An unusual case of spinal column metastasis after orthotopic transplantation for cardiac sarcoma

Case report

GREGORY S. MCLoughlin, M.D.,1 DANIEL M. SChiubba, M.D.,2 S. KAIser Ali, M.B.B.S.,4 JUSTIN G. WEinkauf, M.D., F.R.C.P.C.,3 AND DARYL R. FOURney, M.D., F.R.C.S.C.1

1Division of Neurosurgery, University of Saskatchewan, and 4Saskatoon Cancer Centre, Saskatoon, Saskatchewan; 1Department of Medicine, University of Alberta, Edmonton, Alberta, Canada; and 2Department of Neurosurgery, Johns Hopkins University, Baltimore, Maryland

The authors describe a patient who underwent orthotopic cardiac transplantation after an undifferentiated cardiac sarcoma was diagnosed. While receiving immunosuppressive therapy, the patient developed spinal column metastases and cauda equina syndrome requiring surgical decompression and stabilization. This occurred despite an exhaustive search for metastatic disease prior to the transplantation. To the authors’ knowledge, this represents the first reported case of an undifferentiated cardiac sarcoma metastasis to the spine.

This previously healthy 18-year-old woman presented with a myocardial infarction. Investigations revealed a left atrial tumor, which was resected. Following local recurrence, the patient underwent extensive studies to rule out systemic disease. Orthotopic heart–lung transplantation was then performed. While receiving postoperative immunosuppressive therapy the patient presented with cauda equina syndrome secondary to metastatic tumor compression at the L-5 level.

Despite a comprehensive screening process to exclude metastatic disease prior to transplantation, spinal metastases occurred while this patient was receiving immunosuppressive therapy. This represents a previously unreported and clinically significant complication for undifferentiated cardiac sarcoma. (DOI: 10.3171.SPI.2008.9.10.377)

Key Words • cardiac sarcoma • metastasis • spine • transplantation

Primary cardiac sarcomas are rare, aggressive neoplasms that have a notoriously poor prognosis.6,8,21,28 Optimal treatment consists of wide resection and chemotherapy, which has prolonged survival.19,20 Recently, cardiac autotransplantation has been associated with improved outcomes.22–24 Orthotopic cardiac transplantation has been used to treat both benign and malignant tumors, although the usefulness of this procedure in patients with malignant tumors is debated. Reports of systemic disease following immunosuppressive therapy raises the concern that viable tumor cells proliferate in this environment.7,11,29 This has not been proven, however, and cases of prolonged, disease-free survival following transplantation exist.17

The authors present the case of a patient in whom an undifferentiated cardiac sarcoma was diagnosed and who underwent orthotopic cardiac transplantation after systemic disease was excluded. Postoperatively, while receiving immunosuppressive therapy, the patient presented with cauda equina syndrome secondary to metastatic spine disease. To our knowledge, this represents the first reported case of an undifferentiated cardiac sarcoma metastasizing to the spine.

Case Report

History and Examination. This previously healthy 18-year-old woman presented to the emergency department following an acute episode of chest discomfort and palpitations. An electrocardiogram and cardiac enzyme assays were performed, revealing she had suffered a posterolateral myocardial infarction. Transthoracic and transesophageal echocardiograms identified a lesion within the posterior left atrium, extending laterally to the right pulmonary vein. A second, separate lesion was found to lie within the atrial septum. Of concern, the mitral valve leaflets were involved and particles of free-floating material were visualized within the left ventricle.
Operation. The patient was medically stabilized and taken to the operating room for resection of the tumor. At operation, a left atrial wall mass measuring 3.2 × 2.3 × 1.8 cm was resected. The mitral valve was extensively involved with tumor, precluding the placement of an artificial valve. Invasion of the right upper and lower pulmonary veins similarly limited the amount of tumor that could be removed. Histopathological analysis of the tissue confirmed the tumor as a high-grade cardiac sarcoma. Chemotherapy was implemented, consisting of 4 cycles of ifosfamide, carboplatin, and etoposide. Unfortunately, local recurrence occurred within a month of surgery, and given her young age, consideration was given to a heart–lung transplant.

