Multimodality Treatment for Cardiac Angiosarcoma

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Abstract

Primary cardiac angiosarcoma is a rare and highly malignant condition. Besides performing complete surgical excision, it remains controversial as to whether survival can be improved with additional treatment. We herein describe a 30-year-old man with a right atrial angiosarcoma. He underwent two operations for the resection of the primary lesion, and the patient's metastatic lesions involved an intestinal segment. With chemotherapy, radiotherapy, and molecular targeted therapy, he survived for 33 months. The literature describing adjuvant therapy for cardiac angiosarcoma, which is mostly case reports, is also reviewed. In conclusion, the limited evidence suggests that multimodality treatment for cardiac angiosarcoma is a beacon of hope to improve the survival of such patients.

Key words: cardiac angiosarcoma, chemotherapy, radiotherapy, molecule targeted therapy

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Introduction

Primary cardiac angiosarcoma accounts for around 33% of all primary malignant cardiac tumors, which make up approximately 25% of the primary cardiac tumors (1, 2). Delayed diagnosis is frequent because the symptoms are not specific, and the incidence of the disease is rare. Once a patient is confirmed to have the disease, the high malignancy of cardiac angiosarcoma is associated with a very poor prognosis. Nonetheless, the therapies for cardiac angiosarcoma remain controversial. Surgical resection has been demonstrated to improve survival (3-6). Researchers have studied the effects of numerous adjuvant therapies, including chemotherapy, radiotherapy, and molecular targeted therapy. Some reports have published negative results for adjuvant therapies that failed to modify the natural course of primary cardiac angiosarcoma. On the other hand, numerous studies have described an increased survival with additional treatments after surgery. However, no randomized controlled trials have been performed to provide evidence that supports or opposes the administration of adjuvant therapies. We herein describe a patient with primary cardiac angiosarcoma who received multimodality adjuvant treatments and survived for 33 months, reinforcing the hope of extending the

survival of cardiac angiosarcoma patients with multimodality adjuvant treatments.

Case Report

A 30-year-old man had fever and chest tightness for more than 40 days. Echocardiography performed in the local hospital showed an ejection fraction (EF) of 45% and a large pericardial effusion. He was diagnosed with tuberculous pericarditis and received anti-tuberculosis treatment, including rifampin, isoniazid, pyrazinamide, and ethambutol for two weeks. Thereafter the symptoms subsided. Repeat echocardiography showed that the pericardial effusion had been absorbed, and the EF was 73%. However, an abnormal echo signal next to the right atrium was found at this time (Fig. 1), and he was therefore referred to our hospital. Magnetic resonance imaging revealed bilateral pleural effusion, and an abnormal pericardial signal adjacent to the right atrium (Fig. 2). The radiologists considered it to possibly be a mesenchymal tissue tumor. Positron emission tomography scanning confirmed high metabolic activity in the right atrial mass (Fig. 3A) and revealed another high metabolic nodule in the anorectal area. The nodule was resected during a colonoscopy and was confirmed to be an adenoma by pathologists. No other systemic metastases were found.

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Figure 1. The patient's ultrasound cardiograph showed a pericardial mass measuring approximately 3.7×3.9 centimeters in size on a two-dimensional display. The mass compressed the right atrium outside of the free wall, which was closely adjacent to and maybe invaded by the mass.

Figure 3. Positron emission tomography confirmed high metabolic activity in the right atrial mass (A). One year after the surgery, positron emission tomography showed the patch used for right atrial reconstruction, and the residual lesion adjacent to the patch showed no evidence of progression (B).

Three months after the first diagnosis, the patient underwent resection of the right atrial mass. He had an extensive adhesion between the pericardium and the right atrium. The mass was located at the anterior inferior wall of the right atrium. The size was approximately 5×4×3 cm. The tumor also invaded the right ventricle adjacent to the right atrial tumor. After cardiopulmonary bypass was established, the tumor was resected along the tricuspid annulus and atrioventricular groove, and a Gortex patch was used to reconstruct the right atrium. The patient's postoperative recovery was uneventful. The pathological report confirmed the diagnosis of a highly differentiated angiosarcoma (Fig. 4A, B), and the margin of the specimen was determined to be tumor tissue. The immunohistochemistry results were as follows:

Figure 2. A magnetic resonance imaging scan revealed that the tumor (white arrow) had an isotense to slightly high-intensity signal on a T1-weighted image (A), and an isotense to slightly low-intensity signal on a T2-weighted image (B).

Figure 4. A photomicrograph revealing oval-to-spindle cells with frequent mitoses. There was a vascular neoformation with intraluminal red blood cells (AB). The immunohistochemistry findings were positive for CD31 (C) and F8 (D).

vimentin (+), CD34(+), CD31(+) (Fig. 4C), F8(+) (Fig. 4D), Ki67 40%(+), actin (-), desmin (+), CD117(-), DOG-1(-), S-100(-), and CK(-).

Fourteen days later, he began to receive chemotherapy with docetaxel 120 µg once a month. He underwent radical radiotherapy 2 months later. One year after the surgery, in

Figure 5. Capsule endoscopy of the jejunum revealed multiple masses with smooth surfaces and focal bleeding.

the 15th month after he was first diagnosed, a follow-up positron emission tomography scan indicated that the residual lesion had not progressed (Fig. 3B).

