Clinico-pathological profile of pancytopenia patients in a single health care centre of northern India

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ABSTRACT

Background: Pancytopenia is a clinical outcome of various pathological conditions ranging from bone marrow suppression, bone marrow infiltration, infections, hypersplenism, haemolysis, and haematological malignancies. As such is the most common cause in drug induced (chemotherapy) bone marrow suppression. As most of these patients first contact their primary care physicians, a quick workup will resolve many diagnosis and can give a hint towards a life threatening condition too. Material and Methods: We included all patients admitted with pancytopenia at our tertiary care centre except those who were drug induced. They were evaluated and given appropriate treatment. Results: We observed 73 patients in a year, after excluding drug-induced pancytopenia, and showed aplastic anaemia was the foremost cause (31.5%) followed by vitamin B12 deficiency (19.2%), infections (13.7%), hypersplenism and haematological malignancies. Conclusion: Majority of adult patients admitted with pancytopenia are diagnosed to have curable cause like vitamin deficiency and infections but significant number was also of aplastic anaemia, a condition that requires specialist care. Keywords: Aplastic anaemia, chronic liver disease, haemolytic anaemia, megaloblastic anaemia, pancytopenia

Introduction

Pancytopenia is defined as decrease in all peripheral blood lineages[1]. The most common cause is drug especially chemotherapy induced bone marrow suppression. Other causes include bone marrow infiltration, marrow aplasia, ineffective haemopoiesis, and bone cell destruction or sequestration.²,³ Rare causes are haemophagocytic lymphohistiocytosis (HLH), waldenstrom macroglobulinemia, storage diseases, and congenital disorders.⁴ It is associated with multitude of disease state. Its presentation may be influenced by nutritional status, geography, socioeconomic conditions, and endemic illnesses. After excluding drug induced bone marrow suppression, Vitamin B12 deficiency and aplastic anaemia are the two most common cause of pancytopenia in India.⁵-⁷ Aplastic anaemia is a common haematological problem in eastern part of our country. Although accurate data are not available, its high incidence expected to be due to high use of fertilizers used in growing crops in the field.

Pancytopenia is not a disease entity; it is a haematological finding secondary to some underlying pathology. Hence, clinical presentation depends on the underlying cause, severity of pancytopenia and predominantly affected cell line. Common symptoms are lethargy, malaise, fever, and rash over body (petechiae, purpura). Detailed history and examination are key to diagnosis. History regarding onset and progression of illness, medication history, exposure to toxic substances is important. It is imperative to look for lymphadenopathy, hepatomegaly, splenomegaly, and bony tenderness during examination. Basic work up includes complete blood count, peripheral smear, reticulocyte count, rk-39, bone marrow aspiration and biopsy and ultrasound abdomen. Importance to know the cause is indeed necessary as significant numbers of patient can be treated with cheap and affordable measures. Cost

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effective evaluation and treatment at right time can decrease the morbidity of patients. Primary workup will guide family physicians to treat or refer them appropriately.

Here, we present our experience of patients presented to us with pancytopenia in a year.

Material and Methods

This study was a prospective observational study conducted at All India Institute of Medical Sciences, Patna. This study was approved by Institute Ethical Committee. (AIIMS/Pat/IEC/2019/374).

Inclusion criteria

All adult patients presented with pancytopenia on laboratory investigation who consented to be the part of study.

Exclusion criteria

1. Patients who got recent blood or blood product transfusion
2. Patients who were on chemotherapy or radiotherapy.

All patients presented with pancytopenia during period of one year (April 1, 2019 to March 31, 2020) were included in the study. Detailed history and examination were done for all patients. Patients underwent battery of investigations including complete blood count, liver function test, kidney function test, Vitamin B12, and folate level (wherever indicated), viral markers, ultrasound abdomen, coagulation profile (where indicated), and bone marrow aspiration and biopsy (where indicated). Bone marrow aspiration and biopsy was done with Jamshidi needle after taking consent. Other ancillary tests like antinuclear antibody and Coomb's test were done wherever indicated. Case-based treatment was offered to all patients.

Results

A total of 73 patients were recruited in the study during the defined time period.

Of total patients, 40 were male and 33 were female (M: F: 1:2.1). Mean age of study population was 46.97 years. Age and diagnosis-based distribution is shown in Figure 1. The most common presenting complaints were fatigue and lethargy, fever, weight loss, and bleeding manifestation in descending frequency. On examination, common findings were – pallor which was present in all (100%) patients, followed by splenomegaly in 35 (47.9%), rash in 15 (20.5%), and lymphadenopathy in 7 (9.5%) patients. Mean Hb was 5.27 gm%, (range 1.8–10.8 gm%); 29 patients (39.7%) had Hb < 5 gm %. Mean total leucocyte count was 2.08 × 10³/cumm; 8 patients (10.9%) had severe leukopenia (<1500/cumm). Mean platelet count was 59.7 × 10³/cumm. Severe thrombocytopeny, that is, <20,000/cumm was found in 17 patients (23.3%) [Table 1].

Patients were divided into three categories as per their reticulocyte index (RI) – high RI (>2.5%); 10 (14%), normal RI (1-2.5) - 30 (41%), and low RI (<1) – 33 (45%) [Figure 2].

