OMCR

Oxford Medical Case Reports, 2019;01, 32–34

doi: 10.1093/omcr/omy118
Case Report

CASE REPORT

Cerebral venous thrombosis as an initial manifestation of acute myeloid leukemia

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Abstract

Cancer-associated thromboembolism is not an uncommon complication in patients with malignancies. No study has reported the occurrence of thromboembolism prior to the diagnosis of acute myeloid leukemia (AML). Most reports are anectodal and data are scarce on this subject. In this report, we present a case of extensive cerebral venous thrombosis (CVT) that was detected a few weeks before the diagnosis of AML, in which case the patient responded well to chemotherapy and anticoagulation.

INTRODUCTION

It is not uncommon for patients with malignancies to have cancer-associated thromboembolism complications [1, 2]. Though the association between solid tumors and thrombosis is well recognized, most reports, however, remain anecdotal and data are scarce on this subject i.e. risk of thrombosis in acute myeloid leukemia (AML) [3]. No study has reported the occurrence of thromboembolism prior to diagnosis of AML. In this paper, we present a case of extensive cerebral venous thrombosis (CVT) that was detected a few weeks before the diagnosis of AML.

CASE REPORT

A 29-year-old woman, with no underlying medical illness, developed a week-long history of severe headache, altered mental status and generalized weakness. On examination, she appeared drowsy with fluctuating consciousness. Vital signs were stable and afebrile. Neurological examination showed power 4/5 in all limbs with no meningism. Other physical examinations were unremarkable. Laboratory investigations showed bicytopenia (hemoglobin 6.4 g/dL, leukocyte 5.4×103/μl, platelet 100 ×103/μl) and elevated LDH. Serum electrolytes, coagulation profile, renal and liver profile were all within normal range. Initial full blood picture (FBP) was reported as severe, normochromic, normocytic anemia with no blasts. Contrasted computed tomography (CT) of brain showed features of left transverse, straight and posterior aspect of superior sagittal sinus thrombosis, with left temporal intra-parenchymal bleeding. Intravenous Unfractionated heparin (UFH) commenced with a remarkable symptomatic improvement. The patient was discharged with oral warfarin as anticoagulation.

Three weeks later, during an outpatient clinic follow-up, her white cell count had elevated to 48.7×103/μl with persistent bicytopenia (Hb 7.2 g/dL, platelet 80×103/μl). A repeated FBP showed the presence of 55% blast cells. Her bone marrow biopsy was consistent with AML-M4 (French-American-British (FAB) criteria). Immunophenotyping reported a 10% cluster of myeloblasts and 66% cluster of blast expressing monocytic

Received: July 6, 2018. **Revised:** October 1, 2018. **Accepted:** November 1, 2018

marker with cytogenetic studies indicating an aberrant expression of 7, with no molecular abnormality. Induction chemotherapy DA (daunorubicin and cytarabine) 3 + 7 was started and warfarin was changed to subcutaneous Low Molecular Weight Heparin Tinzaparin 10 000 units daily (LMWH). Tinzaparin was withheld whenever the platelet count was below 50×10^9/l. The patient did not go into remission with the first induction and was re-induced with a high dose of AraC. She responded very well, as evidenced by the rapid recovery of her neurological status, and the repeated bone marrow studies showed that the disease was in remission. The high doses of AraC chemotherapy treatment were maintained and the patient has been undergoing monthly chemotherapy for the last 3 months. No bleeding episodes or recurrence of thrombosis was observed throughout the chemotherapy. A platelet count above 50×10^9/l was used as the level to start LMWH, and when any platelet count was below 50×10^9/l, LMWH was stopped.

DISCUSSION

CVT is relatively common in Acute Lymphoblastic Leukemia (ALL) patients, as treatment of ALL with L-asparaginase is known to produce a pro-thrombotic state leading to overt thrombosis [4, 5]. Several studies reported thrombosis complications in acute promyelocytic leukemia (APL) patients [6]. However, limited data are available for the occurrence of CVT in non-APL AML patients. One study has found that thrombosis was evident in 3.4% of the whole cohort at diagnosis: 9.6% in APL and 3.2% in non-APL AML patients [5]. Of the latter population, none were reported to have CVT.

Due to its non-specific manifestations, CVT may be difficult to diagnose clinically. The associated symptoms and signs may vary widely. These include headaches, vomiting, focal neurological deficits and seizure. Multiple factors have been identified, which also vary according to different geographical profile, including coagulopathies, connective tissue disorders, tumors and infections [7, 8]. Therefore, it is of paramount importance to determine the underlying etiology, as the mainstay of therapy is to treat the underlying cause, in addition to starting standard anticoagulation. The fact that almost half of the brain CTs were found to be normal added to the clinical difficulty in the diagnosis of CVT [9]. This highlights the rationale for ordering cerebral venography in highly suspicious cases of CVT even in the presence of normal brain CT findings.

One study reported that venous thromboembolism (VTE) before or during diagnosis of acute leukemia was not related to poor prognosis, as the authors found similar overall survival, disease-free survival, and remission duration between patient groups with and without VTE [10]. However, the VTE events in this study did not include CVT and hence, it was unable to predict the outcome of CVT in AML patients.

Patients with hematological malignancies are often thrombocytopenic due to disease and/or chemotherapy. It has always been a debate regarding the safety of anticoagulation in the treatment of VTE in such subset of patients. Current recommendations suggest a full anticoagulation dose of LMWH be used in patients with platelet count above 50×10^9/l with dose adjustment if below 50×10^9/l [11–13]. In our case, LMWH is withheld whenever the thrombocyte count is less than 50×10^9/l. No bleeding or recurrent thrombotic episodes have been observed. Anticoagulation may be considered in patients with low platelet count, on a case-by-case basis, taking the risk of bleeding and thrombosis into consideration.

Data from the International Study on Cerebral Vein and Dural Sinus Thrombosis (ISCVT) study suggest that LMWH may be more effective and safer than UFH [14]. However, no direct comparisons between UFH and LMWH are available up to date. Such decision should be based on individual cases. The rationale of choosing UFH at the initial acute stage of presentation in our case is due to the concern of bleeding risks and the potential reversibility of UFH. The short half-life of UFH is preferred over LMWH for clinically unstable patients. The contrasted brain CT of our patient demonstrated left temporal intraparenchymal bleeding. It has been shown that concomitant intracerebral bleeding at the time of CVT diagnosis should not contraindicate the use of anticoagulant treatment [14, 15]. Anticoagulant with a shorter half-life should be administered over the first days of therapy and the introduction of warfarin should be postponed until the patient is clinically stable [14, 15].

CONCLUSION

The mechanism responsible for CVT in our patient remains speculative. The risk of thrombosis is not negligible in patients with AML. Clinical suspicion should be heightened with the onset of neurological symptoms and signs. The occurrence of thromboembolism is possible even prior to the diagnosis of AML. Anticoagulation is safe and feasible during chemotherapy for AML.

ACKNOWLEDGMENTS

No other persons have made substantial contributions to the manuscript other than the authors.

CONFLICT OF INTEREST STATEMENT

The authors declare that they have no competing interest.

FUNDING

The authors declare no financial disclosure.

ETHICAL APPROVAL

No ethical approval is required. Each of the authors warrants that the enclosed article is original and does not infringe any copyright or violate any other right of any third parties, and the article has not been published elsewhere, has not been submitted for publication, and is not being considered for publication elsewhere in any form, except as explained to the Editor.

CONSENT FOR PUBLICATION

Written permission for publication has been obtained from the patient.

GUARANTOR: AUTHOR

Author—Siaw Tze, Yeo was nominated as a guarantor of this report

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