Acute pulmonary embolism combined with acute myocardial infarction as the first manifestation of acute leukemia: a case report

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Abstract

Thrombotic complications in acute myeloid leukemia (AML) are uncommon due to coagulation dysfunction and thrombocytopenia. We report a unique case of AML presenting as concomitant pulmonary embolism and atypical acute myocardial infarction. A 67-year-old male experienced persistent bilateral chest pain. Despite an unremarkable electrocardiogram, elevated D-dimer and mildly increased troponin T levels prompted further investigation, leading to the diagnosis of simultaneous pulmonary embolism and acute myocardial infarction. The patient underwent percutaneous coronary intervention and received triple antithrombotic therapy. However, antithrombotic therapy was discontinued following a sharp decline in hemoglobin and platelet counts, and the patient subsequently developed persistent fever. AML was diagnosed via bone marrow biopsy. Chemotherapy was not initiated due to the patient's deteriorating condition, and he ultimately succumbed to presumed intracranial bleeding.

Introduction

Thrombotic complications in acute myeloid leukemia (AML) are rare due to coagulopathy and thrombocytopenia. Paradoxically, thrombocytopenia and thrombosis can coexist, leading to treatment dilemmas, as thrombosis may be fatal and become the primary cause of death. Additionally, concomitant arterial and venous embolisms are seldom reported in association with AML. This case is notable for the simultaneous occurrence of acute pulmonary embolism and acute myocardial infarction as the initial manifestation of AML, which was treated with antithrombotic therapy until the final diagnosis of acute leukemia. Atypical clinical presentations of acute myocardial infarction may signify early-stage AML.

Case presentation

A 67-year-old male patient was admitted to the hospital with a complaint of bilateral chest pain and weakness lasting for five days. The patient reported that the pain was persistent, albeit tolerable, and not associated with exercise or breath. He denied experiencing symptoms such as cough, dyspnea, diaphoresis, or lower limb edema. His pertinent medical history included a well-controlled hypertension for three years and a recent weight loss of 10 kg over the past year. The patient was a non-smoker and reported infrequent alcohol consumption.

The patient's vital signs upon admission were within normal limits, with a blood pressure reading of 115/72 mmHg, a heart rate of 80 bpm, a respiratory rate of 18 bpm, and an oxygen saturation (SpO2) of 98% while breathing room air. Physical examination revealed scattered moist rales across the bilateral lower lung fields. Cardiac and abdominal examinations were unremarkable, with no evidence of edema in the lower extremities.

The results of the complete blood count (CBC) revealed a white blood cell count of 8.51×10^9/L, a hemoglobin level of 114 g/L, and a platelet count of 96×10^9/L. The coagulation panel showed a prothrombin time (PT) of 12.6 seconds, a D-dimer level of 94.83 ug/mL (normal range (NR) 0-0.5), a
fibrinogen level of 6.53 mg/dL (NR 1.8–3.5), and fibrinogen degradation products (FDP) level of 270.70ug/ml (NR 0–5). The cardiac marker showed a high-sensitive troponin T level of 0.357 µg/L (NR 0-0.014). Liver and renal function tests were unremarkable, while procalcitonin levels were elevated at 0.29ng/ml (NR 0-0.05).

The electrocardiogram showed no ST segment changes but a Q wave in lead III (Fig. 1). The computed tomography (CT) of the chest revealed a 1.0×1.1cm solid nodule in the right upper lobe of the lung, with a shallow lobulated edge, and mild to moderate homogeneous enhancement, and exudation in the lower lobe of the lungs, mild bilateral pleural effusion. CT angiography showed embolization in the left upper branches of the pulmonary arteries and bilateral lower pulmonary arteries (Fig. 2). However, no thrombus was found in the lower limb veins. Pulmonary embolism was diagnosed, and the patient was given 0.6ml enoxaparine subcutaneously every 12 hours for anticoagulation.

Initially, acute coronary syndrome was not considered due to the absence of angina and no ST segment change in the electrocardiogram. However, moderate stenosis in the left coronary artery was identified by CT angiography. Subsequent coronary angiography revealed occlusion in the middle segments of the left circumflex artery (LCX), 50% stenosis in the middle segment of the left anterior descending artery, and 80% stenosis in the middle segment of the right coronary artery. A drug-eluting stent (DES) was successfully implanted in the middle segment of the LCX, achieving thrombolysis in myocardial infarction (TIMI) grade III flow (Fig. 3). The patient was given 100mg aspirin with 75mg clopidogrel daily for antiplatelet aggregation and 20mg atorvastatin to stabilize the plaque after the procedure. To identify the cause of concomitant thrombosis in the pulmonary arteries and coronary artery, autoantibody spectrum, anticardiolipin antibody, tumor markers of the respiratory system, rheumatoid factor, and immunoglobulin levels were tested, but no abnormalities were found.

