TMJ
Case report

Published by OJS
Doi: doi.org/10.4314/tmj.v30i1.275

OPEN ACCESS JOURNAL

Causes of pancytopenia based on bone marrow examination in adult patients presenting at Muhimbili National Hospital

*Magesa P. M.[1], Magesa A. S.[2], Rwezaula S. S.[2], Meda E. C.[2]

[1]Department of Haematology and Blood Transfusion, Muhimbili University of Health and Allied Sciences, Tanzania

[2]Department of Laboratory Services, Muhimbili National Hospital, Tanzania.

*Corresponding author
Dr. Pius M. Magesa
E-mail: mwitap42@gmail.com

TMJ
Case report
Published by OJS
Doi: doi.org/10.4314/tmj.v30i1.275

OPEN ACCESS JOURNAL

Abstract

Background

Pancytopenia is the simultaneous presence of anaemia, leucopenia and thrombocytopenia. The aetiological spectrum of pancytopenia is wide and variable. We aimed to determine the common causes of pancytopenia by analyzing bone marrow aspiration records of adult patients seen at Muhimbili National Hospital, a tertiary care centre.

Methods

This was a retrospective descriptive cross-sectional study of all adult patients who presented with pancytopenia for a period of one year from January 2013 to December 2013. All patients with pancytopenia, i.e. Hb < 10 g/dl, WBC < 4 x 109/l and platelet count < 150 x 109/l; aged ≥ 18 years; and of both sexes were included in the study. The data obtained were entered on excel sheets, cleaned and analyzed for averages and ranges for numerical data. Categorical data were summarized by averages of frequencies and proportion.

Results

A total number of 216 adult patients had bone marrow examination in one year. A full blood picture was retrieved in 153 patients and among these, 26.8% (n = 41) had pancytopenia. The common causes of pancytopenia were aplastic anaemia (48.8%); haematological malignancies (29.3%); and nutritional anaemia (17.0%). Acute myeloid leukaemia was the commonest malignancy comprising 50% of all haematological neoplasms and iron deficiency occurred in 71.4% of nutritionally anaemic patients.

Conclusion

Aplastic anaemia was the most common aetiological factor followed by haematological malignancies among adult patients presenting with pancytopenia at Muhimbili National Hospital. The high frequency of iron deficiency anaemia with pancytopenia was unusual.

Key words: pancytopenia, aetiology, bone marrow, adult patients

Published by OJS
Doi: doi.org/10.4314/tmj.v30i1.275

Introduction

Pancytopenia is the simultaneous presence of anaemia, leucopenia and thrombocytopenia. Therefore, it is not a disease entity. The cut-off points for defining anaemia, leucopenia and thrombocytopenia differ in terms of age, gender, physiological variations, geographical location, socioeconomic status and ethnicity. In industrialized countries, pancytopenia in adults is defined as the haemoglobin (Hb) of less than 13.0 g/dl in males or 12.0 g/dl in females; the leucocyte counts of less than 4 x 10^9/l and the platelet count of less than 150 x 10^9/l [1]. Adult haematological reference values in Tanzania, a less industrialized country, have been published. The cut-off points at 95% confidence interval were Hb of less than 13.7 g/dl in males or 11.1 g/dl in females; the leucocyte count of less than 3.0 x 10^9/l; and the platelet count of less than 150 x 10^9/l [2]. Pancytopenia is commonly encountered in clinical practice and determining its cause is often challenging to the attending clinician. The commonest clinical manifestations of pancytopenia are usually fever (86.7%), fatigue (76%), dizziness (64%), weight loss (45.3%), anorexia (37.3%), night sweats (28%), pallor (100%), bleeding (38.7%), splenomegaly (48%), hepatomegaly (21.3%), and lymphadenopathy (14.7%) [3]. Initially, mild impairment in marrow function may go undetected and pancytopenia may become apparent only during times of stress or increased demand (e.g., bleeding or infection). The severity of pancytopenia and the underlying pathology determine the management and prognosis of the patients [4]. Varieties of haematopoietic and nonhaematopoietic conditions manifest with features of pancytopenia. The underlying mechanisms are: decrease in haematopoietic cell production, marrow replacement by abnormal cells, suppression of marrow growth and differentiation, ineffective haematopoiesis with cell death, defective cell formation which are removed from the circulation, antibody mediated sequestration or destruction of cells and trapping of cells in a hypertrophied and over active reticuloendothelial system [3, 5, 6].

