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Case Report

New curative approach using embolization followed by moderate-dose radiotherapy after surgical failure for large right heart metastasis

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ABSTRACT

Purpose: Cardiac metastasis is a rare fatal event. An intracavitary right tumor mainly in the ventricle is difficult to manage. Literature reports suggest that cardiac surgery in oligometastatic patients could offer median survival of 1 year. We investigated salvage treatment comprising transcoronary tumor embolization followed 15 days later by cardiac radiotherapy (40.5 Gy/15 fractions).
Cases: We report two cases of severe right cardiac metastasis with a history of abdominal cancer managed by this salvage treatment following residual cardiac mass after previous cardiac surgery.
Conclusion: Both symptomatic patients improved progressively and were locally controlled for at least 1 year without toxicity.

Introduction

Cardiac metastasis (CM) is a rare and rapid life-threatening stage in an oncological process between the sixth and eighth decades of life, with few therapeutic options [1]. Whereas the usual therapeutic strategy for a metastatic disease is palliative, oligometastatic cases have prompted a change in our attitudes in the last decade by treating the metastatic site as well as the primary cancer. In fact, local treatment with a curative intent of a large cardiac tumor is difficult, even impossible.

Three decades ago, our team first used curative brachytherapy boost in base of tongue tumors after large moderate-dose radiotherapy (RT) bath [2]. At the same time, we wondered whether moderate-dose cardiac RT, boosted by a non-RT focal treatment as tumor embolization, with no cross-toxicity, could be a "curative" treatment option for CM, and in what sequence.

We used transcoronary embolization, followed 2–3 weeks later by moderate-dose RT in 2 cases of large right (R) ventricular metastasis derived from an abdominal tumor, following cancer recurrence after cardiac surgery.

Reports

Case 1

A 51-year-old man came to the emergency room in October 2019 because of syncope and dyspnea. He had a large right ventricular metastasis, following cardiac surgery 8 months previously with tumor exeresis (100 g, 5 cm) followed by failed oral chemotherapy (3 months) and then treatment with a nuclear export inhibitor.

The patient had a history of a left 15 cm mesocolic undifferentiated liposarcoma treated in January 2014 by abdominal surgery followed by adjuvant chemotherapy. Locoregional recurrence occurred three times and was treated by salvage abdominal surgery (last one in 2017, with preoperative chemotherapy). A new recurrence on the other side of diaphragm, in the form of a R ventricular mass (Fig. 1A-1A'-1A''), was treated by incomplete surgery. The heart lesion was developed in the R lateral wall up to the tricuspid valve (54 x 42 mm on MRI) and was life-threatening because of mechanical compression (retrosternal).

Because at the time there was no standardized treatment, we decided to offer the patient a salvage procedure. Coronarography showed that the R coronary artery accounted for 90% of the blood supply to the tumor, and it was occluded by coil (Fig. 1B-B'). We waited for 14 days for clinical improvement and then implemented focal RT (40.5 Gy/15