On the second day of hospitalization, the patient's hemoglobin level decreased to 106g/L, and platelet counts dropped to 55×10^9/L. Furthermore, the D-dimer levels increased, and urinary occult blood was detected. Suspecting heparin-induced thrombocytopenia, the patient's medication was switched from enoxaparin to rivaroxaban, with a daily dose of 10 mg. Following the switch, the urinary occult blood became negative on two consecutive tests. On the third day, the patient developed a fever, and piperacillin sodium, tazobactam, and cephalotazidine moxifloxacin were administered to treat the infection. Hepatitis virus screening and autoimmune hepatitis tests, along with tests for antibodies to EB virus, cytomegalovirus, rubella virus, and herpes simplex virus, galactomannan tests, and blood bacterial cultures were all negative.

On the sixth day of hospitalization, pancytopenia with 13% blasts was detected in the patient's peripheral blood. The following day, ecchymosis was observed at the vein puncture site on the wrist, and the white blood cell counts dropped to 2.61×10^9/L, with hemoglobin at 61g/L and platelets at 8×10^9/L, with 17% blasts. The coagulation panel revealed disseminated intravascular coagulation, as evidenced by a prolonged PT (22.8 seconds), elevated D-dimer levels (> 20.00 µg/mL), and decreased fibrinogen levels (5.03 mg/dL), with FDP levels > 150.00µg/mL. The Coombs test was negative. Following consultation
with a hematologist, aspirin, clopidogrel, and rivaroxaban were discontinued, and red cell and platelet transfusions were administered, resulting in platelet counts increasing to $37 \times 10^9 / L$ and PT decreasing to 15.2 seconds. Fortunately, no fresh ecchymoses or massive hemorrhage occurred. A bone marrow smear revealed hyperplasia of nucleated cells with necrotic cell remnants, confirming the diagnosis of acute myeloid leukemia (AML). The bone marrow biopsy showed a large amount of necrosis in the bone marrow tissue, with hyperactive proliferation of blasts in the necrotic part and few megakaryocytes and lymphocytes (Fig. 4). Immunophenotyping was not performed due to few nucleated cells. Immunohistochemical examination revealed CD117 (-), CD34 (-), MPO (granulocyte+), CD68 /PG-M1 (+), CD71 (nucleated red blood cell+), CD61 (megakaryocyte+), CD3 (-), CD20 (-), CK-L (-), TTF-1 (-), NapsinA (-), CK7 (-), PSA (-), and P504s (-).

Despite the initial improvement, the patient's condition deteriorated in the following days, with persistent fever and unstable hemodynamics. The platelet count fell to $6 \times 10^9 / L$, and chemotherapy was not initiated due to the worsening condition. On the 16th day of admission, the patient lost consciousness, and his heart rate gradually decreased, with blood pressure eventually collapsing, leading to presumed cerebral bleeding and subsequent death.

**Discussion**

Thrombosis is a rare and atypical complication of acute leukemia that may lead to misdiagnosis and improper treatment at the early stages of the disease. In this case, an elderly male patient presented with acute pulmonary embolism combined with acute myocardial infarction, received percutaneous coronary intervention and triple antithrombotic therapy. However, the progressive decline in hemoglobin and platelet count suggested hematological disease, and the patient was ultimately diagnosed with acute leukemia. This case is relatively rare clinically since anemia and bleeding are common initial presentations, as normal bone marrow hematopoietic function is inhibited by leukemic cell proliferation and thrombocytopenia. However, in recent years, thrombotic complications have been reported sparsely, including venous thrombosis [1], arterial embolism like stroke, acute myocardial infarction, or lower extremity arterial embolism [2, 3], or arteriovenous thrombosis [3].

