A STUDY ON CASES OF PANCYTOPENIA WITH EVALUATION OF VARIOUS CLINICAL SYMPTOMS AND AETIOLOGIES

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ABSTRACT

BACKGROUND

Several diseases can cause bone marrow failure, resulting in greatly reduced to absent haematopoiesis with subsequent pancytopenia. Pancytopenia which includes deficiency of all three cellular elements of blood resulting in anaemia, leucopoenia and thrombocytopenia is a common haematological entity that we have come across in routine practice. Hence a detailed clinical examination, thorough haematological investigation and bone marrow study of patients usually helps in identification of the underlying cause and adds to the pathologist's role as a consultant to the patient's treating physician.

MATERIALS AND METHODS

The study included 100 consecutive cases (both adult and children) with peripheral pancytopenia in the department of haematology (pathology) at SCB MC, Cuttack from January 2017 to April 2018. Patients receiving chemotherapy/radiation were excluded. Apart from detailed clinical examination, complete blood count, peripheral smear examination and bone marrow study (aspiration/trephine biopsy) were conducted. This was a cross sectional study.

RESULTS

The 100 consecutive cases showed a male predominance (58%). Most common clinical presentation was generalised weakness followed by fever. Most common cause for pancytopenia in adults was aplastic anaemia (40%) and acute leukaemia in children (60%). This was closely followed by Megaloblastic Anaemia (36%) whereas aplastic anaemia (40%) was second most common cause for pancytopenia among paediatric age group. Other causes included MDS with excess blast and hypersplenism.

CONCLUSION

Out of 100 consecutive cases, aplastic anaemia was most common cause of pancytopenia closely followed by megaloblastic anaemia in adults; whereas in paediatric cases, acute leukaemia was the most common cause followed by aplastic anaemia. The role of bone marrow study along with detailed clinical and haematological evaluation plays a very important role.

KEYWORDS

Pancytopenia, Bone Marrow, Aplastic Anaemia, Megaloblastic Anaemia.

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BACKGROUND

Pancytopenia is characterised by a decrease in all the three cellular elements of the peripheral blood below the lower limit of normal range, red blood corpuscles, white blood corpuscles and platelets.[1] It is a manifestation of a wide variety of disorders which primarily or secondarily affects the bone marrow, resulting in anaemia, leucopoenia and thrombocytopenia.[2] As such pancytopenia is not a disease but an important feature of many serious and life threatening illnesses.[3] The frequency of various diagnostic entities causing pancytopenia has been attributed to differences in the methodology and stringency of diagnostic criteria, geographic difference and underlying exposure to various drugs and infectious microbial agents, especially virus.[4] The severity of pancytopenia and the underlying pathology determines the management and prognosis of the disease. Hence early diagnosis of the cause for pancytopenia is essential for effective management.

Pancytopenia mainly results from either failure of production of progenitors in bone marrow or malignant cell infiltration or antibody mediate bone marrow suppression or ineffective haematopoiesis and dysplasia or peripheral sequestration of blood cells in over active reticuloendothelial system. The main causes are aplastic anaemia, nutritional deficiencies leading to megaloblastic anaemia, myelodysplastic syndrome, hypersplenism, sub-acute (acute) leukaemia, infectious agents like viruses and bacteria.

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MATERIALS AND METHODS

The study was carried out in the department of pathology (haematology section) at SCB MC, Cuttack from January 2017 to April 2018, a period of 16 months. 100 consecutive cases presenting with Pancytopenia on initial investigations requiring bone marrow study were included. Patients on myelotoxic chemotherapy or radiation were excluded from the study. The criteria applied for Pancytopenia was:

- Hb <10.0 gm/dl
- WBC <4 X 10^9/L
- Platelet <150 X 10^9/L

Complete blood count (CBC) was done along with absolute neutrophil count (ANC) and reticulocyte count. CBC was performed on automated haematology analyser confirmed by manual method. ANC was done by direct and indirect methods.

RESULTS

100 consecutive cases with a haematological diagnosis of Pancytopenia requiring bone marrow study from 2017 January onwards in the haematology section of department of pathology, SCB MC, Cuttack. From 100 patients, 58 were males (58%) and 42 females (42%) which showed a male predominance.

