Case Reports

Angiosarcoma Causing Cardiac Constriction Late after Radiation Therapy for Breast Carcinoma

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Therapeutic radiotherapy rarely causes sarcoma, and this occurs years after completion of the intended treatment. In treating breast carcinoma, careful planning in the application of modern radiotherapeutic techniques usually can shield the heart and pericardium.

We report a rare case of angiosarcoma of the pericardium, which presented in a 41-year-old woman as constrictive pericarditis 8 years after irradiation for cancer of the left breast. To our knowledge, this is only the 2nd report of angiosarcoma of the pericardium after radiotherapy. ***(Tex Heart Inst J 2016;43(1):81-3)***

Pericardial constriction remains a difficult diagnosis that requires a high degree of clinical suspicion, careful clinical examination, and multimodality imaging. The cause of the constriction can be challenging to ascertain and often becomes evident only at the time of surgical resection. Such is the case we present.

Primary tumors of the pericardium are extremely rare, with an incidence of between 0.001% and 0.28% in an autopsy study[1]; approximately 8% of those are angiosarcoma. In a study by Kirova and colleagues[2] of 16,705 patients who received radiation therapy (RT) for breast cancer, only 13 patients developed angiosarcoma of the breast, chest wall, or skin after a median follow-up period of 9.3 years. Pericardial angiosarcoma after RT is rare but has been described.[1] To our knowledge, this is the 2nd report of angiosarcoma of the pericardium after RT.

Key words: *Angiosarcoma; constrictive pericarditis; neoplasms, radiation-induced; pericardium/radiation effects; postradiation tumor; radiotherapy/adverse effects*

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Case Report

A 41-year-old woman presented with 8 weeks of progressive dyspnea, orthopnea, and cough. Her history included intracystic papillary carcinoma of the left breast 8 years earlier (treated with lumpectomy and postoperative RT). The details of the protocol and dosage of radiation used during the treatment were not available. The physical examination was consistent with pleural and pericardial effusions. The white cell count was elevated, as were the serum creatinine level (2 mg/dL [normal range, 0.6–1.1 mg/dL] and the blood urea nitrogen level (46 mg/dL [normal range, 6–21 mg/dL]). Her other laboratory tests—coagulation profile, autoimmune/rheumatologic disease assay, and urinalysis—were within normal limits. A chest radiograph revealed bilateral pleural effusions. Computed tomography (Fig. 1) revealed a large amount of pericardial fluid extending to the aortic root, with an increased density suggesting hemorrhage or high protein content and a possible anterior mass over the right atrium, thought to represent an ill-defined mass or organized hematoma and pleural effusions.

Transthoracic echocardiography revealed preserved left ventricular ejection fraction, diastolic dysfunction, bilateral pleural effusions, and evidence of effusive-constrictive pericarditis. Thoracocentesis and pericardiocentesis through a pericardial window revealed no malignant cells. Laboratory evaluation of the effusions for autoimmune and rheumatologic disease was negative.

The patient underwent open-chest pericardiectomy for constrictive pericarditis. On the visceral pericardium, there were nodular masses—7-mm thick, rubbery, and dark red-brown—adherent to the parietal pericardium.

Microscopically, these were spindle-cell neoplastic cells with marked nuclear pleomorphism, consistent with angiosarcoma (Fig. 2). The malignant cells expressed vimentin, factor VIII, podoplanin, and CD31, with focal expression of CD34. The

