Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/jptcp.v31i3.5125

CLINICAL AND ETIOLOGICAL PROFILE OF PATIENTS PRESENTING WITH PANCYTOPENIA IN A TERTIARY CARE CENTRE OF ARUNACHAL PRADESH.

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Abstract:
Pancytopenia is a clinical phenomenon characterized by reduction in 3 cell lineage-erythrocytes, leukocytes and platelets[1].Whenever a clinician encounters a case of pancytopenia, major challenge is to reach a diagnosis and rule out causes of pancytopenia[2]. Here we present case series of 7 patient who presented with pancytopenia and was diagnosed with varied etiology.

Background :
Causes of pancytopenia can be divided into Marrow causes and non-marrow causes[3].
Marrow causes includes Aplastic anemia, acute leukemias, bone marrow fibrosis, myelodysplastic syndrome and infiltrative diseases mainly due to malignant cells are major causes of bone marrow failure.
Non marrow causes include Hypersplenic state, systemic lupus erythematosus, infections (Tuberculosis, HIV, leishmaniasis and brucellosis) and nutritional deficiency (folate, B12). Chemotherapeutic agents, antibiotics (chloramphenicol, sulphonamides), antiepileptic drugs (Carbamazepine, Phenytoin, Valproic acid), and heavy metals such as gold are known therapeutic agents associated with increased risk of aplastic anaemia.[4]Virus such as parvovirus B19, hepatitis viruses (non-A, non-B, non-C, non-G hepatitis) and HIV are known viral causes of aplastic anaemia.

Patients with history of ethanol ingestion and proven chronic liver disease were excluded from the study. In this study all patients with history of Chronic ethanol ingestion and documented chronic liver disease were excluded, since patient with Chronic liver disease have hypersplenism and may manifest as pancytopenia. Also ethanol ingestion can cause bone marrow suppression[7].

Key words : Pancytopenia, Hypersplenism, Bone Marrow

Case details:

Case 1:
60 years old male with no previous comorbidities presented to our Centre with complaints of increased fatiguability for 1 month duration. On examination he had pallor, splenomegaly around 6 cm below left costal margin and mild hepatomegaly. Other systemic examination was within normal limits. Routines showed pancytopenia. Hb 9.5 gm/dl, TLC 3300/mm3, PLC 44000. Peripheral smear

showed leukopenia with borderline neutropenia, thrombocytopenia. Other routines were within normal limits. In view of pancytopenia and organomegaly, there was high suspicion of leukemia.
So, we proceeded with bone marrow study which showed hypercellular bone marrow, 49 % blast suggestive of Acute myeloid leukemia.

Case 2:
25 years old female presented with breathlessness and swelling of feet and periorbital edema of 10 days duration. Past history of arthralgia was present. On examination patient had pallor, pitting pedal edema. Breath sounds were decreased bilaterally, Other systemic examination was within normal limit. Routine showed Hb 7.6gm/dl, TLC 1500/mm3, PLC 20000. Other routines were within normal limit. Peripherial smear showed leukopenia with severe neutropenia. Urine AC ratio was high. In view of Young female, arthralgia and serositis all were suggestive of autoimmune etiology. So ANA IF was sent which was positive, dsDNA was also positive. So she was diagnosed as a case of SLE and lupus nephritis.

Case 3:
60 year old female presented with giddiness and increased fatiguability for one month duration. She also had complaint of multiple bony aches and pain. On examination she had pallor, systemic examination was within normal limits. Routines showed pancytopenia and very high ESR and reversal of albumin globulin ratio. Peripheral smear showed Rouleux formation and pancytopenia. In view of anemia, high ESR, AG reversal and multiple ache and pain X ray skull was sent which showed lytic lesion.
Simultaneously, Bone marrow was done which showed 49 % atypical immature plasma cells suggestive of multiple myeloma. Serum protein electrophroresis showed M band. Hence, confirming our diagnosis of multiple myeloma.

Case 4:
A 50 year old male with mixed diet but preferably on vegetarian diet now presented with increased fatigability since 2 months. On examination, he had lustreless hair, hyper pigmented knuckles and pallor.

fig 1. Lustreless hair and hyper pigmented knuckle.

Other systemic examinations was within normal limits. Routine showed Pancytopenia, Hb 7g/dL, TLC 2000 /mm3, platelet count 1.5 lakhs/mm3, MCV 120 fL. Clinical features and CBC was suggestive of Megaloblastic Anemia. Peripherial smear showed normocytic to macrocytic RBCs. Mild thrombocytopenia with hyper segmented neutrophils. Bone marrow aspirate showed hyper cellular bone marrow with trilineage hematopoiesis and erythroid hyperplasia. Bone marrow trephine biopsy showed trilineage hematopoiesis with erythroid hyperplasia with normoblastic to megaloblastic maturation. Patient was managed with methylcobalamine injection and folic acid supplementation. On review, his CBC were within normal limits.

Case 5:
A 62 year old male presented with complaints of multiple ache and pains and dyspnea on exertion. On examination patient had pallor, other systemic examination was within normal limits. Routines showed Pancytopenia, peripherial smear showed leukopenia and thrombocytopenia. Bone marrow aspirate showed trilineage hematopoiesis along with a mild dyserythropoiesis, dysmyelopoiesis and mild dysmegakaryopoiesis suggestive of myelodysplastic syndrome with multilineage dysplasia. MDS FISH was positive confirming our diagnosis of myelodysplastic syndrome.

