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CASE REPORT

Microwave Ablation (MWA) for the Treatment of a Solitary, Chemorefractory Testicular Cancer Liver Metastasis

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Abstract We present a case of a patient with stage IIIC metastatic seminoma with a persistent chemorefractory liver lesion. The patient was deemed a poor surgical candidate due to the tumor's aggressive biology with numerous other liver lesions treated with chemotherapy and a relatively high probability for additional recurrences. Further chemotherapy with curative intent was not a feasible option due to the fact that the patient had already received second-line high-dose chemotherapy and four cycles of third-line treatment complicated by renal failure, refractory thrombocytopenia, and debilitating neuropathy. After initial failure of laser, microwave ablation of the chemorefractory liver metastasis resulted in prolonged local tumor control and rendered the patient disease-free for more than 35 months, allowing him to regain an improved quality of life.

Keywords Interventional oncology · Ablation · Liver/hepatic · Cancer

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Introduction

Testicular cancer is a model of a curable malignancy even in the setting of metastatic disease [1]. The revolutionary development of cisplatin-based chemotherapy has resulted in a cure rate of 70 to 80 % for those with advanced disease [2–4]. These historic outcomes have been validated through multiple, well-designed, clinical trials allowing evidence-based and efficacious treatment regimen choices based on accurate risk stratification [5]. However, in the setting of chemorefractory oligometastatic disease, locoregional therapies may play a role. We present the case of a patient with stage IIIC metastatic seminoma and a persistent chemorefractory liver metastasis successfully treated by MWA, rendering the patient disease-free for 35 months.

Case report

A 56-year-old man with an otherwise unremarkable past medical history presented to an outside hospital emergency room (ER) in September 2008 with left inguinal pain. A lesion detected on the left testicle using sonography led to left radical orchiectomy. Pathology reported a 4.5-cm

classic seminoma, with lymphovascular invasion, no rete testis involvement, and negative tumor margins. The patient was diagnosed with stage IB seminoma and treated with 2,550 cGy of adjuvant radiation to the retroperitoneal lymph nodes.

He remained asymptomatic for 9 months after surgery when he presented to the ER again, with symptoms of left pelvic pain and hematuria. Computed tomography (CT) scan demonstrated left-sided hydronephrosis and three liver lesions suspicious for metastases. Further workup with cystoscopy and retrograde left ureteroscopy demonstrated an obstructing mass in the proximal ureter involving the lower pole and pelvis of his left kidney. The patient was referred to surgery.

Based on intraoperative diagnosis suspicious for urothelial cancer, the patient underwent a complete left nephroureterectomy, left adrenalectomy, and partial retroperitoneal lymph node dissection. However, the final pathology demonstrated a 6.2 × 3.0 × 2.5 cm irregular mass consistent with metastatic testicular seminoma, lymphovascular invasion, and tumor extension into the periureteral space and the renal hilar adipose tissue. In addition, the pathology report noted that the tumor had brisk mitotic activity and large areas of necrosis with aggressive behavior.

Approximately 1 month after his surgery, a CT scan demonstrated numerous pulmonary and liver metastases as well as extensive retroperitoneal recurrence. The patient was restaged as intermediate-risk, stage IIIC (pT2cN3M1bS0) seminoma metastatic to the lungs, liver, kidney, ureter, and lymph nodes. He was treated at an outside hospital with BEP (bleomycin, etoposide, and cisplatin), but the second dose of bleomycin during cycle #1 was complicated by neutropenic fever as well as abdominal pain and diarrhea. He was admitted to the hospital for further evaluation and treated with broad-spectrum antibiotics and GM-CSF (granulocyte macrophage colony-stimulating factor). Upon recovery, he received a third dose of bleomycin in the hospital, this time complicated by septic shock requiring resuscitation in the intensive care unit. Thus, bleomycin was discontinued and the last three cycles were continued with EP alone. The patient's CT scan following completion of chemotherapy demonstrated marked decrease in size of pulmonary nodules and significant improvement in retroperitoneal lymphadenopathy; however, multiple liver lesions had increased in size.

