Case Report
Acute myocardial/cerebral infarction as first/relapse manifestation in one acute promyelocytic leukemia patient

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Abstract: In the clinical setting, bleeding is a common manifestation of acute promyelocytic leukemia (APL), whereas thrombosis is relatively rare, especially as an initial symptom. Here, we report an unusual case of APL with acute myocardial infarction as the first manifestation and cerebral infarction as the relapse manifestation in a healthy young woman. This unique case emphasizes that a thrombotic event could be the first manifestation of an underlying hematological disorder such as APL and could also be a sign of relapse. Rapid detection of the underlying disorder and the timely use of anticoagulation therapy and ATRA are crucial for preventing further deterioration of the disease and saving the patient’s life.

Keywords: Acute promyelocytic leukemia, initial symptom, acute myocardial infarction, cerebral infarction

Introduction

Acute promyelocytic leukemia (APL) is a subtype of acute myelogenous leukemia characterized by abnormal hypergranular promyelocytes in the bone marrow and peripheral blood [1]. Patients of APL characteristically present with pancytopenia and coagulopathy [2]. The coagulopathy has been proved to cause the occurrence of DIC, which includes hypercoagulable state and hemorrhage. In clinical, bleeding is a more common manifestation while thrombosis is relatively rare, such as cerebral infarction and acute myocardial infarction. Here we report an exceeding rare case with acute myocardial as first manifestation of APL and cerebral infarction as relapsed in a healthy young woman. To the best of our knowledge, there is no report like this before.

Case report

A 33-year-old female was admitted to our emergency department with a chief complaint of chest pain for one day. There was no remarkable past medical history, with no history of hypertension, diabetes, stroke or coronary artery disease. She denied smoking or alcohol abuse. Her physical examination was normal except for a pale appearance. The initial electrocardiogram (ECG) showed an abnormal Q wave and 1-2 mm ST-segment elevation in leads II, III and AVF (Figure 1A). Routine blood testing showed WBC 3.9×10⁹/L, with 52% lymphocytes, hemoglobin 61 g/L and normal platelets. Hemocoagulation parameters revealed a slightly prolonged prothrombin time (14.4 s, normal range (NR) 10-13.5 s), normal activated partial thromboplastin time (APTT), low fibrinogen (0.6 g/L, NR 2.0-4.0 g/L) and raised D-dimer level (1403 ug/L, NR 0-700 ug/L). Troponin I was elevated at 2.4 ng/mL (NR<0.1 ng/mL). Cardiac enzymes were also tested, showing creatine kinase (CK) 1831 (NR 38-174 U/L), CK-MB 143 (NR 0-25 U/L) and AST 102 (NR 90-40 U/L). Echocardiogram demonstrated hypokinesis of the inferolateral wall of the left ventricle. The woman was then given aspirin, clopidogrel bisulfate and low-molecular-weight heparin due to concerns of acute myocardial infarction.

Although we thought she would have a good outcome, in the coming ten days, the patient developed an isolated neutropenia, with her neutrophils dropping to 0.70×10⁹/L (NR 2.0-7.0×10⁹/L). A bone marrow aspiration was per-
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formed, which demonstrated a diffuse infiltration of abnormal promyelocytes (Figure 2A). Cytogenetic and molecular diagnostic examination confirmed t(15;17) and PML-RARα fusion protein. The diagnosis of APL was established. After treatment with all-trans retinoic acid (ATRA) (40 mg/day) and ATO (0.16 mg/kg) for 25 days, the patient achieved complete remission. Half a year later, echocardiogram demonstrated normal kinesis at the inferolateral paries of the left ventricle, with ejection fraction of 62%, and ECG showed sinus rhythm with the axis leaning slightly to the right (Figure 1C).

Following chemotherapy of IDA (10 mg/m², d1-3) for three cycles and ATO (0.16 mg/kg) d1-14 for one cycle, the patient refused to continue treatment after October 2012.

Figure 1. ECG gradually normalized over time. A. ECG at admission, showing ST-segment elevation in leads II, III and AVF; B. ECG two months after infarction, showing T wave inversion in leads III and AVF; C. ECG half a year after infarction, showing normal sinus rhythm with the axis leaning slightly to the right.

