

Reirradiation of pulmonary artery intimal sarcoma: A case report

Ilaria Chiola¹ | Liliana Belgioia^{1,2}  | Elena M. L. Vaccara³ | Marco Gusinu³ | Renzo Corvò^{1,2}

¹Health Science Department (DISSAL), University of Genoa, Genoa, Italy

²Radiation Oncology Department, IRCCS San Martino Hospital, Genoa, Italy

³Medical Physics Department, IRCCS San Martino Hospital, Genoa, Italy

Correspondence

Liliana Belgioia, Health Science Department (DISSAL), University of Genoa, Via Pastore 1, 16132 Genoa, Italy.
Email: liliana.belgioia@unige.it

Abstract

We report here the case of a patient with 4 years long-term survival after treatment with surgery, chemotherapy, and radiotherapy with good local control. This case highlights the possible role of radiation therapy in this tumor.

KEYWORDS

case report, helical tomotherapy, intensity modulated RT, pulmonary artery sarcoma, reirradiation

1 | INTRODUCTION

Intimal sarcoma of the pulmonary artery is a rare tumor with poor oncological outcomes. We report here the case of a patient with 4 years long-term survival after treatment with surgery, chemotherapy, and radiotherapy with good local control. This case highlights the possible role of radiation therapy in this tumor.

Primary pulmonary artery sarcomas (PAS) are the most frequent sarcoma of the great arteries. Most PAS are derived from the embryologic bulbus cordis area, mainly from the pulmonary artery. Intimal sarcoma of the pulmonary artery (PAIS) is a rare tumor with an estimated incidence between 0.001% and 0.003%,¹ which is likely an underestimate due to frequent misdiagnosis and late detection during surgery or autopsy.² Median overall survival (OS) of approximately 17 months is reported in the literature for PAIS patients.³ Surgery remains the mainstay of management for patients with PAIS, even though the use of various chemotherapy agents has been reported.^{3,4} To date, the role of radiotherapy remains unclear.⁵

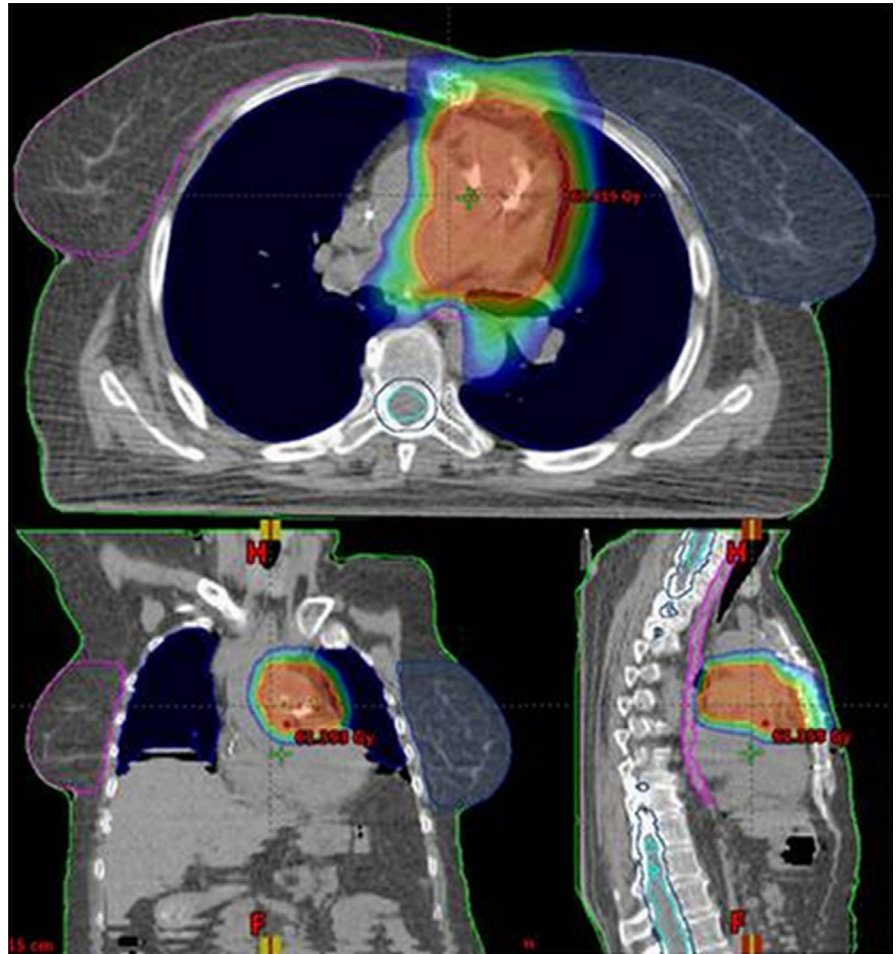
Below, we report the case of a woman with long-term survival from PAIS who was initially treated with surgical