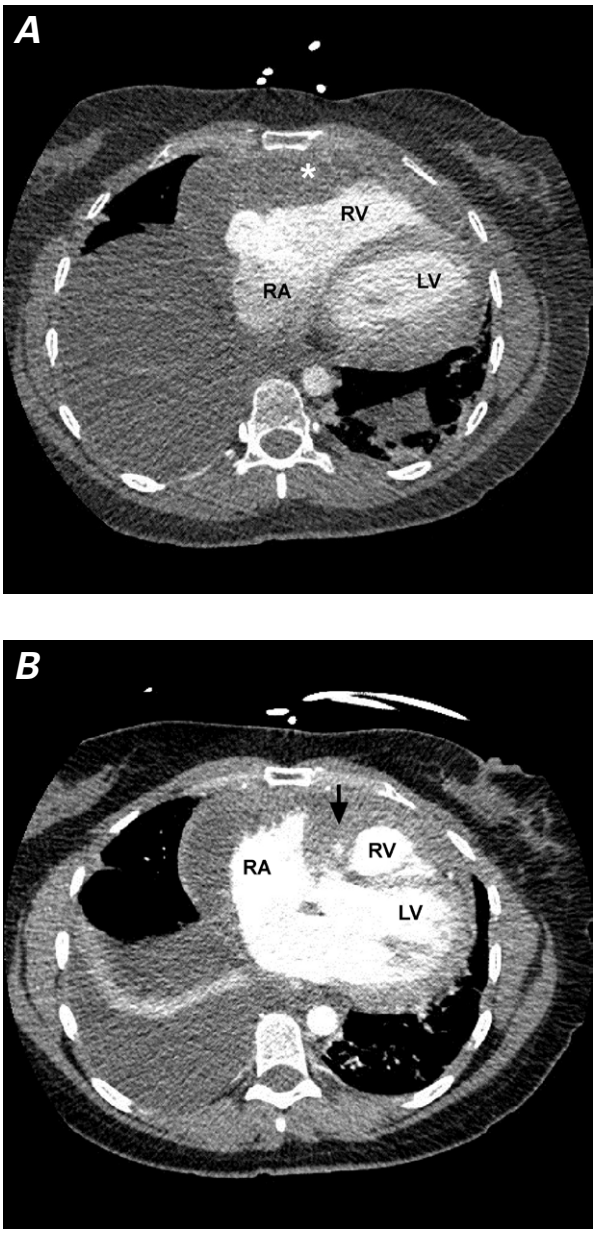

Fig. 1 *Computed tomograms of the chest with contrast medium show **A**) a large pericardial effusion with an ill-defined soft tissue mass (asterisk) anterior to the right ventricle and right atrium and **B**) the mass extending along the atrioventricular groove (arrow). A large right-sided pleural effusion is also present.*

LV = left ventricle; RA = right atrium; RV = right ventricle

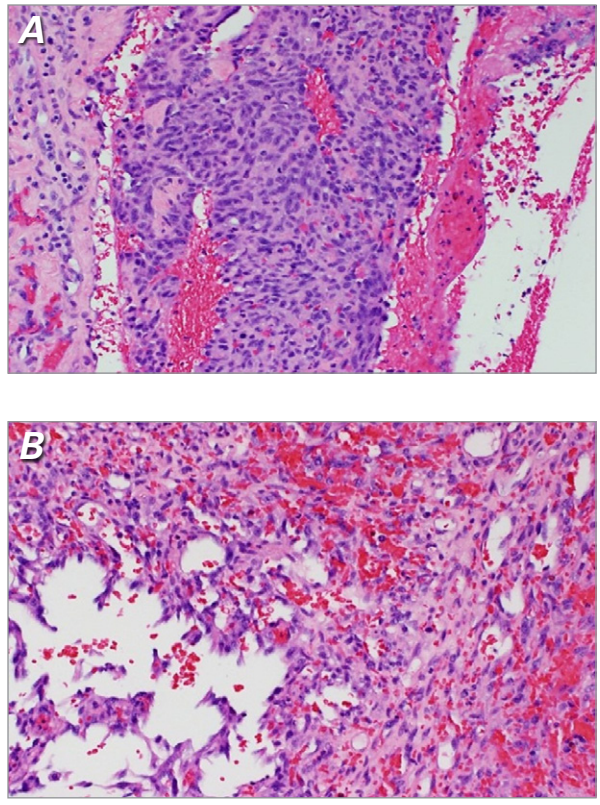

Fig. 2 *Photomicrographs of angiosarcoma in the pericardium show **A**) solid fascicles and **B**) vascular channels (H & E, orig. ×200).*

malignancy was not amenable to complete resection. The patient was started on paclitaxel for palliative treatment.