The aetiological spectrum of pancytopenia is therefore wide and variable. It commonly includes aplastic anaemia [7, 8, 9]; acute leukaemia [7, 8, 9]; megaloblastic anaemia [7, 8]; and infections [10, 11]. Myelodysplstic disorders [12] and paroxysmal nocturnal haemoglobinuria [13] are occasionally reported as causes of pancytopenia. Iron deficiency anaemia is rarely reported as a

Published by OJS
Doi: doi.org/10.4314/tmj.v30i1.275

cause of pancytopenia [14, 15]. To the best of our knowledge, no similar studies have been reported in Tanzania and in Eastern Africa. The purpose of this study was to determine the common causes of pancytopenia by analyzing bone marrow aspiration records of adult patients seen at Muhimbili National Hospital (MNH), a tertiary care centre.

Methods

Study design

This was a retrospective descriptive cross-sectional study of all adult patients who presented with pancytopenia for a period of one year from January 2013 to December 2013.

Study area and population

This study was conducted at MNH in Dar es Salaam in the Department of Haematology and Blood Transfusion. MNH is the largest referral hospital in Tanzania, catering for patients from all over the country including public and private hospitals. The study analyzed bone marrow aspiration reports of all adult patients seen at the MNH facilities.

Inclusion criteria

All patients with pancytopenia, i.e. Hb < 10 g/dl, WBC < 4 x 10^9/l and platelet count < 150 x 10^9/l; aged ≥ 18 years; and of both sexes were included in the study.

Exclusion criteria

Patients without full blood picture (FBP) report or bone marrow aspiration (BMA) report were excluded from the study. Patients who had more than one FBP or BMA report, only one diagnostic report was used.

Procedure and Data collection

The following clinical information from hard and soft copies of the bone marrow report was entered on a data sheet for each patient: (i) report serial number; (ii) hospital registration number; (iii) age in years; (iv) sex; (v) presence or absence of pallor, fever, bleeding, hepatomegaly, splenomegaly and lymphadenopathy. The following haematological information was collected and

entered on the data sheet: (i) FBP, i.eHb g/dl, mean cell volume (MCV) fl, white blood cell (WBC) count x 10^9/l and platelet count x 10^9/l; (ii) peripheral blood film report; and (iii) bone marrow aspiration report. Under bone marrow report the following data were captured: report serial number; bone marrow number; bone marrow cellularity whether normal, decreased, or increased; bone marrow abnormal infiltration; bone marrow iron stain if positive, negative or not suitable; and bone marrow diagnosis.

Data management and statistical analysis

The data obtained were entered on excel sheets, cleaned and analyzed for averages and ranges for numerical data. Categorical data were summarized by averages of frequencies and proportions.

Ethical clearance

Permission to perform this study at MNH was obtained from the Director of Clinical Support Services. For confidentiality, only registration numbers were used to record patient data.

Results

A total number of 216 adult patients had bone marrow aspiration examination in 2013. FBP was retrieved in 153 patients and among these, 26.8% (n = 41) had pancytopenia. Analyses on these patients with pancytopenia were done. The mean age was 37.9 (range 18 – 80) years. There were 27 males and 14 females. The other clinical information was missing in the majority of cases. Hence, no further analysis on clinical information was performed. The FBP mean results were Hb 6.1 (range 3.2 – 9.7) g/dl; MCV 87.1 (range 57.9 – 109) fl; WBC 2.0 (range 0.4 – 3.6) x 10^9/l; and platelets 42.4 (range 2.8 – 135) x 10^9/l. The aetiological spectrum of the pancytopenia showed aplastic anaemia in 48.8% (n = 20) cases; haematological malignancies in 29.3% (n = 12) cases; nutritional anaemia in 17.0% (n = 7) cases; and normal bone marrow appeared in 4.9% (n = 2) cases.

Among the 20 patients with aplastic anaemia, two had splenomegaly and a third patient had lymphadenopathy. Acute myeloid leukaemia was found in 50% (n = 6/12) cases with haematological malignancies. It was followed by acute lymphoblastic leukaemia, 16% (n = 2/12); non-Hodgkin

Published by OJS
Doi: doi.org/10.4314/tmj.v30i1.275

lymphoma, 16.7% (n = 2/12); chronic myeloid leukaemia, 8.3% (n = 1/12); and multiple myeloma, 8.3% (n = 1/12). Iron deficiency anaemia occurred in 71.4% (n = 5/7) among patients with nutritional anaemia. The remaining 28.6% (n = 2/7) of patients with nutritional anaemia had megaloblastic anaemia. The two patients with normal bone marrow, one had fever, hepatomegaly and lymphadenopathy; and the other was only pale.

