Profile of fever with Pancytopenia

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Abstract
Background: Pancytopenia is defined as presence of anemia, leucopenia and thrombocytopenia and it results from a number of disease processes.
Aim:This study was carried out to investigate for and to identify the causes of pancytopenia, to find out the frequency of different causes especially fever and to determine the incidence of pancytopenia in relation to sex and age.
Methods:This study was conducted in the Department of Pathology, Siddhartha Medical College, Vijayawada over a period of two years (October 2015 to November 2017). All the patients referred to the clinical laboratory for routine complete blood count and peripheral smear examination from both the outpatient and the inpatient departments, were screened for pancytopenia. 250 cases that fulfilled the diagnostic criteria were selected. Detailed hematological investigations were performed according to standard methods to ascertain the causes of pancytopenia. Bone marrow aspiration was done wherever indicated.
Results: A definite male preponderance was observed, the male to female ratio being 1.4:1. The majority of cases were encountered in 3rd and 4th decades. Infections (77.2%), Anaemias (17.6%), malignancies (3.6%), Drug induced (0.8%) and Idiopathic thrombocytopenic purpura (ITP 0.8%) were the four most common causes.
Conclusion:As a large proportion of causes for pancytopenia are treatable and reversible, accurate diagnoses and timely intervention maybe lifesaving and will certainly have impact on the morbidity and mortality in these vulnerable patients. Knowing the exact etiology is thus important for specific and timely treatment and for prognostication.
Keywords: Pancytopenia, Infections, Megaloblastic anemia,Dengue

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I.   Introduction

Pancytopenia is defined as reduction in all three major formed elements of blood to levels below their lower normal limit leading to simultaneous presence of anemia, leucopenia and thrombocytopenia. [1].Identifying the correct etiopathology of underlying pathology to assess the severity of pancytopenia in a given case is crucial and helps in implementing timely and appropriate treatment.

II.   Aims &Objectives

This study was conducted mainly with the aims of diagnosing the patients with pancytopenia who presented with fever, finding out the common disease entities responsible for pancytopenia and also assessing the age and sex distribution.

III.   Methods

This study was carried out over a period of two years(October 2015 to November 2017) in the Department of Pathology, Siddhartha Medical College, Vijayawada. All the patients referred to the clinical laboratory of the hospital for routine hematological investigations from both outpatient and inpatient departments were screened for pancytopenia. 250 cases were selected, based on the following criteriae (Fever, Hemoglobin level – below 13.5 g/L for males and below 11.5 g/L for females,Total Leucocyte Count - below 4 $\times 10^9$/L, Platelet count – below 150×10^9/L.

In all patients, a complete clinical history including age, sex, smoking status, alcohol intake, history of any treatment, intake of or exposure to potentially toxic chemicals, agents or drugs, radiation exposure, history of symptoms such as fever, bone pains, night sweats, malaise, weight loss and pruritus was taken. A detailed physical examination of every patient was done for pallor, jaundice, hepatosplenomegaly, lymphadenopathy, sternal tenderness and gum hypertrophy. Evidence of primary malignancy was searched for whenever necessary.

Basic hematological investigations like complete blood count, reticulocyte count and peripheral smear examination were performed in each case. Blood counts were done and were again cross checked manually during peripheral smearexamination. Bone marrow aspiration was done wherever indicated. Other investigations were performed included erythrocyte sedimentation rate (ESR), urine examination, liver and renal function tests, serological investigations for enteric fever, blood culture, ELISA for HIV, hepatitis B and C viruses, chest and bone radiographs, abdominal ultrasonography based on suspected underlying pathology and the provisional diagnoses. In all the patients, cause of pancytopenia was ascertained and the data was analyzed on the basis of etiology, clinical and hematological findings.

