be locoregional versus systemic therapy. Rather, the question should be how to optimally combine these therapies for synergistic effect. The treatment approach advocated by our multidisciplinary tumor board for locally advanced HCC patients with preserved liver function/performance status is liver-directed therapy with radioembolization, followed by systemic therapy (historically sorafenib). We have had success with this treatment paradigm, downstaging several patients to liver resection and/or liver transplant after sustained tumor response and demonstration of good tumor biology. Radioembolization offers well-tolerated outpatient therapy with high tumor response rates and competitive survival outcomes, especially in Child-Pugh A patients with PVTT not extending to the main portal vein. Adjuvant systemic therapy offers the promise of reducing local/systemic disease progression. By themselves, systemic therapies are limited by poor tumor response rates and tolerability. The role of this combination therapy (radioembolization plus sorafenib) is currently being studied in the STOP-HCC trial (NCT01556490).

Although sorafenib is the gold standard systemic agent for locally advanced HCC patients based on a 2- to 3-month survival advantage over placebo,[3] it might not be the ideal systemic agent for combination/adjuvant therapy given negative results from prospective randomized trials of sorafenib plus chemoembolization,[7] as well as a recent negative trial of sorafenib in the adjuvant setting.[8] There is tremendous enthusiasm for immunotherapy in this patient population. Our current treatment approach to the patient proposed in this scenario would be to enroll him in a clinical trial with radioembolization plus nivolumab (NCT02837029). Although nivolumab has been

shown to promote long duration of tumor response, it is limited by poor tumor response rates. There is promise in using a locoregional therapy such as radioembolization to improve local tumor response rates and present antigen, enhancing innate tumor surveillance and tumor destruction.

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CASE 3

WITH JUSTIN D. BLASBERG, MD; FRANK C. DETTERBECK, MD, FACS, FCCP; ALEXANDER LAM, MD; AREO SAFFARZADEH, MD; EMI J. YOSHIDA, MD; AND ETAY ZIV, MD, PHD

A 55-year-old woman, a lifelong nonsmoker with no past medical history of cancer, is incidentally found to have a new 1.5-cm nodule in segment 1 of the left lung, nonadjacent to the pleura. The biopsy results in the diagnosis of *KRAS* wild-type adenocarcinoma.

Dr. Ziv: The International Association for the Study of Lung Cancer, American Thoracic Society, and European Respiratory Society introduced a new classification of lung adenocarcinoma in 2011, dividing lung adenocarcinoma into five histologic subtypes: lepidic, acinar, papillary, micropapillary, and solid.[1] This classification has important prognostic and predictive utility in the setting of early stage lung adenocarcinoma. The histologic subtypes can be identified on core needle biopsy, and therefore, the first question that needs to be addressed is whether a core biopsy was performed, and if so, which histologic subtypes were identified on the specimen.

Micropapillary and solid components are well-established indicators of worse outcomes. This includes higher local recurrence rates after surgery,[2] ablation,[3] and stereotactic body radiation therapy (SBRT).[4] The presence of micropapillary and/or solid histologic subtype in clinically N2-negative patients was predictive of occult N2 lymph node metastasis,[5] suggesting that radical lymph node dissection was necessary in these subgroups. Indeed, in patients with stage IA lung adenocarcinoma with micropapillary subtype, recurrence rates were lower if patients underwent lobectomy rather than limited resection.[6] Therefore, if micropapillary or solid components are identified in the biopsy specimen, the most appropriate treatment for this patient is lobectomy with hilar and mediastinal lymph node dissection.

No randomized controlled trials exist to compare ablation and minimally invasive surgery. Comparisons between prospective trials are limited, as they are not stratified for the most important prognostic indicators—histologic subtype and *KRAS* mutation status.[3,7] However, despite similar overall survival rates compared with surgery, local recurrence rates for lung ablation are high.[8] Therefore, in a

patient with no medical comorbidities and no contraindications to surgery, surgical resection is the most appropriate treatment. In a nonsmoker with presumably normal pulmonary and cardiac function, I would recommend surgical resection (lobectomy or limited resection based on the histologic subtype). At present, ablation for primary lung adenocarcinoma should be reserved for patients who are not surgical candidates.

