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Case Report

Complete metabolic response after Partially Ablative Radiotherapy (PAR) for bulky retroperitoneal liposarcoma: A case report ☆,☆☆

Federica Medici, MD[a,b,*], *Silvia Strolin, PhD*[c], *Paolo Castellucci, MD*[d], *Savino Cilla, PhD*[e], *Viola Laghi, MD*[a,b], *Erika Galietta, MD*[a,b], *Maria Vadalà, MD*[d], *Lidia Strigari, PhD*[c], *Alessio Giuseppe Morganti, MD*[a,b,1], *Silvia Cammelli, MD*[a,b,1]

[a] *Department of Medical and Surgical Sciences, DIMEC, Alma Mater Studiorum University of Bologna, Bologna, Italy*
[b] *Radiation Oncology, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy*
[c] *Department of Medical Physics, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy*
[d] *Nuclear Medicine, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy*
[e] *Medical Physics Unit, Gemelli Molise Hospital – Università Cattolica del Sacro Cuore, Campobasso, Italy*

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ABSTRACT

In the management of symptomatic inoperable retroperitoneal sarcomas (RPS), palliative radiotherapy (RT) is a potential treatment option. However, the efficacy of low doses used in palliative RT is limited in these radioresistant tumors. Therefore, exploring dose escalation strategies targeting specific regions of the tumor may enhance the therapeutic effect of RT in relieving or preventing symptoms.

In this case report, we present the case of an 87-year-old patient with rapidly growing undifferentiated liposarcoma in the retroperitoneum, where surgical and systemic therapies were ruled out due to age and comorbidities. RT was administered using volumetric modulated arc therapy, delivering 20 Gy in 4 fractions twice daily to the macroscopic tumor and 40 Gy in 4 fractions twice daily (simultaneous integrated boost) to the central part of the tumor (Gross Tumor Volume *minus* 2 cm). An ^{18F}–FDG-PET-CT scan performed after RT demonstrated a complete metabolic response throughout the entire tumor mass. Although the patient eventually succumbed to metastatic spread to the bone, liver, and lung after 9 months, no local disease progression or pain/obstructive symptoms were observed.

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* Corresponding author.
E-mail address: federica.medici4@gmail.com (F. Medici).

[1] These authors contributed equally to the work and shared the senior authorship.

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This case highlights the technical and clinical feasibility of delivering ablative doses of RT to the central region of the tumor and suggests the potential for achieving a complete metabolic response and durable tumor control.

Introduction

The recent classification by the World Health Organization (WHO) provides a comprehensive overview of soft tissue and bone primary tumors, including the diverse histologic subtypes of soft tissue sarcomas (STSs) [1]. Among these subtypes, liposarcomas (LPs) are the most common, although with a low estimated incidence [1]. LPs are characterized by unique morphological, immunohistochemical, and molecular features, which contribute to their tailored diagnosis and treatment [2,3].

Primary STSs can arise in various mesenchymal tissues throughout the body, leading to heterogeneity in clinical presentations and management approaches [4]. Retroperitoneal sarcomas (RPS) account for a significant proportion of STSs and pose challenges due to their large size and involvement of adjacent organs, making complete surgical resection difficult [4–6]. Local relapse is a common pattern of treatment failure in RPS, emphasizing the importance of local adjuvant treatments [7].

Radiotherapy (RT) plays a role in the management of unresectable or bulky STSs, with recommended doses depending on the clinical context and patient factors [8,9]. However, in the case of palliative RT, concerns arise regarding the adequacy of low doses for symptom relief in bulky RPS [9]. To address this, our previous planning study explored the feasibility of delivering highly heterogeneous doses, and in particular, ablative doses to part of the tumor, using volumetric modulated arc therapy (VMAT) and simultaneous integrated boost (SIB) to achieve palliative effect in symptomatic large tumors [10].

Here we present, based on CARE guidelines [11], the case of an 87-year-old male patient with a bulky RPS (>10 cm) who received partially ablative radiotherapy (PAR) using VMAT-based SIB after surgical and systemic treatment options were ruled out due to age and comorbidities.

Case report

The patient's medical journey began with the discovery of a sizable pararenal mass during a CT scan performed for abdominal swelling and worsening constipation, with findings on palpation of a hard and painless mass in the right hypochondrium. This mass exhibited a complex nature, displaying a central necrotic core surrounded by vascularized solid septa, causing displacement of the adjacent kidney and encroaching upon the ipsilateral psoas muscle.

