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ACUTE MYELOID LEUKEMIA PRESENTING WITH ACUTE THROMBOSIS OF THE PORTAL VEIN, SUPERIOR MESENTERIC VEIN, AND SPLENIC INFARCT: A CASE REPORT

Gastroenterology

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ABSTRACT

Background: Acute myeloid leukemia (AML) is a rapidly progressing cancer affecting the myeloid cells. The most common risk factor for AML is the presence of an antecedent hematologic disorder, the most common of which is myelodysplastic syndrome (MDS). Some congenital disorders that predispose to AML include Bloom syndrome, Down syndrome, congenital neutropenia, Fanconi anemia, and neurofibromatosis. Persons who smoke tobacco have a small but statistically significant (odds ratio:1.5) increased risk of developing AML. In several studies, the risk of AML was slightly increased in people who smoked compared to those who did not. Exposure to soot, creosote, inks, dyes, tanning solutions, and coal dust have also been associated with AML.[1] Thrombosis is a common complication in patients with acute leukemia. The clinical outcome of thrombosis in adult patients with acute myeloid leukemia (AML) is scarce. This case report demonstrates acute myeloid leukaemia causing acute thrombosis of the portal vein, superior mesenteric vein, and splenic infarct in a chronic smoker but an otherwise healthy person.

KEYWORDS

Case Presentation:
A 36-year-old Asian male with no notable past medical history presented to emergency medicine with 2 weeks of severe fatigue, myalgia, anorexia, malaise, left sided abdominal pain, especially left hypochondriac and lumbar region. Patient had a history of frequent and multiple visits to healthcare providers for stomach upsets, GERD-like symptoms, and flank pain all of which were symptomatically treated and evaluated by routine investigations, which were found to be within normal limits.

Since the patient was presented with severe abdominal pain (pain scale 8-9/10), not relieved by over-the-counter analgesics or proton pump inhibitors, CT abdomen was advised with contrast. The report suggested an enlarged spleen with multiple wedge-shaped hypo densities consistent with infarctions with an enlarged splenic vein, portal vein, and superior mesenteric vein with large extensive filling defects consistent with acute extensive thrombosis. Liver of normal size and outline, no focal lesion or dilated intrahepatic biliary passages. GB and CBD were normal with no stone.

Hence, to get the etiology for non-hepatic causes of the acute thrombosis, the patient was advised for thrombophilia and vasculitis screen, tests to rule out PNH, Polycythemia, and hyper-homocysteinemia. The reports came within the normal limits, except for the mild elevation of liver enzymes and platelets and a higher D –dimer of 3.62mg/dl.

Peripheral blood smear showed >42 % Blast Cells, which were round to oval, medium to large in size with a high N/C ratio and scanty pale grayish blue cytoplasm. Nuclear chromatin was smooth. A minor amount of blast cells had distinct nucleolus and Auer rods. Promyelocytes were not increased and monocytic features were not seen. These cytomorphological features were consistent with Acute Myeloid Leukemia (AML).

The patient was started on therapeutic anticoagulation with enoxaparin and warfarin with close monitoring of INR. After 2 days of treatment the patient's pain decreased, started tolerating oral intake. The haematology department was consulted for further evaluation. The patient was advised for flow cytometry and bone marrow biopsy for confirmation.

Flow cytometry analysis showed an abnormal population of myeloblasts comprising up to 40% of total events with the following features:

Positive for: CD45 (dim), CD34, CD56 (minor subset), CD19 (minor subset dim, mostly negative), CD38 (bright), CD200, CD13 (dim, partial), HLA-DR (bright), CD123 (dim, partial), CD117 and MPO
Negative for: CD3, CD5, CD10, CD20, kappa, lambda, CD2, CD4, CD5, CD7, CD8, CD16, CD64, CD14, CD11b, CD15, CD33, TdT, cyCD3 and cyCD79a

These features were highly suggestive of Acute myeloid leukemia. When the patient was informed about the condition, he wanted to do further evaluation and treatments from his hometown, hence, was discharged with oral anticoagulation with proper education about his disease and prognosis.

DISCUSSION

Acute myeloid leukemia (AML) is a malignant disease of the bone marrow in which hematopoietic precursors are arrested in an early stage of development. Most AML subtypes are distinguished from other related blood disorders by the presence of more than 20% blasts in the bone marrow.