At this point, he was referred to our institution. Upon evaluation, tumor markers (β-HCG, AFP, LDH) had increased. Liver biopsy was consistent with metastatic seminoma to the liver. The decision was made to treat him with high-dose chemotherapy using the TI-CE (paclitaxel-ifosfamide) regimen [6]. He received two cycles of paclitaxel plus ifosfamide and G-CSF with stem-cell mobilization followed by 1 cycle of high-dose carboplatin and etoposide with autologous stem-cell reinfusion, complicated by the development of renal insufficiency and prolonged physical and hematological recovery. In addition, patient developed severe diarrhea, thrombocytopenia, and neuropathy. However, response to treatment with normalization of tumor markers as well as liver function tests was noted. Imaging at this point revealed a dramatic improvement in his liver, lung, and retroperitoneal metastases. Despite significant response, he was still not considered a surgical candidate because of the multitude of liver lesions and extrahepatic disease. Due to his poor glomerular filtration rate and tolerability, further cycles of high-dose chemotherapy could not be administered either. Because it was unlikely that he had achieved a full remission with only one cycle of high-dose chemotherapy (curative therapy generally consists of 2 or 3 cycles), it was decided to administer four additional cycles of conventional-dose chemotherapy with gemcitabine plus oxaliplatin, plus paclitaxel (GOT). This regimen was specifically selected due to its lack of renal toxicity. This first cycle was

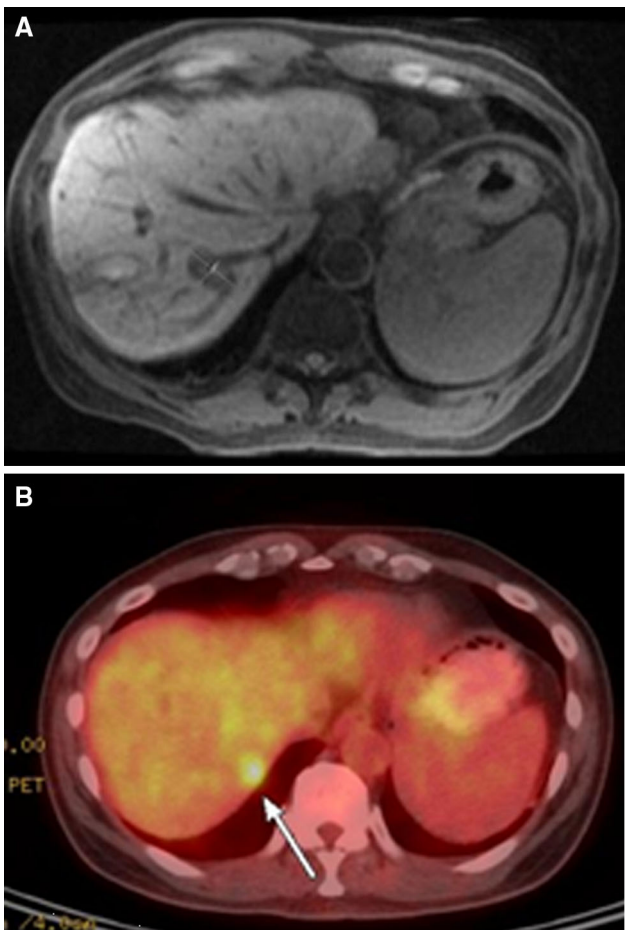

Fig. 1 MRI (**A**) and PET (**B**) imaging before percutaneous ablation shows one residual lesion in segment 7