Approximately 1 month later, further assessment via an 18F-FDG-PET/CT scan revealed heightened metabolic activity within the peripheral region of the tumor (SUVmax: 7.3), emphasizing its pathological nature (Fig. 1).

Therefore, the patient was evaluated within the Urology Department at our institution. Given the patient's age, underlying health issues, and personal preferences, a consensus was reached that surgical intervention was not a suitable course of action. Instead, a percutaneous ultrasound-guided biopsy was undertaken, confirming the presence of a malignant mesenchymal spindle cell and polymorphic neoplasm, characteristic of a high-grade dedifferentiated liposarcoma.

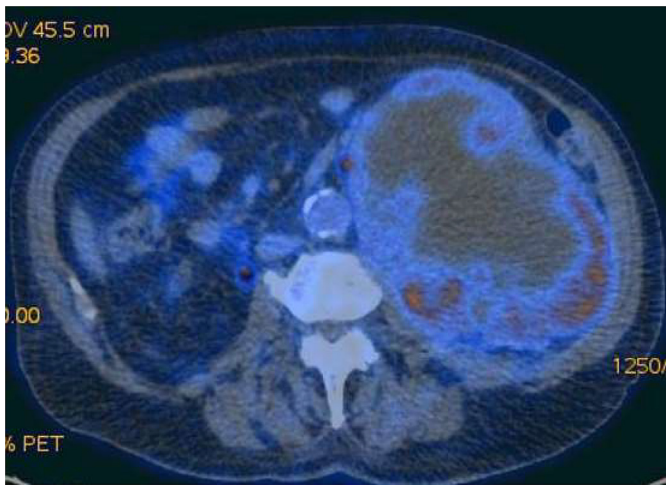

Fig. 1 – The image shows a bulky abdominal tumor on pretreatment $^{18F-}$FDG-PET/CT (SUV_{max} 7.7).

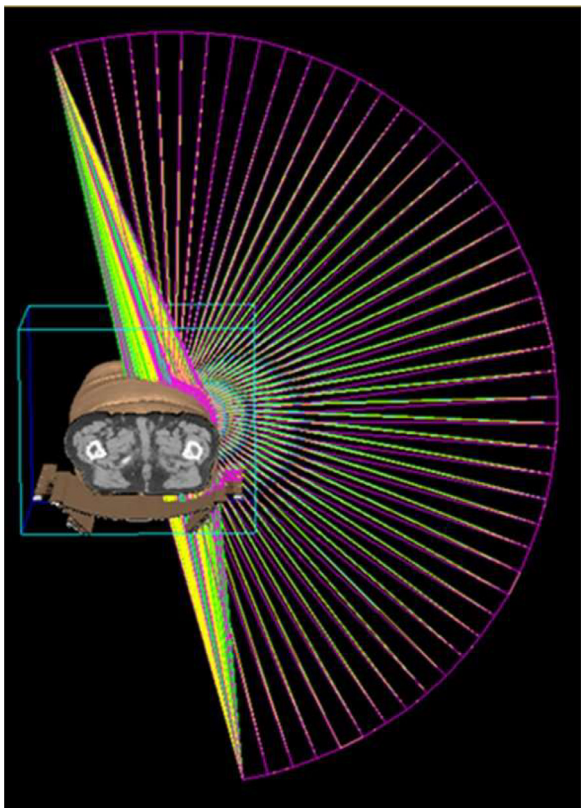

Fig. 2 – The image shows the treatment technique, based on 2 partial and noncoplanar arches.

In time, approximately 10 months after the initial diagnosis, the patient was referred to the Medical Oncology Department for further consultation. Due to the patient's age and comorbidities, the medical team opted against systemic treatments and instead advised radiation therapy (RT) and the initiation of home care services.

Approximately 3 months later, follow-up 18F-FDG-PET/CT scans indicated a gradual increase in tumor size, prompting the decision to start palliative RT. At this stage, the patient showed worsening general conditions due to asthenia and constipation, possibly attributable to the mass's pressure on nearby structures.