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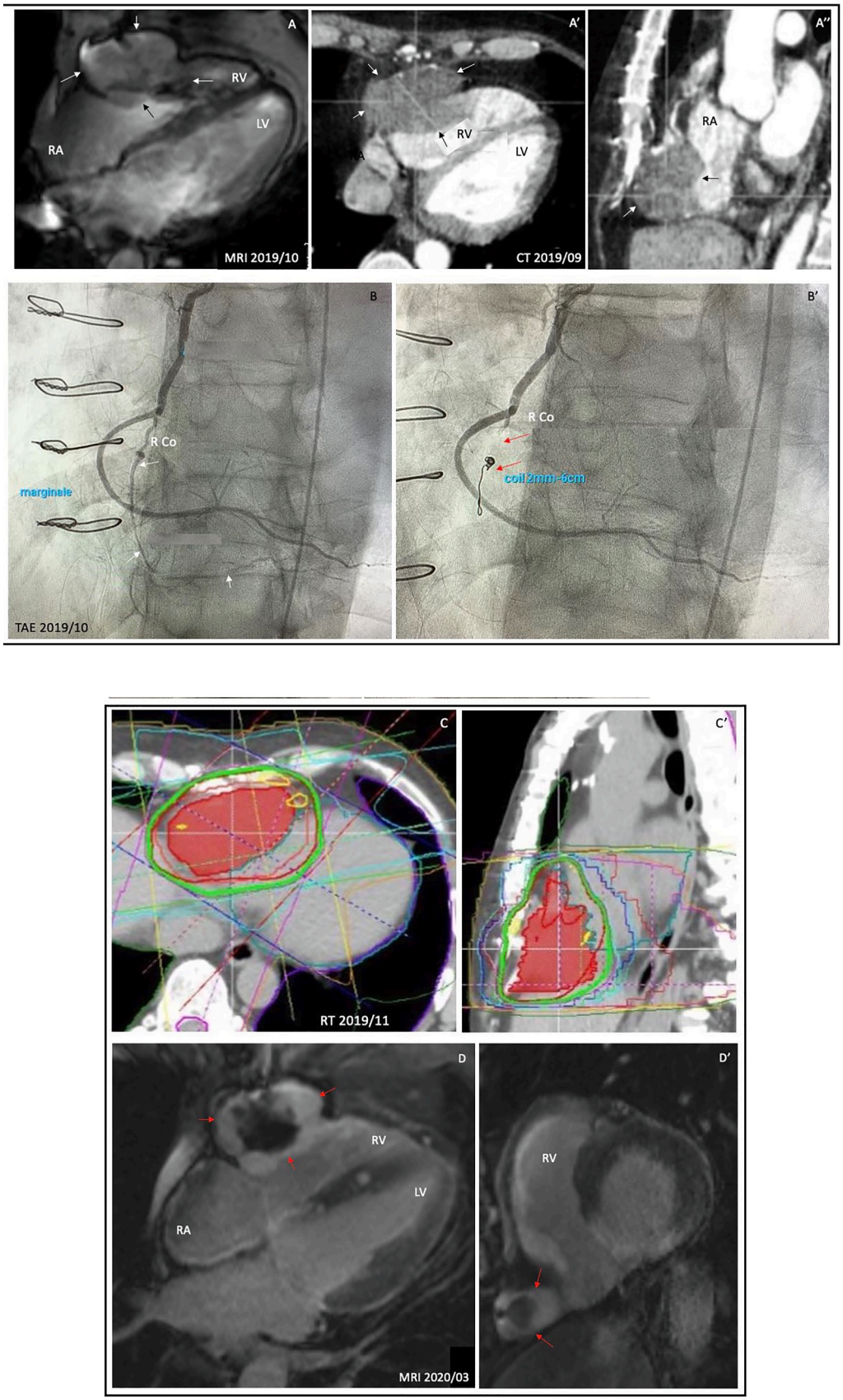

Fig. 1. Case 1. Cardiac right ventricular metastatic tumor recurrence after surgery: axial MRI T2 weighted (A); axial (A') and sagittal (A'') CT-scan; before (B) and after embolization with coil (B') in right coronary artery; radiation dosimetry: green line 40.5 Gy axial (C) and sagittal (C'); axial (D) and sagittal (D') MRI showing right cardiac wall tumor necrosis. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

fractions/30 days; PTV 250 cm^3; RX 6MV, mid-programmed 7 days split) (Fig. 1C-C') boosted by daily oral radiosensitive chemotherapy (etoposide 25).

During and after RT, we observed progressive clinical improvement every week, with reduction in thoracic pain and then in cardiac dyspnea. Six months later, the patient was asymptomatic with a reduced necrotic R ventricular lesion (39 × 27 mm) without late MRI raising (Fig. 1D-D'). One year later, the patient's cardiac condition was stable after tumor reduction, but subcutaneous metastases were observed.