IV. Results

In this study two main causes for pancytopenia were infections (77.2%), anaemia (17.6%) followed by malignancies (3.6%), drug induced (0.8%) and ITP (0.8%) as shown in Table 1. All of them presented as pyrexia of unknown origin (PUO); their CBC reports showing varying degree of pancytopenia. The maximum number i.e., 58 (23%) cases occurred between the age group of 41-50 years, followed by 31-40 and 51-60 years each constituting 50 cases (20%).as shown in the Table 2. Of the 250 cases studied, 148 (59%) were males and 102 (41%) females as shown in Table 3. A definite male preponderance was seen, the overall male to female ratio being 1.4: 1. All the patients were presented with fever and pallor. The other signs and symptoms noted were bleeding tendencies, splenomegaly, hepatomegaly and lymphadenopathy as described in Table 4. Among 193 cases of infections, Pancytopenia was observed most commonly in Dengue fever cases (33%) followed by other viral fevers 24%, malaria and HIV 20.5% cases each and tuberculosis 2% as shown in Table 5. Of the 44 (17.62%) cases of anaemias, most of them were megaloblastic anemias constituting 31 (70.4%) followed by aplastic anemia 7(15.9%) and dimorphic anemia 6 (13.7%).

Table 1: Distribution of pancytopenia cases with fever based on etiology

Etiology	No. of cases	Percentage
Infections	193	77.2%
Anemias	44	17.6%
Malignancies	9	3.6%
Drug induced	2	0.8%
ITP	2	0.8%
Total	250	100%

Table 2: Age distribution of Pancytopenia cases presented with fever

Age group(years)	No. of cases	Percentage
>1	0	0%
1-10	5	2%
11-20	12	5%
21-30	35	14%
31-40	50	20%
41-50	58	23%
51-60	50	20%
61-70	28	11%
71-80	12	5%
Total	250	100%

Table3: Sex distribution of Pancytopenia cases

Sex	No. of cases	Percentage
Male	148	59%
Female	102	41%
Total	250	100%

Table 4: Clinical features of Pancytopenia cases

Clinical feature	Percentage
Fever	100%
Pallor	100%
Bleeding tendency	28%
Splenomegaly	23%
Hepatomegaly	20%
Lymphadenopathy	7%

Table 5: Types of infections among Pancytopenia cases

Type of Infection	No. Of cases	Percentage
Dengue	64	33%
Malaria	39	20.5%

HIV	39	20.5%
Tuberculosis	4	2%
Other viral	47	24%
Total	193	100%
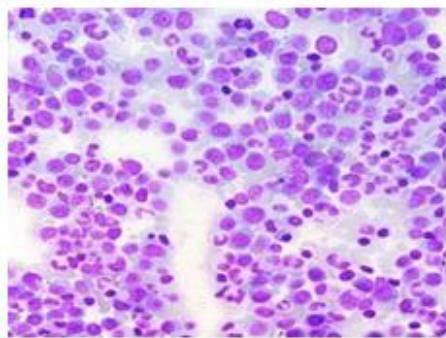
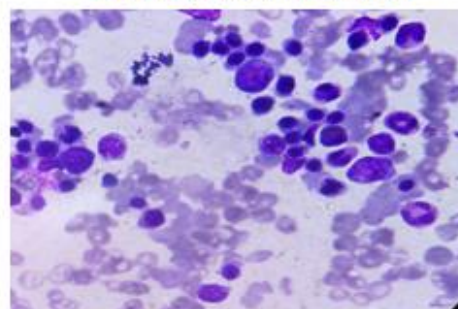Megaloblastic anaemia 40X
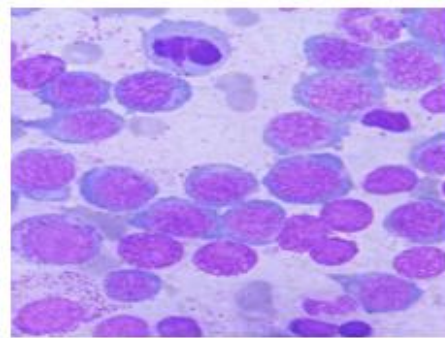
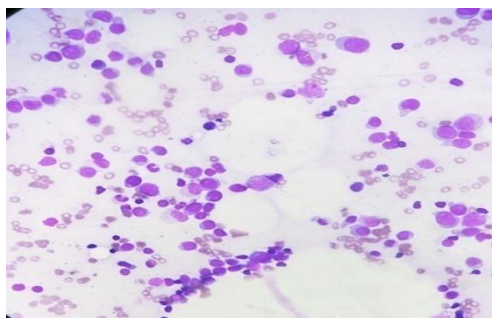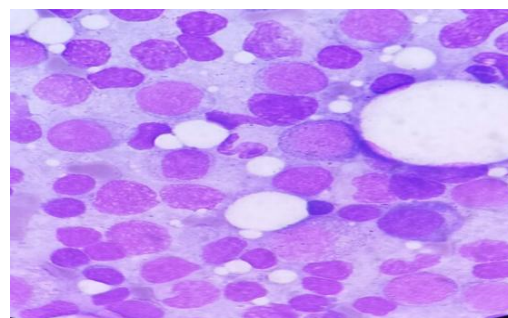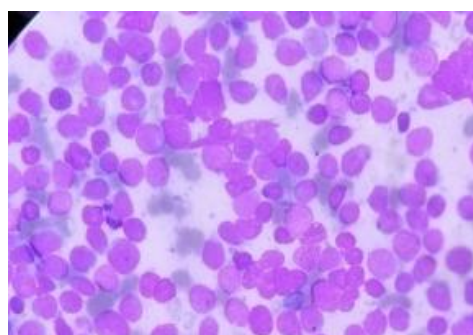Megaloblastic anaemia 100X
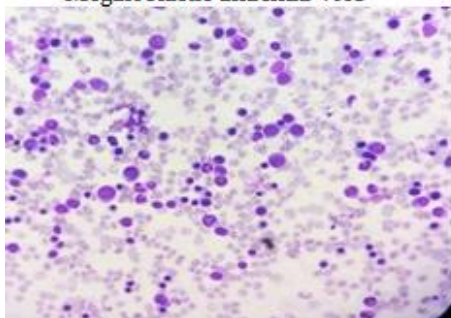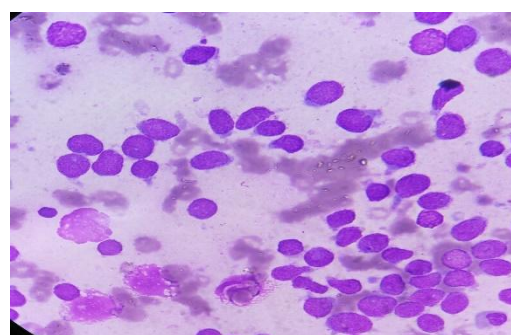

