Low R-Wave Amplitude in the Right Precordial Leads in Children with Symptomatic Doxorubicin Cardiomyopathy

Masakazu Umemoto, Eiichi Azuma, Masahiro Itoh, Yoshihiro Komada, Masaru Ido, Hajime Kawasaki, Hirohito Kita, and Minoru Sakurai

Department of Pediatrics, Mie University School of Medicine, Mie-Ken, Japan

SUMMARY. Electrocardiographic (ECG) findings were studied in four patients with doxorubicin cardiomyopathy. In all patients with congestive heart failure (CHF), the ECGs had a low R-wave and low R/S ratio in lead V1. Our study suggests that increased injury to myocardial cells in the regions of the anterior septum and anterior left ventricular wall may be important in the pathogenesis of doxorubicin cardiomyopathy. Eight years later, cardiac recovery from CHF occurred with a normal ECG and left ventricular ejection fraction in one patient, indicating that CHF may be reversible in certain cases.

KEY WORDS: Doxorubicin — Cardiomyopathy — Electrocardiogram

Cardiomyopathy is a well-documented complication of anthracycline-derivates and related to the cumulative dose. A cumulative dose of 550 mg/m2 body-surface area doxorubicin is considered the limit for the development of congestive heart failure (CHF) in adults [7, 9].

In children, most centers have lower limits for treatment. Recently, however, the risk of CHF has been reported as occurring during or within the first year of completing doxorubicin chemotherapy [3].

In this report, we describe the electrocardiographic (ECG) data of three children who developed congestive cardiomyopathy (CCM) and one patients in the initial stages of an evolving cardiomyopathy during doxorubicin treatment.

Patients

Case 1

A 4-year-old girl with Wilms' tumor and multiple lung metastase was treated with vincristine (V), actinomycin-D (A), cyclophosphamide (C), and doxorubicin (D).

Case 2

A 3-year-old boy with Wilms' tumor and multiple lung metastase was treated with VAC and D.

Case 3

A 1-year-old boy with acute myelogenous leukemia (AML) was treated with cytosine arabinoside, predonisone, and D.

Case 4

A 2-year-old boy with malignant teratoma was treated with V, A, C, and D.

Clinical Presentations and Outcome

The initial presentation with CHF was at ages 1–4 years, (i.e., 1.5–2 years after doxorubicin chemotherapy) (Table 1). Three patients had symptoms of tachypnea and dyspnea. Two patients died of CHF. Patient 1 had progressive CHF and died 2 months after her initial presentation. Patient 2, now 16 months after his initial presentation of ECG and echocardiographic abnormalities, has no clinical signs of heart failure. Patient 3 died 1 month after her initial CHF presentation. Patient 4, now 8 years
Table 1. Patient population: Age, diagnosis, time to development of CHF, and clinical outcomes

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Diagnosis</th>
<th>Age at cancer diagnosis (yr)</th>
<th>Cumulative doses of Adriamycin (mg/m²)</th>
<th>Time to CHF after last Adriamycin dose (yr)</th>
<th>Clinical outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Wilms' tumor</td>
<td>4</td>
<td>420</td>
<td>1.5</td>
<td>Death (2 mo)</td>
</tr>
<tr>
<td>2</td>
<td>Wilms' tumor</td>
<td>3.5</td>
<td>420</td>
<td>1.5</td>
<td>Alive (14 mo)</td>
</tr>
<tr>
<td>3</td>
<td>AML</td>
<td>1</td>
<td>510</td>
<td>1</td>
<td>Death (1 mo)</td>
</tr>
<tr>
<td>4</td>
<td>Malignant teratoma</td>
<td>2.5</td>
<td>510</td>
<td>2</td>
<td>Alive (96 mo)</td>
</tr>
</tbody>
</table>

Subclinical CHF.

(a) (b)

1. There had been no ECG and echocardiographic evidence of doxorubicin cardiac toxicity at 5 years of age. R-wave amplitude was 1.0 mV and R/S ratio was 1.0. The EF was normal (0.70). Six months later, CHF developed, which ultimately caused the patient's death. At this time, R-wave amplitude had decreased to 0.3 mV and R/S ratio to 0.2. The chest x-ray showed cardiomegaly with a cardiothoracic ratio (CTR) of 65% and the EF decreased to 0.28.

2. There had been no ECG evidence of doxorubicin cardiac toxicity at 3.5 years of age. R-wave amplitude was 0.8 mV and R/S ratio was 1.0. Eighteen months later, the EF decreased to 0.54. R-wave amplitude decreased to 0.3 mV and R/S ratio to 0.2. Repeat ECG and echocardiographic examinations have not now demonstrated any significant changes.

3. There had been no ECG evidence of doxorubicin cardiac toxicity at 1 year of age. R-wave amplitude was 0.7 mV and R/S ratio was 1.4. One year later, the EF had decreased to 0.43 with CHF. R-wave amplitude decreased to 0.2 mV and R/S ratio to 0.5.

4. There had been no ECG evidence of doxorubicin cardiac toxicity at 4 years of age. R-wave amplitude was 1.2 mV and R/S ratio was 0.9. The EF was

ECG Findings in Lead V₁

In all patients, the ECGs showed a low R-wave and a low R/S ratio in lead V₁ (Fig. 1). Echocardiograms obtained at the time of onset of CHF for each patient showed reduced left ventricular ejection fraction (EF).

Patient 1

Patient 2

Patient 3

Patient 4