resection and postoperative chemotherapy, which was successfully treated with repeated (fractionated) courses of radiotherapy.

2 | CASE REPORT

The patient, a 62-year-old woman, reported a history of pulmonary hypertension since March 2010 with findings of a high D-dimer, shortness of breath, and chest pain. In April 2014, during follow-up for her pulmonary hypertension, chest computed tomography (CT) revealed the presence of a solid mass originating from the main pulmonary artery with a maximal extension of 37 mm and involvement of the pulmonary valve but without signs of extravascular invasion. The subsequent 18-fluorodeoxyglucose positron emission tomography (18 FDG PET/CT) confirmed chest CT findings with pathologic uptake at the pulmonary trunk. In May 2014, she underwent pulmonary endarterectomy (PEA) and paratracheal lymphadenectomy. The definitive histological diagnosis was poorly differentiated mesenchymal tumor with strong fibroblastic differentiation at

FIGURE 1 Dose distribution of helical tomotherapy plan



immunohistochemistry, consistent with pulmonary arterial intimal sarcoma (KI67 30%, G3, mitotic index >20, necrosis <50%); negative nodes (0/6) but positive margins (right and left margin of pulmonary artery and the margin of ventricular). Due to the negative CT re-evaluation 1 month after surgery, the patient received four cycles of adjuvant chemotherapy combining adriamycin and ifosfamide between June and September 2014. The fourth chemotherapy cycle was complicated by neurological toxicity and a diagnosis of encephalopathy, which resolved completely. From October to December 2014, the patient underwent adjuvant radiation treatment, which was delivered by Hi-Art helical tomotherapy and daily image guided radiotherapy (IGRT). A CT simulation scan with 2.5 mm slices was acquired, and the following volumes were identified: clinical target volume (CTV), including the surgical areas of pulmonary artery; planning target volume (PTV), defined adding 5 mm to CTV; organs at risk (OARs), such as spinal cord, esophagus, heart, and right and left lungs. The prescribed dose was 60 Gy in 30 fractions, five fractions per week (Figure 1). The radiotherapy treatment was well tolerated with no relevant toxicity. At the end of the radiotherapy, the patient started a regular clinical and radiological follow-up. In May

2016, 19 months after external beam radiotherapy (EBRT), a chest CT revealed a solid nodule of 7 × 6 mm located nearby the inferior wall of the pulmonary artery descending branch. The lesion was suspicious for recurrence, but was too small to be defined. Close radiological follow-up with repeated chest CTs in July 2016, October 2016, and January 2017 revealed stability in nodule size. In July 2017, the CT scan revealed a pulmonary descending artery filling defect; however, the defect increased in size three times compared to its original size. No evidence of distant metastases was observed. From September to November 2017, the patient underwent second-line chemotherapy (Docetaxel and Gemcitabina—4 cycles). This regimen was interrupted because of disease progression at CT re-evaluation (lesion of 30 mm in maximum size that involved the whole lumen of the inferior right pulmonary artery). Particle radiations treatment was evaluated at Protontherapy Center, Pavia, but the site of the lesion was not compatible and photon re-irradiation concomitant to pazopanib was proposed. This second radiotherapy treatment (reRT) was delivered in February 2018 by VMAT technique with LINAC (VARIAN Trilogy). The re-RT dose prescribed was 24 Gy in 4 fractions, once a week, with energy of 6 MV. The CTV included