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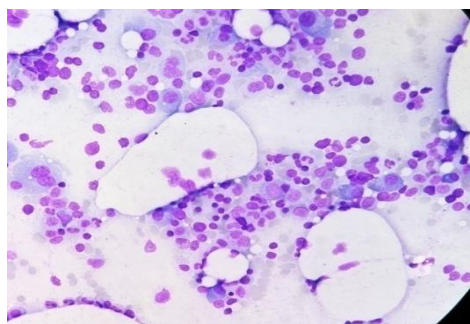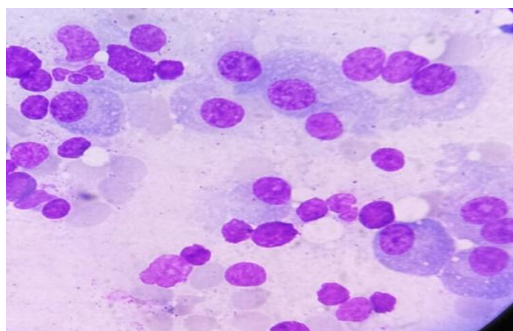

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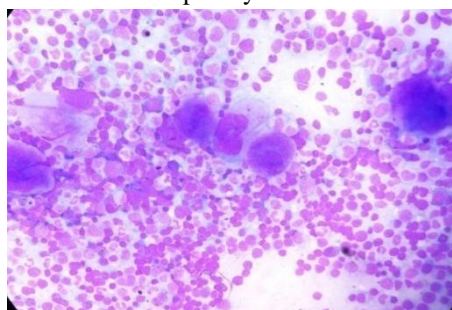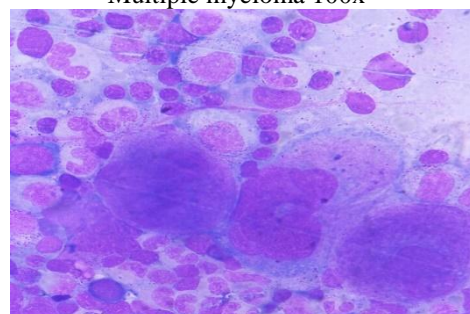Acute Myeloid Leukemia M2 40XAcute myeloid leukemia M2 100X