Discussion

Sarcoma is a rare sequela of RT. Its incidence and its relative risk in an individual patient are difficult to estimate because of the rarity of this malignancy. In studies that examine the incidence of sarcoma after RT, the estimated rate of occurrence lies between 0.017% and 0.17%.[3,4] The histologic subtypes of post-RT sarcoma include osteosarcoma (most common), malignant fibrous histiocytoma, angiosarcoma, lymphangiosarcoma, and spindle-cell sarcoma.

A published case of pericardial angiosarcoma[1] has been summarized and compared with the case presented (Table I).

An early-stage diagnosis of pericardial angiosarcoma is little more than a strong clinical suspicion. The clinical presentation can be that of acute pericarditis, pericardial effusion with or without tamponade, effusive constrictive pericarditis, or pericardial constriction. Cytologic results of effusions in patients with advanced angiosarcoma can be negative, even after repeated testing.[5] The differential diagnosis of a nodular mass in the pericardium includes metastatic tumor, soft-tissue sarcoma, rhabdomyosarcoma, melanoma, mesothelioma, and Kaposi sarcoma. The criteria by which a tumor is considered a post-irradiation sarcoma were originally proposed by Cahan and colleagues[6] and were subsequently revised by Murray and associates.[7] The salient points in the revised criteria are these: 1) the sarcoma must arise within the field of prior irradia-

TABLE I. Reported Cases of Angiosarcoma of the Pericardium after Radiation Treatment

Reference	Pt. Sex, Age (yr), and Original Malignancy	Criteria for Post-RT Sarcoma		Management	Outcome
		Field of Irradiation	Latency Period after Irradiation (yr)		
Killion MJ, et al.[1] (1996)	M, 54, seminoma	Supraclavicular areas and mediastinum	15	Pericardiectomy; postoperative adriamycin and isophosphamide	Died 3–4 mo after onset of symptoms
Current case	F, 41, breast papillary carcinoma	Left mediastinum	8	Pericardiectomy; postoperative paclitaxel	Palliative treatment

F = female; M = male; Pt = patient; RT = radiation treatment

tion; 2) the sarcoma was not present at the onset of RT, as shown by no evidence of sarcoma before irradiation and by a latent period after the RT; and 3) the sarcoma must be proven histologically and must be of a different histologic makeup than the original malignancy.

Angiosarcoma of the heart has a poor prognosis (mean survival is <9 mo).[8] Metastasis often involves the pleura, but can be widespread—involving the liver, lymph nodes, bone, spleen, and central nervous system. The tumor is frequently nonresponsive to radiation, and surgical treatment in advanced disease is often difficult because of metastasis and extensive local infiltration by tumor. If the tumor is detected in the early stages, careful surgical resection with clean margins and aggressive chemotherapy might be offered in select instances.[9] In patients with an early diagnosis and no metastases, several reports have described improved survival rates and increased disease-free intervals consequent to aggressive surgical and multimodal treatment with chemotherapy and RT.[8-10] These patients were alive and symptom-free at their follow-up evaluations 9 months or more after therapy.

Newer treatment options include immunotherapy with interleukin-2, selective coronary embolization, and (less often) a heart transplant—or a total artificial heart implant while awaiting transplantation—to look for evidence of metastases.[10] The risk of a patient's developing post-RT sarcoma can be reduced by careful selection of cancer patients in accordance with established guidelines on radiosensitive tumors and by choosing targeted therapy, such as intensity-modulated proton-beam RT over conventional RT. Proton-beam therapy, however, is not yet widely available and not yet proven.

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