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Case Report

A case of acute limb ischemia

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ABSTRACT

Thromboembolism is a well-recognized complication of hematological malignancy. The incidence of symptomatic thrombosis at diagnosis is relatively low in AML (acute myeloid leukemia) patients, though its incidence increases on treatment with anthracyclines. We reported a case of 69 year old female with T2DM who presented with DVT and later on acute limb ischemia of the same lower limb. On hematological evaluation, she had leukocytosis and thrombocytopenia. Further evaluation revealed AML. Thromboembolism as a rare presentation of AML in adults with leukemic hyperleukocytosis has seldom been reported. In the absence of clear guidelines, early diagnosis and management are desirable.

Keywords: Acute myeloid leukaemia, Deep vein thrombosis, Leukocytosis, Peripheral arterial occlusive disease

INTRODUCTION

AML is a neoplasm characterised by infiltration of the blood, bone marrow and other tissues by proliferative, clonal, poorly differentiated cells of hematopoetic system. AML is associated with complications related to the excess production of undifferentiated myeloid blasts such as leukostasis, tumor lysis syndrome (TLS) and disseminated intravascular coagulation (DIC).[1] Venous thrombosis in AML is less common compared to bleeding manifestations; therefore in patients with AML, venous and arterial thrombosis is a rare phenomenon especially at initial presentation.[2] Although the total leukocyte count (TLC) is usually higher in acute lymphoblastic leukemia (ALL), patients with AML are more likely to have serious complications and organ dysfunction related to high white blood cell (WBC) count.[3]

CASE REPORT

A 69 year old female, known case of T2DM on oral antidiabetic agents with no other co-morbidities, presented with history of right lower limb pain for 2 days, more so in the calf region that aggravated with movement. On examination, she was found to have significant pallor, her right posterior tibial artery was feeble with impalpable dorsalis pedis artery. There was tenderness in right calf region with no varicosities or discolouration. On evaluation, she was found to have a WBC count of 27000 cells/cumm, hemoglobin level of 9.5 g/dl, platelet count of 57000 cells/cumm with ESR 70. USG venous Doppler of right lower limb showed deep venous thrombosis of right posterior tibial vein, extending for a length of 2.7 cm. She was treated with unfractionated heparin (UFH) and warfarin, meanwhile cause for DVT was evaluated. CT pulmonary angiogram and 2D ECHO was done and pulmonary thromboembolism was ruled out.

On day 3 of admission, patient developed bluish discolouration of right big toe and 2nd toe with no palpable pulse up to femoral artery of right lower limb (Figure 1). Arterial Doppler of right lower limb and later CT aortogram showed monophonic flow up to right common femoral artery and diffuse atherosclerotic changes in arch and abdominal aorta with non-opacification of right common iliac and external and internal iliac arteries below bifurcation for a length of 10 cm with no onward flow to femoral, popliteal and tibioperoneal trunk. She was started on anti-platelets and statins.

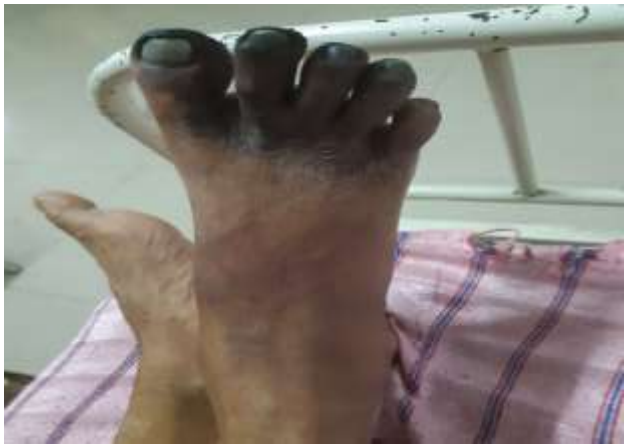

Figure 1: Dry gangrene of right toes.

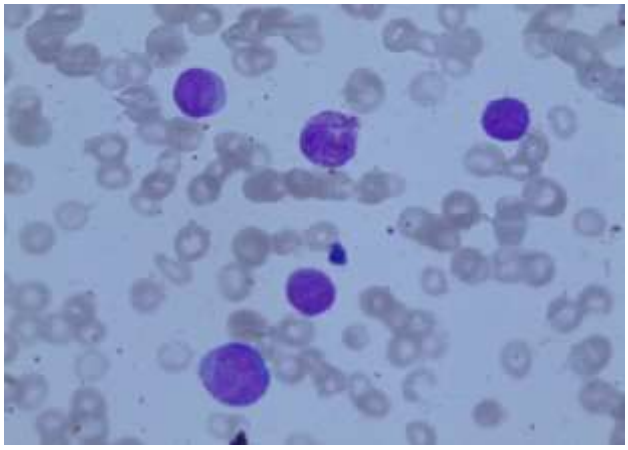

Figure 2: Peripheral smear.

Table 1: Classification of myeloid leukemia.[5]

WHO	Incidence (%)	FAB type	Incidence (%)
AML with recurrent genetic abnormalities			
t(8;12((q22;q22)	30-40	M2	25-30
inv(16) (p13q22) or t(16;16)(p13;q22)		M4eo	5-15
t(15;17) (q22;12), (PML/RARA) and variants		M3	5-10
11q23(MLL) abnormalities			
AML with multi lineage dysplasia; following MDS or MDS/MPD; without antecedent MDS or MPD, with dysplasia in atleast 50% of cells in 2 or more myeloid lineages	10-15		
AML and MDS , therapy related; alkylating agents/radiation related; topoisomerase 2 inhibitor related others	5-10		
AML, not otherwise categorised; minimally differentiated	30-40%	M1	10-15
Without maturation		M0	2-5
With maturation			
Acute myelomonocytic leukemia		M4	5-15
Acute monoblastic/monocytic leukemia		M5	15-25
Acute erythroid leukemia		M6	-3
Acute megakaryoblastic leukemia		M7	5-10
Acute basophilic leukemia			
Acute panmyelosis with myelofibrosis			
Myeloid sarcoma			

MDS-myelodysplastic syndrome; MPD-myeloproliferative syndrome.

