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Case Report

Yttrium-90 radioembolization in desmoplastic small round cell tumor with recurrent hepatic metastasis following hyperthermic intraperitoneal chemotherapy ☆,☆☆

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ABSTRACT

We report a case of a 26-year-old male who was diagnosed with metastatic desmoplastic small round cell tumor initially treated with systemic chemotherapy followed by tumor debulking and hyperthermic intra-peritoneal chemotherapy. The patient was in complete remission by clinical and imaging criteria for 11 months, until he developed bi-lobar hepatic disease, which was successfully treated with selective internal radiation therapy by Yttrium-90. The patient demonstrated liver-specific complete response on follow-up imaging obtained 18 months after the procedure.

Introduction

Soft tissue sarcomas (STS) are a rare group of tumors comprising less than 1% of adult malignancies and 15% of pediatric malignancies [1]. In 2020, an estimated 13,130 people (adult and children) will be diagnosed with soft tissue sarcoma in the United States, resulting in approximately 5,350 deaths [2]. A subgroup of these tumors, desmoplastic small round cell tumor, was identified as a separate entity in 1989 by Gerald and Rosai after recognizing a pathognomonic chromosomal translocation {t (11;22) (p13: q12)} that fuses the Ewing sarcoma gene (*EWSR1*) with the Wilms tumor suppressor gene (*WT1*) [3]. Desmoplastic small round cell tumor (DSRCT) is a highly aggressive mesenchymal tumor with median survival ranging from 17 to 32 months [3,4]. However, in patients affected with liver metastases, the prognosis is even poorer.

Multimodality management of DSRCT includes aggressive treatments such as polychemotherapy, debulking surgery, and whole abdominal radiation. Among these, cytoreductive surgery remains the mainstay of therapeutic strategy with

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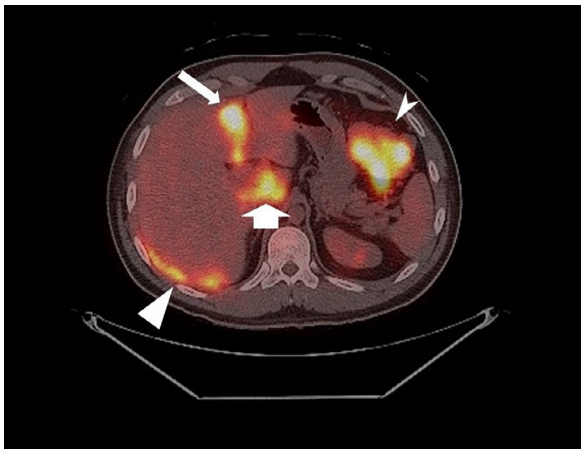

Fig. 1 – Axial PET/CT showing hypermetabolic abdominal mass (pointed arrow), FDG avid hepatic metastasis (arrow), hepatic surface implants (arrowhead) and porta hepatis lymphadenopathy (thick arrow).

promising outcomes [4,5]. Yttrium-90 (^{90}Y) is an effective intra-arterial-directed therapy for treatment of unresectable primary hepatic malignancy and metastatic disease to the liver. Only a few studies have reported effectiveness of selective internal radiation therapy (SIRT) for hepatic STS, primarily leiomyosarcoma [6,7]. To the best of our knowledge, only two prior case reports have described the role of radioembolotherapy with yttrium-90 microspheres on this extremely rare subtype of sarcoma [8,9].

Case report

A 26-year-old man with no significant past medical history presented with intermittent abdominal and groin pain for the past month. He was transferred from an outside hospital, where the initial computed tomography (CT) scan showed an abdominal mass and lymphadenopathy, which was concerning for lymphoma. As a result, positron emission tomography – computed tomography (PET/CT) was obtained for staging and interventional radiology was consulted for diagnostic CT-guided biopsy of the abdominal mass (Fig. 1). Histological and immunohistochemistry analysis of the specimen revealed a

