Clinical Characteristics of Children With Eosinophilic Cardiac Disease

Arene Butto, MD; Deipanjan Nandi, MD, MSc; Matthew J. O’Connor, MD

Patient A
A 13-year-old boy with relapsed eosinophilic leukemia was admitted to the oncology service with acute chest pain. On physical examination, a new gallop was auscultated. The initial troponin was 5.94 ng/mL and peaked at 14.32 ng/mL during the following 24 hours (normal <0.3 ng/mL). The ECG demonstrated inferolateral T-wave inversions with low QRS voltage. An echocardiogram (echo) demonstrated biventricular hypertrophy without outflow tract obstruction, moderate mitral regurgitation (MR), normal systolic shortening, and a thick posterior pericardial effusion (Figure 1A and 1B; Movies I and II in the Data Supplement). Normal findings were seen on an echo performed 2 months before at another institution. Intravenous methylprednisolone and chemotherapy were administered, with marked reduction of the troponin within 48 hours. There was no ventricular hypertrophy on echo 10 days after treatment and no visible MR on echo 2 months later.

Patient B
A 10-year-old boy was admitted for diagnostic evaluation of peripheral eosinophilia. After extensive infectious, rheumatologic, and oncological work-up, he was diagnosed with hypereosinophilic syndrome. Nine days into his hospitalization, he developed acute chest pain with a peak troponin of 6.89 ng/mL and B-natriuretic protein of 2510 pg/mL (normal <10.0 pg/mL). ECG showed ST depression in the precordial leads and T-wave flattening in the inferior leads (Figure 2). Echo demonstrated moderate MR and low—normal systolic function, in addition to an increase in a right-sided pleural effusion. Additionally, spontaneous contrast in the left ventricle was seen, prompting concern for increased risk of intracardiac thrombus formation. Despite clinical improvement on steroid therapy and anticoagulation with enoxaparin, he had persistent moderate MR on subsequent echo studies.

Patient C
A 13-year-old boy presented with 1 month of cough and shortness of breath, with cardiomegaly and pleural effusions on chest x-ray. He was initially diagnosed with eosinophilic leukemia at a referring institution, but subsequent studies at our institution demonstrated pre-B-cell acute lymphoblastic leukemia with paraneoplastic hypereosinophilic syndrome. An echo performed after transfer to our institution demonstrated atrial dilation and severe diastolic dysfunction, consistent with restrictive cardiomyopathy (Figure 3A and B; Movies III and IV in the Data Supplement). Subsequent echoes demonstrated that the posterior mitral valve leaflet was thick and tethered, with moderate-to-severe MR. He was treated with chemotherapy but had persistent moderate MR on later studies. A cardiac catheterization performed 2 months after presentation showed a mildly elevated pulmonary capillary wedge pressure of 14 mmHg after administration of a fluid bolus and did not have hemodynamic findings of restrictive physiology.

Discussion
Eosinophilic infiltration into cardiac tissue is a rare but important form of cardiac injury with a wide range of underlying causes, including oncological and rheumatologic disease. This series demonstrates a representative range of findings in 3 children with eosinophilic cardiac disease, which is a rare diagnosis at any age, who presented to our institution between August 2014 and July 2015.1 The clinical, laboratory, and imaging findings for these patients, aged 10 to 13 years, are summarized in the Table. Two of the patients had underlying malignancies and 1 had isolated hypereosinophilic syndrome. Of note, biopsy and cardiac magnetic resonance imaging were not used to establish the diagnosis in any of the cases; their use has been reported in previous studies.2

In the acute phase of this disease, eosinophilic infiltration may cause necrosis of cardiac myocytes, leading to clinical signs of myocarditis.3 Both patients A and B had transient but marked troponin elevation consistent with this diagnosis. In patient A, the combination of low-voltage QRS on ECG and ventricular hypertrophy on echo may have resulted from interstitial myocardial edema.3 As the disease progresses, thrombi may develop along the cardiac myocardium, particularly in the apex and along the outflow tracts. There had been concern for the development in this process in patient B, whose management included prophylactic...
Buttø et al  Children With Eosinophilic Cardiac Disease

enoxaparin. The last stage of this process causes irreversible changes, with fibrosis of the ventricles or the subvalvar apparatus of the mitral or tricuspid valves. Patient C presented in this stage with mitral leaflet fibrosis and restrictive cardiomyopathy.

All patients in this series had mitral valve involvement, with persistent moderate MR in 2 patients despite systemic treatment. Notably, these 2 patients were diagnosed with cardiac involvement later in the course of their illnesses. It is unclear if earlier administration of steroid therapy could reduce long-term sequelae of the disease. Additional research into appropriate timing of medication therapy is warranted. Cardiologists should remain vigilant for this rare disease and its diversity of presentations.

