Case Report

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A Rare Case of Portal Hypertension

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Presenting Complaints: A 47-year-old male patient presented with complaints of breathlessness and easy fatiguability for two months.

History of Presenting Complaints: The patient was apparently in the usual state of health until about two months back, after which he developed complaints of breathlessness – insidious in onset. Initially grade 2 dyspnea which progressed to grade 3 dyspnea in 2 months. No history of orthopnea and paroxysmal nocturnal dyspnea.

- H/o easy fatiguability for two months.
- H/o loss of weight present – patient not able to mention the number of kgs or the duration of weight loss.
- h/o palpitations on exertion present
- No h/o chest pain.
- No history of cough with expectoration
- No history of bilateral lower limb swelling
- No history of abdominal distension/ pain.
- No history of frothy urine/ decreased urine output/ painful micturition
- No history of bleeding manifestations.
- No history of vomiting up of blood or black-colored tarry stools, blood in sputum.
- No history of fever, evening rise of temperature.
- No history of headache, blurring of vision. No history of ENT complaints.
- History of loss of appetite present.

Past History: Not a known case of diabetes, hypertension, coronary artery disease, chronic kidney disease, tuberculosis, thyroid diseases, bronchial asthma.

No history of prior hospitalizations, no history of previous blood transfusions.

No history of similar complaints in the past

Personal History: The patient has been a chronic alcoholic for the past 25 years. The patient reports daily consumption of alcohol, around 2 to 3 quarters per day, with increased intake on the weekends and other special occasions. Due to the symptom onset, the patient has refrained from alcohol intake over the last two months. Chronic smoker for 25 years. Quit two years back.

Occupational History: Painter by occupation.

Family History: Nil significant

Drug History: Nil significant

General Examination: The patient was conscious, oriented, afebrile with good hydration.

PALLOR ++, no icterus, no cyanosis, no clubbing, minimal grade 2 pitting pedal edema, no significant cervical, axillary, inguinal lymphadenopathy.

JVP elevated

- **CVS:** S1S2 heard, Hemic murmur heard. No other added sounds.
- **RS:** Bilateral normal vesicular breath sounds heard in all lung fields. No added sounds.

P/A: On Inspection, Skin appears normal, with no scars, sinuses, or dilated veins. Umbilicus in the midline. The abdomen is flat, not distended, and has no visible mass. All quadrants move equally with respiration.

Palpation: An enlarged liver palpable around 3cm below the right intercostal margin is felt. The margins are regular, firm in consistency, non-tender, and move with respiration.

- On palpation from the right iliac fossa, diagonally to the left hypochondrium, a mass that moves with inspiration is firm in consistency, and non-ballotable was felt immediately above the umbilicus—measured around 12cm from the left costal margin. It was confirmed to be the spleen.

Percussion: Liver Span – 15 cm Traube's Space – Obliterated.

CNS: No focal neurological deficit.

Investigations:

Complete Blood Count: on admission

Total Count: 12000

Hemoglobin: 3.2 g/dl

HCT: 11.0 %

MCV: 106.8 fl

Platelet: 1,81,000

Random Blood Sugar – 77mg/dl

PERIPHERAL SMEAR

- Dimorphic anemia, macro ovalocytes, teardrop cells, severe poikilocytosis. Neutrophilic predominance with hypersegmented neutrophils.
  - *Corrected Retic Count* – 0.5%
- Impression: *Dimorphic Anemia With Neutrophilic Leukocytosis*

LFT and RFT:

UREA – 18

CREATININE -0.7

Na+- 145

K+ - 4.8

Bilirubin – 1.0

SGOT – 11

SGPT – 43

ALP – 88

Total Protein – 6.0 ALB – 3.9, Globulin – 2.1

- In the meantime, the patient was treated with one dose of T. Albendazole and two packed cell transfusions.
  - Other investigations:

  Serum folic acid: 24.80 ng/ml (5.90 – 24.80)

  Serum Vitamin B12 - >1500 pg/ml (180.00 – 914.00)

  LDH : 590 U/L (135-214)

  ESR: ½ HOUR – 28mm

  1 hr – 66mm

  PT, APTT, INR - WNL

  Viral Markers – HIV, HbSAg, Anti HCV - Negative

Ultrasound abdomen: liver – normal echoes, spleen measuring 23cm. Portal vein diameter of 25mm. Splenomegaly with portal hypertension. Possibility of Extrahepatic portal vein thrombosis to be ruled out and suggested CECT abdomen.