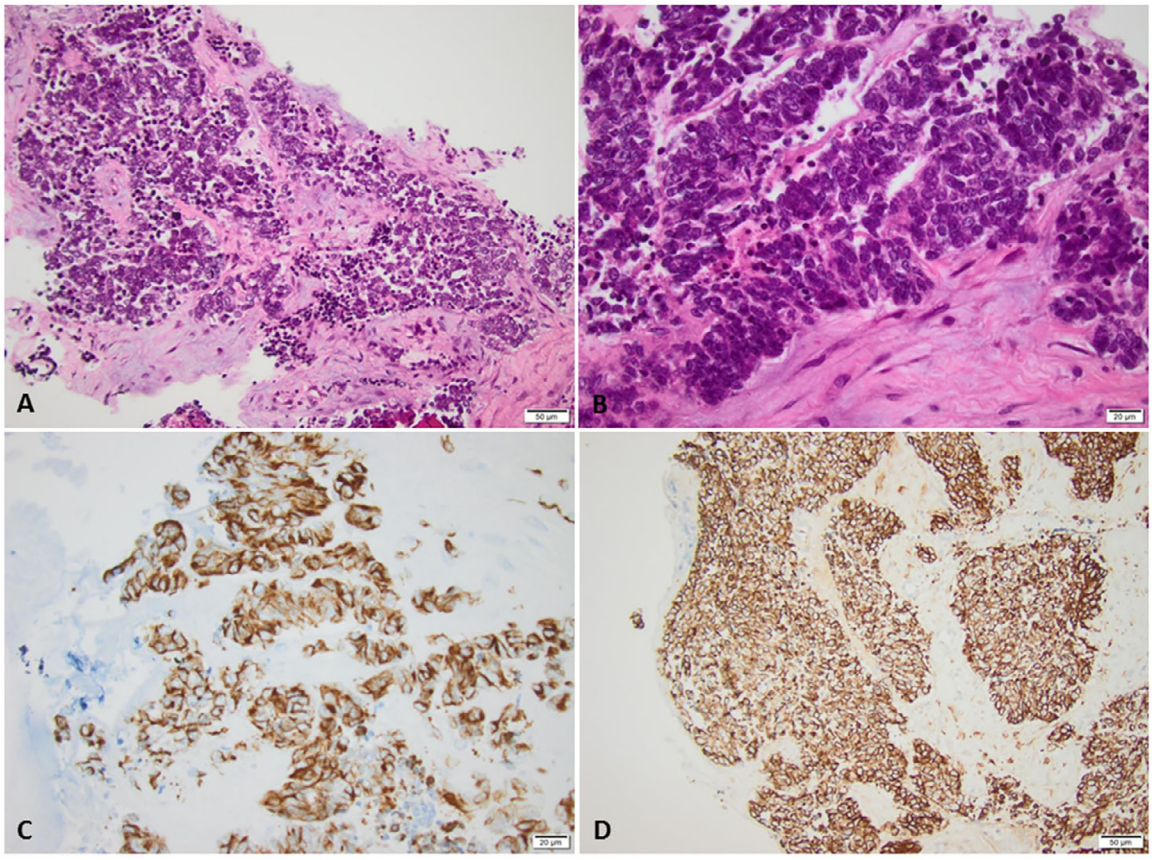

Fig. 2 – CT-guided biopsy of abdominal mass with histopathology. (a) Low power image (H&E): The tumor is highly cellular with cohesive nests of primitive small round to oval cells surrounded by desmoplastic stroma. (b) High power image (H&E): The tumor cells display nuclear hyperchromasia, inconspicuous nucleoli, nuclear crowding with prominent mitosis and karyorrhexis. (c, d) Immunohistochemical stain shows diffuse positive staining for desmin and Pan-Cytokeratin.