Case 2

A 68-year-old asymptomatic woman presented with a single right ventricular cardiac metastasis in November 2019. The patient had a history of metastatic colorectal adenocarcinoma (November 2018; T4N2; blood carcinoembryonic antigen [CEA] 132 ng mL^{-1}) treated first by chemotherapy (Folfirinox) then complex R hepatectomy (8 metastases), left colectomy-omentectomy in May 2019, followed by 3 months of chemotherapy (Folfox) with complete remission (CEA 1.5 ng mL^{-1}).

A polylobed cardiac lesion was discovered three months later in the R ventricle against the interventricular septum and tricuspid valve (53 × 49 × 64 mm on MRI), together with a parietal thrombus in the R atrium, without any abdominal recurrence. Cardiac biopsy was followed by pericardial tamponade. Chemotherapy (cetuximab-FOLFIRI) over the next four months was stopped after local progression (Fig. 2A-A'). In April 2020, the patient underwent incomplete R ventricular surgery with valve change (Fig. 2B-B'), followed by pneumothorax and bilateral pleural effusion.

Because at this time there was no standardized treatment, we decided to offer the patient a salvage procedure. Three weeks later, coronarography showed that a marginal (from R coronary) artery was supplying blood to the remnant tumor, and it was occluded by two 4 × 50 mm coils in May 2020 (Fig. 2C-C'), CEA level was 5.5. After two weeks, there was clinical improvement (postoperative cardiac failure reduced by diuretic and erythropoietin) and in June 2020 we implemented focal RT (40.5 Gy/15 fractions/30 days; 150 cm^3; RX 6MV; mid-programmed 7 days split) (Fig. 2D-D') boosted by daily oral radiosensitive chemotherapy using capecitabine (June 2020: CEA 6.3).

During and after RT, we observed progressive cardiac improvement. Three months later, the patient was asymptomatic (CEA 2.2) with disappearance of septal thickening and a 1 cm R ventricular tip (ropes), without MRI raising in September 2020 (Fig. 2E-E'). However, the patient suffered a local borderline recurrence in December 2020, including obstruction of the superior vena cava and a R hilar node and CEA equal to 10 ng mL^{-1} (Fig. 2F). A new salvage treatment was possible using a cava stent (Fig. 2F') followed by focal RT.

Discussion

CM is rare, although its true frequency may be underestimated, with an incidence ranging from 2.3 to 18.3% in the literature: Bussani et al discovered in 18,751 autopsies, 622 CM (9%) among 7289 malignancies (39%) [3], i.e. a rate 20 to 40 times that of a primary cardiac tumor [4]. The CM is usually small and multiple rather a single large lesion, while two-thirds of CM invade the pericardium, one-third the myocardium, and 5% the endocardium.

Cardiac metastases spread mainly by direct external invasion (for intrathoracic cancer) up to the pericardium; a hematogenous or