Thrombosis is a common complication in patients with acute leukemia. The pathogenesis of thrombosis in leukemia is multifactorial.[2] Blasts secrete prothrombotic products such as tissue factor (TF), cancer procoagulants,[3] and cytokines.[4] Additional risk factors for venous thromboembolism in AML patients include the increased expression of tissue factors in leukemic cells, its activation on cellular surfaces, and hyperleukocytosis.[5]

Portal vein obstruction was first reported in 1868 by Balfour and Stewart, who described a patient presenting with an enlarged spleen, ascites, and variceal dilatation. Most of the studies on portal vein obstruction/thrombosis are done on ALL patients, who are mostly children and thus the studies on adult leukemic patients about the pathophysiology are lacking. Myeloproliferative disorders and inherited or acquired hypercoagulable disorders account for 10-12% of cases in adults. Approximately 8-15% of cases have been reported to be idiopathic in the recent literature. In adults, cirrhosis is accused to be the major etiology, accounting for 24-32% of cases of portal vein thrombosis. Neoplasms including hepatocellular and pancreatic carcinoma are another cause accounting for 21-24% of cases of portal vein obstruction.[6] These tumors cause portal vein compression or direct invasion and by inducing a hypercoagulable state, leading to thrombosis.[7] Although less common, intra-abdominal infections with *Bacteroides fragilis* with associated bacteremia play an important role in portal vein thrombosis. The other less common etiologies include

abdominal trauma, surgery, and local ablative therapies for hepatocellular carcinoma or metastatic disease.

Studies indicate that the risk of thrombosis in hematologic patients may be similar or even higher than in those with solid neoplasms. Among hematologic malignancies, the incidence of venous thromboembolism (VTE) is known in myeloma (5%), non-Hodgkin lymphoma (4.8%) and Hodgkin disease (4.6%) [8] whereas, the information is lacking in acute leukemia. In addition to the procoagulant activity of malignant cells, chemotherapy, high doses of steroids, infections, and central venous catheter (CVC) insertion also contribute to thrombosis in acute leukemia. The study of Ku et al. [8] indicates that female sex, older age, number of chronic comorbidities and presence of a CVC are predictors of VTE development within 1 year from the diagnosis of AML. In a large study of AML patients, advanced age (>65 years) and intermediate/high cytogenetics risk [9] were found to anticipate VTE development. [10]

In a prospective cohort study done in a large population of adult AML patients, Libourel et al. found that the incidence of thrombosis was 8.4% (4.7% venous, 4% arterial) in younger adults and 10.4% (4.4% venous, 5.9% arterial) in elderly patients. Overall, the incidence of arterial thrombosis was higher than expected. Based on a set of biomarkers of disseminated intravascular coagulation (DIC) the authors calculated the DIC score, which could significantly predict venous and arterial thrombosis, and, among the DIC biomarkers, a high D-dimer level was the best predictor of thrombosis. [11]

From a retrospective study by Khorana et al., one of the most used risk-scoring systems for thrombosis, the Khorana Risk Score (KRS), was developed by studying patients with non-hematologic cancers receiving outpatient chemotherapy treatments. The score is based on body mass index (BMI) and white blood cell, hemoglobin, and platelet counts. [12]

To reduce the incidence of thrombosis, therapeutic agents like all-trans retinoic acid (ATRA) was shown to diminish the expressions of TF and cancer procoagulants, attenuating the procoagulant, fibrinolytic and proteolytic activity of the leukemic blasts. However, some studies suggest that ATRA-induced modifications in the balance between procoagulant and fibrinolytic properties of leukemic promyelocytes might favor the development of thrombosis, especially during ATRA syndrome and in patients with hyperleukocytosis. [13]

Thus the treatment guidelines should be based on prospective studies conducted on patients with acute leukemia and should be designed separately, according to leukemia subtype (ALL, AML, and APL), since each acute leukemia subtype represents a different pathogenic setting favoring the development of thrombosis. A systematic review by Azin et al. found that there is a significant lack of data in this area with a high degree of heterogeneity in the choice of anticoagulant, dose adjustments for thrombocytopenia, and duration of anticoagulation for the treatment of venous thromboembolism in acute leukemia.[14]

The role of newer anticoagulants needs to be explored in multicenter clinical trials, and risk factors should be standardized to provide adequate treatment to these patients within a complicated set of thrombosis and hemorrhage.

CONCLUSION

Venous thrombosis is a serious complication seen in Acute myeloid leukemia patients, although the data regarding its incidence, pathogenicity, and the risk factors involved are lacking with respect to adult patients. The current case report about an adult patient with acute myeloid leukemias having acute thrombosis of the major abdominal veins can increase awareness about this unexplored condition. Further studies are required to develop guidelines and suggestions for the treatment of VTE in Acute Leukemia.

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