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Systematic Review
Cardiac Manifestation of Rosai-Dorfman Disease: A Case Report and a Systematic Review

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Abstract
Background: Rosai-Dorfman disease is a rare condition that typically presents as a nodal disease. Cardiac involvement is extremely uncommon, occurring in 0.1–0.2% of cases, which has hindered our understanding. We report a case of Rosai-Dorfman disease (RDD) related cardiac manifestation in a patient without nodal involvement. Further, we conduct a comprehensive review of the literature to consolidate data on how patients with cardiac manifestations of RDD are typically managed and treated.

Methods: A systematic review of PubMed, Web of Science, and Embase was conducted to identify cases of RDD with cardiac involvement. Out of 464 studies identified, 42 publications encompassing 43 patients met the criteria and were incorporated in this review. We gathered data on patient demographics, as well as their management and treatment approaches. Additionally, we share our own experience with a patient who presented with a cardiac mass related to RDD.

Results: Out of the 43 patients, only 20.9% (n = 9) had a documented history of RDD prior to cardiac manifestations. Nodal involvement was reported in 32.6% (n = 14), while extranodal extracardiac involvement was reported in 46.5% (n = 20). Upon presentation, the most prevalent symptoms were dyspnea (48.8%, n = 21), chest discomfort (41.9%, n = 18), and lower extremity edema (16.3%, n = 7). Cardiac manifestations were most frequently found in the right atrium (41.9%, n = 18) and pericardium (18.6%, n = 8). Treatment encompassed systemic medical therapy (34.9%, n = 15) and cardiac surgery (39.5%, n = 17). The median follow-up period was 12 months (with a range of 1 to 36), and 8 patients (18.6%) experienced mortality. Our patient, who had a cardiac mass in the left atrium, underwent resection and has remained symptom-free without any recurrence for the past 5 years. Conclusion: The frequency of cardiac related-RDD manifestations may be greater than initially perceived. These results underscore the significance of identifying RDD and its cardiac-related manifestations, facilitating timely diagnosis and treatment for affected individuals.

Keywords
Rosai-Dorfman disease; cardiac mass; myxoma; histiocytosis

Introduction
Rosai-Dorfman disease (RDD), also known as sinus histiocytosis with massive lymphadenopathy, is a rare histiocytic disorder of non-neoplastic nature [1]. First described in 1965 [2], this disease entity was characterized by Rosai and Dorfman in 1969 and 1972 [3,4], with further delineation by additional reports [5]. Rosai-Dorfman disease is a rare disease that typically presents as a nodal disease in young children. The etiology of the disease is currently unknown. Although concurrent extranodal involvement of various systems and tissues have been reported, manifestation in the cardiovascular system is extremely uncommon. Moreover, isolated extranodal involvement has been reported in only a handful of cases, limiting our understanding of this disease. We report a case of Rosai-Dorfman disease in the heart, without clinical evidence of nodal involvement. Additionally, we perform a systematic review of patients with cardiac manifestations of RDD which aims to summarize the data regarding patterns of patient presentation, management, and treatment of this patient population.

Case Presentation
With the patient’s consent, we report a case of a 46-year-old otherwise healthy female (body mass index 39.4) who presented with progressively worsening dyspnea on exertion. She otherwise denied fever, chest pain, cough, sputum, recent illness, night sweats, leg swelling, paroxysmal nocturnal dyspnea, or weight loss. Her vital signs were normal. Physical examination, including cardiovascular, respiratory, abdominal, and skin, were unremarkable.
No head and neck, suprascapular, axillary, oringuinallymphadenopathy was appreciated.

At this time, complete blood count was only significant for leucocytosis (14,080 cells/µL), anaemia (hemoglobin count of 9.7 g/dL, and hematocrit of 29.8%), andthrombocytopenia (118,000/µL). Other laboratory parameters were unremarkable. Electrocardiogram revealed sinus rhythm with first degree atrioventricular block. Transthoracicechocardiography (TTE) demonstrated a 4.0 × 3.0 × 3.0 cm mass in the left atrium (LA) prompting referral for surgical evaluation.