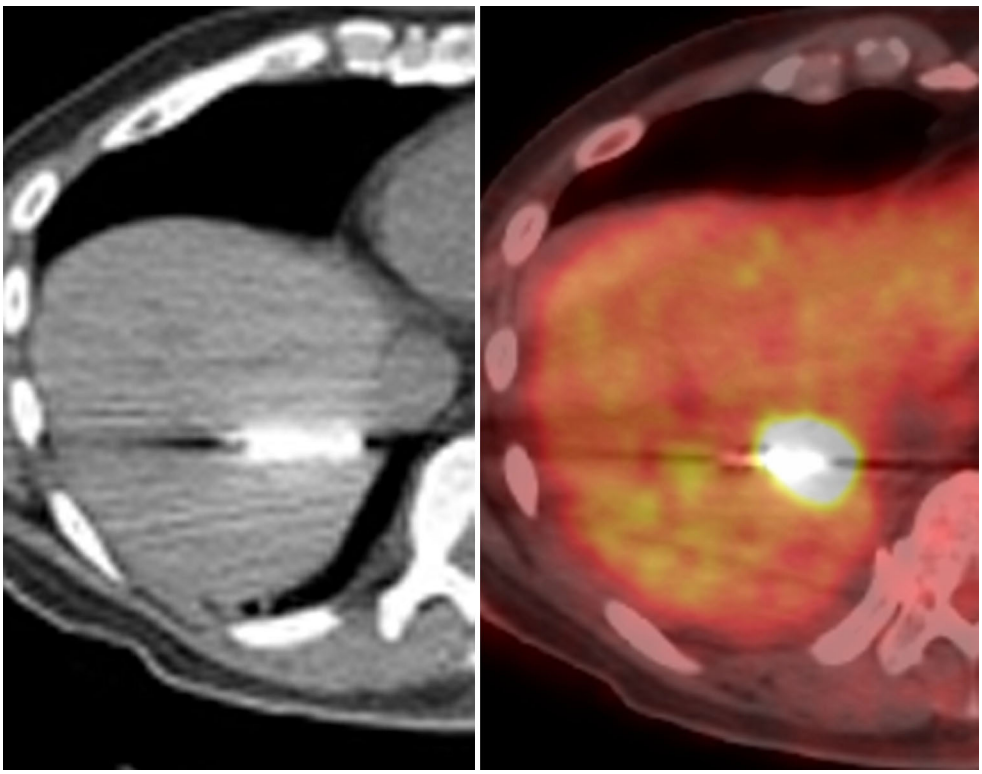

Fig. 2 PET CT-guided MW ablation of segment 7

complicated by thrombocytopenia and worsening debilitating neuropathy, which led to discontinuation of paclitaxel. He completed three additional cycles of gemcitabine plus oxaliplatin within 12 months after his primary surgery, which resulted in further response of liver disease and persistently negative tumor markers. A PET scan demonstrated no evidence of FDG uptake within any of the hepatic or pulmonary lesions and the patient was placed on active surveillance.

Repeat imaging with PET and MRI 4 months following completion of chemotherapy demonstrated a sustained response in the lungs and liver, with the exception of a solitary lesion in hepatic segment 7, which had increased in size and was FDG-avid on PET. All other lesions appeared treated with no apparent enhancement on MRI and no PET activity.

Due to prolonged cytopenias and progression of disease despite extensive prior chemotherapy, he was not eligible for any additional systemic therapy. In addition, surgery was not offered due to the high likelihood for future recurrences and the relatively challenging tumor location, requiring extended hepatectomy to achieve clear margins (Fig. 1). At a multidisciplinary discussion, it was decided that image-guided percutaneous thermal ablation was the best option for tumor control.

Initially, the lesion was treated with MR-guided laser ablation, which was unsuccessful with residual tumor at the first postablation imaging evaluation. Sixty days after the initial ablation, the patient underwent PET-CT guided MWA using the split-dose technique [7]. According to this technique a total of 4 mCi (148 MBq) of FDG was administered before the procedure for localization and imaging guidance. After ablation was completed, an additional 8 mCi (296 MBq) of FDG was administered to assess ablation adequacy [7] (Fig. 2). Limited-contrast CT and PET/CT examination was performed to localize a hypodense and hypermetabolic posterior sector lesion, measuring 17 × 14 mm abutting the inferior vena cava (IVC) and hepatic vein. Two microwave needles were utilized and overlapping ablations were performed to cover completely the target lesion with sufficient margins. Track ablation was performed. CT and PET/CT examination was performed immediately after the procedure demonstrating good coverage of the lesion by the ablation zone, without evidence of bleeding or residual tumor. Six weeks later, his first follow-up MRI and PET/CT imaging showed successful ablation completely covering the prior metabolically active segment 7 tumor, with no evidence of residual disease (Fig. 3). The patient was subsequently followed with clinical assessments, tumor markers, and imaging follow-up every 2–4 months (Fig. 3). He remains without evidence of disease for more than 35 months post-MWA. At the same time, his ECOG score is 0 with dramatic improvement in his overall activity.

