THE STUDY OF CLINICO-AETIOLOGICAL PROFILE OF PANCYTOPENIA IN ELDERLY POPULATION

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ABSTRACT

BACKGROUND

Pancytopenia is a common problem in clinical practice. Pancytopenia is defined as haemoglobin less than 9 gm/dL, total leucocyte count less than 4,000/dL and platelet count less than 1 lakhs/dL. Causes of pancytopenia vary from nutritional deficiencies, bone marrow failure status and malignancies. Pancytopenia is a common problem in geriatric population also. In this study, we try to find common causes of pancytopenia in geriatric population in a tertiary care hospital.

MATERIALS AND METHODS

40 consecutive patients who are more than 60 years of age attending General Medicine Outpatient Department were included in the study. Pancytopenia due to acute infections like viral fever and sepsis were excluded. Patients suspected to be having malignancies like lymphadenopathy and hepatosplenomegaly were also excluded. These patients were subjected to detailed history taking and clinical examination. Routine investigations like complete blood count, peripheral smear, reticulocyte count, Coombs test, serum cobalamin levels, renal function tests and liver function tests were done. Bone marrow examination was done in cases where indicated. Upper gastrointestinal endoscopy and anti-intrinsic factor antibody and antiparietal cell antibody were done where indicated.

RESULTS

Out of 40 patients included in the study, 25 were males and 15 were females. 28 patients were aged between 60-70 years, 10 patients between 70-80 years and 2 were more than 80 years old. Mean age of the patients was 68 years. Fatigue was the most common symptom (70%), fever was seen in 15% cases, mild cognitive impairment was reported in 10% patients and bleeding manifestations were seen in 5% cases. Most common cause of pancytopenia was cobalamin deficiency (60%). Others causes were aplastic anaemia (7.5%), chronic liver disease (5%), myelodysplasia (5%), drug induced (2.5%) and HIV associated (2.5%) cases. In this study, we saw that most common of pancytopenia was cause of cobalamin deficiency. We found that mean MCV was 88 fL (p=0.2) in all these patients.

CONCLUSION

Vitamin B12 deficiency is the most common cause of pancytopenia in elderly population. Symptoms of vitamin B12 deficiency maybe vague in elderly. High index of suspicion is required for the diagnosis. Mean corpuscular volume may not be raised in all cases. Hence, all patients in geriatric population presenting with must be tested for vitamin B12 deficiency.

KEYWORDS

Pancytopenia, MCV, Cobalamin.

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BACKGROUND

Pancytopenia presents as a major challenge in the diagnosis and management in day-to-day practice. Pancytopenia are often are very difficult to diagnose and treat often owing to its varied aetiologies. Causes may range from infections, nutritional deficiencies to malignancies. Pancytopenia is defined as haemoglobin of <9 g/dL, WBC <4000 cells/cumm and platelets <1 lakhs /cumm. Severe pancytopenia is defined as absolute neutrophil count <500/cumm, platelet count <20,000/cumm and corrected reticulocyte count <1%. Megaloblastic anaemia, hypersplenism (congestive splenomegaly, malaria leishmaniasis), aplastic anaemia, myelodysplastic syndrome, subleukaemic leukaemia's, military tuberculosis, multiple myeloma and PNH are some of the aetiologies presenting with pancytopenia. Identifying the etiopathology of pancytopenia is important for a given case for timely treatment of the disease.[1] The presenting features of pancytopenia are attributable to anaemia and thrombocytopenia, but leucopenia may cause life-threatening infections.[2] There are many studies conducted

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in India regarding aetiology of pancytopenia. But, such study conducted in elderly population is rare. Hereby, we have conducted a study on finding aetiology of pancytopenia in geriatric population who presented to Department of General Medicine.

Aims and Objectives- To study the clinico-aetiological profile of pancytopenia in elderly population in a tertiary care hospital.

MATERIALS AND METHODS

40 patients more than 60 years who had pancytopenia for at least 2 weeks presenting to Department of Internal Medicine of Ramaiah Hospitals, Bangalore, were included in the study.