Preoperative transesophageal echocardiography (TEE) revealed a 6.0 × 3.4 cm mass in the left interatrial septum with projection into the LA appendage and the anterior leaflet of the mitral valve, resulting in reduced mobility of the mitral valve leaflet. TEE also revealed moderate-to-severe mitral regurgitation with no evidence of mitral stenosis and moderate dilation of the LA. The left ventricular ejection fraction was preserved at >55%. The patient was suspected to have an atrial myxoma for which shewas advised to undergo surgical resection.

After median sternotomy, central cannulation, and induction of cardiopulmonary bypass, a rightatriotomy was performed. A solid pink-to-tan mass was visualized originating from the interatrial septum and protruding bilaterally into both the atrial chambers, extending apically towards the interventricular septum for unknown length. The tip of the right atrial protrusion was in proximity to the inferior vena cava and the left atrial protrusion was riding over the anterior leaflet of the mitral valve. An intraoperative frozen section was obtained, revealing a benign neoplasm with dystrophic calcification. Although the relatively extensive process of the mass prevented a complete resection, a radical septectomy with reconstruction using bovine pericardial patch was performed. The subsequent pathology report of the excised mass revealed RDD.

Follow up TTE at 4 months revealed a normal ejection fraction without any recurrence of the LA mass. The patient has been symptom free with no evidence of recurrence for the past 5 years.

Systematic Review Method

Search Strategy

In accordance with the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) [6], three databases (PubMed, Embase, and Web of Science) were systematically searched to identify all published cases on cardiac manifestations of RDD from each database’s inception until July 30th, 2023 (Supplementary Table 3). We used the Covidence Systematic Review Software for article screening and data extraction tool for conducting systematic reviews. Search term “Rosai-Dorfman” was used interchangeably with the terms “heart”, “cardiac”, “pericardium”, “pericardial”, “epicardium”, “epicardial”, “myocardium”, “myocardial”, “atria”, “ventricle”, “cardiovascular”, or “artery”, using the Boolean operator AND. Two authors independently screened the titles and abstracts found in the initial search and extracted data. Following selection, we conducted a full text review for confirmation and data extraction.

Inclusion and Exclusion Criteria

We included all literature describing cardiac manifestations in patients with a confirmed diagnosis of RDD, whether discovered prior to or during the onset of cardiac manifestations, or through autopsy findings. Cardiac diagnostic testing, such as biopsy, was not required for inclusion. The selected publications were assessed for additional references that were not detected in the initial database.

We applied the following exclusion criteria: (1) involvement of the great vessels (e.g., aorta, pulmonary artery) or mediastinal structures, without concurrent pericardial, myocardial, and endocardial involvement, (2) lack of histopathologic diagnostic testing for RDD, (3) review articles and commentaries that did not specifically describe individual cases. Fig. 1 displays the publication selection flow diagram and type of articles included.

Data Extraction

We included all data from the available literature as defined by the publishing authors. The heterogeneity of the data in the identified studies prevented a formal analysis. As a result, we conducted descriptive analyses only.

Using a predesigned collecting table, we extracted the author, year of publication, age, comorbidities, clinical presentation, diagnostic workup, treatment, follow up, and outcome when provided. One foreign language article was translated using Google translate. Pooled data and calculations in this review are derived from studies that provide individualized data.

Results

The systematic search strategy generated 464 citations and the manual full text review resulted in three additional articles. Ultimately 42 studies, including 34 case reports and 8 case abstracts, met inclusion criteria and were extracted, representing a total of 43 patients [5,7–45].

Most patients were female (60.5%) with a median age of 51 years (range 12 to 79 years). 32.6% had nodal involvement and 46.5% had extranodal extracardiac involvement. Not all non-cardiac manifestations of RDD were clinically apparent at the time of presentation and some were detected radiographically and/or during autopsy. Due to the heterogeneity of included studies, we only report cumulative data. More granular data on patient characteristics can
At the time of presentation, 20.9% had a known history of RDD, and reported symptoms of dyspnea (48.8%), chest discomfort (41.9%), and lower extremity edema (16.3%). Most patients had an echocardiogram (65.1%), cardiac magnetic resonance imaging (cMRI) (44.2%), and chest computed tomography (CT) scan (39.5%). Diagnosis of RDD was frequently with a biopsy (60.5%) or surgical resection (27.9%) in patients without a prior biopsy or those with inconclusive findings. Overall, 35 (81.4%) out of 43 patients had confirmed RDD-related cardiac manifestations, diagnosed with biopsy, surgical resection, or autopsy. The remaining 8 (18.6%) cases underwent biopsies from alternative sources (e.g., skin, lymph node, or testicle),

be found in Supplementary Tables 1,2.