Drs. Saffarzadeh, Blasberg, and Detterbeck: To usefully frame the discussion, we will assume this is a peripheral, mostly solid lesion (not ground-glass) and that the patient has normal pulmonary function, no significant comorbidities, and there is no evidence of metastasis. We assume that she is at a high-volume center that frequently performs both minimally invasive lobectomy as well as SBRT and ablation.

We need to ground decision-making on available evidence and then use clinical judgment to individualize the approach based on nuances of tumor-, patient-, and setting-related factors. To date, there is no adequately powered randomized evidence regarding lobectomy versus ablation or SBRT in fit, healthy patients with clinical stage I non–small cell lung cancer (NSCLC).[9] With respect to ablation, there is minimal evidence on the long-term outcomes of ablation for fit, healthy patients. Early data from the ACOSOG Z4033 trial of 54 medically inoperable patients with stage IA NSCLC treated with radiofrequency ablation showed 40% local recurrence rate at 2 years,[8] which is higher than the established recurrence rates for lobectomy or sublobar resection. If we are to ground decision-making on available evidence, the use of ablation for healthy individuals with stage I NSCLC cannot be routinely recommended over surgery at this time.

For comparisons of surgery versus nonsurgical therapies, we can also look at nonrandomized studies between surgery and SBRT. Nonrandomized comparisons are prone to confounding, but if a study can adjust for virtually all possible confounding factors, it can be viewed as a "possibly only slightly confounded" comparison.[10] Such a study does exist; using the National Cancer Database, it restricted patients to those without comorbidities and with stage I NSCLC who underwent either lobectomy or full-dose SBRT.[11] Propensity matching for essentially all known prognostic factors was done (> 20 variables), as well as several sensitivity and subset analyses that confirmed the results. Among 1,781 propensity-matched pairs, 5-year OS was better after lobectomy (59% vs 29%; $P < .001$). This evidence argues strongly for lobectomy. Additional arguments based on surrogate outcomes can be made. The operative mortality for video-assisted thoracoscopic surgery lobectomy in large studies is 1% to 1.5% (all comers)—and should be much less in the patient described in this case who is a nonsmoker and younger than average.[12-14]

Therefore, lobectomy remains the standard in fit individuals.[15] SBRT is an excellent alternative in patients with limited pulmonary reserve or comorbidities that significantly increase perioperative mortality. The role of ablation is still to be determined. Age or comorbidities that limit life expectancy have less impact on the relative role of surgery versus nonsurgical therapy and mostly impact whether any treatment is warranted. Finally, although it is ultimately the patient's decision, patient preference is a valid reason only when unrealistic fears or expectations have been addressed and short- and long-term outcomes can be rationally weighed.

At the current time, we view surgery and nonsurgical therapies such as SBRT and ablation as complementary, not competitive. We place the patient first and find that the most effective decision-making occurs during a joint consultation between thoracic surgery, other treatment providers, and the patient and his/her family. This allows an open, honest discussion and a decision supported by all parties, which avoids having the patient feel that they are pitting one provider against another.

Drs. Yoshida and Lam: Our first recommendation in the management of this patient would be completion of her workup, including pulmonary function testing, fluorodeoxyglucose PET/CT, consideration of additional molecular evaluation (epidermal growth factor receptor [EGFR], *ALK*, *ROS1*, *BRAF*, programmed death ligand-1), and discussion of pathologic mediastinal lymph node evaluation. Importantly, she should be assessed by a thoracic surgical oncologist for possible resection.

If further workup does not reveal regional or distant disease, the patient would be staged with IA2 NSCLC, and the preferred treatment based on current National Comprehensive Cancer Network guidelines is surgical resection with or without adjuvant therapy. If the patient is deemed medically inoperable or refuses surgery, an alternative local therapy, such as SBRT, is indicated. SBRT is generally composed of up to five high-dose radiation treatments delivered to a small volume. Advanced technology is required to plan and deliver a conformal radiation dose to the tumor while minimizing dose to surrounding normal tissue.