Bone marrow aspiration and biopsy was indicated in 49 patients. But it could be done for 43 patients only. Rest six patients were very sick and succumb to their illness before subjecting to any procedure. Of 43 patients, for whom bone marrow biopsy was done, majority of patients had bone marrow report suggestive of aplastic anaemia. Other findings in bone marrow were erythroid hyperplasia with megaloblastoid maturation, hyper cellular marrow with multilineage dysplasia suggestive (MDS) of Myelodysplastic syndrome, haemophagocytic syndrome, and acute leukaemia and LD bodies [Table 2].

The most common cause of pancytopenia in present study was aplastic anaemia followed by megaloblastic anaemia, infections, autoimmune haemolytic anaemia, hypersplenism, and haematological malignancies [Table 3].

Twenty-three (31.5%) patients were diagnosed with aplastic anaemia; 14 (19.2%) patients were diagnosed to have megaloblastic anaemia. All cases of megaloblastic anaemia were caused by Vitamin B12 deficiency, while no patient had folate deficiency. Patient suffering from megaloblastic anaemia were found to be younger in comparison to those with aplastic anaemia. Among 10 patients with infectious aetiology for pancytopenia, 4 patients had dengue, and 2 each of HIV, kala azar, and malaria. Six patients had autoimmune haemolysis (AIHA) as a cause of pancytopenia. Of these, three patients were male and three females. Five out of these six patients were ANA positive. One male patient was Rheumatoid factor positive.

A total of 10 patients were diagnosed with malignancy. Out of these, 4 patients diagnosed with acute leukaemia (2 patients expired), Three – non-Hodgkin's lymphoma (NHL) and two – haemophagocytic histiocytosis (both expired), and one patient had myelodysplastic anaemia.

Total seven patients expired in our study – two patients died of acute leukaemia, two of HLH, and three patients expired.
remained undiagnosed. In three months follow-up, 29 patients improved and rest patients referred to haematology department for definitive treatment.

**Discussion**

Pancytopenia is a common manifestation of various illnesses. Its severity and underlying cause define its way of presentation. Severe anaemia leads to lethargy and fatigue, low leukocyte count can lead to increased risk of infections and low platelets lead to haemorrhagic manifestations. In our study, the mean age was 47 years, suggest that our patient population is slightly older in comparison to few previous studies. Most patients were in age group of 21–40 and 41–60 years.

The most common presenting complaint was fatigue and lethargy, followed by fever, weight loss, and bleeding manifestation. This was similar to the findings of study done by Niazi and Razii. Initial evaluation detected that most patients were having hypoproliferative anaemia, that is, reticulocyte index <1 (45.3%), followed by normal and hyper proliferative anaemia (41% and 13.7%). The most common diagnosis in our study was aplastic anaemia (n = 23; 31.5%). Similar results were reported by Kumar DB, Raghupathi AR and by GK Santra an BK Das. However few other large studies had reported megaloblastic anaemia as the most common cause.

The exact incidence of aplastic anaemia is not known. Worldwide, it varies from 10 to 52.7%. Incidence of aplastic anaemia was 31.5% in our study. Half of the aplastic anaemia patients are found in first three decades of life. In our study, 43% patients of aplastic anemia belong to the 21–40 year age group. Important causes of aplastic anaemia are viral infections, autoimmune injury and inherited or acquired clonal/genetic abnormalities. The diagnosis is confirmed by bone marrow examination which shows hypocellular marrow and it is filled with fat and stromal cells. Flow cytometry and cytogenetics should be done to rule out coexisting disorders like paroxysmal nocturnal hemoglobinuria, MDS, and acute leukaemia. Due to unavailability of these investigations, we referred these patients to department of Haematology. In our study, aplastic anaemia has emerged as the most common cause of pancytopenia in our state, yet bone marrow transplant is not readily available. So, this facility needs to be developed in public sector. This study also showed that there are other treatable causes of pancytopenia such as megaloblastic anaemia, infections, hypersplenism, and haematological malignancies. These are important to recognise. Infections like dengue, acute viral illness, enteric fever, and HIV, malaria and kala azar are important causes of pancytopenia. These cases respond well with treatment.
Haematological malignancies like acute leukaemia, lymphoma, and hemophagocytic syndrome are also differentials of pancytopenia. These are diagnosed by peripheral smear and bone marrow examination.

Haemolysis can also present with pancytopenia, but these patients will also have indirect hyperbilirubinemia. In our study, we had significant number of patients with haemolysis secondary to autoimmune diseases.

Chronic liver disease (CLD) also manifests as pancytopenia secondary to hypersplenism due to portal hypertension. It is a poor prognostic marker in CLD. If pancytopenia becomes severe, it can be corrected by splenectomy. None of our patients had severe pancytopenia due to CLD. So, they were offered standard treatment of CLD and vaccination advised for meningococcus and pneumococcus.

Mortality in pancytopenia depends upon the underlying cause. Prognosis and outcome of patients with vitamin deficiencies, infections, and autoimmune diseases are usually favourable, while aplastic anaemia and haematological malignancies carries poor prognosis.

**Conclusion**

Aplastic anaemia is the single most common final diagnosis of pancytopenia, followed by megaloblastic anaemia and other causes. These patients are mostly middle-aged and a candidate for bone marrow transplant therapy. We should urge for this facility in our area. Treatable causes are important to recognise as appropriate steps at right time will decrease morbidity and mortality of the patients.

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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**Conflicts of interest**

There are no conflicts of interest.

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