ALL L2 40XALL L2 100X

Multiple myeloma 40X
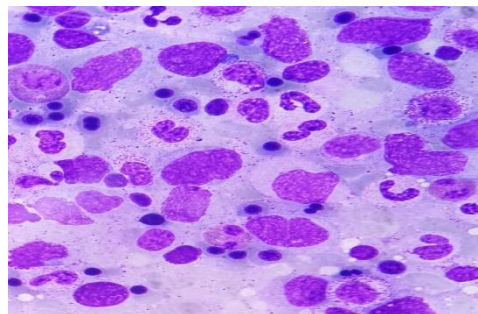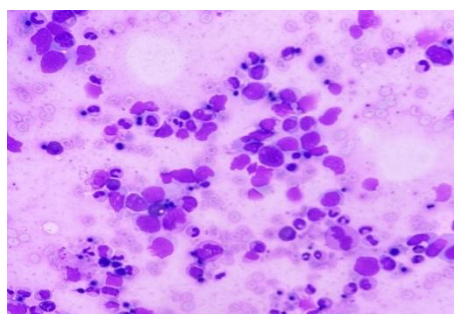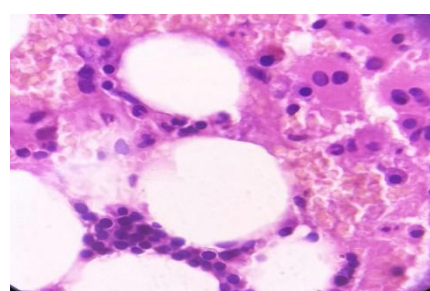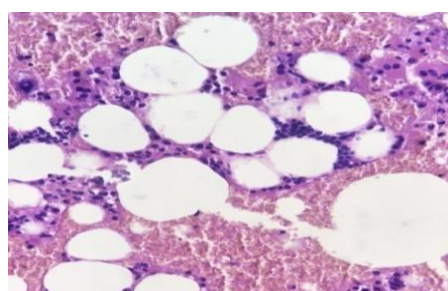

Multiple myeloma 100x

ITP 40X

ITP 100X

NHL 40XNHL 100X

Miliary Tuberculosiss 40XMiliary tuberculosis 100X

V. Discussion

A definite male predominance observed in our study has been reported by many other similar studies. In our study, majority (23%) cases presented in 4th and 5th decades. Infections causing pancytopenia was the commonest cause of pancytopenia 193 (77.2%) cases in our study. Of these, the majority were patients suffering from Dengue constituting 64 cases (33%) and other viral infections 47 (24%) cases. HIV infection and tuberculosis are known to cause various hematological manifestations including pancytopenia as observed in similar studies [2-10].

Increase in incidence of pancytopenia in malaria in our study may also be related to the increased prevalence of malaria, kala azar and other infectious diseases in India, malaria in particular being endemic. In tropical countries, the incidence is as high as the frequency of splenic enlargement caused by tropical parasitic infections: malaria, leishmaniasis, brucellosis, and schistosomiasis [11].

Tuberculosis is a common disease in India and in many other countries. Miliary (disseminated) tuberculosis is known to cause pancytopenia and there are sporadic reports of pulmonary tuberculosis too causing pancytopenia. Although pancytopenia appears to be a rare presentation of tuberculosis, it is advised to always consider tuberculosis as differential diagnosis in patients presenting with pancytopenia, unexplained pyrexia and weight loss. Degree of pancytopenia is influenced more by duration of infection than by its severity [13,14]. We also had 4 patients in this group presenting with fever and weight loss diagnosed to be suffering from tuberculosis CBC reports of these patients showed moderate pancytopenia with normocytic normochromic anemia. Few other studies too have reported infections like tuberculosis, HIV etc. as independent causes of pancytopenia similar to our study. [3,4,7,9,12,13,14,15]. Relative to other studies, the overall incidence of infections causing pancytopenia appears to be high in our study. The likely explanation being that our hospital, as a tertiary care center caters to the poor rural population where the overall health awareness is suboptimal. Thus, patients frequently arrive in hospital after considerable delay, with advanced disease and overwhelming widespread infections, which are difficult to control even with advanced therapy.