Prospective trials of definitive SBRT for medically inoperable, early stage, localized NSCLC have demonstrated excellent local control of approximately 95% and reasonable OS rates of approximately 60% at 3 years.[16-18] Although multiple randomized trials comparing surgery and SBRT for operable NSCLC have been initiated, all

were stopped early due to slow accrual. A pooled analysis of two trials (STARS and ROSEL) randomizing patients to SBRT versus lobectomy demonstrated a 3-year OS of 95% versus 79% in favor of SBRT (hazard ratio [HR], 0.14; $P = .037$) despite similar recurrence-free survival rates of 86% versus 80% (HR, 0.69; $P = .538$).[9] Although one large population-based study comparing SBRT and surgery found a survival decrement associated with SBRT,[19] most prospective phase 2 and retrospective studies have reported comparable OS rates to surgical outcomes. Ongoing prospective randomized trials (SABRTOOTH, POSTILV, STABLE-AMTES) comparing SBRT and surgery are anticipated to answer this question.

Due to the small size and peripheral location of this tumor, there are several acceptable dose and fractionation treatment paradigms. Commonly used in the United States, 54 Gy delivered in three fractions of 18 Gy allows treatment completion in 1.5 to 2 weeks. This strategy's safety and efficacy were established in RTOG 0236, a phase 2 trial for medically inoperable patients with T1/T2(< 5 cm)N0M0 NSCLC. At 3 years, the primary tumor control rate was 97.6%. Grade 3 to 4 toxicity was reported in 15% of patients, and no grade 5 adverse events were reported.[16]

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CASE 4

WITH RYAN HICKEY, MD; HOWARD S. HOCHSTER, MD; ZELJKA JUTRIC, MD; MANSI R. SHAH, MD; AND RONALD F. WOLF, MD

A 51-year-old man with no past medical history of cancer was recently diagnosed with adenocarcinoma of the descending colon and synchronous bilobar metastatic disease of the liver with at least 30% tumor burden and liver replacement. There is no sign of extrahepatic metastases on staging CT.

Dr. Hickey: The presence of synchronous liver metastases and lack of extrahepatic metastases indicate stage IV colon cancer with M1 metastatic disease. The most important question to answer when a patient presents with this stage of disease is whether the hepatic metastases would be eligible for curable treatment, meaning that all hepatic disease could be eliminated with surgical resection and/or ablation. Surgical resection remains the preferred treatment for resectable disease, but ablative therapies may be used alone or in conjunction with surgical resection provided that all sites of disease can be addressed.[1] Resection and/or ablation can be performed in conjunction with removal of the primary tumor, either prior to or after a course of systemic chemotherapy, or hepatic resection can be staged to follow both removal of the primary tumor and a course of adjuvant systemic chemotherapy.

However, considering that this patient has bilobar metastases replacing approximately 30% of the liver volume, he is likely not a candidate for curative resection and/or ablation. In this circumstance, the patient should be treated with systemic chemotherapy consisting of FOLFOX (folinic acid [leucovorin], fluorouracil, and oxaliplatin), CAPEOX (capecitabine and oxaliplatin), or FOLFIRI (folinic acid, fluorouracil, and irinotecan) with or without bevacizumab. Panitumumab or cetuximab may be used in place of bevacizumab if the tumor expresses the wild-type *KRAS/NRAS* gene. The patient should be evaluated for conversion to resectability or ablative therapy every couple of months while on systemic therapy.[2]

It is important to note that based on the combined results of the FOXFIRE, SIRFLOX, and FOXFIRE Global studies, transarterial therapy with Y-90 radioembolization is not recommended as part of the standard first-line treatment of patients with hepatic metastases of colorectal cancer. Although the combined analysis indicated superior control of hepatic metastatic disease when radioembolization was combined with first-line systemic chemotherapy compared to systemic chemotherapy alone, this did not translate to an improvement in OS (22.6 vs 23.3 months; HR, 1.04; $P = .61$).[3] Based on current evidence, radioembolization of colorectal cancer liver metastases should be reserved for patients with chemorefractory or chemoresistant hepatic metastases and preserved liver function.[2,4,5] Further investigation is necessary to evaluate the optimal role of Y-90 radioembolization early in the treatment of colorectal liver metastases, such as for the treatment of metastases of right-sided primary tumors, as a consolidation therapy, and as a means to facilitate hepatic resection by inducing preoperative hypertrophy of the future liver remnant.