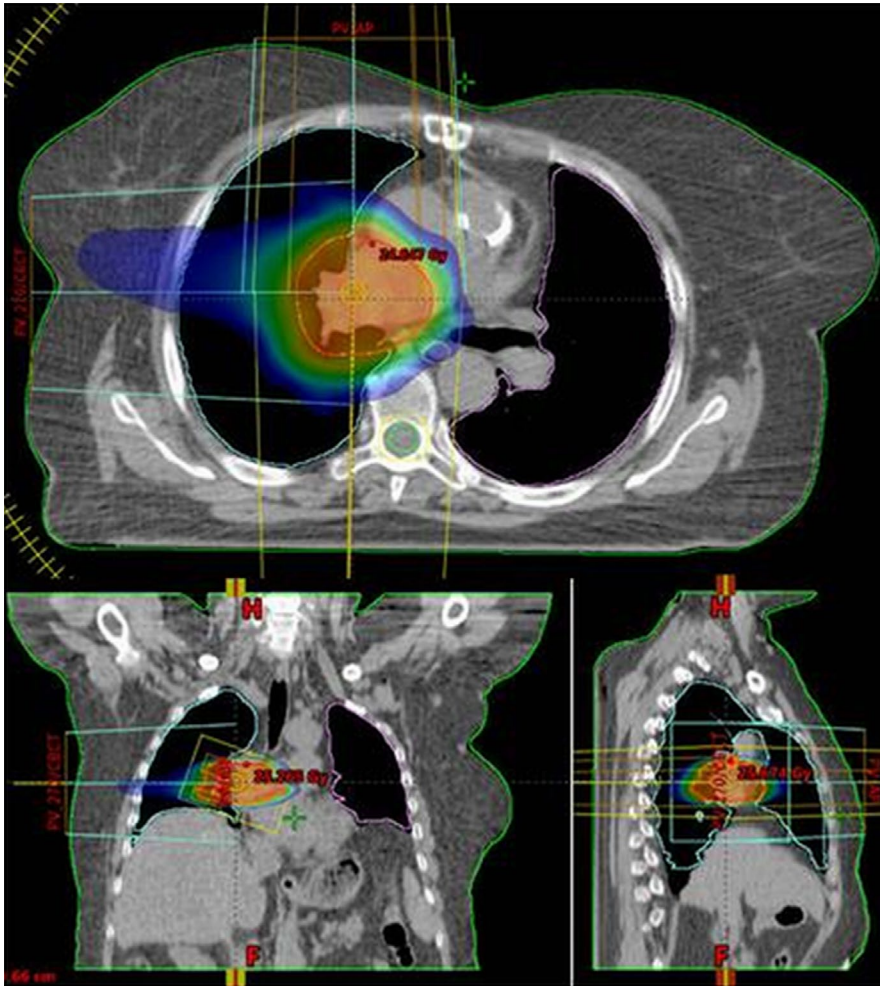


FIGURE 2 VARIAN Trilogy dose distribution

the macroscopic disease plus a 5 mm margin (Figure 2). Like the first one, this EBRT treatment was well tolerated. An early CT performed 1 month after reRT revealed a partial response with maximum lesion size reduction from 3 to 2 cm. In June 2018, a further CT scan showed stable disease. In view of the lack of change and reasonable tolerability, the patient will continue Pazopanib treatment.

