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Acute Myeloid Leukemia presenting with Acute Thrombosis of the Portal vein, Superior Mesenteric vein and Splenic infarct: a case report.

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ABSTRACT

Background:-

This case report demonstrates Acute myeloid leukemia causing acute thrombosis of portal vein thrombosis , superior mesenteric vein , and splenic infarct in otherwise healthy man. Patient is chronic smoker , with pack years of 20 . Thrombosis is a common complication in patients with acute leukemia. The clinical outcome of thrombosis in adult patients with acute lymphoid leukemia (ALL) or acute myeloid leukemia (AML) is still scarce. The most common risk factor for AML is the presence of an antecedent hematologic disorder, the most common of which Myelodysplastic syndrome (MDS), Some congenital disorders that predispose patients to AML include **Bloom syndrome**, **Down syndrome**, congenital neutropenia, **Fanconi anemia**, and **neuro fibromatosis**. Persons who smoke tobacco have a small but statistically significant (odds ratio, 1.5) increased risk of developing AML[1]. In several studies, the risk of AML was slightly increased in people who smoked compared with those who did not smoke. Exposure to benzene is associated with aplastic anemia and pancytopenia. Exposure to soot, creosote, inks, dyes, and tanning solutions and coal dust have also been associated with AML

I. CASE PRESENTATION:

A 36-year-old Asian male with no notable past medical history presented to his primary care provider with 2 weeks of severe fatigue, left sided abdominal pain , mainly left hypochondriac and lumbar region ,anorexia, and malaise, associated with myalgia's. Patient has a history of frequent and multiple visits to healthcare providers for stomach upsets , GERD like symptoms , flank pain all of which were symptomatically treated and evaluated by routine investigations ,which were found to be within normal limits .

Initial presentation to emergency with severe abdominal pain , not relived by over the counter pain medications , proton pump inhibitors .Patient has no significant past medical history .

As the patient presented with severe pain abdomen , pain scale 8-9/10 , not relived by analgesics , patient underwent computed tomography of abdomen with contrast . The report suggested Enlarged spleen with multiple wedge shaped hypo densities consistent with infarctions with enlarged splenic vein , portal vein and Superior Mesenteric Vein with large extensive filling defects consistent with acute extensive thrombosis .Liver of normal size & outline , no focal lesion seen ,not dilated intrahepatic biliary passages, normal GB & CBD , no stone .

Hence in an effort to get to the etiology all the routine investigations were done , basically searching for non hepatic causes of the acute thrombosis . Patient was worked up for thrombophilia screen , vasculitis screen, tests to rule out PNH , Polycythemia and hyper-homocyteinemia .

Initial blood work up were all with in normal limits , except for D –dimer being higher 3.62mg/dl , mild elevated liver enzymes and platelets .

peripheral blood smear was suggestive of :- Blood smear shows Blast Cells (>42 %) round to oval in shape, medium to large in size with high N/C ratio and scanty pale grayish blue cytoplasm. Auer rods seen in rare blasts. Nuclear chromatin is smooth. Rare blast cells show distinct nucleoli. Promyelocytes are not increased. Monocytic features not seen. Cytomorphological features are consistent with Acute Myeloid Leukemia (AML).

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Patient was started on therapeutic anticoagulation with enoxaparin and bridging with warfarin with close monitoring of INR .

Hematology department was consulted for further evaluation . After 2 days of treatment patient pain decreased , started tolerating oral intake . Since we are in secondary setup the patient needed evaluation with Flow cytometry and bone marrow biopsy for confirmation .

Flow cytometry report was done:- Flow cytometry analysis shows an abnormal population of myeloblasts comprising up to 40% of total events with the following:

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

Highly suggestive of Acute myeloid leukemia .

Patient was referred for bone marrow biopsy and evaluation by hemato-oncologist in higher centre , but due to the patients request to return to his home country to be with his family and to receive treatment, He was discharged with oral anticoagulation with proper education about his disease condition and prognosis .

II. DISCUSSION :-

In the English literature, 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 [3]

In adults, cirrhosis is the major aetiology , accounting for 24-32% of cases of portal vein thrombosis. Neoplasms are another major cause, accounting for 21-24% of cases of portal vein obstruction, with hepatocellular carcinoma and pancreatic carcinoma causing most of these cases. [3]These tumours can cause compression or direct invasion of the portal vein or lead to thrombosis by inducing a hyper coagulable state[4]

Local ablative therapies for hepatocellular carcinoma or metastatic disease have been linked to its development. Although less common than in children, infections (predominantly intra-abdominal) still play an important role, with a particular association with Bacteroides fragilis bacteraemia.

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. For other less common aetiologies, such as abdominal trauma, surgery, and inflammatory bowel disease, see the image below.

Acute myeloid leukaemia (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

Additional risk factors for VTE in AML patients include the increased expression of tissue factor in leukemic cells, its activation on cellular surfaces, and hyperleukocytosis.[5]

The pathogenesis of thrombosis in leukaemia is multifactorial [6]. Blasts secrete prothrombotic products such as tissue factor (TF), cancer procoagulant [7] and cytokines [8].

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 information in acute leukemia is severely lacking .

In addition to procoagulant activity of malignant cells, chemotherapy, high doses of steroids, infections and central venous catheter (CVC) insertion also contribute to thrombosis in acute leukemia. Among therapeutic agents, all-trans retinoic acid (ATRA) was shown to diminish the expressions of TF and cancer procoagulants, thus attenuating procoagulant, fibrinolytic and proteolytic activity of the leukemic blasts. However, some studies also suggest that ATRA-induced modifications in the balance between procoagulant and fibrinolytic properties of leukemic promyelocytes might favor development of thrombosis, especially during ATRA syndrome and in patients with hyperleukocytosis [9].

The study of Ku et al.[10] 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 [11] were found to anticipate VTE development [12]

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In a prospective study done in 2001, including a cohort of 272 adult patients and an independent 'validation' cohort of 132 adults with newly diagnosed AML, Libourel et al. measured a set of biomarkers of disseminated intravascular coagulation (DIC) (fibrinogen, D-dimer, α-2-antiplasmin, ant thrombin, prothrombin time and platelet count) and calculated the DIC score (according the International Society of Thrombosis and Haemostasis) (13)

The authors 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, incidence of arterial thrombosis was higher than expected.

The calculated DIC score significantly predicted venous and arterial thrombosis and, among the DIC biomarkers, a high D-dimer level was the best predictor of thrombosis(14)

Another study done from collection of data from 2000-2018 by Khorana AA et al , ,One of the most commonly 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 KRS is based on body mass index (BMI) and white blood cell, haemoglobin, and platelet counts (15)

In a study conducted by Azin et al, The Treatment of venous thromboembolism in acute leukaemia: A systematic review:- they concluded 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. Further studies are required to develop guidelines and suggestions for treatment of VTE in Acute Leukaemia (16)

III. DISCUSSION:-

Thrombosis is a common complication in patients with acute leukaemia. Most of the information on ALL patients has been obtained from studies in children and the information in adult patients is lacking.

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

Ideally, guidelines should be based on prospectively designed studies conducted only in patients with acute leukaemia. Furthermore, they should be designed separately, according to leukaemia subtype (ALL, AML, and APL). It is very probable that each acute leukaemia subtype represents a different pathogenic setting favouring the development of thrombosis.

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