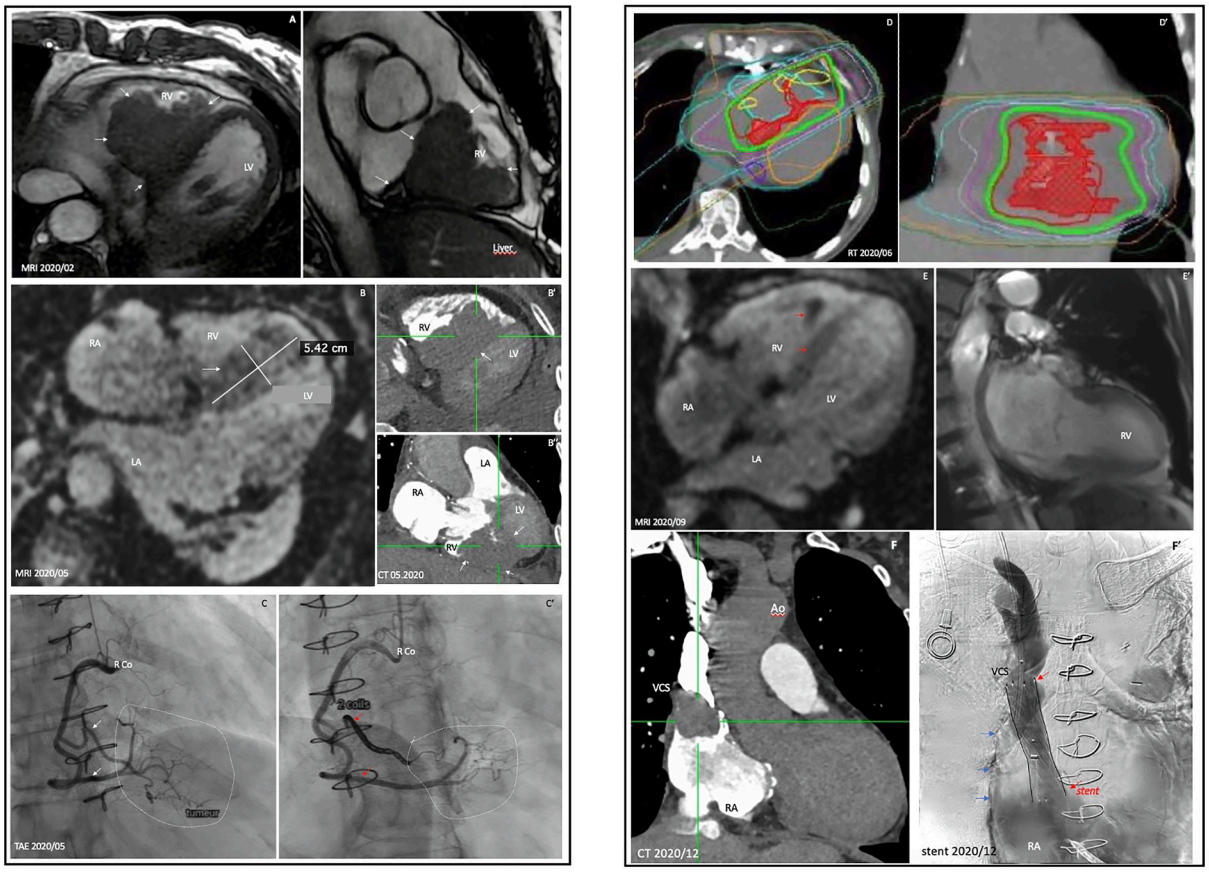

Fig. 2. Case 2. Cardiac right ventricular metastatic tumor before surgery: axial (A) and sagittal (A') MRI; residual tumor after surgery: axial MRI (B), axial (B') and frontal CT-scan (B"); before (C) and after embolization with two coils (C') in right coronary artery; radiation dosimetry: green line 40.5 Gy axial (D) and frontal (D'); axial (E) and sagittal (E') MRI with right cardiac control. Recurrence in superior vena cava: frontal angio-CT view (F) and salvage stent (F'). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

lymphatic route preferentially up to the myocardium (as for lymphoma or breast cancer); and direct intracavitary invasion through the inferior vena cava (mainly intra-abdominal cancer) to the endocardium, followed by a possible secondary retrograde migration towards the epicardium.

Intracavitary CM from the abdomen via the inferior vena cava is mainly located in the right ventricle or atrium, favored by physical cardiac conditions as low intracavitary pressure, slow blood flow, and lighter contractile strength and abdominal conditions such as extensive sub-diaphragmatic or hepatic surgery [5,6]. Whereas cardiac valves are usually not involved because of their lack of vascularization and constant movement [3], an obstruction is expected to damage valve function in the case of a large intraventricular mass.

The diagnosis of CM is not specific, and clinical manifestations vary according to the type of cancer invasiveness, such as pericardial (effusion) or myocardial signs (asymptomatic, conduction disturbance, heart failure). The most efficient multimodal imaging methods today in characterizing a cardiac mass (thrombus, benign or malignant tumor) and planning its management are transesophageal ultrasound, ^{18}FDG-positron emission tomography- CT scan and cardiac MRI [7].