Drs. Shah and Hochster: Hepatic metastases are present in two-thirds of patients with colon cancer. In patients with isolated liver lesions, several liver-directed options are available in combination with systemic chemotherapy as a route to possible cure. The combination of surgery with systemic therapy is the only potentially curative treatment, with 5-year survival rates of 20% to 50% in multiple retrospective series.[6] Initial resectability and recurrence due to persistence of micrometastases after liver surgery are major concerns. In this case, anatomic issues related to bilobar involvement, location of the specific metastases, and the extent of local resection may influence the approach. Multidisciplinary consultation on the best approach and possible need for portal vein embolization and timing are essential. We generally favor perioperative chemotherapy as the approach most likely to reduce the size and number of metastases, render them more easily resectable, and improve survival based on controlled trials.

In patients with synchronous disease that is amenable to resection, perioperative chemotherapy has been used to assess disease trajectory and chemotherapy responsiveness, thereby enhancing patient selection for surgery. EORTC 40983, a phase 3 randomized controlled trial, compared the use of perioperative chemotherapy (FOLFOX4, 3 months pre- and postsurgery) with surgery versus surgery alone for patients with liver metastases in 364 patients.[7] At a median follow-up of 8.5 years, the trend for median OS (61.3% vs 51.2%) and 5-year progression-free survival (38% vs 30%; HR, 0.81; $P = .068$) favored the combined

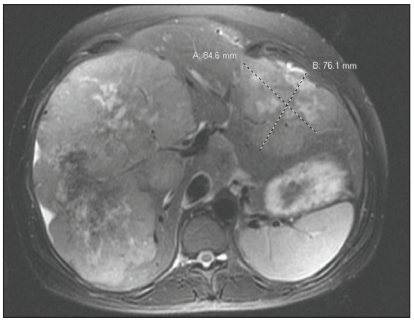

Figure 1. Initial CT scan for a 33-year-old otherwise healthy woman demonstrating significant liver replacement by tumor. The majority of liver segments are involved, including the caudate lobe.

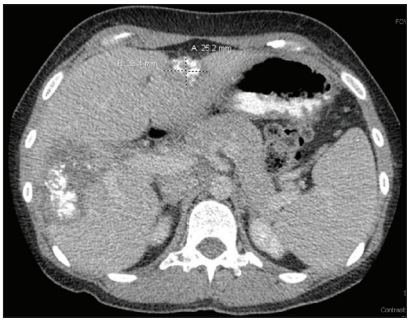

Figure 2. Response after preoperative FOLFOX therapy.

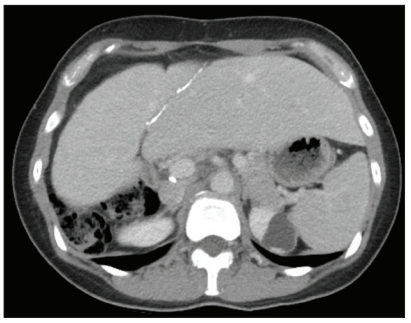

Figure 3. No evidence of disease 7 years after resection. Note the significant hypertrophy of the remnant liver.

modality arm. Although the study did not meet statistical significance for the intent-to-treat population, when those ineligible for surgery were excluded from the analysis, the difference was significant and similar to the effect of adjuvant chemotherapy in the setting of stage III colon cancer. Additionally, 83% and 84% of patients were successfully resected in the combination group and the surgery alone group, respectively, indicating that perioperative chemotherapy did not render patients ineligible for surgery due to delay. Finally, the overall mortality rate was not affected even though postoperative complications were higher in the chemotherapy group. It should be noted that this trial was limited to patients with four or fewer metastases and clearly resectable disease. If these lesions are clearly resectable, this patient would meet that definition.