Peripheral smear report showed acute leukaemia with 75% blasts, MPO and PAS inconclusive (Figure 2). Her autoimmune and APLA work up turned negative. Peripheral blood flow cytometry was sent which was suggestive of AML with CD45 dim population (30% of total atypical cells) which were positive for CD117 (precursor marker), CD13, CD15 (subset), CD33, MPO and CD11c. CD59 and CD55 were present which ruled out paroxysmal thrombocytopenic purpura. Bone marrow study and molecular genetic study was suggested for further classification of AML, however patient was not willing for the same (Table 1). Hemato-oncology consultation was sought and induction therapy with cytosine arabinoside was initiated.

On day 2 of induction therapy patient developed focal seizures of left upper limb for which an NCCT brain was ordered. It revealed a hemorrhagic infarct in right fronto temporal region. Patient subsequently developed aspiration pneumonia and succumbed to her illness.

DISCUSSION

AML can be classified based on morphology (FAB) and etiology (WHO) (Table 1). Common presentations of

AML are anemia, hemorrhage, recurrent infections and organomegaly resulting from organ infiltration with leukemic cells. Hemorrhagic or thrombotic events may occured in patients with AML, but thrombotic events were less common because of thrombocytopenia with its accompanying coagulopathy in these patients.[4] Thrombosis if occured, commonly involved the venous system though the arterial system may also be affected. DeStefano et al reported venous thrombosis in 80% and arterial thrombosis in 20% of patients with acute leukemia and thrombosis.[6]

The association between AML and thrombosis was rarely but very well documented; however the pathogenesis of thrombosis in AML remained unclear. The pathogenesis of the cancer-related prothrombotic state was complex and reflected the action of different mechanisms including activation of blood coagulation via procoagulant substances, impairment of fibrinolytic pathways, alterations of endothelium towards a thrombogenic state, occlusion of the blood vessel by a leukemic thrombus, leukostasis syndrome.[6] It was worthy to note that the heighest WBC count in this patient was 47000 cells/cumm, hence leukostasis was less likely and prothrombin time, activated partial thromboplastin time was well within normal limits. Hence disseminated intravascular coagulation was also less likely.

This patient on treating with UFH developed further reduction in platelet count, hence a possibility of heparin induced thrombocytopenia was also considered and UFH was switched to injection fondaparinux 5 mg subcutaneous OD. Although acute leukemia patients have high risk of thromboembolism, the preventive treatment of this complication was still controversial due to the higher risk of hemorrhage in the patients. Till now, there was no standard protocol of anticoagulant therapy in acute leukemia patients, except APL with high TLC or at high risk of developing all-trans retinoic acid syndrome.[7,8]

Later on with induction chemotherapy patient's counts improved but unfortunately she developed a hemorrhagic infarct which could possibly be due to anti coagulation and thrombocytopenia and succumbed to her illness.

CONCLUSION

In conclusion, the above is a case report of AML in a patient presenting with arterial and venous thrombosis, including a DVT of the right leg, peripheral occlusive arterial disease of right lower limb caused by thromboembolism of right common iliac artery. It sums up the need for considering haematological malignancy as an important differential while evaluating a case of thromboembolism, especially in elderly so that an early diagnosis can be clenched leading to early initiation of treatment. It is also important to estimate the risk of bleeding when anticoagulation therapy is being considered for AML patients with multiple vascular thromboembolism and thrombocytopenia. Only few cases have reported the vascular paradox of thrombosis and thrombocytopenia in literature and data regarding therapeutic strategies to tackle such situations in sparse.

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REFERENCES

1. Bewersdorf JP, Zeiden AM. Hyperleukocytosis and leukostasis in acute myeloid leukemia: can a better understanding of the underlying molecular pathophysiology lead to novel treatments? Cells. 2020;9(10):2310.
2. Ali AM, Mirrakhimo AE, Abboud CN, Cashen AF. Leukostasis in adult acute hyperleukocytic leukemia: a clinician's digest. Haematol Oncol. 2016;34(2):69-78.
3. Creutzig U, Ritter J, Budde M, Sutor A, Schellong G. Early deaths due to hemorrhage and leukostasis in childhood acute myelogenous leukemia. Associations with hyperleukocytosis and acute monocytic leukemia. Cancer. 1987;60(12):3071-9.
4. Liang H, Ba M, Li C, Li H, Guo Z, He P, et al. A case of acute myelogenous leukemia characterized by arterial and venous thrombosis. Cardiovasc Diagn Ther. 2020;10(5):1332-40.
5. Hess CJ, Ameziane N, Schuurhuis GJ. Hypermethylation of FANCC and FANCL promoter regions in sporadic acute leukemia. Cell Oncol. 2008;30(4):299-306.
6. DeStefano V, Sorà F, Rossi E, Chiusolo P, Laurenti L, Fianchi L, et al. The risk of thrombosis in patients with acute leukemia: Occurrence of thrombosis at diagnosis and during treatment. J Thromb Haemost. 2005;3(9):1985-92.
7. Chong BH, Lee SH. Management of thromboembolism in hematologic malignancies. Semin Thromb Hemost. 2007;33(4):435-48.
8. Singh NK, Sangwan G. Low platelet counts in cancer patients: Should heparin for venous thromboembolism prophylaxis be instituted? J Clin Oncol. 2008;26(11):1906.

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