When the heart is the only site of metastasis, with limited tumor invasion, surgery is an option if resection is technically feasible in selected patients with good performance status and long life expectancy [8]. Postoperative survival after CM resection varies in the literature: from hours to 26 months in 10 case reports between 1971 and 1981 [4], and 2–34 months in 4 patients in 2012 [8]. Two-thirds of primary malignant cardiac tumors are sarcomas. In a single institution, after surgery (two-thirds in the right heart) with curative intent, median survival was 11 months in 21 patients during the 1964–89 period and 23.5 months in 27 patients during the 1990–2006 period, thanks to neoadjuvant/adjuvant chemotherapy (1 adjuvant RT) and salvage treatments (15 resection R0, 7% perioperative death) [9].

Radiotherapy has long been known to reduce the risk of local recurrence after oncological surgery or to control cancer symptoms transiently, using a postoperative moderate-dose level of 45–50 Gy (9–10 Gy/week). However, this “moderate-dose” RT must be increased to 70–80 Gy if the intent is curative. This is not feasible for a large cardiac volume, because it is not tolerated by the heart [10]. Thus, in the literature, RT for CM is mainly palliative in intent: in 11 patients without surgery, 7 irradiated survived longer (5–24 months) than 4 non-irradiated ones (0–5 months) [11]. In 10 irradiated patients, 2 survived 7 and 11 months after surgery and postoperative RT versus 8 patients 0–11 months after RT alone (2 of whom worsened after a 5 Gy daily fraction) [12]; one patient was treated by stereotactic body RT (SBRT 30 Gy/5 fractions) with a stable lesion at 2 months [13].

In one recent case, a curative dose using SBRT with a single 20 Gy fraction proved safe and successful [14]. A mean 2 cm interventricular nodular CM, revealed by a syncope, helped to diagnose a small right apical lung adenocarcinoma: the patient was treated by chemotherapy for 3 months, then SBRT, followed by conventional RT-chemotherapy for lung cancer, allowing complete cancer remission for 9 months [14].

Cardiac SBRT was also recently used to control tachyarrhythmia in a safe and successful manner, applied to a moderate elongated volume, and long nerve path (median PTV 25 and 61 cm^3) [15,16]. However, for our patients, the cardiac tumor was a large recurrence (>5–7 cm), in scar tissue, the bed of the previous surgery, and with incomplete cardiac reversion. The risk of radiation necrosis with SBRT was too high [17]. We thought that conformal fractionated RT at a “moderate dose” after embolization was then possibly an option.

Transcatheter arterial embolization (TAE) is an established method of treatment used, after catheterization of the main artery, to occlude the high-flow feeding artery of the tumor that provides remarkable neovascularization. TAE has been used for the control of large tumors, alone or together with RT after insufficient pain reduction, allowing tumor size decrease and tumor necrosis [18].

The sequence of administration of TAE and RT is not clear in the literature. On the one hand, there is a theoretical reduction of tissue radiosensitivity under hypoxic conditions induced by embolization. On the other hand, vascular obliteration rate, in cerebral arteriovenous malformations, is significantly lower in embolized RT versus non-embolized RT tissue, suggesting that embolization protects adjacent normal tissue [19]. A recent meta-analysis in hepatocellular carcinoma showed that patients receiving TAE plus RT had a significantly better survival rate and complete response than those receiving TAE alone, and a better response if TAE was performed less than 28 days before RT [20].

We speculated that administration of TAE followed by RT may present synergic therapeutic mechanisms: (a) TAE damages a large number of cancer cells, mainly in the center of the tumor, thus promoting peripheral residual cells from a non-proliferative phase into a proliferative and more radiosensitive phase, especially a short period of time after TAE; (b) after TAE, residual cancer cells at the tumor periphery are still viable because of peripheral circulation; (c) TAE decreases tumor volume, thus reducing the RT target volume and related complications; (d) RT after TAE extends intratumoral retention of lipiodol, and therefore its efficacy [20].

Conclusion

Transcoronary embolization followed by immediate moderate-dose RT with curative intent was feasible and useful without complication at 10 months, in two oligometastatic patients with a large right ventricular tumor.

Informed consent statement

The two patients gave their written consent for publication of these cases.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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