Case 6:
A 17-year-old male presented with fever and arthralgia of 5 days duration. On examination pallor was present, he was febrile. On examination, mild hepatomegaly and traubes space was dull. Other systemic examinations were within normal limits. Routines showed Hb of 8.8 g/dL, TC of 3000/mm3, and PLC of 70000/mm3. Mild transaminitis was present. Patient was managed with antibiotics, antipyretics and other supportive measures. ESR was high. Peripheral smear showed microcytic hypochromic RBCs with presence of target cells, pencil cells, mild thrombocytopenia and leucopenia.
Bone marrow study showed trilineage hematopoiesis with normoblastic erythroid hyperplasia. All were suggestive of viral fever syndrome with bone marrow suppression. Patient was started on hematinics once fever subsided and on follow up his counts improved.

Case 7:
50 years old male presented with fever and increased fatiguablity for 3 months, history of significant loss of weight and appetite present. He also had history of pulmonary tuberculosis 1 year ago. He had completed one full course of fixed dose anti tuberculous drug. On examination he had grade 2 clubbing. Respiratory system examination showed barrel shaped chest, movement decreased on right upper and lower part both anteriorly and posteriorly. Per abdomen examination revealed hepatomegaly and moderate splenomegaly. Routines showed pancytopenia, high ESR, serum ferritin was 1282, Mantoux was strongly positive. Peripheral smear showed microcytic hypochromic anemia with occasional target cells. His triglyceride was very high 300 mg.
We proceeded with CECT Thorax which showed fibrosis bilaterally. Bone marrow examination showed cellular bone marrow, with erythroid hyperplasia, myeloid maturation, increase in macrophages with hemophagocytosis.

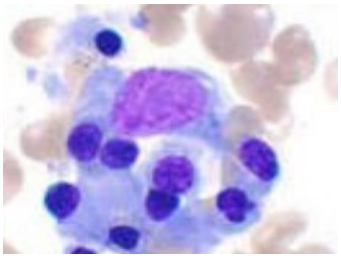

Fig 2: macrophage with hemophagocytosis

Modified 2009 HLH criteria

- At least three of the following:
  - Fever
  - Splenomegaly
  - Cytopenia affecting at least two cell lines:
    - Hemoglobin <9 g/L
    - Platelets <100 b/L
    - Absolute neutrophil count <1000 b/L
  - Hepatitis
- At least one of the following:
  - Ferritin elevation
  - Elevated soluble CD25 (soluble IL2-receptor)
  - Hemophagocytosis seen on tissue biopsy
  - Low/absent NK-cell activity
- Other supportive features (not required)
  - Hypertriglyceridemia
  - Hypofibrinogenemia
  - Hyponatremia

Fig 3: New diagnostic criteria for HLH[8]

So as per new criteria, our final diagnosis was pulmonary tuberculosis with secondary hemophagocytic lymphohistiocytosis.

DISCUSSION:

Sl. no	Age	Total count	Hb	Platelet count	Splenomegaly	Peripheral smear	Bone marrow	Final diagnosis
1	60 years	3300	9.5	44000	Yes	Pancytopenia	49 percent blast	Acute myeloid leukemia
2	25 years	1500	7.6	20000	No	Pancytopenia	Not done	Systemic lupus erythematosus with lupus nephritis
3	60 years	1800	8.2	34000	No	Pancytopenia with rouleux formation	49 percent atypical immature plasma cells	Multiple myeloma
4	50 years	2000	7	1.5 lakhs	No	Pancytopnia, hypersegmented neutrophils	Normocytic to megaloblastic maturation of RBC	Megaloblastic anemia due to vitamin b 12 deficiency
5	62 years	2300	7	49000	No	Pancytopenia	Dyserythropoisis, dysmyelopoisis, dysmegakaryopoisis	Myelodysplastic syndrome
6	17 years	3000	8.8	70000	No	Pancytopenia	Normal marrow	Viral fever induced bone marrow supression
7	50 years	1400	6.2	43000	Yes	Pancytopenia	Macrophages with hemophagocytosis	Pulmonary tuberculosis with secondary HLH

Table 1: Comparisons of age and biochemical profile of patient under study.

In our study, age ranged from 17 years to 62 years. Complete blood count showed pancytopenia in all the patients. Splenomegaly was present in two patient. Peripheral smear showed pancytopenia in all patients. Rouleux formation was seen in multiple myeloma[5]. Hyper segmented neutrophils was seen in megaloblastic anemia[6]. Bone marrow examination helped confirm our diagnosis in 6 cases.
This study highlights the importance of proper diagnostic approach while managing patients with pancytopenia. Patient who presents with pancytopenia can range from as simple as viral fever with bone marrow suppression to serious blood dyscrasias like Acute myeloid leukemia and hemophagocytic lymphohistiocytosis. Proper clinical history and examination is very importance while managing a case of pancytopenia. Dietary history will give clue regarding vitamin B12 deficiency and well as clinical examination correlation like hyperpigmented knuckles, lustreless hair, beefy tongue. Search for organomegaly will give us clue regarding blood dyscrasia and hypersplenism. Young patient especially female who presents with pancytopenia must be screened for autoimmune disease.

CONCLUSIONS:

Number of cases with pancytopenia is alarmingly high and of great concern. The hematologic alteration in most of the patients is found to be very grave with severe clinical conditions like Leukemia and HLH. Hence proper history, examination and proper investigation like peripheral smear and bone marrow examination depending on clinical profile like age of presentation, signs and symptoms at presentation is of paramount importance in clinching diagnosis.

Conflict of interest : None

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