Figure 2. A. Bone marrow aspiration showing diffuse infiltration of abnormal promyelocytes; B. Diffusion-weighted magnetic resonance imaging (DWI-MRI) revealing acute infarcts in the left frontoparietal lobe.
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In Feb 2013, the patient appeared at the emergency department again with declined mental status, slurred speech, and right-sided weakness. Neurologic examination showed a right-sided paralysis with 0/5 motor strength. Upon investigation, her WBC was 3.1×10^9/L, hemoglobin was 119 g/L, and platelets were 95×10^9/L. Her coagulation profile showed low fibrinogen (0.7 g/l) and a high D-dimer level (4980 ug/L), similar to the parameters in the previous year when she suffered the myocardial infarction. Diffusion-weighted magnetic resonance imaging (DWI-MRI) was conducted, revealing acute infarct in the left frontoparietal lobe (Figure 2B). The patient was stabilized with treatment of decreasing intracranial pressure and anticoagulation.

With no clot or regional wall motion abnormality revealed by echocardiography and her sinus rhythm by ECG, cardiogenic cerebral embolism was preliminarily excluded despite her prior myocardial infarction. Considering her history of APL and coagulation abnormality, relapse of the leukemia seemed possible. Bone marrow aspiration was performed, and a large number of abnormal promyelocytes was found. The patient achieved complete remission a second time with therapy of ATRA, ATO and IDA. Half a year later, her right hemiparesis was improved, but the aphasia was remained.

Discussion

Patients with APL characteristically present with coagulopathy as a result of complex interactions between leukemia promyelocytes and the coagulation system [1]. One main factor is the release of procoagulant activities by promyelocytic blast cells. In the clinical setting, bleeding is a more common manifestation of such coagulopathy, whereas thrombosis is relatively rare. Recently, a report showed that the incidence of all thromboses in APL was approximately 7.9% [2] and tissues involved were varied such as cardiac events, cerebral events, deep vein thrombosis, hepatic vein thrombosis et al [1]. Among them, only 8 cases were reported as having acute myocardial infarction presenting as an initial symptom [1]. Here we summarized clinical details of APL patients with myocardial infarction (MI) as the first manifestation (Table 1). Most of the patients summarized were young and had no remarkable past medical history, their WBC counts were relatively low and DIC only appeared in three of the cases. All these features showed us that underlying hematologic disease such as APL should be considered when a relatively “special” MI patient is admitted.

Our case is another typical example presenting with APL and MI simultaneously. However, different from the cases reported previously, our patient suffered a second thrombotic event, cerebral infarction, half a year after complete remission, which provided a clue as to her relapse of APL.

To the best of our knowledge, there are only 5 reports describing 4 patients with thrombosis occurring in relapsed APL. V Runde reported a relapsed APL patient developing an acute thrombosis of the right arm after 5 days using ATRA [11, 12]; Fujiwara H described a man presenting cerebellar infarction during all-trans retinoic acid therapy [13]; In another case, a 32-year-old man was reported having hepatic vein thrombosis [14]; and in 2000, a 27-year-old female with left middle cerebral artery infarct was reported [15]. All the four patients developed thrombosis during the use of ATRA, which may be a result of ATRA syndrome. The patient we report herein suffered thrombosis prior to the use of any medicine, making this case unique and the first with acute myocardial infarction as a first manifestation of APL and cerebral infarction as a relapse manifestation.

<table>
<thead>
<tr>
<th>Time</th>
<th>Age</th>
<th>Gender</th>
<th>Past history</th>
<th>DIC</th>
<th>WBC (×10^9/L)</th>
<th>Outcome</th>
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<td>1980 [3]</td>
<td>46</td>
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<td>n/a</td>
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<tr>
<td>2007 [7]</td>
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<td>2013 [10]</td>
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<td>Yes</td>
<td>3.9</td>
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<tr>
<td>Our case</td>
<td>33</td>
<td>F</td>
<td>No</td>
<td>No</td>
<td>3.9</td>
<td>Alive</td>
</tr>
</tbody>
</table>
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Thrombotic events, such as cardiac infarct or stroke, could be the first or relapse manifestation of an underlying hematological disorder such as APL. Such cases require a higher awareness in the young and those without past illness. Obvious coagulopathy, abnormality in routine blood indexes and “no risk factors” for thrombosis may be hints of underlying hemopathy. The rapid detection of such disorders and the timely use of the corresponding therapy are crucial in preventing further deterioration of the disease and saving the patient's life.

Disclosure of conflict of interest

None.

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