Various presenting complaints were generalised weakness (60%) and fever (50%). Bleeding manifestation like gum bleeding, epistaxis and purpura was also present in about (22%) of cases. About 4% presented with joint pain. Almost all patients had pallor on clinical examination. Hepatomegaly was found in 20%, splenomegaly in 12% and lymphadenopathy in 4% of cases. Among the paediatric cases (38), the most common cause for Pancytopenia was subleukaemic leukaemia (60%) followed by aplastic anaemia (40%). Among the adult cases aplastic anaemia accounted for the main cause for Pancytopenia (40%) closely followed by megaloblastic anaemia (36%). Other causes included were sub leukaemia leukaemia (12%) MDS with excess blast and hypersplenism.

Generalised Weakness	60%
Fever	50%
Bleeding manifestation	22%
Joint pain	4%

Table 1. Presenting Complaints

Pallor	100%
Hepatomegaly	20%
Splenomegaly	12%
Lymphadenopathy	4%

Table 2. Clinical Findings

Paediatric Case (38)		Adult Case (62)
Aplastic anaemia	15 (40%)	25(40%)
Subacute leukaemia	23 (60%)	8(12%)
Megaloblastic anaemia	NIL	23(36%)
MDS C excess blast	NIL	2(4%)
Hypersplenism	NIL	2(4%)
Normal marrow	NIL	2(4%)

Table 3. Causes for Pancytopenia

	(15) children	(25) adults
Non-severe	14 > 95%	24>95%
Severe	NIL	1
Very severe	1	NIL

Table 4. Aplastic Anaemia Types (Acquired)

Bone Marrow Cellularity	No. of Cases
<10%	2
10%-25%	38
>25%	NIL

Table 5. Bone Marrow Findings of Aplastic Anaemia Cases

Absolute Neutrophil Count	No. of cases
>500/cu.mm	38
500-200/cu.mm	1
<200/cu.mm	1

Table 6. Absolute Neutrophil Count in Aplastic Anaemia Cases

DISCUSSION

Pancytopenia is one of the common conditions observed in our day to day practice. It is not a disease but a triad of findings which results from a number of disease processes primarily or secondarily involving the bone marrow.[5]

In our study prevalence of Pancytopenia was noted more in males (58%) than in female (42%). In a similar study Das et al observed an incidence of 58% male and 42% female varies other studies by Prasad et al, Agarwal et al, Kumar et al, Hirachand et al as show in table 6 shows a dominance of male over female in the cause of Pancytopenia.

Sl. No.	Authors	No. of Cases	Age Range (yrs.)	M:F
1.	Tilak V et al (1999)	77	5-70	1.14:1
2.	Kumar R et al (2008)	166	12-73	2.1:1
3.	Khodke K et al (2001)	50	3-69	1.3:1
4.	Khunger JM et al (2002)	200	2-70	1.2:1
5.	Jha A et al (2008)	148	1-79	1.5:1
6.	Al- Khalisi KA et al (2011)	104	15-75	1.3:1
7.	Hirachand S et al (2013)	52	12-82	1.2:1
8.	Deepa Takewani et al	100	12-80	1.7:1
9.	Present study	100	2-8	1.4:1

Table 6. Age and Sex Distribution Compared to Other Studies

Our study showed generalised weakness (60%) followed by fever (50%) as the first and second mode of presentation for Pancytopenia. This was followed by bleeding manifestation (22%) and joint pain (4%). Our study was comparable with the study by Niazi M et al (2004)[6] which showed generalised weakness (68.2%) was the commonest symptom, followed by fever (47.7%) and bleeding manifestation (33.7%). In another study by Gayathri and Rao et al (2011)[7] generalized weakness (70.83%) was the most common symptom followed by fever (6.25%) and bleeding manifestation (6.25%). In yet another study by BB et al (2013)[8] generalised weakness (97%) was the most common symptom, followed by fever (70%), weight loss (38%) and dyspnoea (32%).

In the present study, most common clinical finding was pallor (100%) followed by hepatomegaly (20%), splenomegaly (12%) and lymphadenopathy (4%). This was comparable with study by Gayathri and Rao[7] et al (2011), the most common physical finding was pallor (100%) followed by splenomegaly (35%) and hepatomegaly (26.97%).

In another study by Kumar DP et al (2012),[9] pallor (45%) followed by splenomegaly (33%) and lymphadenopathy (6.25%). In the study by Khodke K et al (2001)[10] Shal SN et al (2014)[11] pallor was the most common 100%, followed by splenomegaly (40%), hepatomegaly (21%) and lymphadenopathy (3%).