The course of RT proceeded as planned: using a dual arc volumetric modulated arc therapy (VMAT) (Fig. 2), a dose of 40 Gy was delivered in 4 fractions twice daily in the central tumor core (GTV minus 2 cm) as a simultaneous integrated boost, and 20 Gy were delivered in 4 fractions twice daily to the GTV plus 1 cm (Fig. 3). Table 1 shows the Equivalent Dose in 2 Gy/fraction and the Biologically Effective Dose of the delivered PAR. Dose specification and reporting were based on ICRU recommendations 83 and dose-volume constraints to the organs at risk were based on QUANTEC guidelines [12]. The patient reported good tolerance to the treatment, without significant adverse effects related to radiation.

Initial RT follow-up, approximately 2 months after treatment, revealed a fair general clinical condition, albeit with some increase in asthenia and constipation. The massive abdominal lesion, although nonpainful, persisted in the left hypochondrium.

Subsequent 18F-FDG-PET/CT scans, conducted about 6 months after RT, showed a complete metabolic response (SUVmax: 1.9) (Figs. 4A and B). The patient's overall condition improved slightly during this period, marked by increased appetite and a 20% reduction in the size of the abdominal lesion.

However, another 18F-FDG-PET/CT scan performed about 10 months after initial diagnosis unveiled signs of disease progression, manifesting as metastases in the liver, lungs,

Table 1 – Biologically effective dose (BED) and equivalent dose in 2 Gy/fraction (EQD2) delivered to the planning target volumes (PTVs).

	PTV 2 (GTV + 1 cm)	PTV 1 (GTV – 1 cm)
$BED_{\alpha/\beta=3}$	53.3 Gy	104.0 Gy
$BED_{\alpha/\beta=10}$	30.0 Gy	66.7 Gy
$EQD2_{\alpha/\beta=3}$	32.0 Gy	173.3 Gy
$EQD2_{\alpha/\beta=10}$	25.0 Gy	80.0 Gy

GTV, gross tumor volume.

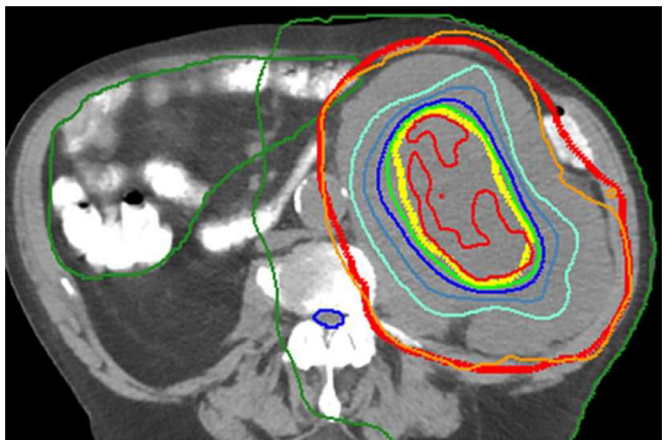

Fig. 3 – The image shows the dose distribution in the treatment plan in an axial CT scan. Planning target volume 1 (Gross Tumor Volume *minus* 2 cm) is shown in blue and planning target volume 2 (Gross Tumor Volume *plus* 1 cm) is shown in red.

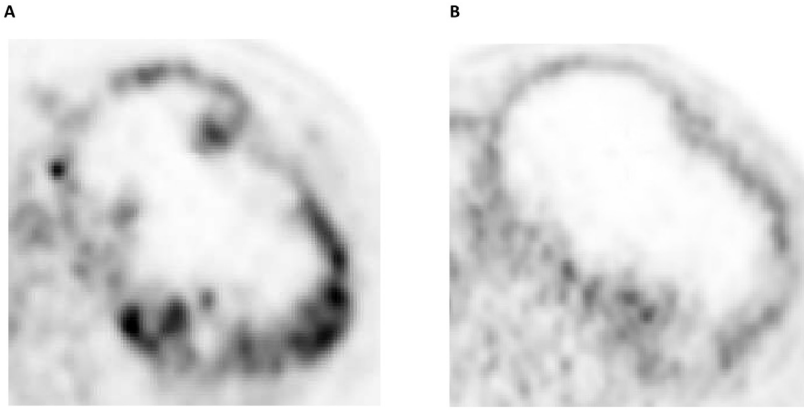

Fig. 4 – The images show a complete metabolic response after treatment: pre- (A) vs post-treatment (B) $^{18F-}$FDG-PET/CT.

and bones. Despite the unfavorable development, the patient's passing approximately 13 months after diagnosis occurred without the occurrence of painful or obstructive symptoms.