Table. Clinical, Laboratory, and Imaging Characteristics of Patients A, B, and C

<table>
<thead>
<tr>
<th></th>
<th>Patient A</th>
<th>Patient B</th>
<th>Patient C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Underlying diagnosis</td>
<td>Eosinophilic leukemia</td>
<td>Hypereosinophilic syndrome</td>
<td>Pre B-cell acute lymphoblastic leukemia, paraneoplastic HES</td>
</tr>
<tr>
<td>Peak peripheral eosinophil count, µL</td>
<td>15,126</td>
<td>12,430</td>
<td>26,130</td>
</tr>
<tr>
<td>ECG findings</td>
<td>Inferolateral T-wave inversion</td>
<td>ST depression in precordial leads, inferior T-wave flattening</td>
<td>Nonspecific T-wave changes, repolarization abnormality</td>
</tr>
<tr>
<td>Peak troponin, ng/mL</td>
<td>14.32</td>
<td>6.89</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Peak BNP, pg/mL</td>
<td>1008.7</td>
<td>2510.0</td>
<td>69.0</td>
</tr>
<tr>
<td>Mitral valve abnormalities</td>
<td>Moderate MR</td>
<td>Moderate MR</td>
<td>Moderate-to-severe MR, thick and tethered posterior valve leaflet</td>
</tr>
<tr>
<td>Diastolic function</td>
<td>Mildly impaired; lateral E/e’=15.5</td>
<td>Mildly impaired; reversed mitral E/A ratio</td>
<td>Moderately impaired; septal E/e’=17</td>
</tr>
<tr>
<td>Additional echo findings</td>
<td>Biventricular hypertrophy, septal hypertrophy</td>
<td>Spontaneous contrast in left ventricular cavity</td>
<td>Atrial dilation; echo-bright anterolateral papillary muscle of the mitral valve</td>
</tr>
<tr>
<td>Effusions</td>
<td>Moderate pericardial, small pleural</td>
<td>Moderate pleural</td>
<td>Trivial pericardial</td>
</tr>
</tbody>
</table>

BNP indicates B-natriuretic protein; E/A, the ratio of the early (E) and late (A) peak Doppler velocities of flow across the mitral valve; E/e’, the ratio of the peak E to the peak early diastolic velocity by Tissue Doppler (e’); HES, hypereosinophilic syndrome; and MR, mitral regurgitation.

Disclosures

This work was in part supported by the National Institutes of Health research grant T32-HL007915 to Dr Nandi.

References


Figure 1. Still images from echocardiogram for patient A. A, Apical 4-chamber view with color demonstrating moderate mitral regurgitation and complex pericardial effusion. B, Parasternal long-axis view demonstrating hypertrophy of the left ventricular posterior wall and interventricular septum.
Figure 2. ECG for Patient B. Notable findings include precordial ST depression and T-wave flattening in the inferior leads.

Figure 3. Still images from echocardiogram for Patient C. A. Apical 4-chamber view demonstrating tethering of the posterior mitral valve leaflet and dilated left atrium. B. Parasternal long-axis view with color demonstrating moderate-to-severe mitral valve regurgitation.
Clinical Characteristics of Children With Eosinophilic Cardiac Disease
Arene Butto, Deipanjan Nandi and Matthew J. O'Connor

Circ Heart Fail. 2016;9:e003172
doi: 10.1161/CIRCHEARTFAILURE.116.003172
Circulation: Heart Failure is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2016 American Heart Association, Inc. All rights reserved.
Print ISSN: 1941-3289. Online ISSN: 1941-3297

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circheartfailure.ahajournals.org/content/9/6/e003172

Data Supplement (unedited) at:
http://circheartfailure.ahajournals.org/content/suppl/2016/06/09/CIRCHEARTFAILURE.116.003172.DC1

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation: Heart Failure can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation: Heart Failure is online at:
http://circheartfailure.ahajournals.org/subscriptions/
SUPPLEMENTAL MATERIAL

Online Data Supplements

Video 1:
Transthoracic echocardiogram performed on Patient A. Apical 4-chamber sweep with color, demonstrating moderate mitral valve regurgitation, left ventricular and septal hypertrophy without left ventricular outflow tract obstruction, and a complex pericardial effusion.

Video 2:
Transthoracic echocardiogram performed on Patient A. Parasternal long-axis sweep demonstrating hypertrophy of the left ventricular posterior wall and interventricular septum, as well as the complex pericardial effusion.

Video 3:
Transthoracic echocardiogram performed on Patient C. Apical 4-chamber view demonstrating right and left atrial dilation with preserved ventricular systolic function, consistent with restrictive cardiomyopathy, as well as tethering of the posterior leaflet of the mitral valve.

Video 4:
Transthoracic echocardiogram performed on Patient C. Apical 4-chamber view with color demonstrating moderate to severe mitral regurgitation as a result of tethering of the posterior mitral valve leaflet.