Sr. No.	Study	Country	Year	No. of Cases	Age Range (yr.)	M.F	Most Common Cause	2nd Most Common Cause
1	Tilak V & Jain R et al	India	1998	77	5-70	1.14:1	Megaloblastic anaemia (68%)	aplastic anaemia (7.7%)
2	Khodkeetal	India	2000	50	3-69	1.3:1	Megaloblastic anaemia (44%)	aplastic anaemia (14%)
3	Khunger J.M. et al	India	2002	200	5-70	1.2:1	Megaloblastic anaemia (74%)	aplastic anaemia (14%)
4	Jha et al	Nepal	2008	148	1-79	1.5:1	Hypoplastic Anaemia 29.5%)	Megaloblastic anaemia (23.6%)
5	Gayathri B N et al	India	2011	104	2-80	1.2:1	Megaloblastic anaemia (74%)	aplastic anaemia (18.26%)
6	Goli N et al	India	2016	54	-	-	Megaloblastic anaemia (54.5%)	Malignant & premalignant conditions (20.5%)
7	Deepa Takewani et al	India	2014	100	12-80	1.7:1	Megaloblastic anaemia (78%)	Aplastic anaemia (12%)
8	Present study	India	2018	100	2-80	1.4:1	Aplastic anaemia (adults 40%), acute leukaemia (children 60%)	Megaloblastic anaemia (adult 36%), aplastic anaemia (children 40%)

Table 7. Different Causes of Pancytopenia and its Comparison with Other Studies

A total of 100 cases of Pancytopenia was studied. Age, presenting complaints, peripheral blood picture, complete blood marrow count, ANC, retic count and bone Marrow examination was studied in all the cases. In our case, the most common cause for Pancytopenia in adults was aplastic anaemia whereas in paediatric age group it was subleukaemic leukaemia. Incidence of aplastic anaemia varies from 10% to 52% among Pancytopenia patients 10. In our case it was seen in 40% of the cases (adult and children) which was comparable with many studies like Gayathri BN et al and Jha et al.

Among adults, megaloblastic anaemia was second common cause (36%) that was comparable to the studies by Goli N et al and Jha et al aplastic anaemia is relatively common, and is seen in both children and adults (Table 7). Although the majority of the causes are idiopathic, this disease can be caused by multiple aetiologies, including drugs and viruses. In our study, most patients had history of drug intake, mostly antibiotics and NSAIDS. Children mostly had a previous history of fever, indicating a viral aetiology for aplastic anaemia. About >95% of AA in both adults and children were of non-severe type.

Haematopoietic neoplasms, most commonly acute leukaemia causes pancytopenia in both children and adults. Pancytopenia results from replacement of bone marrow by blast cells. In our case acute leukaemia was most common cause for pancytopenia in children. Common signs and symptoms were pallor, hepatosplenomegaly and bone pair. Megaloblastic anaemia is the most frequent cause of pancytopenia in several studies but was the second most common second cause in our present study (36%) (Table 7). Nutritional deficiency is the common cause for pancytopenia where patients present with anaemia, weakness and neurological symptoms. MDS is another cause in adults for pancytopenia in which there is bone marrow failure. We had encountered a few MDS with excess blasts cases. Bone marrow biopsy and CD34 had helped in the diagnosis. Malarial infection should be kept in mind in hypersplenism. Hypersplenism was also a cause for

pancytopenia, in our case (4%). Few cases (4%) with pancytopenia also revealed a normal bone marrow picture.

CONCLUSION

Causes of pancytopenia are vast and extremely varied. Our study helped us to gather some common causes of pancytopenia in both children and adults. Aplastic Anaemia was common in adults (40%) and was also 2nd common cause in children (40%). Megaloblastic anaemia (36%) was second most common in adults followed by acute leukaemia, MDS and hypersplenism. Acute leukaemia was the most common cause (60%) in children. However, this list is by no means complete and patients with complex conditions may have multifactorial causes of pancytopenia. The diagnosis especially in the absence of obvious neoplasm, can be extraordinarily challenging even in the presence of sharp clinical acumen. Hence various studies like detailed history and clinical examination, complete blood count, bone marrow aspiration and biopsy including immunohistochemistry are often required to make an accurate diagnosis.

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