Malignant Extrarenal Rhabdoid Tumor of the Heart in an Infant: Case Report and Literature Review

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Abstract

Malignant extrarenal rhabdoid tumors (MERT) are aggressive malignancies of infancy with dismal prognosis; cardiac localization is extremely rare. A 5-month-old male was diagnosed with a cardiac MERT after finding a large heterogenous mass attached to the left ventricular wall. He responded well to initial intensive chemotherapy but developed tumor progression 4 months after diagnosis. Palliative treatment with ipilimumab and nivolumab was administered; however, he died within one week. New treatment options are essential to improve survival in patients where complete tumor resection is unattainable.

Introduction

Initially described as a "rhabdomyosarcomatoid" variant of Wilms tumor because of the resemblance of its cells to rhabdomyoblasts, malignant extracranial rhabdoid tumor is a rare, highly aggressive malignancy of early childhood with a poor prognosis[1-2]. It is most common in the kidney, comprising 1.6% of pediatric renal tumors. Malignant extrarenal rhabdoid tumors (MERT) can occur at any site; cardiac localization is rare[3], with only three cases reported in the literature[4-5]. Regardless of location, these tumors frequently contain alterations in chromosome 22q11.2 in the*hSNF5/INI1/SMARCB1* gene.

Treatment with chemotherapy derives from high-risk protocols from the National Wilm's Tumor Study (NWTS) and the European Pediatric Soft Tissue Sarcoma Study Group (EpSSG NRSTS 2005). The NWTS reported an overall survival (OS) of 15.9% for patents with high grade tumors[6]. The EpSSG prospectively studied 100 patients with malignant rhabdoid tumor and reported OS of 38% at 3 years utilizing courses of vincristine, doxorubicin, and cyclophosphamide alternating with cyclophosphamide, carboplatin and etoposide[7]. Metastases, less than 2 years of age, no radiotherapy, and tumor unresectability were associated with poorer prognosis[8-9]. Retrospective review of German and Chinese registries studies have shown similar poor prognoses[10-11]. Here, we present the case of a 5-month-old male diagnosed with cardiac MERT as well as a review of the current literature.

Case Report

A 5-month-old African-American male presented with respiratory distress for two days. Evaluation included an echocardiogram which showed a pericardial effusion with tamponade and hypertrophic cardiomyopathy. Infectious workup was positive for non-COVID19 Coronavirus. Two days later, rapid clinical deterioration prompted re-intubation and transfer to our facility. Arrival was complicated by cardiac arrest. A repeat echocardiogram showed pericardial effusion requiring pericardiocentesis and a large heterogeneous mass. The mass was further characterized by cardiac MRI (Figure 1A) which showed a heterogeneously enhancing mass in the left ventricle and interventricular septum, extending outward through pericardium and infiltrating into the superior mediastinum, encasing the great vessels.

The patient underwent a median sternotomy (Figure 2A) for an excisional biopsy of the tumor. Pathology report confirmed the diagnosis of extrarenal malignant rhabdoid tumor: *INI-1* showed diffuse loss of nuclear positivity (Figure 2B, C). Due to the complexity of the mass and the degree of infiltration into the myocardium, his tumor was deemed unresectable. In the post-operative period, he experienced bradycardic spells with ST segment changes on telemetry requiring cardiac pacing.

Treatment following Children's Oncology Group Protocol AREN0321, Regimen UH-1 was initiated[12]. Due to cardiac dysfunction, the anthracycline-containing first cycle of the protocol was omitted. He received carboplatin, cyclophosphamide, and etoposide. Following this cycle, the pericardial and pleural effusions resolved and the cardiac pacemaker was removed. Follow up chest MRI after 2 cycles per UH-1 showed no change in size of the tumor.

The patient's case was presented at the National Rare Tumor Board sponsored by Texas Children's Hospital. Based on their recommendations, it was decided to intensify his chemotherapy regimen, using an individualized rhabdoid tumor protocol consisting of vincristine (0.067 mg/kg/dose) on day 1, high-dose cyclophosphamide (40 mg/kg/dose) on days 1 and 2, and doxorubicin (1.25 mg/kg/dose) with dexrazoxane (12.5 mg/kg/dose). After three cycles of this regimen, there was 75% reduction in tumor size (Figure 1B).

One month later an echocardiogram resulted with a large complex fluid collection along the inferior heart border with external compression of the left ventricular cavity and the right ventricular outflow tract (ROVT), as well as worsening mitral regurgitation. A chest CT confirmed the presence of a cystic and solid soft tissue mass throughout the mediastinum and pericardium (Figure 1C) requiring placement of a drainage catheter to treat ROVT obstruction. Biopsy by was performed for identification of possible targeted therapies; genomic studies confirmed loss of *SMARCB1* but no other targetable lesions.