Discussion

The most common aetiological factor among adult patients presenting with pancytopenia at MNH was aplastic anaemia which occurred in 48.8% of the cases. Our findings are higher than those reported in studies from Asia where the incidence of aplastic anaemia is known to be 2-4 times higher than it is in Europe, Canada and America [16, 17, 18]. Makheja et al in 2013 [7] reported a frequency of 19.4% of aplastic anaemia in their prospective study of 62 adult patients with pancytopenia in India. Similar frequencies of aplastic anaemia in all age groups of 18.26% and 16.7% were reported by Gayathri et al [8] in 2011 from India and Isho et al [9] in 2016 from Iraqi, respectively. We did not find similar studies from Africa. The high frequency of aplastic anaemia in the present study could be due to several reasons: study design; using different age groups; using different definitions of pancytopenia; applying different inclusion and exclusion criteria; lack of confirmation of aplastic anaemia by bone marrow trephine biopsy; small sample size; geographical factors; and other reasons.

The second most common cause of pancytopenia among our adult patients was malignancy which comprised of 29.3% cases. Acute leukaemia was the leading malignancy accounting for 19.5% of all adult cases and 50% of all patients found to have malignancy in our series. Acute myeloid leukaemia was three times commoner than acute lymphoblastic leukaemia (6 versus 2 cases, respectively). The diagnosis of acute leukaemia was based on morphology alone and this technique may miss-classify the main types of acute leukaemia. The other less common malignancies found in our study included two cases of non-Hodgkin lymphoma, and one case each of chronic myeloid leukaemia and multiple myeloma. The frequency of malignancies in our study is lower when compared with similar studies. One prospective study in India reported acute myeloid leukaemia in 27.4% among 62 adult patients with pancytopenia [7]. Isho et al, 2016 [9], in

Published by OJS
Doi: doi.org/10.4314/tmj.v30i1.275

their prospective study in Iraqi reported haematological malignancies in 51.7% among 60 patients aged 1 – 80 years with pancytopenia. In their study, acute leukaemia was found in 35% of cases. On the other hand, Gayathri and Rao, 2011 [8] in their prospective study in India did not find malignancy as a cause of pancytopenia in their series of 104 patients aged 2 – 80 years. From their study the main causes of pancytopenia were megaloblastic anaemia (74.0%) and aplastic anaemia (18.9%). These differences in prevalence of haematological malignancies as causes of pancytopenia by different authors could arise from different reasons as explained previously.

The third commonest cause of pancytopenia in ours study was nutritional anaemia which had a frequency of 17.1%. Iron deficiency anaemia was detected in 12.2% and megaloblastic anaemia in only 4.9% of all adult patients with nutritional anaemia. This is in contrast to previous studies which give high prevalences of megaloblastic anaemia compared with iron deficeciency anaemia. Makheja et al, 2013 [7] reported megaloblastic anaemia as the single most common cause of pancytopenia in their series with a frequency of 41.9%. Similarly, Gayathri and Rao [8], reported megaloblastic anaemia as the commonest cause of pancytopenia in their study with a prevalence of 74.0%. The low frequency of megaloblastic anaemia in our study population may be due to lack of testing for serum levels of vitamin B12 and folic acid. Iron deficiency anemia is commonly associated with thrombocytosis and normal leukocyte count. Thrombocytopenia has occasionally been reported in iron deficiency anemia, but pancytopenia is very rare. Case studies [14, 15] have shown that some patients who presented with iron deficiency anaemia associated with pancytopenia, improved with iron replenishment. A study of the causes of iron deficiency anaemia was beyond the scope of the present study. It would be of interest to exclude paroxysmal nocturnal haemoglobinuria (PNH) in these patients because PNH can present with pancytopenia, bone marrow erythroid hyperplasia or hypoplasia and iron deficiency anaemia [8, 13]. The iron deficiency anaemia in PNH is due to chronic intravascular haemolysis resulting in iron loss through haemosiderinuria. Common causes of iron deficiency anaemia like nutritional deficiency and chronic gastrointestinal haemorrhage should be excluded as well.

Published by OJS
Doi: doi.org/10.4314/tmj.v30i1.275

Conclusion

Aplastic anaemia was the most common aetiological factor followed by acute leukaemia among adult patients presenting with pancytopenia at MNH. The higher frequency of iron deficiency anaemia than megaloblastic anaemia in pancytopenia was unusual. It would be of interest to verify the findings in this small retrospective study by a large prospective one.

Acknowledgements

The authors thank the following individuals for their valuable contributions in this study: The staff of Haematology Section, Department of Laboratory Services at Muhimbili National Hospital; and the patients whose bone marrow records were used in this study. No funds were received for this research.