At the time of presentation, 20.9% had a known history of RDD, and reported symptoms of dyspnea (48.8%), chest discomfort (41.9%), and lower extremity edema (16.3%). Most patients had an echocardiogram (65.1%), cardiac magnetic resonance imaging (cMRI) (44.2%), and chest computed tomography (CT) scan (39.5%). Diagnosis of RDD was frequently with a biopsy (60.5%) or surgical resection (27.9%) in patients without a prior biopsy or those with inconclusive findings. Overall, 35 (81.4%) out of 43 patients had confirmed RDD-related cardiac manifestations, diagnosed with biopsy, surgical resection, or autopsy. The remaining 8 (18.6%) cases underwent biopsies from alternative sources (e.g., skin, lymph node, or testicle),
and it was assumed that their cardiac manifestations were also related to RDD. Table 1 demonstrates presentation and workup of patients with cardiac involvement in RDD.

Cardiac involvement usually involved the right atrium (RA) (41.9%) and the pericardium (18.6%), and less frequently involved other chambers in no particular pattern. Most patients were treated with systemic medial therapy (34.9%) and/or cardiac surgery (39.5%). Table 2 demonstrates characteristics of cardiac involvement, treatment, and outcomes, where reported.

**Treatment**

Of 43 cases, 8 patients were treated solely with steroids. When follow-up data was provided, 3 out of 8 of these patients died, 3 developed partial/complete resolution of symptoms, and 1 developed minimal worsening of symptoms. Four patients received chemotherapy in addition to steroids. However, follow-up data is only reported for 2 patients who continued to suffer from progressive disease. One of these patients required surgical resection at the 1-year. Two patients received immunotherapy in addition to steroids. One of them required debulking at 2 months due to progressive disease, while the other showed symptom improvement at 6 months. One patient exclusively received immunotherapy but required debulking and pericardiocentesis due to extensive disease with resolution of symptoms at the 2-year follow-up.

Out of 14 patients who underwent surgical resection of their cardiac mass, only 7 provided interval follow-up outcomes, ranging from 1 to 18 months (median 5 months), none of whom experienced recurrent cardiac manifestations. One patient who underwent heart transplant had no recurrent symptoms at 18 months. Overall, there was an 18.6% mortality rate in this patient cohort. Information regarding individual cases and treatment is detailed in Supplementary Table 2.

**Discussion**

RDD is a rare histiocytic disorder that is largely considered idiopathic, with a prevalence of 1:200,000 [46]. The most common variant of RDD is sporadic in nature (e.g., nodal, extranodal, neoplasia-associated, and autoimmune-associated), while less common forms include familial (e.g., H syndrome and autoimmune lymphoproliferative syndrome) and cutaneous [47]. Roughly 30–50% [48] of sporadic cases have lymph node involvement and up to 40% can have extranodal manifestations [49]. Generally, extranodal disease coincides with lymphadenopathy and can involve virtually all organ systems [49] with skin (10–50%), lung (10–20%), and bone (5–15%) being the most frequently affected [47,48,50]. In up to 23% [51] of instances, the initial disease manifestation of the disease solely involves extranodal symptoms, which is linked to a more aggressive course [49,52,53].

Cardiac manifestations of RDD are exceedingly rare, occurring in 0.1–0.2% of cases [54]. In the absence of extracardiac disease, RDD can be extremely difficult to diagnose. Our systematic search identified 43 patients with cardiac manifestations of RDD, most of whom presented with heart failure symptoms. Our patient’s only presenting symptom was dyspnea and her LA mass was initially misdiagnosed as a myxoma, which is a common occurrence in these patients. A retrospective study (n = 38) utilizing position emission tomography-CT (PET-CT) in patients with RDD found cardiac involvement in 13.2% [55], suggesting that cardiac-related RDD manifestations may be more prevalent than previously understood—although not all instances may result in noticeable symptoms. These findings highlight the importance of recognizing RDD and cardiac-related manifestations.