Discussion

We presented the case of an elderly patient with RPS who was not amenable to surgery or systemic therapies. Palliative RT was administered using PAR to prevent local symptoms. Our previous planning study proposed the feasibility of planning and delivering PAR through SIB [10]. In this case, we used a fractionation regimen (4 fractions in 2 days) due to its convenience for the patient, considering the overall brevity of the treatment, and based on the efficacy of this regimen as shown by our previous studies[13–15]. Recently, Wittenstein et al. reported preliminary results of a multicenter feasibility study where PAR was delivered with the intention of administering a dose of 150%-200% of the prescribed dose to the core of the metastases [16]. The authors concluded that based on short-term follow-up, PAR is feasible and free of severe acute side effects or unexpected toxicities.

To the best of our knowledge, ours is the first reported case of treating a primary bulky tumor, specifically RPS, with PAR. Our case demonstrated no serious short- or intermediate-term toxicity, and the disease did not progress locally despite the large size and rapid pretreatment growth, resulting in 6 months of symptom-free survival.

In patients with inoperable or residual RPS, several studies have tested RT with partially satisfactory results. Sobiborowicz et al. conducted a literature review and reported a 2-year local control rate of 50%-53% in patients treated with conventional RT techniques such as 3D-conformal RT, intensity-modulated RT, and VMAT [17], indicating the potential for future improvements. Consequently, innovative irradiation methods like spatially fractionated radiotherapy (SFRT) have been proposed.

SFRT is a technique that involves delivering radiation to a target area using multiple small radiation fields, as opposed to a single large field. It spatially divides the radiation dose into subfields separated by nonirradiated gaps or valleys. This approach allows for high radiation doses to the tumor while minimizing the dose to surrounding healthy tissues.

The underlying principle of SFRT is to exploit the phenomenon of "dose sparing" in normal tissues within the gaps. By dividing the radiation dose into fractions and strategically arranging the fields, SFRT aims to achieve a more favorable therapeutic ratio by maximizing tumor control while reducing normal tissue toxicity.

SFRT encompasses different approaches, including grid therapy, lattice therapy, and interlaced brachytherapy. Grid therapy employs a grid-like pattern of radiation fields, while parallel opposed fields converge at the target. The lattice technique, a specific form of SFRT, utilizes a lattice-like pattern of radiation beams to create a highly conformal dose distribution, enhancing the therapeutic ratio in select cases. Interlaced brachytherapy involves the insertion of radiation sources into the tumor or surrounding tissues.

SFRT has been investigated and employed for various cancers, including large and recurrent tumors and those located in challenging anatomical or radiosensitive areas. This technique has shown promise in improving local control and reducing toxicity, although further research is necessary to determine its optimal use, efficacy, and potential benefits compared to conventional RT approaches [18].

In the treatment of soft tissue sarcomas (STS), both the GRID [19] and lattice [20] techniques have been tested for bulky tumors, with promising preliminary results. However, the approach used in our case was more practical and pragmatic, as it relied on a widely available technique (VMAT-SIB). In our case, we hypothesized that ablating part of the tumor, considering the low α/β ratio of STSs [21], would be more easily achievable with ultra-hypofractionated treatments, potentially enhancing the palliative effect without invasiveness. On the other hand, traditional SFRT techniques (GRID, lattice, interlaced brachytherapy) have been suggested to induce immunogenic effects, bystander effects, and microvasculature alterations, which can contribute to therapeutic outcomes [22].

Nevertheless, it is noteworthy that in our patient, the complete metabolic response was not limited to the region treated with the ablative dose (40 Gy in 4 fractions) but also included the region exposed to the palliative dose (20 Gy in 4 fractions). This observation suggests that mechanisms beyond simple

radio-induced cell killing may have contributed to the complete metabolic response.

Conclusion

In conclusion, our case study highlights the tolerability and efficacy of PAR, which did not produce unexpected side effects despite delivering an ablative dose to a large tumor volume. Our findings support further studies to evaluate the tolerability and effectiveness of PAR in palliative treatment for bulky RPS and to compare its results with more traditional SFRT methods.

Authors contribution statement

FM and AGM had the idea for the article; SS, PC, VL, and LS performed data and figures collection; FM, SC, AGM, and SC drafted the manuscript; all authors critically revised the work.

Patient consent

The patient described in this case report gave written consent for the scientific use of his documentation and imaging.

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