Echo: NO RWMA, EF-60%, Normal LVSF.

Direct Coombs Test, Indirect Coombs Test – Negative

Stool Occult Blood–Negative

Urine Routine Examination – Sugar and Albumin – Nil

Blood Grouping and Typing – O+ve

CT Chest:

- Multiple enlarged necrotic prevascular, pretracheal, right paratracheal nodes were noted as the largest, measuring 1.3*0.6 cm.
- Lung fields normal
- CECT Abdomen and Pelvis: Liver measuring 16 cm in size. The portal vein appears dilated, measuring 25mm.
- Gall bladder – appears normal in contour and wall thickness. No evidence of mass lesion. Calculus measuring 3.5 mm was noted in the neck of the gall bladder.
- Spleen – Spleen appears grossly enlarged, measuring 24 cm. Multiple perisplenic, periportal, perigastric collateral noted. The splenic vein appears grossly dilated, measuring 1.7cm at the hilum.
- **Impression:** Hepatosplenomegaly with portal hypertension, portal vein thrombosis
- Cause for splenic vein thrombosis and portal hypertension was being evaluated, and the repeat investigations showed a progressive exponential increase in WBC counts

Date	WBC Count	Platelets	Hemoglobin
04.12.2021	12000	181000	3.2
09.12.2021	17300	155000	3.4
11.12.2021	25000	202000	5.5
14.12.2021	35800	238000	6.1
16.12.2021	57920	506000	6.6

Repeat Peripheral Smear

RBC – Reduced in number, predominantly normocytic, normochromic admixed with macrocytic RBCs, few polychromatophilic cells.

Nucleated RBCs - 2/100 WBCs. Moderate anisocytosis, mild poikilocytosis. No inclusions or hemoparasites were seen.

WBC: Counts markedly increased, with the shift to the left comprising of myeloid series, including band forms, myelocytes, metamyelocytes, and mild basophilia.

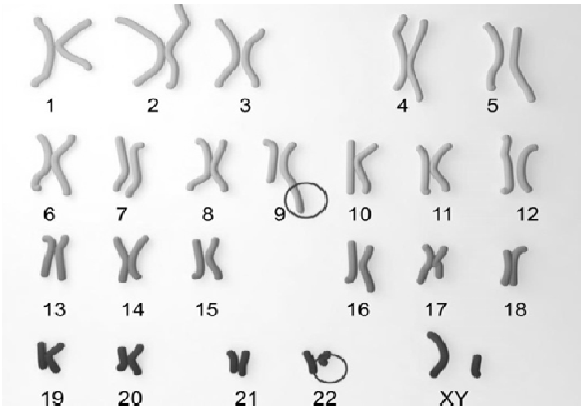
Neutrophils – 53%, lymphocyte – 2%, metamyelocyte – 14%, Myelocyte – 16%, Band – 2% Basophils – 2%

Platelets: Increased in number. Occasional giant platelets are seen.

Impression: Leukoerythroblastic blood picture possibility of chronic myeloid leukemia – chronic phase.

Diagnosis: Chronic Myeloid Leukemia – Chronic Phase induced Hypercoagulable State Resulting in Portal Venous Thrombosis and Portal Hypertension

Discussion: Chronic myeloid leukemia is caused mainly due to translocation of 9:22 BCR-ABL mutation. The foreshortened chromosome number 22 with the BCR-ABL translocation is called the Philadelphia chromosome.



The Formed BCR-ABL Fusion Protein Can Exist in 2 Forms – 210 KDa (most common), 190 KDa (less common).