Because metastasis contraindicates transplantation at our institutions, the patient underwent an extensive screening process. A lumbar spine MR imaging study was significant for heterogeneous marrow signal changes of the L-3 and L-5 VBs. These regions also showed enhancement after administration of Gd contrast (Fig. 1). These findings implicated possible metastatic disease or incidental vertebral hemangiomas. The bone scan was negative. A PET scan demonstrated some increased uptake, but only within the L-3 VB.

The patient underwent a total of 3 separate spinal biopsy procedures. Initially, a radiologist performed a CT-guided biopsy of the L-3 VB. The specimen was thought to be inadequate on pathological examination, and therefore a spine surgeon performed an open biopsy of L-3. A subsequent transpedicular trocar biopsy of L-5 was also performed by another surgeon. All histopathological results were negative for malignancy. Although the MR imaging signal changes at the L-3 and L-5 levels persisted, the patient remained asymptomatic and the neuroimaging findings did not change for 1 year after the biopsies. Follow-up bone scans also remained negative. Therefore, a heart–lung transplant proceeded, with the patient making a good recovery. The postoperative immune suppression regimen consisted of tacrolimus initially and then sirolimus.

Histopathological Analysis. The explanted cardiac tumor measured 6 × 3.5 × 1.1 cm. The lungs and hilar lymph nodes did not harbor evidence of malignancy. Microscopically, the tumor was cellular and exhibited nuclear pleomorphism, hyperchromasia, and frequent mitotic figures. Spindle-shaped cells predominated, with oval, multinucleated cells interspersed (Fig. 2). Immunocytochemical evaluation demonstrated strong immunopositivity for vimentin and immunonegativity for myosin, desmin, and smooth-actin myosin. The histopathological diagnosis was again consistent with an undifferentiated pleomorphic cardiac sarcoma.

Postoperative Course. Several months after transplantation, the patient began experiencing low-back pain.

![Fig. 1. Sagittal T1-weighted (A) and T2-weighted (B) MR images demonstrating the heterogeneous signal changes within the VBs of L-3 and L-5. Postcontrast sagittal (C) and axial (D) T1-weighted images (L-5 spinal level) demonstrating enhancement of these regions.](image-url)
This was associated with occasional episodes of transient weakness of the lower extremities. An MR imaging study revealed that the signal change at L-5 had been replaced by an extradural tumor involving the VB and right pedicle. Interestingly, the signal change at L-3 remained unchanged. The PET images now demonstrated prominent uptake within the L-5 VB. Additional investigations revealed sacral and hepatic lesions, and analysis of biopsy samples proved these to be metastatic cardiac sarcoma.

**Second Operation and Outcome.** The patient was referred for palliative radiation therapy. In the interim, however, she developed an acute onset of bilateral foot drop, loss of the left ankle reflex, and diminished sensation throughout the L5–S1 distribution. Bowel and bladder function were preserved. An emergency MR image demonstrated complete replacement of the VB and right pedicle with tumor, loss of VB height, and anterior epidural compression resulting in complete canal block (Fig. 3). Cauda equina syndrome secondary to epidural tumor compression was diagnosed. The patient was taken to the operating room for emergency L4–5 laminectomy and epidural decompression, L4–S1 posterolateral instrumented fusion with pedicle screws, and L-5 bipedicular vertebroplasty. The histopathological analysis of the resected L-5 tumor was consistent with the primary cardiac tumor.

Following surgery the patient’s neurological status improved. She retained her ability to walk, and continued to progress with physiotherapy. Unfortunately, several weeks after surgery and despite an initially encouraging recovery, the patient died.