**Clinical Presentation**

RDD typically presents in children or young adults, with an average age 20.6 years, primarily among individuals of African American descent [46]. While RDD is generally more prevalent in males, cutaneous manifestations are most common in females [46]. The classic presentation of nodal RDD includes massive painless lymphadenopathy (cervical or generalized), fever, night sweats, and weight loss [47]. In cases of lymphomas or malignancies, constitutional symptoms can also arise. Therefore, in the absence of lymphadenopathy and/or extranodal disease, diagnosing RDD with cardiac involvement can be challenging.

Specifically in patients presenting with cardiac involvement, classical RDD symptoms were rarely present. Therefore, a high index of suspicion and histologic confirmation is required in patients presenting with heart failure symptoms and evidence of intracardiac mass.

The dominant cardiac manifestation of RDD is an intracardiac mass with or without underlying infiltration. Intracardiac masses frequently present with multifocal cardiac involvement, mainly arising from the RA (41.9%), but LA involvement is uncommon (7.0%). Intracardiac RDD is associated with hemodynamic implications such as flow obstruction as well as conduction abnormalities (e.g., AVB and electrical storm). A minority of the patients in this cohort required a permanent pacemaker placement (9.3%) or electrical cardioversion (4.7%). Pericardial involvement is also common (18.6%), which frequently manifests as pericardial effusion with or without cardiac tamponade.

**Diagnosis**

Given its rarity, RDD is often undiagnosed during its early stages, which may be partially responsible for frequent diagnosis of RDD in late-adulthood, even though the majority of RDD emerge during childhood [56]. Cardiac
Table 1. Presentation, and management of patients with Rosai-Dorfman disease-related cardiac manifestations (N = 43).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, Years</td>
<td>51 (12–79)</td>
</tr>
<tr>
<td>Female</td>
<td>26 (60.5)</td>
</tr>
<tr>
<td>Known History of RDD</td>
<td>9 (20.9)</td>
</tr>
<tr>
<td>Nodal Involvement</td>
<td>14 (32.6)</td>
</tr>
<tr>
<td>Extranodal Extracardiac Involvement*</td>
<td>20 (46.5)</td>
</tr>
<tr>
<td>Skin</td>
<td>7 (35.0)</td>
</tr>
<tr>
<td>Kidney</td>
<td>7 (35.0)</td>
</tr>
<tr>
<td>Bone</td>
<td>6 (30.0)</td>
</tr>
<tr>
<td>Orbital</td>
<td>5 (25.0)</td>
</tr>
<tr>
<td>Lung</td>
<td>4 (20.0)</td>
</tr>
<tr>
<td>Presenting Symptom*</td>
<td></td>
</tr>
<tr>
<td>Dyspnea</td>
<td>21 (48.8)</td>
</tr>
<tr>
<td>Chest discomfort</td>
<td>18 (41.9)</td>
</tr>
<tr>
<td>Lower Extremity Edema</td>
<td>7 (16.3)</td>
</tr>
<tr>
<td>Arrhythmia/Palpitations</td>
<td>5 (11.6)</td>
</tr>
<tr>
<td>Dizziness/Presyncope</td>
<td>3 (7.0)</td>
</tr>
<tr>
<td>Initial Workup</td>
<td></td>
</tr>
<tr>
<td>Echocardiogram</td>
<td>28 (65.1)</td>
</tr>
<tr>
<td>Cardiac MRI</td>
<td>19 (44.2)</td>
</tr>
<tr>
<td>Chest CT scan</td>
<td>17 (39.5)</td>
</tr>
<tr>
<td>Electrocardiogram</td>
<td>16 (37.2)</td>
</tr>
<tr>
<td>Chest X-Ray</td>
<td>9 (20.9)</td>
</tr>
<tr>
<td>PET-CT scan</td>
<td>9 (20.9)</td>
</tr>
<tr>
<td>Diagnostic Workup</td>
<td></td>
</tr>
<tr>
<td>Biopsy†</td>
<td>26 (60.5)</td>
</tr>
<tr>
<td>Myocardial/Pericardial</td>
<td>14 (53.8)</td>
</tr>
<tr>
<td>Lymph Node</td>
<td>5 (19.2)</td>
</tr>
<tr>
<td>Skin</td>
<td>4 (15.3)</td>
</tr>
<tr>
<td>Other (adrenal, parotid, pleural)</td>
<td>3 (11.5)</td>
</tr>
<tr>
<td>Pericardiocentesis</td>
<td>2 (4.7)</td>
</tr>
<tr>
<td>Surgical Resection</td>
<td>12 (27.9)</td>
</tr>
<tr>
<td>Autopsy** (in patients without a prior RDD diagnosis)</td>
<td>3 (7.0)</td>
</tr>
</tbody>
</table>