This increases kinase activity, and the kinase is now called BCR-ABL kinase. This fusion kinase has increased activity and hence accelerates the formation of granulocytes and neutrophils.

Classification:

- **Chronic Phase:** Contains <10% blasts in the bone marrow. It is associated with thrombocytosis.
- **Accelerated Phase:** 10-19% blasts in the bone marrow. Basophilia of more than 20%. Platelets start to drop.
- **Blast Crisis:** >20% blasts in the bone marrow.

The anemia usually seen is caused due to diversion of the myeloid precursor cells to the production of granulocytes.

Clinical Features: Usually, the patients tend to be asymptomatic. Constitutional symptoms include low-grade fever, evening rise of temperatures, easy fatiguability, abdominal pain, and a dragging sensation secondary to an enlarged spleen. Anemia induced easy fatiguability and exertion aldyspnea. Easy bruising, bleeding manifestations, or symptoms secondary to a hypercoagulable state like chest pain, blurring of vision, CVA, etc.

Other Investigations: Peripheral Smear: Leucocytosis with Left-sided shift with good myeloid maturation. Basophilia with or without thrombocytosis, with or without anemia.

BONE MARROW: Hypercellular with an increase in Myeloid to erythroid ratio.

M:E – 3:1 – NORMAL

CML – 10:1 or greater.

KARYOTYPE: Philadelphia chromosome.

Cause of Splenomegaly In CML: Increased blood cell circulation and extramedullary hematopoiesis induced an increase in splenic reticular cells proliferation

Cause of Hypercoagulability in CML: Increase in white blood cells and thrombocytosis

contribute to the hypercoagulable state. The coagulation profile is usually unaltered.

The role of anticoagulants like heparin and warfarin is questionable. The treatment lies in the treatment of the underlying disease status. As per studies, the hypercoagulable state settles down with the reduction in the counts.

Increased VIT B12 in CML: The aetiological profile of high serum cobalamin was primarily composed of potentially serious diseases, where early diagnosis is often a determinant prognostic factor.

Normal vit b12 levels – upto 950 pg/ml.

Vitamin B12 levels though high, can manifest with symptoms of deficiency due to functional deficiencies.

This occurs because of the following reasons, Vitamin B12 circulating in the blood binds to transcobalamins.

Transcobalamins are of 3 different types. The TC I and TC III are 60-70 kDa molecular weight proteins. They belong to the haptacorrin superfamily, in which they represent the serum forms. These are derived from the granulocyte line and are the markers of neutrophilic secondary granules, which explains their increase in myeloproliferative neoplasms.

TC II is the functional component that plays a role in delivering vitamin B12 to the tissues for uptake. Decrease in uptake by the cells and increase in the circulating forms account for the high serum levels of vitamin B12 with clinical symptoms due to functional deficiency.

Alcoholism and CML: A study – Alcohol consumption and risk of leukemia: A multicentric case-control study – Even though their study did not show a clear association between alcohol intake and leukemia risk, some of the patterns of risk estimates (a possible J shaped dose-response curve between alcohol intake and ALL, AML and CML and the positive association between alcohol and CML may be suggestive.

Treatment: Tyrosine Kinase Inhibitors Like Imatinib

Months	Optimal	Sub Optimal
Three months	BCR-ABL <10%	Complete hematological response
Six months	BCR-ABL <1% + partial cytological response	Ph >35%
12 months	BCR-ABL <0.1% (major molecular response) + complete cytological response	Ph > 1%
Anytime		Loss of major molecular response

If an optimal response is maintained with imatinib therapy and a complete molecular response sustained for 2 years, the TKI therapy can be withheld with careful follow-up.

Other Drugs:

- Interferon-alpha - useful in pregnancy
- Hydroxyurea
- Omacetaxine is used after more than two tyrosine kinase inhibitors fail.

Dosage – 1.25mg/m^2 subcutaneously twice daily for 14 days for induction, seven days of maintenance every month.

Allogenic hematopoietic stem cell transplant can be used upfront when the patient is in the accelerated phase or blast crisis.