3 | DISCUSSION

Primary pulmonary artery sarcomas (PAS) are the most frequent sarcomas of the great arteries characterized by local growth, with only a slight ability to metastasize.² They typically affect middle-aged people, particularly women, with a mean age at diagnosis of 48 years.² Our patient had an older age of onset than is generally reported in literature. The aim of this paper is to report our experiences with a patient who had long-term (50 month) survival with PAS, considering that this disease has a poor prognosis and a median OS of 17 months.³ Diagnosis of PAS is difficult and often delayed due to the nonspecific nature of the symptoms. It is often confused with pulmonary thromboembolism and is therefore

treated inappropriately with prolonged anticoagulation or thrombolysis.⁶ Common symptoms at the time of presentation are progressive dyspnea, cough, chest pain, and weight loss. The patient described here presented with all the above symptoms but had been diagnosed with pulmonary hypertension 4 years prior. This misdiagnosis is quite common as PAS starts with nonspecific symptoms and it can be easily confused with pulmonary embolism; however, the onset of the symptoms is usually more gradual with PAS than pulmonary embolism.¹ In our patient, this missed diagnosis led to a delay in therapy that could have affected outcomes. Surgical treatment remains the mainstay of management for patients with PAIS and can include pulmonary endarterectomy, lobectomy, or pneumonectomy depending on mono or bilateral disease.⁷ The correct surgical approach must be evaluated individually, according to the tumor presentation, the presence of pulmonary hypertension, and the patient's clinical condition.⁸ Surgery can prolong survival and often improve symptoms but margin status, like in this case, is rarely clear. For this reason, the patient underwent adjuvant treatment.³ Chemotherapy is normally given postoperatively, although cases of improved outcome with neoadjuvant chemotherapy have been described. It is not clear if adjuvant chemo and

radiotherapy bring any improvement, but some data reported an increased OS in patients who received multimodality therapy vs patients who received one single therapy⁹ and our patient received both chemo and radiotherapy. Several perioperative agents have been reported in the literature, including anthracyclines, ifosfamide, gemcitabine, taxanes, platinum, and immunotherapy. Anthracyclines, either alone or in combination, are the most commonly used agents. In our case, first-line chemotherapy was adriamycin and ifosfamide.^{3,4} The role of postoperative radiotherapy remains unclear.⁵ Chemotherapy regimens are normally followed by intensity modulated RT (IMRT) at a radical dose of 60 Gy in 30 fractions to surgical bed as happened in our patient.¹⁰ Helical tomotherapy allows the delivery of higher doses to target volumes along with better sparing of normal tissues and to perform daily IGRT permitting us to correct any possible setup errors at every application, increasing the precision of the treatment and reducing interfraction changes.¹¹ In our case, the patient had a disease-free survival and was symptom-free for 19-months after first EBRT. At recurrence, the patient was clearly refractory to the second chemotherapy therapeutic regimens and presented with disease progression. For this reason, a second RT course concomitant to new targeted therapy was proposed. This re-RT was delivered with a weekly fractionation in order to exploit a radiobiological rationale designed to increase the therapeutic index.¹² The only targeted agent approved for use in soft tissue sarcoma at present is the tyrosine kinase inhibitor pazopanib, based on the results of the PALETTE trial.¹³ Pazopanib should be considered in patients with intimal sarcoma of the pulmonary artery that is unresectable or recurrent after surgery or cytotoxic chemotherapy.¹⁴ This case suggests that the combination of RT and pazopanib is safe and well tolerated and that disease recurrence may well respond precociously (re-evaluation after 1 month) and effectively to RT.

4 | CONCLUSION

In this case, we can confirm the beneficial role of postoperative radiotherapy and the safety of reirradiation on residual recurrence. Early diagnosis could be an essential prerequisite to optimal management of PAS, especially by a multidisciplinary team. Being a rare and radioresistant cancer, more studies are still necessary to better understand the role of adjuvant treatment and the role and timing of RT, which, as this case suggests, can be delivered more than once when disease recurs.

CONFLICT OF INTEREST

None declared.

AUTHOR CONTRIBUTIONS

IL, LB: contributed equally to this work, wrote the paper, and reviewed final manuscript; EMV, MG: review and editing of final manuscript, provided insight into how results relate to medical physics; RC: review and editing of final manuscript, provided insight into how results relate to radiation oncology.

INFORMED CONSENT

Consent was obtained from patient for the publication of this report and any accompanying images.

ORCID

Liliana Belgioia  <https://orcid.org/0000-0003-0508-6344>

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