Values are presented as n (%) or median (range). *Indicates five most common variables reported are demonstrated in the table. †Excludes diagnostic studies with inconclusive results. Several cases underwent biopsies from multiple areas, detailed in Supplementary Table 2. **Only includes those without prior conclusive diagnostic studies. CT, Computed tomography; RDD, Rosai-Dorfman Disease; MRI, Magnetic resonance imaging; PET-CT, Positron emission tomography computer tomography.

manifestations of RDD most often trigger an investigation into progressing symptoms. Where reported, electrocardiogram (ECG) often revealed a heart block or arrhythmia. Chest X-rays were often non-specific, demonstrating pericardial/pleural effusion or cardiomegaly in some cases. Chest CT often detected an intracardiac mass, prompting additional assessment through echocardiography, cMRI and/or PET-CT scans [56].

When encountering a patient with a cardiac tumor, the range of potential diagnoses is extensive. This is due to the fact that over 99% of cardiac tumors are secondary, with many attributed to metastatic disease (e.g., breast, lung, melanoma), particularly for right-sided tumors [57,58]. In contrast, primary cardiac tumors are rare, and almost 90% of them are benign—with approximately 80% being myxomas—and the remaining 10% are malignant, of which 95% are sarcomas and 5% are lymphomas/mesotheliomas [58].

In patients with RDD, echocardiography and cMRI features often resemble those of malignant primary tumors, attributed to local invasion into surrounding structures, location in the RA, involvement of the pericardium, and a lack of a stalk, which distinguishes it from myxomas [58]. Nevertheless, in cases where the tumor originates from the LA
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Table 2. Characteristic and treatment of Rosai-Dorfman disease-related cardiac manifestations (N = 43).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Size of Intracardiac Mass, cm*</td>
<td>2.9 (0.8–9.0)</td>
</tr>
<tr>
<td>Cardiac Involvement†</td>
<td></td>
</tr>
<tr>
<td>Right Atrium</td>
<td>18 (41.9)</td>
</tr>
<tr>
<td>Interal atrial septum</td>
<td>4 (9.3)</td>
</tr>
<tr>
<td>Interventricular septum</td>
<td>3 (7.0)</td>
</tr>
<tr>
<td>Left Atrium</td>
<td>3 (7.0)</td>
</tr>
<tr>
<td>Left Ventricle</td>
<td>3 (7.0)</td>
</tr>
<tr>
<td>Right Ventricle</td>
<td>3 (7.0)</td>
</tr>
<tr>
<td>Pericardium</td>
<td>8 (18.6)</td>
</tr>
<tr>
<td>Epicardium</td>
<td>4 (9.3)</td>
</tr>
<tr>
<td>Myocardium</td>
<td>3 (7.0)</td>
</tr>
<tr>
<td>Treatment</td>
<td></td>
</tr>
<tr>
<td>Systemic Medical Therapy</td>
<td>15 (34.9)</td>
</tr>
<tr>
<td>Steroids</td>
<td>8 (53.3)</td>
</tr>
<tr>
<td>Steroids + Chemotherapy</td>
<td>4 (26.7)</td>
</tr>
<tr>
<td>Steroids + Immunotherapy</td>
<td>2 (13.3)</td>
</tr>
<tr>
<td>Immunotherapy</td>
<td>1 (6.7)</td>
</tr>
<tr>
<td>Cardiac Surgery</td>
<td>17 (39.5)</td>
</tr>
<tr>
<td>Resection</td>
<td>14 (82.4)</td>
</tr>
<tr>
<td>Debulking</td>
<td>2 (11.8)</td>
</tr>
<tr>
<td>Transplant</td>
<td>1 (5.9)</td>
</tr>
<tr>
<td>Permanent Pacemaker Placement</td>
<td>4 (9.3)</td>
</tr>
<tr>
<td>Electrical Cardioversion</td>
<td>2 (4.7)</td>
</tr>
<tr>
<td>Follow Up, Months**</td>
<td>12 (1–36)</td>
</tr>
<tr>
<td>Mortality</td>
<td>8 (18.6)</td>
</tr>
</tbody>
</table>