Declaration of Interest

The authors have no conflict of interest in this work.

Related Papers/Manuscripts

We have submitted a related manuscript to the East African Journal of Public Health regarding causes of pancytopenia in children.

References

1. Lewis SM (2006). **Reference ranges and normal values**. In Lewis SM, Bain BJ and Bates I (Eds.), Dacie and Lewis Practical Haematology (pp. 11-24). Philadephia PA: Churchill Livingstone.
2. Saathoff, E, Schneider P, Kleinfeldt V, Geis S, Haule D, Maboko L, Samky E, de Souza M, Robb M and Hoelscher M (2008). **Laboratory reference values for healthy adults from southern Tanzania.** Tropical Medicine and International Health, 13(5): 612-625. DOI: 10.1111/j.1365-3156.2008. 02047.x
3. Imbert M, Scoazec JY, Mary JY, Jouzult H, Rochant H, Sultan C. **Adult patients presenting with pancytopenia: a reappraisal of underlying pathology and diagnostic procedures in 213 cases.** Hematol Pathol. 1989; 3:159-167.

Published by OJS
Doi: doi.org/10.4314/tmj.v30i1.275

4. Tilak V & Jain R (1999). Pancytopenia - **A clinico-haematologic analysis of 77 cases**. Indian J Pathol Microbiol; 42:399-404.
5. Jha A, Sayami G, Adhikari RC, Panta AD, Jha R. **Bone marrow examination in cases of pancytopenia**. J Nepal Med Assoc. 2008; 47:12-17.
6. Varma N, Dash S. **A reappraisal of underlying pathology in adult patients presenting with pancytopenia.** Trop Geogr Med. 1992; 44:322-327.
7. Makheja KD, Maheshwari BK, Arain S, Kumar S, Kumari S, Vikash. **The common causes leading to pancytopenia in patients presenting to tertiary care hospital.** Pak J Med Sci 2013 Sept-Oct; 29(5): 1108 – 1111.
8. Gayathri BN and Rao KS. **Pancytopenia: A clinico-hematological study**. J Lab Physicians 2011 Jan-Jun; 3(1): 15 – 20. DOI: 10.4103/0974-2727.78555.
9. Isho AI, Mohamed NS, Nooruldin SA. **A clinical – haematological study of pancytopenia in patients attending Nanakaly Hospital in Erbil City**. Iraqi J Haematology; May 2016; 5(1): 129-142.
10. Memon S, Shaikh S, Nizamani MA. **Aetiological spectrum of pancytopenia based on bone marrow examination in children.** J Coll Physicians Surg Pak. 2008 Mar; 18(3): 163 – 7. doi: 03.2008/JCPSP.163167.
11. Gupta V, Tripathi S, Tilak V, Bhatia BD. **A study of clinico-haematological profiles of pancytopenia in children.** Trop Doct. 2008 Oct; 38 (4): 241 – 3. DOI: 10.1258.td.2008.070422.
12. Shano Naseem, Neelam Varma, Reena Das, Jasmina Ahluwalia, Man Updesha Singh Sachdeva, Ram Kumar Marwaha. **Pediatric patients with bicytopenia/pancytopenia: Review of etiologies and clinico-hematological profile at a tertiary center**. Indian J Patholo Microbiol 2011; 54(1): 75 – 80.
13. Kinoshita T, Inone N. **Relationship between aplastic anemia and paroxysmal nocturnal hemoglobinuria**. Int J Hematol. 2002 Feb; 75(2): 117 – 22.
14. Jhamb R, Kumar A. **Iron deficiency anemia presenting as pancytopenia in an adolescent girl.** Int J Adolesc Med Health. 2011; 23(1): 73 – 4

Published by OJS
Doi: doi.org/10.4314/tmj.v30i1.275

15. Ganti AK, Shonka NA, Haire WD. **Pancytopenia due to iron deficiency worsened by iron infusion: a case report.** J Med Case Rep. 2007 Dec 7; 1: 175. DOI: 10.1186/1752-1947-1-175.
16. **The International Agranulocytosis and Aplastic Anaemia Study. Incidence of aplastic anaemia: The relevant diagnostic criteria**. Blood 70: 1718, 1987.
17. Mary JY, Baumelou E, Guiguet M: **Epidemiology of aplastic anaemiain France: A prospective multicentre study**. Blood 75: 1646, 1990.
18. Chongli Y and Ziaobo Z: **Incidence survey of aplastic anaemia in China**. Chin Med Sci J 6: 203, 1991.