**Discussion**

Primary cardiac tumors are rare, occurring with an estimated incidence of 0.0017–0.0028%. Although benign myxomas comprise the majority of these neoplasms, 25% are malignant, with a clear predilection toward sarcoma. Undifferentiated sarcomas, which comprise the majority of the sarcoma variants, are unique in that they lack a clear tissue lineage and do not demonstrate a histological and immunohistochemical profile.
Independent of histological type, however, cardiac sarcomas have a uniformly poor prognosis, with mean survival times ranging between 9 and 16.5 months.\(^{6,8,20}\)

Wide excision combined with chemotherapy is the preferred treatment for cardiac sarcomas.\(^{4}\) Margin-free resections have been demonstrated to improve survival by up to 50%.\(^{19,20}\) Recently, cardiac autotransplantation has been used successfully to facilitate resection.\(^{22-24}\) In this case, the patient underwent a heart–lung transplant because the tumor involved the pulmonary veins. Less clear, however, is the role for orthotopic transplantation for unresectable tumors.\(^{10}\) In theory, this approach provides an opportunity for radical resection, which would translate into a lower incidence of systemic recurrence.\(^{31}\) However, this is often not the case. Metastases in the setting of immunosuppression have been reported, in some cases when systemic disease had been excluded prior to the transplant.\(^{7,21,29}\)

To our knowledge, this represents the first case of an undifferentiated cardiac sarcoma metastasizing to the spinal column and producing cauda equina syndrome. This occurred following an exhaustive search for metastatic disease prior to the transplantation, including 3 separate biopsy procedures and ongoing use of the most advanced imaging technologies available. In this case, the possibility remains that immunosuppression led to the proliferation of an otherwise clinically and radiographically silent disease. The fact that no single diagnostic test has 100% sensitivity and specificity for detecting spinal column metastases is important, because most authors believe that progression to transplantation should be done only when systemic disease has been excluded. Magnetic resonance imaging, in particular short tau inversion recovery images, is reported to be the most sensitive modality for spinal column metastases. For this purpose, MR imaging has a sensitivity and specificity of 93% and 97%, respectively.\(^{30}\) Bone scintigraphy is less sensitive than MR imaging, especially if there is a lack of cortical bone involvement.\(^{30}\) The modality \(^{18}F\) fluorodeoxyglucose–PET has recently been used for metastatic spine disease, with reports of sensitivity of up to 98%.\(^{16}\) With respect to biopsy procedures, a CT-guided needle biopsy has a diagnostic accuracy of 71–89%, whereas a transpedicular trocar biopsy has an accuracy rate of 92%.\(^{2,12,14}\) Despite the fact that this patient underwent all of these procedures on numerous occasions, in this case a definitive diagnosis of metastatic disease eluded investigators.

Systemic disease in patients with cardiac sarcoma is not uncommon. Although metastases are more frequent with sarcoma variants localized to the left side of the heart, all types are capable of metastasizing, and they represent an important factor in the patient mortality rate.\(^{4,9,13,18}\) Metastatic disease of the spinal column is distinctly uncommon, however, especially for an undifferentiated sarcoma.\(^{12}\) A high degree of clinical suspicion is required to diagnosis this condition because patients may report only nonspecific back pain; subtle neurological deficits may be present on examination or occur in a delayed fashion as the tumor gradually compresses the spinal cord or nerve roots.\(^{3,26,27,32}\) It is important to differentiate between spinal cord involvement and cerebral lesions, because intracra-

nial metastases are fairly common with cardiac sarcomas.\(^{25}\)

The multidisciplinary team involved in caring for these patients should recognize that metastases may occur after transplantation despite negative results on pre-transplantation screening studies. Reports of back pain should prompt a thorough clinical and radiographic assessment to rule out spinal column metastases. Although cerebral metastases are well documented in patients with cardiac sarcoma, it should be recognized that neurological deficits may be precipitated by spinal cord compression. This may allow for timely intervention to minimize neurological morbidity.

**Conclusions**

The role of orthotopic transplantation for cardiac sarcoma has yet to be defined. Although this procedure allows for radical resection, it remains unclear how post-transplantation immunosuppressive therapy relates to the development of systemic disease. This case provides an example of rare spinal metastases following transplantation in a patient receiving immunosuppressant therapy.

**Disclaimer**

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

**References**

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