Values are presented as n (%) or median (range). *Size reported by n = 21 studies; †Only the major site of cardiac involvement is included, unless the patient had two or more separate nodules. **Follow-up interval was reported by n = 22 studies.

and does not infiltrate the surrounding tissue—as seen in our case—the tumor can be easily misdiagnosed as a myxoma. PET-CT scan in RDD is typically characterized by avid fluodeoxyglucose-18 (FDG) uptake, likely due to underlying inflammatory process. While PET-CT cannot provide useful information concerning the intracardiac mass, it can rule out metastatic disease and identify a suitable biopsy site, which may be especially valuable for patients for those whom cardiac biopsy is not safe [10,55].

A definitive diagnosis is accomplished through histological assessment and identification of emperipolesis—histiocytes containing intact lymphocytes within their cytoplasm [38]. However, the lesion often appears as a non-specific fibroinflammatory lesion, and emperipolesis can be quite subtle, especially in cases of extranodal RDD [55]. This scenario expands the range of potential differential diagnoses to encompass inflammatory pseudotumor, fibrohistiocytic tumor, non-specific chronic inflammation, and even histiocytic sarcoma in cases displaying atypia [49,52]. This often necessitates multiple biopsies to confirm RDD.

When dealing with nodal histiocytic proliferation, the list of differential diagnoses is also extensive, including sinus histiocytosis, Langerhans cell histiocytosis, infectious disorders, and lymphoproliferative disorders [59].

Immunohistochemical staining plays a critical role in distinguishing RDD. Histiocytes in RDD are positive for S100, CD68, and CD163 and negative for CD1a and CD207 [47]. RDD also shares certain morphological features with IgG4-related disease, and it often displayed elevated IgG4 to IgG ratios at both nodal and extranodal sites [47]. Current guidelines recommend incorporating immunohistochemistry for IgG4, especially when numerous plasma-cells are present. Flow Cytometry and cytogenetic testing are used to rule out lymphoproliferative disorder, but their utility in the diagnosis of RDD remains limited [38,46].

**Management**

The progression of RDD is often unpredictable, marked by episodes of worsening symptoms followed by periods of improvement lasting several years. RDD is often linked to a favorable prognosis, and it can resolve spontaneously in up to 50% of patients with asymptomatic RDD and/or uncomplicated adenopathy [46]. On the other hand, extranodal involvement has a poor prognosis and is fatal in approximately 7–12% of patients due to dysfunction or failure of involved vital organs [46]. Given the diverse array of ways RDD can manifest and unclear underlying etiology, there is no standardized approach to managing patients with RDD.

The approach to treatment varies depending on the extent of RDD, the affected site(s), and the presenting symptoms, necessitating an individualized approach [60]. For cases involving RDD-related cardiac manifestations, the primary approach to managing intracardiac masses and their associated symptoms is surgical resection or debulking. When reported, patients who underwent surgical resection did not experience disease progression during follow-up periods ranging from 1 to 18 months.

In patients with symptomatic RDD, multifocal extranodal disease, and nonresectable cardiac tumors, systemic treatment is required. In patients without RDD-related cardiac manifestations, corticosteroids have demonstrated favorable responses, but the optimal duration of treatment remains unclear [46]. In our cohort, 8 (18.6%) were treated solely with steroids, most of which had extensive multiorgan involvement. Three out of these 8 cases died, and the remaining cases displayed minimal disease progression or had partial/complete resolution of their symptoms. In the literature, corticosteroid therapy has been associated with frequent relapse in patients with extranodal RDD [46]. This dynamic is less clear in the context of cardiac-related RDD.