In the 22nd month, he had manifestations of gastrointestinal bleeding, associated with such symptoms as malena, dizziness, and fatigue. The patient's hemoglobin level decreased to 5.6 g/dL. However, we found a normal gastrointestinal appearance with gastroendoscopy once and colonoscopy twice. Finally, capsule endoscopy allowed gastroenterologists to confirm multiple metastases in the jejunum (Fig. 5). In the 23rd month, gastrointestinal surgeons resected the metastatic lesions, which were located 80, 100, and 140 centimeters distal to the treitz ligament and were 2×1.5, 2×2, and 2×1.5 cm in size, respectively.

The pathological analysis of the lesions revealed angiosarcoma with transmural invasion (Fig. 6A). Immunohistochemistry showed that the specimens were positive for vimentin, CD34, and CD31 (Fig. 6B). The resected intestinal segment was 80 centimeters long, and the ends were free of tumor tissue. No evidence of any mesenteric lymphnode metastasis was found.

The chemotherapy plan was changed to doxorubicin and ifosfamide. He also received bevacizumab (Avastin) for targeted therapy. However, the primary lesion progressed rapidly and metastasized extensively to the bilateral lungs, pleura, liver, and peritoneum. The patient died of circulatory and respiratory failure 33 months after he first presented at the hospital.

Discussion

Angiosarcoma is the most common primary cardiac malignant tumor. The incidence is extremely rare, with a post-mortem incidence of 0.0001% (7). The clinical diagnosis of angiosarcoma is often difficult because there are no specific symptoms associated with the disease. Some of the more common cardiac symptoms are chest pain, palpitations, and symptoms of congestive heart failure or acute right heart failure secondary to a pericardial tamponade (8). Systemic symptoms occur in approximately 10% of cases and include fever, night sweats, and weight loss (9). Metastases occur in approximately 66-89% of cases at the time of diagnosis and

Figure 6. A photomicrograph showing that the metastatic lesion exhibited a spindle cell pattern similar to the primary tumor (A). Immunohistochemistry of the lesion revealed labeling for CD31 (+) (B).

are mostly found in the lungs, liver, bone, lymph nodes, and central nervous system (10). The present patient had fever and pericardial effusion, which was diagnosed as tuberculous pericarditis despite the absence of night sweats and weight loss. Doctors in the local hospital did not perform pericardiocentesis or administer any other drugs besides the anti-tuberculosis therapy. However, the symptoms remitted, and the patient's effusion decreased after the therapy.

Surgical resection remains the first-line treatment of choice. The applications and benefits of adjuvant therapy, including chemotherapy, radiotherapy, targeted therapy, and others, are debatable.

However, chemotherapy and radiotherapy have well-established postoperative roles because of the high probability of metastasis (11). If the tumor is resectable, a multidisciplinary approach with adjunctive chemotherapy and radiotherapy can offer the potential of improved survival (3, 11-25) (Table).

With regard to molecular targeted therapy, phase II trials of sorafenib (26), imatinib (27), and bevacizumab (28) for the treatment of advanced or metastatic angiosarcoma have demonstrated the efficacy of these anti-angiogenic drugs. Imatinib was not found to be an active agent against advanced sarcoma. Sorafenib exerts activity against angiosarcoma, with 3.8 and 14.9 months progression-free survival and overall survival, respectively. While sorafenib provides a better progression-free survival, the response rate is lower than those for standard cytotoxic agents. Bevacizumab is effective for angiosarcoma with 57% (13/23) patients showing a response and no progression.

The longest survival of a patient with cardiac angiosarcoma in the literature was reported by Look et al. in 2012. The patient survived for 84 months following treatment with surgery, chemotherapy, and radiotherapy. The second-longest survivor was described by Kim et al. in 2008; that patient survived for 64 months and also received multidisciplinary treatment.

Our patient could only undergo a palliative debulking resection of the primary lesion. Twenty months later, he underwent a second palliative surgery to excise the metastatic

Table. Literature Review of Cardiac Angiosarcoma: Treatment Modality and Survival

Treatment	Reference	Published Year	n	Age (Years)	Survival (Months)
Surgical resection alone	3	2012	1	31	5+
	12	2013	1	80	11
	13	2010	1	41	6
	14	2009	1	56	6
	15	2009	1	NR	0.5
Chemotherapy alone	12	2013	2	35-38	7-17
	16	2012	1	43	12+
	16	2012	1	55	12-
	17	2011	1	60	3+
	18	2007	1	29	3
Surgery plus adjuvant chemotherapy or radiotherapy or both	15	2009	8	NR	2-58
	16	2012	3	20-45	12+
	18	2007	2	31-47	13+ -16
	19	2012	11	24-53	1-84
	20	2008	10	20-61	1-64
	21	1997	1	8	53+
	22	2005	1	57	48
	23	2012	1	37	32
Chemotherapy plus molecular targeted therapy	11	2013	1	25	27+
	15	2009	1	NR	33+
	24	2012	1	31	10+
	25	2006	1	32	6+

n: number of patients, NR: not reported,

+: survive for more months, -: survive for less months

lesion involving the intestinal segment. With the combination of aggressive surgical treatment, chemotherapy, radiotherapy and targeted therapy, the patient survived for 33 months. However, two events should be noted regarding this case. Firstly, the local hospital misdiagnosed the patient with tuberculosis and administered anti-tuberculosis therapy, which did have some effect on improving his symptoms. This did allow us to discover the cardiac mass and estimate the malignancy using imaging technologies without the influence of effusion. Secondly, this is the first report describing intestinal metastasis from cardiac angiosarcoma.

The authors state that they have no Conflict of Interest (COI).

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