Inclusion Criteria

- Patients aged >60 years who were admitted with pancytopenia (haemoglobin of <9 g/dL, WBC <4000 cells/cumm and platelets <1,00,000/cumm).
- Lab values indicative of pancytopenia persisting for 2-3 weeks.

Exclusion Criteria

- Patients suspected to be having malignancy or found to be having haematological and other malignancy.
- Acute causes secondary to sepsis, DIC excluded.

The study was conducted from May 2016 to March 2017. This prospective study was carried out over a period of one years in the Department of General Medicine in a Tertiary Care Hospital. In all patients, a complete medical history including age, sex, smoking status, alcohol intake, history of any treatment, intake of drugs and radiation exposure. A detailed physical examination of every patient was done for pallor, jaundice, hepatosplenomegaly, lymphadenopathy, sternal tenderness and gum hypertrophy. Basic haematological investigations like complete blood count, reticulocyte count and peripheral smear examination were performed in each case. Serum cobalamin (vitamin B12) levels were done in all the cases by ELISA method. Serum cobalamin level of <150 pg/dL were considered to be having deficiency. Bone marrow aspiration studies were done wherever indicated and possible except cases where the cause for pancytopenia was obvious. Other investigations like Erythrocyte Sedimentation Rate (ESR), urine and stool examination, liver and renal function tests, blood culture, ELISA for HIV, hepatitis B and C viruses, chest and bone radiographs, abdominal ultrasonography and urinary Bence-Jones proteins and serum electrophoresis in selected cases. Upper gastrointestinal endoscopy, cytogenetic analysis as and when indicated. The patients who were suspected of having malignancy were excluded from the study. All the patients thus selected were investigated in a systematic manner and cause of pancytopenia was ascertained. Clinicopathological correlation was done in all cases before reaching a definitive diagnosis.

RESULTS

Out of 40 patients included in the study, 25 were males and 15 were females. 28 patients were aged between 60-70 years, 10 patients between 70-80 years and 2 were more than 80 years old. Mean age of the patients was 68 years. Fatigue was the most common symptom (70%), mild cognitive impairment was reported in 10% patients and bleeding manifestations were seen in 5% cases.

Haemogram Parameters	Values
Mean haemoglobin	7.5 gm/dL (SD ± 3.5)
Mean total leucocyte count	2,500/dL (SD ± 1260)
Mean platelet count	52,000/dL (SD ± 25400)
Mean corpuscular volume	88 fl (SD ± 5)

Cause of Pancytopenia	Percentage of Cases
Cobalamin deficiency	60%
Aplastic anaemia	7.5%
Chronic liver disease	5%
Myelodysplasia	5%
Drug induced	2.5%
HIV associated	2.5%
Systemic lupus erythematosus	2.5%
Cause not established	2.5%

Most common peripheral smear finding was dimorphic anaemia followed by normocytic normochromic anaemia with pancytopenia.

Bone marrow examination was done in 25 of 40 patients. Megaloblastoid changes were found in 60%, erythroid hyperplasia in 15% and aplastic changes in 7.5% cases. Marrow dysplastic changes were seen in 5% cases. Serum cobalamin deficiency was found in 60% cases, aplastic anaemia 7.5% and myelodysplastic in 5%. There was one case of HIV associated pancytopenia where cause could not be found, one case of methotrexate-induced pancytopenia and one case of systemic lupus erythematosus. Main symptom in patients having cobalamin deficiency was fatigue (80%), mild cognitive impairment (20%), unsteadiness of gait (10%) and paraesthesia in 10%. In majority of cases, the cause of vitamin B12 deficiency was attributed to nutritional deficiency (70% cases). Among them, 50% of patients were strict vegetarians and other 20% had history of ethanol abuse. Pernicious anaemia was a cause in 1 of cases where antiparietal cell antibody was positive. Drug-induced cobalamin deficiency was seen in 5 cases of which 4 were on long-term metformin therapy in high doses and one patient was on phenytoin therapy. Cause of cobalamin deficiency could not be ascertained in 10% cases. Out of 40 cases of pancytopenia, 8 patients had raised MCV. Remaining 32 patients had normal MCV (p=0.2). 24 patients had low serum cobalamin levels (p=0.01), which was statistically significant.