Even when steroids were used in conjunction chemotherapy (n = 4) or immunotherapy (n = 2), 2 pa-
tients required subsequent surgical intervention due to progressive disease. In patients with RDD, in the absence of cardiac manifestations, chemotherapy outcomes have been inconsistent and are typically reserved for cases that are recurrent or unresponsive to other treatments, or as an initial strategy in cases of multifocal and life-threatening disease [46]. Radiotherapy was administered in a single case and is generally reserved as a last resort for providing palliative relief.

While the available data is limited for making definitive recommendations, it seems that surgical intervention is preferred whenever feasible. Nonetheless, for patients with nonresectable cardiac involvement and extensive disease, systemic medical therapy is indicated.

Follow Up

For patients undergoing systemic therapy, generally 6-to-12 months of therapy is recommended [46]. Initial follow-up appointments should be more frequent but can be extended to intervals of 6-to-12 months once the disease has stabilized and entered remission. PET-CT scans are highly sensitive in gauging response to therapy and can be used annually following remission to monitor for potential relapse.

In patients who receive curative surgical resection and lack other extranodal manifestations, annual follow-ups utilizing echocardiogram or cMRI may be more practical [34]. This approach, coupled with comprehensive physical examinations and routine laboratory studies, can avoid unnecessary radiation exposure.

Limitations

This study is constrained by a limited sample size drawn from case reports and abstracts, which may be attributed to the rarity of RDD and the challenges associated with its diagnosis. Some patients with symptomatic RDD may not undergo diagnostic testing and/or autopsy, thus were excluded from this study. RDD also appears to be more prevalent in third world countries, where diagnostic and reporting capabilities may be limited. We did not find any retrospective studies, precluding a comprehensive statistical analysis and generalizability of our findings. Second, it is reasonable to assume a positive outcome bias in most studies. Some of the studies included may have focused only on pertinent findings and work-up, potentially influencing our results. To enhance prompt RDD diagnosis and gather prospective data, we aim to raise awareness about RDD and advocate for patient enrollment in international registries.

Conclusion

RDD is a rare histiocytic disorder that often presents with nodal involvement, but it can affect any organ, often with a poor prognosis. Cardiac involvement, reported in just 43 cases so far, is particularly uncommon. In this group, most patients lacked a history of RDD or nodal involvement, but approximately half had extra-cardiac manifestations. As a result, diagnosis of RDD is often challenging, especially when presenting with isolated cardiac masses, which can be misdiagnosed. Our patient, with no evidence of concurrent nodal or extracardiac involvement, presented with a LA mass, initially diagnosed as a myxoma based on imaging.

Diagnostic studies, when possible, are crucial for determining etiology and guiding treatment. Due to limited data and considerable heterogeneity in reported literature, the optimal management approach remains unclear. Surgical resection appears to be the most effective, with medical management reserved for unresectable masses and multi-organ involvement. Notably, our patient has remained symptom-free for 5 years after surgical resection, marking the longest reported follow-up to date.

We hope that our findings raise awareness in the medical community to improve accurate diagnosis of RDD. We encourage patient enrollment in international registries to facilitate prospective studies aimed at improving our understanding of how to best manage these patients and optimize their outcomes. The CARE checklist was used when writing this case report (Supplementary Table 4).

Abbreviations

cMRI, cardiac magnetic resonance imaging; CT, computed tomography; RA, Right atria; RDD, Rosai-Dorfman disease; TTE, Transthoracic echocardiography; TEE, Transesophageal Echocardiography; LA, Left atria; PET-CT, position emission tomography-computed tomography.

Author Contributions

NST performed data gathering, data analysis, manuscript writing, manuscript revisions, and coordination of the study. MHD conceived the study and reviewed the manuscript. DW and PS helped with data gathering, manuscript writing, and manuscript revisions. SNM and SS helped with data gathering and manuscript writing. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work to take public responsibility for the content and to be accountable for all aspects of the work in ensuring that accuracy and integrity of the study.
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Ethics Approval and Consent to Participate

Informed content was obtained from the patient for scientific activity, including publication of this report, thus the case report was deemed exempt by the Institutional Review Board.

Acknowledgment

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Conflict of Interest

The authors declare no conflict of interest.

Supplementary Material

Supplementary material associated with this article can be found, in the online version, at https://doi.org/10.59958/hsf.6887.

References