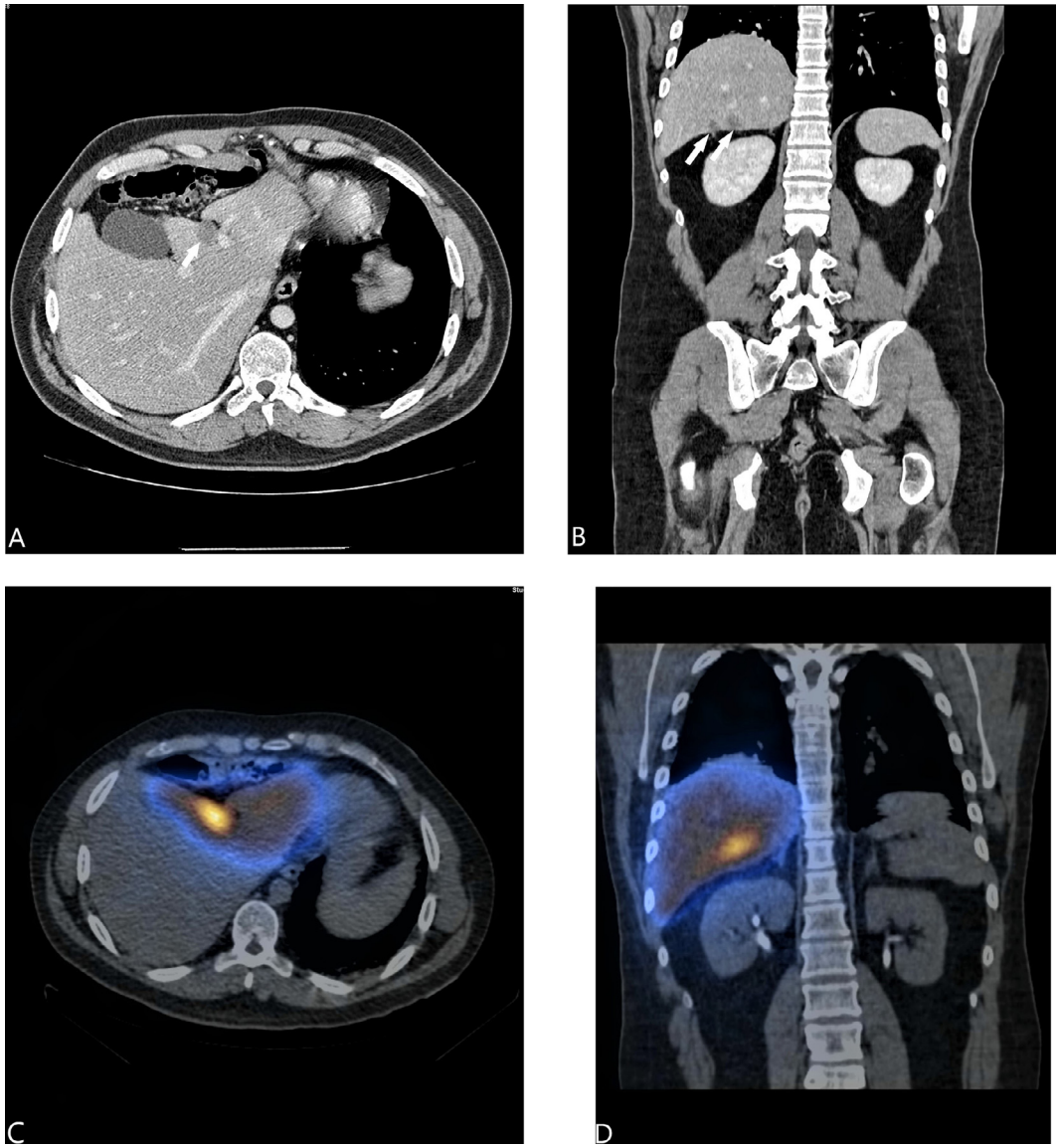

Fig. 3 – Contrast-enhanced CT showing segment 4 (arrow) and segment 5/6 (2 arrows) hepatic lesions on axial and coronal images (a, b). Post yttrium 90 radioembolization SPECT/CT demonstrating targeted radiotracer accumulation (arrow) within these lesions (c, d).

hypercellular tumor composed of primitive small round to oval cells surrounded by desmoplastic stroma (Fig. 2). The tumor cells stained positive for pan-cytokeratin, desmin; and were negative for CD99, myogenin, myoD1, calretinin, S-100, synaptophysin, chromogranin. Fluorescence in situ hybridization testing on the tumor tissue showed *ESWR1-WT1* fusion transcript pathognomonic for DSRCT.

The patient received 3 cycles of neoadjuvant chemotherapy (vincristine, doxorubicin, cyclophosphamide, fosfamide, and etoposide) followed by debulking surgery and hyperthermic intraperitoneal chemotherapy (peritoneal index score: 17). After the surgery, adjuvant chemotherapy was initiated with 2 cycles of VAI (vincristine, actinomycin D, ifosfamide) and 1 cycle of VIT (vincristine, irinotecan, temozolomide). Given a high risk of tumor recurrence, the patient underwent frequent scans (every 3-4 months) while on surveillance and remained in complete remission for 11 months. Unfortunately, recurrent disease was noted in the right and left hepatic lobe requiring systemic chemotherapy. After 4 months of treatment, the patient was referred to interventional radiology for transarterial radioembolization of residual bi-lobar hepatic disease.

The pre ^{90}Y planning angiogram revealed a replaced right hepatic artery arising from the superior mesenteric artery and supplying the majority the right hepatic lobe. The left hepatic artery had conventional anatomy and supplied a majority of the left hepatic lobe. We decided to coil the right gastric artery, which originated from the proximal left hepatic artery, thereby preventing nontargeted distribution of the radiotracer. A lung shunt fraction of 4.3% was calculated after administration of approximately 5 mCi of technetium 99m labeled macro-aggregated albumin. Given the bi-lobar distri-