Pancytopenia	Raised MCV	Normal MCV	P value
40	8	32	0.2

Pancytopenia	Low Serum Cobalamin Level	Normal Serum Cobalamin Level	P value
40	24	6	0.01

DISCUSSION

This study analysed the clinical spectrum of presentation and aetiology of pancytopenia in elderly. The data regarding pancytopenia in general population is available, but limited in geriatric population. In our study, we found that most common cause was cobalamin deficiency. Cobalamin is responsible for the maturation of all the haematopoietic stem cells. Deficiency is commonly seen in elderly people especially who are vegetarians, alcoholics and who are on long-term drugs, which impair cobalamin absorption like phenytoin, metformin and antipsychotic drugs. Symptoms of cobalamin deficiency range from fatigue, restlessness, forgetfulness, unsteadiness and burning sensation of legs. These symptoms are sometimes very subtle in elderly population. Hence, high suspicion of index is required. Also, in our study, we found that MCV was normal in many patients of cobalamin deficiency. Hence, raised MCV may not be present in all cases. Serum cobalamin levels were found to be low and statistically significant. Hence, all patients, especially geriatric population who present with pancytopenia, serum cobalamin should be measured. Serum cobalamin levels are reasonable good markers of vitamin B12 deficiency. Serum transcobalamin levels are promising parameters in the future. Patients suspected of having pernicious anaemia should be tested for antibodies to Intrinsic Factor (Ifab). Patients found to be positive should have lifelong therapy. Patients negative for Ifab with no other cause should be treated as anti-Ifab negative pernicious anaemia. Other causes of pancytopenia were chronic liver disease, SLE and methotrexate induced. This study was conducted in Department of General Medicine. The malignant causes of pancytopenia were excluded from the study. The true prevalence of vitamin B12 deficiency in the general population is not known. The incidence, however, appears to increase with age according to Kumar et al. Megaloblastic anaemia was a common cause of pancytopenia in their study and they stated that it may present acutely in the critically ill patients.[3] According to a study conducted by Asof C. Antony, et al, there is widespread deficiency of cobalamin and folate in Indian population, which can lead to many cardiovascular morbidity due to elevated homocysteine.[4] According to Savage DG et al from Zimbabwe, most common cause of pancytopenia was megaloblastic anaemia and they stated that mean corpuscular volume in these cases was normal or low in one third of cases.[5] According to Lakhey et al from Nepal, major causes of pancytopenia were hypoplastic marrow, megaloblastic anaemia and leukaemia.[6] In the study conducted by Khunger et al in New Delhi, most common cause of pancytopenia was megaloblastic anaemia accounting for upto 72% cases.[7] In the study conducted by Arvind Jain et al, cause of pancytopenia was varied and involved hypersplenism, megaloblastic anaemia and aplastic anemia.[8] According to the study conducted by Gayathri et al from Kolar, most common cause of pancytopenia was megaloblastic anaemia in 74% of cases.[9] According to a study conducted by Robert C et al, true prevalence of vitamin B12 deficiency is not known. The incidence, however, appears to increase with age. 15 percent of adults older than 65 years had laboratory evidence of vitamin B12 deficiency. The use of gastric acid blocking agents may also cause deficiency of vitamin B12.[10] The diagnosis of vitamin B12 deficiency has traditionally been based on low serum vitamin B12 levels usually less than 200 pg per mL (150 pmol per L). However, studies indicate that older patients tend to present with neurological disease in the absence of haematologic findings.[10] Estimation of methylmalonic acid and homocysteine levels have been shown to be more sensitive in the diagnosis of vitamin B12 deficiency than measurement of serum B12 levels alone.[10] Hereby, we conclude that most common cause of pancytopenia in elderly population was vitamin B12 deficiency. Mean corpuscular volume may not be raised in all the cases.

CONCLUSION

In our study, vitamin B12 deficiency was the most common cause of pancytopenia in elderly population. Symptoms of vitamin B12 deficiency maybe vague in elderly. High index of suspicion is required for the diagnosis. Mean corpuscular volume may not be raised in all cases. Hence, vitamin B12 deficiency should be considered in elderly population with pancytopenia.

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