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Commentary: Primary cardiac sarcoma—Systemic disease requires systemic therapy

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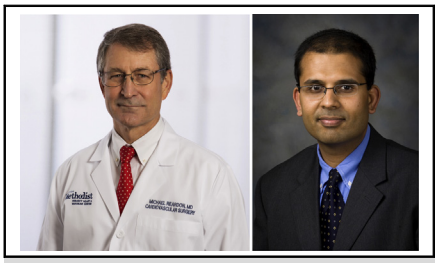

Michael J. Reardon, MD (*left*) and Vinod Ravi, MD (*right*)

CENTRAL MESSAGE

Primary cardiac sarcoma is a rare and deadly disease. Surgical resection for appropriate tumors is first-line therapy. Adjuvant chemotherapy increases survival in this usually systemic disease.

In this issue of the Journal, Hendriksen and colleagues[1] take on the difficult task of examining a rare and deadly malignant disease regarding which there is little treatment consensus or consistency, primary cardiac sarcoma, and attempt to delineate the outcomes of postsurgical adjuvant chemotherapy. Few surgeons and few institutions will have more than a few primary cardiac sarcoma cases, even over expanses as long as decades. The rarity and aggressiveness of primary cardiac sarcoma has often led to a nihilistic approach and infrequent programmatic development of treatment algorithms. Hendriksen and colleagues[1] added considerably to our knowledge base by using the National Cancer Database to identify patients with primary cardiac sarcoma between 2004 and 2015. The study identified 617 patients who were stratified by treatment (surgical, nonsurgical, and none), and treatment was analyzed by stage.

Not surprisingly to those of us who deal in this area, only 24% were identified with early-stage disease. Surgical resection was used in 372 (60.3%), 150 (24.3%) had nonsurgical management (chemotherapy, radiation, or chemoradiation), and 95 (15.4%) received no treatment at all. Surgery alone had a 30-day mortality of 14% whereas the mortality for surgical patients who received adjuvant chemotherapy was 3%. This represents a selection bias, because chemotherapy is only started in patients with a performance status allowing them to tolerate treatment and is often initiated at 4 weeks or more after surgery. At 90 days the mortalities were 26% and 8%, respectively, in these 2 groups.

These results can be difficult to interpret, because postoperative chemotherapy was more common in patients with stage IV and metastatic disease, as well as those with positive margins, all of whom would be expected to have a shorter survival, whereas surgery alone may be chosen because of a negative margin resection or for a patient who never recovered enough from surgery to tolerate systemic therapy. Without a measure of performance status, and in the absence of consistent treatment guidelines, this is difficult to determine. The other interesting and concerning finding in this large patient study was that more surgical patients had positive margins than had negative margins. Primary cardiac sarcoma is an infiltrative disease in an organ in which wide margins are not usually available for resection, and many if not most patients have metastatic systemic disease at presentation. Knowing all of this, how should we approach this difficult disease?

Well over a decade ago, we formed a combined multidisciplinary, multi-institutional cardiac tumor team at the Houston Methodist Hospital and MD Anderson Cancer Center to combine experience in complex cardiac surgery with experienced sarcoma oncology. We have a monthly formal cardiac tumor board meeting of this multidisciplinary group, which is also carried by internet to consult with other institutions. We have also instituted an institutional review board protocol for treating and following these cases. With this programmatic approach, we have established a more consistent approach to the treatment of primary cardiac sarcoma, allowing us to study our results in an organized fashion. Our last publication of our overall primary cardiac sarcoma experience had 95 cases of surgical resection.[2] A current query of our database shows that the number has now risen to 206 surgical cases. This experience has led us to believe that primary cardiac sarcoma, especially cardiac angiosarcoma, should be considered a systemic disease when first seen.

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Our current approach is to obtain a tissue diagnosis for all right-sided tumors thought to be malignant and as many left-sided tumors as reasonable (often from metastatic sites). If these are found to be primary cardiac sarcoma, we begin systemic treatment with doxorubicin-ifosfamide combination chemotherapy. Patients are followed up closely with functional (positron emission tomography and computed tomography) and structural (cardiac magnet resonance imaging) imaging every 2 cycles (6 weeks), and treatment is continued as long as the tumor continues to respond or until the patient is no longer tolerating chemotherapy. Most commonly, patients reach maximal response and early signs of significant toxicity by 6 cycles of chemotherapy. Our early worry that chemotherapy to this extent might increase surgical risks was found not to be true, and in addition this practice doubled our negative margin rate at surgery as well as our survival.[3] Surgical resection is considered only after review by the multidisciplinary cardiac tumor review board.

The goal of surgery is complete resection, with negative margins and maintenance of good cardiac function. Advanced surgical techniques such as cardiac autotransplanation are often needed to achieve this goal, making referral to a reference center for this disease desirable.[4] Even in patients with negative margins, we consider this a systemic disease and recommend adjuvant chemotherapy because of the high rates of metastatic disease. This practice was previously seen to be beneficial by Putnam and colleagues,[5] and it is encouraging to see that Hendriksen and colleagues[1] found the same outcome. We generally do not use radiotherapy unless we have local tumor issues outside the heart or we have decided that further cardiac resection is not possible.

We congratulate Hendriksen and colleagues[1] on an excellent study and thank them for their addition to our current knowledge. Our patients will benefit from this, as will our field.

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Commentary: Adjuvant therapy for cardiac sarcomas: Slowly evolving beyond resection

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Cardiac sarcomas are rare neoplasms with limited survival. Initial presentation can range from nondescript to life-threatening symptoms. Complete resection is

CENTRAL MESSAGE

Survival following resection for cardiac sarcoma may be improved with adjuvant therapy for up to 2 years compared with no adjuvant therapy or other nonsurgical care.

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