This patient had a rapid onset and short course of chest pain, with no risk factors for pulmonary embolism before. When pulmonary embolism and myocardial infarction coexist in the setting of thrombocytopenia, it suggests that the nature of arteriovenous thrombosis is driven by underlying pathology rather than seeming diseases. The mechanism of thrombosis in acute leukemia is not yet clear. Several pathogenic mechanisms have been proposed, including increased blood viscosity due to leukemic blasts and leukostasis resulting from high blast cell count, which impede blood flow. Prothrombogenic cytokines produced by blasts may also contribute to thrombosis [4]. In addition, chemotherapy further promotes thrombus formation [5]. Other reasons related to thrombosis include venous catheter procedures or infections [6]. In this patient, the leukocyte count was normal with no blasts in peripheral blood at admission. The patient neither received chemotherapy nor underwent any invasive procedure before. Therefore, the reasons listed above were inexplicable. It has been reported that...
anticoagulant factor protein C, protein S, and antithrombin III decreased in varying degrees in leukemia patients [7]. Since the patient's anticardiolipin antibody test was negative, antiphospholipid antibody syndrome was excluded. As other anticoagulant factors were not detected in this case, it was speculated that some anticoagulation defects might have given rise to thrombosis in leukemia.

Concomitant acute myocardial infarction and pulmonary embolism are rare and often require double antiplatelet (DAPT) and anticoagulant therapy to reduce new thrombotic events. Unfractionated heparin or low molecular weight heparin is recommended in the acute phase to rapidly extinguish thrombin and fibrin clot generation, which further prevents thrombus extension. Direct oral anticoagulants have been shown to be as effective as conventional treatment for venous thromboembolism [8]. However, in the setting of leukemia with thrombocytopenia, triple antithrombotic therapy is worth exploring, as leukemia-related thrombocytopenia, platelet dysfunction, and systemic coagulation dysfunction increase the risk of bleeding. Managing concomitant bleeding risk caused by antithrombotic drugs and stent thrombosis secondary to drug withdrawal due to bleeding events is challenging. At present, there is no corresponding guideline specifying the management of this particular phenomenon. Although the incidence of stent thrombosis was not significantly different between the two groups in a meta-analysis of all-cause mortality of PCI patients with or without baseline thrombocytopenia, gastrointestinal bleeding, intracranial hemorrhage, and hemorrhagic stroke after PCI were significantly higher than those of patients with normal platelets [9]. To reduce bleeding risk, some experts suggest using bare metal stents or drug-eluting balloons to shorten the time of DAPT [10]. In this case, the patient received DES implantation and was treated with a standard dose of enoxaparin and DAPT without knowing the existence of leukemia. However, on the second day after PCI, enoxaparin was replaced by rivaroxaban due to platelet decline. On the fourth day after PCI, antithrombotic drugs were discontinued due to a sharp drop in hemoglobin and platelets. Platelet transfusion was given when the platelet count was 8000/µL for bleeding prevention. The patient did not develop massive hemorrhage despite low platelets nor stent thrombosis without antithrombotic therapy until he died of irreversible bone marrow necrosis and possible intracranial bleeding. Thus, closely observing changes in the platelet count and adjusting the strategy according to the platelet value is crucial [10]. If the platelet count exceeds 10000/µL, aspirin can be used, while adding clopidogrel if the platelet count exceeds 30000/µL. If the platelet count is less than 50000/µL, the duration of DAPT should be 2 weeks after PTCA, 4 weeks after bare metal stenting, and 6 months after the second and third generation drug-eluting stent implantation. However, Prasugrel, Ticagrelor, and glycoprotein IIb/IIIa antagonists are not recommended [11]. If the platelet count is lower than 20000/µL or the patient has fever, leukocytosis, sudden decrease of platelet count or other blood coagulation disorders, prophylactic platelet transfusion is required [12]. Moreover, multidisciplinary management is also important in tackling the patient's complex situation.

**Conclusion**

The initial symptoms of AML may not be typical, and thrombotic complications such as acute pulmonary embolism and acute myocardial infarction are rare but can present and lead to treatment dilemmas, further increasing the mortality of AML. It is essential to further elucidate the specific mechanism of
arteriovenous thrombosis in the context of thrombocytopenia. Since there is no standard therapy, the strategy should be carefully evaluated based on individual characteristics and should involve multidisciplinary management.

Declarations

Consent

Informed consent was obtained from patient’s daughter.

Conflict of interest

The authors have no conflicts of interest to declare.

Authors’ contributions

All authors made substantial contributions to conception and design, or acquisition of data, or analysis and interpretation of data; ZSZ and LS involved in drafting the manuscript and revising it critically for important content. All authors read and approved the final manuscript

References


**Figures**

**Figure 1**

ECG on admission
Figure 2

A. Coronary angiography showing occlusion in the middle segments of the left circumflex artery (LCX). B. Revascularization of LCX

Figure 3
Computered tomography angiography of chest showing embolization in the left upper branches and bilateral lower pulmonary arteries

Figure 4

Immuohistochemical stainin of bone marrow biopsy(×200)