Megaloblastic anemia was the common cause of pancytopenia among anemic patients.In other studies varies from 0.8 to 74% and 7.7 to 52.7% and our findings are comparable. Diagnosis was established by correlating with estimation of folic acid and vitamin B_{12} levels. Of the 9 cases in malignancies, 5 cases were acute leukemias, 3 were multiple myeloma and 1 case was NHL. The incidence of acute/subleukemic leukemia in other similar studies varies from 1.8 to 14.5%.

Pancytopenia due to infections like Dengue, HIV and Tuberculosis are on rise in today's society, more so in this part of the world and hence should be kept in mind as causes for pancytopenia. Malaria, tuberculosis, megaloblastic anemia are easily treatable and reversible causes of pancytopenia and thus have a good prognosis. Their early diagnosis is important to prevent further complications.

VI.   Conclusions

Detailed clinical history and meticulous physical examination along with baseline hematological investigations provide valuable information in the evaluation of pancytopenic patients, helping in systematic planning of further investigations to diagnose and ascertain the cause, avoiding unnecessary tests which not only add to the expense of treatment but sometimes also may result in delayed diagnoses and treatment.

References

[1].   de Gruchy GC: Pancytopenia, aplastic anemia. In De Gruchy's clinical hematology in medical practice, 5th edition. Edited by Firkin F, Chesterman C, Penington D, Rush B. Berlin, Germany: Blackwell Science; 1989::119-136.
[2].   Williams DM: Pancytopenia, aplastic anemia and pure red cell anemia. In Wintrobe's clinical hematology. 10th edition. Edited by Richard GL, Bithel TC, John F, John WA, John NL. Philadelphia: Lea and Fabiger; 1998::1449-1489.
[3].   Osama I, Baqai HZ, Faiz A, Nisar H: Patterns of pancytopenia patients in a general medical ward and a proposed diagnostic approach. J Ayub Med Coll Abbottabad 2004, 16:3-7.
[4].   Tilak V, Jain R: Pancytopenia – a clinicohematologic analysis of 77 cases. Indian J Pathol Microbiol 1999, 42:399-404.
[5].   Kumar R, Kalra SP, Kumar H, Anand AC, Madan H: Pancytopenia – a six year study. J Assoc Physicians India 2001, 49:1078-1081.
[6].   Kale P, Shah M, Sharma YB, et al.: Pancytopenia with cellular marrow – a clinical study. J Assoc Physicians India 1991, 39:826.
[7].   Savage DG, et al.: Pancytopenia in Zimbabwe. Am J Med Sci 1999, 317:22-32.
[8].   Iqbal W, Hassan K, Ikram N, Nur S: Aetiological breakup of 208 cases of pancytopenia. J Rawal Med Coll 2001, 5:7-10.
[9].   Khunger JM, Arunselvi S, Sharma U, Ranga S, Talib VH: Pancytopenia – a clinicohematological study of 200 cases. Indian J Pathol Microbiol 2002, 45:375-379.
[10].   Niazi M, Raziq F: The incidence of underlying pathology in pancytopenia – an experience of 89 cases.J Postgrad Med Inst 2004, 18:76-79.
[11].   Hamid GA, Shukry SAR: Patterns of pancytopenia in Yemen. Turk J Hematol 2008, 25:71-74.
[12].   Devi PM, et al.: Clinico-hematological profile of pancytopenia in Manipur, India. J Kuwait Med Assoc 2008, 40:221-224.
[13].   Jalbani A, Ansari IA, Chutto M, Gurbakhshani KM, Shah AH: Proportion of megaloblastic anemia in 40 patients with pancytopenia at CMC hospital Larkana. Medical Channel 2009, 15:34-37.
[14].   Tariq M, Khan NU, Basri R, Said A: Aetiology of pancytopenia. Prof Med J 2010, 17:252-256.
[15].   Santra G, Das BK: A cross-sectional study of the clinical profile and aetiological spectrum of pancytopenia in a tertiary care centre. Singapore Med J 2010, 51:806-812.