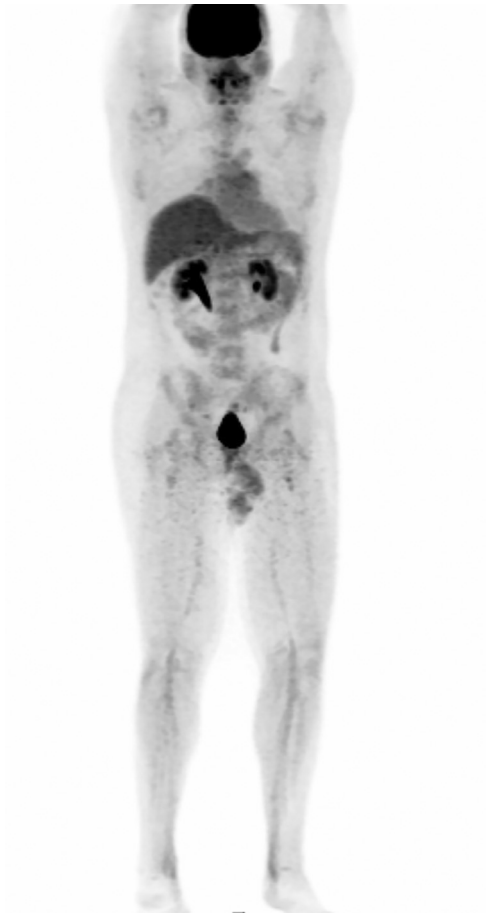

Fig. 4 – PET/CT obtained 18 months post-treatment showed no evidence of hepatic disease burden on the maximum intensity image (MIP).

bution of liver disease, the patient proceeded with a staged SIRT (2-month interval) using ^{90}Y resin radioactive microspheres (SIR-Spheres, Sirtex Medical Limited, North Sydney, New South Wales, Australia) (https://www.sirtex.com/media/169247/ssl-us-14-sir-spheres-microspheres-ifu-us.pdf). Using radial artery access (Barbeau B type circulation), we delivered 21 mCi of ^{90}Y microspheres via the left hepatic artery and 34.2 mCi to the right hepatic tumor split between segments 5 and 6 (Fig. 3). Our targeted location was confirmed on the single-photon emission computed tomography scan (SPECT/CT). On follow-up CT and PET/CT scans obtained up to 18 months after SIRT, the patient remains free of disease burden in the liver (Fig. 4).

Discussion

Desmoplastic small round cell tumor is a highly malignant mesenchymal tumor, most commonly found in adolescent and young adults, with a strong male predominance [4,5]. The presenting symptoms are usually nonspecific such as abdominal pain, mass, and weight loss. Clinically, DSRCT has been shown to have a predilection for serosal surfaces in the abdominopelvic cavity and a majority of cases present with advanced disease. The most common site of extra-peritoneal disease is the liver, followed by the spleen and lungs [6,7]. Diagnosis is based on histopathology with a molecular hallmark of *ESWR1-WT1* fusion protein.

The therapeutic management is challenging due to the rarity and aggressive nature of the disease. A multidisciplinary treatment protocol is necessary for curative intent. Few studies have suggested the use of maximum debulking surgery with HIPEC can improve outcomes, prolonging survival at the cost of an increased toxicity [4,5]. Some authors have proposed whole abdominopelvic intensity-modulated radiation therapy (IMRT) as a part of aggressive multimodality therapy, for patients with metastatic and refractory disease [10]. As described earlier, the liver is the most common site of metastatic disease from DSCRT, hence, an intra-arterial liver directed therapy, such as ^{90}Y, can improve survival by arresting the progression of metastatic disease to the liver [9,10].

Transcatheter liver-directed therapy for hepatic sarcoma is not currently considered the standard of care, and no consensus guidelines exist for malignant DSRCT. ^{90}Y is a beta emitter with an effective radiotherapy range and can induce cell injury through DNA damage for radiosensitive tumors. Hence, the radioisotope can be used preoperatively, to shrink the tumor; postoperatively, to eliminate any residual disease; or as palliative treatment for unresectable disease. In this case, since the patient had bi-lobar metastatic disease, SIRT with ^{90}Y was an ideal option to provide local control and delay progression of disease. Good response was seen on initial post-treatment imaging with no significant adverse effects. During 18 months of imaging surveillance, the patient demonstrated a liver-specific complete response to therapy by clinical and imaging criteria.

Conclusion

DSRCT is an extremely rare and highly aggressive disease with dismal outcomes, despite multimodal treatment. Our case highlights the role of selective internal radiation therapy in controlling liver metastases and expanding treatment considerations in these difficult-to-manage patients. ^{90}Y radioembolization can play a role in extending survival and should be included as a treatment option in multidisciplinary management of metastatic DSRCT.

Patient's consent

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Authors' contributions

Conceptualization and idea: HG; methodology: HG, NS; literature search and data analysis: HG; writing—original draft

preparation: HG, NS; writing—review and editing: HG, WV, ZY; supervision: WV, ZY.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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