Thromboembolism in lower extremity arteries as the initial symptom of acute leukemia: a case report and review of literature

Abstract
Objective Summarized clinical characteristics of aortic thrombosis in patients with leukemia. Method Analysis of a case with aortic thrombosis as the first clinical features, treatment and prognosis of leukemia. Results recommend active anticoagulant therapy in combination with induction chemotherapy in patients with leukemia complicated by thrombosis. This approach would prevent recurrence of thrombosis while treating the underlying leukemia, resulting in improved patient outcomes.

Keywords: leukemia, thrombosis, dorsalis pedis, d-dimer, nadroparin

Introduction
Disorders of the coagulation system are intensively traced in patients with acute leukemia, who usually are plagued by hemorrhagic complications or thrombosis of small vessels. It has been reported that, in leukemia patients, the incidence of bleeding ranges from 20% to 95% and that of thrombosis ranges from 10% to 40%. Acute leukemia may come in hand in hand with thrombosis; Thrombosis usually occurs at the early stage of leukemia and after chemotherapy or infection, especially in acute leukemia with extremely high leukocyte counts, chronic leukemia, or chronic leukemia with acute changes. Thrombosis in leukemia is often seen in veins but rarely in arteries. Leukemia with thrombosis in large arteries as the initial symptoms is especially rare. Here we report such a case.

Case report
A 66-year-old male was admitted to hospital for pain and numbness of the left foot. On the day of admission, physical examination revealed decreased skin temperature below the left knee and cyanosis of the left toes. The left femoral and dorsalis pedis artery pulses were impalpable. An emergency three-dimensional computed tomography (3-D CT) reconstruction of the lower extremity vessels showed thrombosis in the left common, internal and external iliac arteries (Figure 1). A blood routine test (BRT) revealed white blood cell (WBC) count 6900/µL, hemoglobin (Hb) 127g/L, and platelet (PLT) 18×10⁹/L. Coagulation tests showed prothrombin time (PT) 14.7s, activated partial thromboplastin time (APTT) 33.9s, thrombin time (TT) 22.7s, and D-dimer concentration 3200μg/L.

On the afternoon of 29 September, Fogarty balloon catheter thrombectomy was made in the left iliac artery and Nadroparin Calcium was used for anticoagulant therapy. On the same day, blood routine test (BRT) showed WBC 16.6×10⁹/L, Hb 115g/L, and PLT 15×10⁹/L. Blood coagulation tests showed PT 16.1s, APTT 45.8s, indefinite TT, and D-dimer 3780μg/L. Postoperatively his left leg pain was relieved and skin temperature and arterial pulse restored.

Figure 1 3-D CT.

The next day, immature cells were found in the peripheral blood. A bone marrow smear (Figure 2) showed 58% myeloblasts and 35% promyelocytes, bone marrow blasts by the Flow cytometry(BD
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FACSCALIBUR) analysis revealed positive for myeloid markers CD13 and CD33, negative for myeloid markers CD14, negative for lymphoid markers CD3, CD4, CD5, CD8, CD10, and CD19. Fluorescence in situ hybridization (FISH) of Chromosomal analyses showed a normal karyotype 46, XY. The polymerase chain reaction (ProFlex 3 x 32 well PCR System) for the BCR/ABL, PML/RARA, AML1-ETO, or MLL rearrangement was negative. Confirming the diagnosis of acute myeloid leukemia (AML) FAB M2.

Discussion

Patients with acute leukemia may present with thrombosis of vessels, large arterial thrombosis is a rarely-seen complication. De Stefano et al. reported that there were 6.3% people caught by thrombosis, 80% by venous thrombosis, and 20% by arterial. As far as we know, only nine cases of acute leukemia that presents to thromboembolism, the preventive treatment of this complication is still controversial. We reviewed previous similar cases in patients with leukemia complicated by thrombosis. This approach would prevent recurrence of thrombosis while treating the underlying leukemia, resulting in improved patient outcomes.

i. Platelet can be activated by leukemia disease, infection, and medication, also resulting in the hypercoagulable state and thrombosis.

ii. Abnormal coagulation factor levels such as increased levels of plasma fibrinogen, factor VIII, and factor V has been found in leukemia patients complicated with thrombosis by Priest et al. in 1982.

iii. Decreased levels of anticoagulant proteins such as anti-thrombin III and protein C can be found in many leukemia patients. In ALL patients, it is demonstrated that coagulation inhibitors, i.e., anti-thrombin, protein C and proteins S were quantitatively reduced by a large margin during asparaginase therapy.10,11

iv. Leukemia cells can damage the vascular endothelial cells, resulting in activation of factor XII, release of the endothelial cell cytokines, platelet activation, and finally blood clotting and thrombosis.

v. Some leukemia patients have increased plasma a2-antiplasmin levels, leading to decreased fibrinolytic activity on the blood vessel.

vi. In some leukemia patients, the white blood cells show increased vascular adhesion ability, promoting the formation of thrombosis especially tumor thrombus.12

vii. Chemotherapy can kill large numbers of leukemia cells, leading to the release of coagulants into the blood, and therefore the hypercoagulable state and thrombosis.

Although acute leukemia patients are highly vulnerable to thromboembolism, the preventive treatment of this complication is still controversial due to the even higher risks of hemorrhage in these patients. Until now, active anti-coagulant therapy only was used in the acute leukemia patients at high risks of developing thromboembolism. Our patient has lower extremity arterial thrombosis at the time of presentation. Anticoagulant therapy was initiated, but stopped after removal of the thrombus. During induction chemotherapy, further extensive arterial thrombosis occurred. Because the incidence of low platelet counts and bleeding is much higher than that of thrombosis in patients with leukemia, the use of anticoagulants in patients with thrombosis is still controversial. We reviewed previous similar cases and analyzed their treatment and its results. We recommend active anti-coagulant therapy in combination with induction chemotherapy in patients with leukemia complicated by thrombosis. This approach would prevent recurrence of thrombosis while treating the underlying leukemia, resulting in improved patient outcomes.

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None.

Conflict of interest

The author declares no conflict of interest.

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