Additional progress has been made with chemotherapy. Emerging evidence shows that aggressive three-drug first-line chemotherapy can improve progression-free survival and resection rates in those with isolated liver metastases. The phase 3 randomized TRIBE study evaluated the combination of bevacizumab with FOLFOXIRI or FOLFIRI.[8] It showed a significant advantage in OS for triplet therapy of 29.8 versus 25.8 months (HR, 0.8; $P = .030$) and an objective response rate of 65% in favor of triplet therapy versus 53% ($P = .006$) with more liver resections. Moreover, the combination of FOLFOXIRI with an anti–EGFR agent in *RAS* and *BRAF* wild-type tumors has demonstrated remarkable antitumor activity and high subsequent resection rates of 28%, as in the randomized phase 2 MACBETH study.[9] However, the addition of anti-EGFR agents to a triplet backbone significantly increases toxicity, as evidenced by the EPOC study of perioperative FOLFOX and cetuximab, which conversely decreased progression-free survival.[10] We generally favor FOLFIRINOX with a targeted agent such as bevacizumab or anti-EGFR antibody (for *RAS* wild-type, left-sided tumors) prior to surgical resection, followed by metastectomy and resection of primary tumors (often as staged procedures).

We do not favor other means of hepatic-directed therapy in this potentially curable situation. For potential cure, surgery with R0 resection in conjunction with aggressive chemotherapy and targeted agents remains the gold standard treatment.

Drs. Jutric and Wolf: Previous criteria for offering surgery to patients with colorectal liver metastases were based on the number of tumors and tumor size.[11] Considerable experience with more potent chemotherapy and modern surgical techniques has allowed for more inclusive criteria for resectability, with emphasis on the size and blood supply of the future liver remnant (FLR).

Patients are now considered resectable if the surgery will yield adequate liver volume in the remnant liver with remaining two contiguous liver segments (out of eight normally present), preserved vascular inflow/outflow, and intact biliary drainage. A minimum of 30% total liver volume standardized to body surface area is required for safe resection in a patient who has undergone preoperative chemotherapy.[12] Ideally, no more than four to six cycles of preoperative chemotherapy should be administered, as the risk of postoperative liver failure increases after 2 months of chemotherapy.[13]

Patients with bilateral disease, such as the case patient, are candidates for potentially curative surgical resection. We only consider radioembolization in cases in which an adequate FLR cannot be achieved even after preoperative portal vein embolization yields hypertrophy or when inflow/outflow cannot be preserved. Alternatively, if the patient's underlying medical comorbidities preclude aggressive resection, systemic or liver-directed therapies would be considered, in part to lengthen progression-free survival in the liver.[14]

The strategies used for resection are:

- Single-stage hepatectomy (ie, multiple wedge resections), which is used when bilateral liver

metastases are present in a diffuse but mostly peripheral distribution. The focus is on preservation of liver parenchyma.

- Two-stage hepatectomy, which includes limited hepatectomy to remove disease in the FLR as a first stage, followed by a major hepatectomy to clear the remainder of the disease.
- Combination of resection and ablation strategies, which are used to manage bilateral disease, but in cases in which the FLR has a single lesion that is deep within the liver parenchyma. Provided that there are adequate liver volumes, this can be done as a single stage.

With respect to this patient with bilateral metastases and 30% of the liver replaced by tumor, we would suggest four cycles of preoperative FOLFOX chemotherapy, followed by a two-stage hepatectomy, given that an outflow hepatic vein and inflow to the liver can be preserved.

The first stage can be performed laparoscopically at the same time as removal of the primary tumor. This stage also allows for visual and ultrasound assessment of the planned liver remnant for unsuspected additional tumor burden or cirrhosis. Pathologic assessment of the tumor necrosis can be informative to prepare for the second stage hepatectomy. If there is concern for volume based on laparoscopic assessment during the first stage or by liver volumetrics used to calculate volumes, then portal vein embolization should be done in between the two stages. The ability to hypertrophy is the best predictor of FLR function postoperatively.[15]

In general, systemic therapy is offered to all eligible patients at high risk of recurrence, such as this patient, given that modest benefit is demonstrated in similar patients undergoing chemotherapy in lower-risk settings.[16] In the case presented, we recommend an additional eight cycles of chemotherapy postoperatively. Using successful implementation of this strategy, OS of near 60% at 5 years can be expected.[1] Figures 1 through 3 demonstrate our experience with this strategy: a patient with 70% liver replacement by tumor (Figure 1), successful downstaging with modern chemotherapy (Figure 2), followed by R0 resection (Figure 3). The patient remains alive without disease currently. ■

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