A Developmental Therapeutics consult was placed to the team at the University of Alabama Birmingham. Despite being accepted for enrollment he presented two weeks later with respiratory distress due to a large left pleural effusion with rightward shift of mediastinum requiring drainage, which deemed him ineligible. He was treated with palliative immunotherapy: one dose each of ipilimumab (1 mg/kg) and nivolumab (3 mg/kg). However, he continued to deteriorate clinically. The extremely poor prognosis and lack of curative treatment options were explained to the family. He was discharged home on hospice care and died at home a week later.

Discussion

Cardiac MERT is rare and has a dismal prognosis. Absence of metastases, complete surgical resection and intensive chemotherapy are associated with improved survival in patients with extracranial rhabdoid tumor[7-9]. To date, only three patients with cardiac MERT have been reported in the literature; two of them died secondary to disease progression. The first report[4] depicts the case of a 6-month-old female that presented with pericardial effusion, and an echo-dense mass measuring 3.5 x 3.5 x 4.5 cm, later diagnosed with rhabdoid tumor of the heart. She was treated with two courses of doxorubicin (15 mg/m^2/day) for 3 days by continuous intravenous infusion. Three weeks after her second course of doxorubicin, she developed tumor progression and died 3 months after presentation.

The second case report[5] depicts the clinical course of two patients. A 3-week-old male presented with tachypnea; cardiac ultrasound and CT imaging showed tumor in the left thoracic cavity infiltrating the left atrium extending up to the posterior mitral valve causing mitral insufficiency. Biopsy suggested rhabdomyosarcoma, and he received rhabdomyosarcoma treatment with vincristine, dactinomycin and cyclophosphamide. A reference re-evaluation of the initial tumor biopsy eventually confirmed the diagnosis of MERT. The patient experienced rapid tumor progression, dying at 12 weeks of age.

An 11-month-old boy that initially presented with acute otitis media, lethargy, focal seizures of the left arm, and a new holosystolic murmur. An echocardiogram showed an extensive intracardiac tumor within the left ventricle with mitral valve involvement, and a second tumor in the tip of the left ventricle. Histopathological evaluation confirmed the diagnosis of MERT supported by lack of *SMARCB1* expression. Both intracardiac

tumors were completely resected with tumor free margins. He received 6 cycles of chemotherapy with doxorubicin, ifosfamide, carboplatin, etoposide, vincristine, cyclophosphamide and dactinomycin, followed by high dose chemotherapy with thiotepa and carboplatin and peripheral blood stem cell rescue. He is reported to be in complete remission for 42 months after diagnosis.

Unfortunately, due to the complexity and extension of the tumor in our patient, a complete tumor excision was not possible at diagnosis or after 3 cycles of chemotherapy. Similarly, due to infiltration into the superior mediastinum, our patient was not a heart transplant candidate. The extensive infiltration of myocardium and young age in our patient, as well as family wishes precluded radiotherapy. He achieved a partial response to chemotherapy after 3 cycles of an intensified rhabdoid tumor regimen. Unfortunately, like previous cases, rapid tumor progression occurred without options for local control. This case demonstrates the dismal prognosis for those patients in which a complete tumor resection cannot be achieved. Therefore, new targeted therapies are needed to improve survival in these patients.

Conflict of Interest Statement

There are no conflicts of interest to disclose.

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Legend

FIGURE 1 Tumor evolution. (A) Cardiac T1 MRI showing a heterogeneously enhancing mass infiltrating the mediastinum, pericardium, and the myocardium at diagnosis. (B) Cardiac T1 MRI showing 75% tumor reduction after cycle 3. (C) Chest CT showing tumor progression after cycle 4.

FIGURE 2 (A) Gross appearance of tumor, cobblestone appearance of the ventricular myocardium (arrow) caused by infiltration of tumor. (B) Microscopic appearance of tumor, demonstrating 40X H&E staining and (C) 40X power demonstrating loss of INI1 staining.

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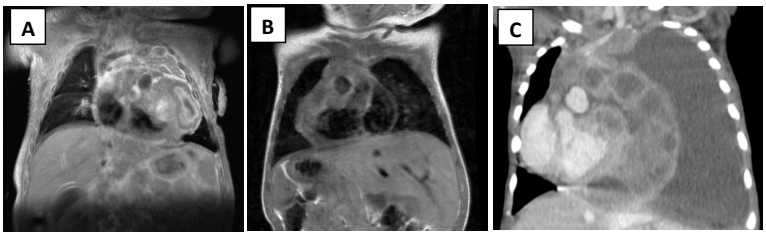

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