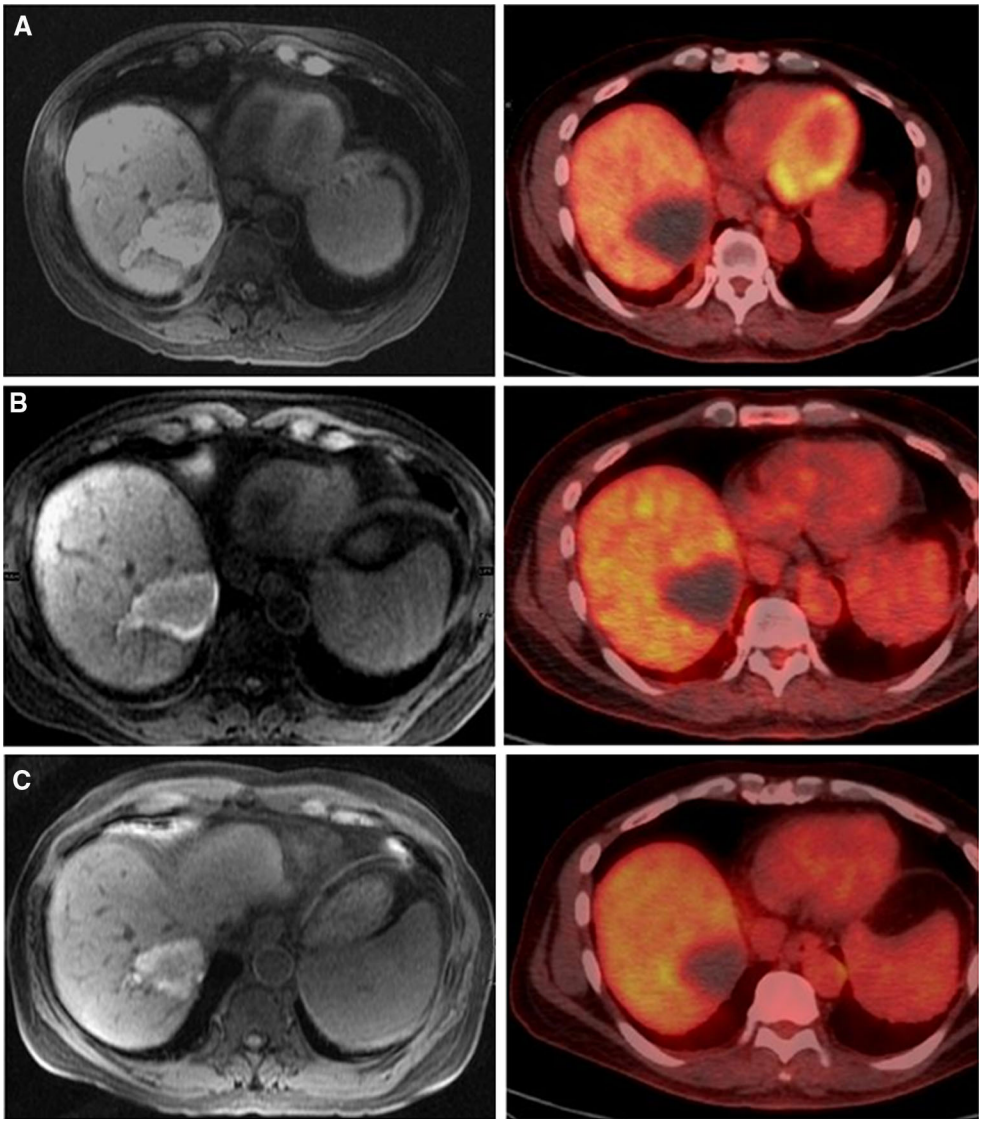

Fig. 3 Follow-up MR (*left* panel) and PET CT (*right* panel) at 3 months (**A**), 6 months (**B**), and 30 months—latest imaging (**C**)

Discussion

To our knowledge, this is the first report documenting long-term remission and probable cure of a germ cell tumor hepatic metastasis refractory to high-dose chemotherapy with MWA. Our patient had intermediate-risk seminoma and relapsed in the liver despite adjuvant radiation therapy, extensive surgery, and three lines of chemotherapy, including eight antineoplastic agents and high-dose chemotherapy with autologous stem-cell transplant. Of note, progression was documented in a persistent FDG-avid, gadolinium-enhancing and enlarging liver lesion in the setting of multiple previously seen hepatic and pulmonary metastases treated with chemotherapy and he remains disease-free more than 35 months after MWA.

The 10-year survival for all patients with seminoma is estimated to be 98 % [8], and even those with intermediate-risk seminoma have a 5-year survival rated of ≥80 %. Even patients with seminoma who relapse after first-line of chemotherapy have been reported to have favorable outcomes with salvage high-dose chemotherapy [9]. Nevertheless, a small proportion of patients with seminoma are refractory to high-dose chemotherapy and generally considered incurable with further chemotherapy. Some of these patients can be cured with "desperation" surgery but this carries high morbidity and may not be possible in some situations [10].

Our patient had an exceptionally aggressive and resistant form of seminoma. At initial diagnosis, he had stage I disease with an expected survival of close to 100 % and

only a 15–20 % risk of recurrence even without adjuvant therapy [11]. Furthermore, he relapsed despite adjuvant radiation, which would have been expected to further decrease his recurrence rate to <4 % [12]. While the typical relapse pattern after radiation is outside the retroperitoneum, our patient's recurrence involved the para-aortic lymph nodes, the left kidney, and ureter. Involvement of the kidney and ureter is also unusual for germ-cell tumors especially when this does not occur as a result of direct extension from retroperitoneal lymphadenopathy. Furthermore, although our patient had >75 % chance of achieving remission after receiving four cycles of cisplatin-based chemotherapy [3, 4], he had incomplete response followed by rapid progression in the liver and lungs. He further had a chemorefractory solitary liver lesion after high-dose TI-CE and 4 cycles of gemcitabine and oxaliplatin-based treatment.

Upon relapse and in the face of persistent chemo-related toxicities with severe thrombocytopenia and neuropathy, further chemotherapy was not considered possible. Surgical resection of the enlarging hepatic lesion was considered, as this has proven efficacious in patients with testicular cancer who have normal serum tumor-marker levels after cisplatin-based chemotherapy [13, 14]. However, due to the unfavorable tumor location, multiple prior hepatic and extrahepatic lesions, the aggressive tumor biology, and his medical comorbidities, he was deemed a poor surgical candidate with a high risk of future recurrence following resection. Similarly, his prior in-field relapse, even following prophylactic radiation to the retroperitoneal lymph nodes, made radiotherapy a less attractive option.

Salvage treatment options for metastatic liver lesions include thermal ablation and hepatic arterially directed therapies, such as bland embolization, chemoembolization, and selective internal radiation therapy [14–19]. Ablation was offered as a less morbid modality that could offer local control with a modified concept of "test of time" [20]. According to this approach, the refractory tumor could be treated while the patient was closely followed to detect possible future recurrences. This would permit repeat ablation or surgery only if there was local recurrence. Surgery could, for example, be considered if late recurrence would occur (more than 6 months after original ablation) and in the face of no other tumor progression. This approach can spare the unnecessary morbidity and possible mortality of surgery in those patients that are treated by ablation and perhaps even more importantly in those unfortunate enough to develop multifocal disease progression during the waiting or follow-up period [21].

Thermal ablation has a very good safety profile and has been effective in the local control of liver metastases from a variety of malignancies, most notably colorectal cancer [16, 21–23]. Microwave is an evolving thermal ablation modality that is less affected by the heat-sink effect [24]. This feature of MWA was considered when choosing this over other ablation modalities. The size of the lesion and the proximity of the tumor to the hepatic vein/IVC was probably one of the causes of laser ablation failure. MWA created an ablation area that completely covered the target tumor with good margins [25] and resulted in good and sustained local tumor control and prolonged progression free survival.

The outcome of our patient with MWA is encouraging, suggesting that ablation as well as other locoregional therapies [15, 16, 19, 26] may be beneficial for the management of patients with refractory GCT and solitary or oligometastatic hepatic disease. While surgical resection remains the standard-of-care for solitary sites of progressive GCT following high-dose chemotherapy, in patients with a high risk of recurrence and/or when resection is considered highly morbid or otherwise contraindicated, thermal ablation and in particular MWA could be considered. This, of course, needs validation in larger clinical series.

Conflict of interest Elena G. Violari, Elena N. Petre, Darren R. Feldman, Joseph P. Erinjeri, Karen T. Brown, Stephen B. Solomon, Michael I. D'Angelica and Constantinos T. Sofocleous have nothing to disclose.

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