Original article:

Clinico-Hematological profile of megaloblastic anaemia in children in Jammu Region- One year retrospective study

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ABSTRACT

Anemias are the most important disorders of blood in infancy and early childhood. Megaloblastic anemia is an important type of anemia. This condition sometimes mimics haematological malignancy like leukaemia ,hence diagnosis assumes great importance. A retrospective study was undertaken in the department of Pathology, Govt. Medical College, Jammu, where 51 children aged less than one year to 14 years admitted with the diagnosis of megaloblastic anemia from April 2016 to March 2017 were included in the study .The inclusion criteria were haemoglobin level < 10 grams and MCV>100fl, macrocytosis in peripheral blood film, hypercellular marrow with megaloblasts and giant metamyelocytes in the bone marrow examination. Case records were accessed for clinical findings, presenting complaints ,PBF and bone marrow findings. Out of 51 children, 27 were males and 26 were females. Male: Female ratio was 1:1.5 .Pallor was present in 44 cases. Bicytopenia was seen in 17 cases (33.33 %). Pancytopenia was present in 18 cases (35.29 %) .Macrocytosis was present in 100% cases. This study showed that the common complaint in Megaloblastic anemia is pallor, macrocytic blood picture and bi or pancytopenia. In any anemic child presenting with bleeding manifestation , a strong suspicion of Megaloblastic anemia should be made .Since it is a treatable condition ,prompt notification and early identification can have positive impact in the further management.

KEY WORDS : Anemia ,Megaloblastic anemia, Bone marrow examination.

INTRODUCTION

Megaloblastic anemia is one of the important cause of anemia in children[2]. Anemias in children differ from those in adults as they tend to be more pronounced and develop rapidly[20]. Megaloblastic anemia is an important reversible cause of neurodevelopmental deterioration[26].It is classically defined as a macrocytic anemia that is characterised by specific megaloblastic bone marrow morphology showing metamyelocytes and megaloblasts, accompanied by leucopenia and thrombocytopenia[26] The recognition and treatment of vitaminB12 deficiency is critical since it is a reversible cause of bone marrow failure and demyelinating nervous system disease[24].Megaloblastic anemia is one of the important causes of anemia.It results from abnormal maturation of hematopoetic cells due to faulty DNA synthesis. Two vitamins, cyanocobalamin,VitB12 and folic acid are essential for DNA biosynthesis .Deficiency of either vitamin results in abnormal nuclear maturation with normal cytoplasmic maturation, apoptosis, ineffective erythropoesis, intramedullary hemolysis, pancytopenia and typical morphological abnormalities in blood and marrow cells [8,13,16].

The most common presenting complaints in Megaloblastic anemia due to vitaminB12 deficiency are anorexia, generalised weakness and irritability manifesting clinically as pallor, hyperpigmentation and hematologically as macrocytic anemia. Regular reports of common presentation of Megaloblastic anemia in various age groups keeps the child care expert vigilant for its early detection.

MATERIAL AND METHODS

In this retrospective observational study all children aged less than one year to 14 years admitted with a diagnosis of Megaloblastic anemia from April 2016 to March 2017 were included. The case records were accessed through admission and discharge database of the hospital. The records were examined and primary outcome measures like chief complaints, mode of diagnosis ,PBF findings and bone marrow findings were noted. The mode of diagnosis considered was either vitaminB12 assay or bone marrow examination .The aim of the study was to evaluate the varying clinico-hematological manifestations in patients diagnosed as Megaloblastic anemia.

RESULTS

Out of 51 cases of megaloblastic anemia, 20 were males and 31 were females with Male to Female ratio of 1:1.5 . Whereas the Age of patients ranged from 5 months to 14 years. Maximum number of children belonged to the age group of 10 to 14 years (Table-I)

TABLE-I: Age & Sex distribution of the cases (n=51)

AGE GROUP	MALE (%age)	FEMALE (%age)	TOTAL (%age)
< 1 Year	2(3.92%)	3(5.88%)	5(9.80%)
>1 Year to 5 Years	1 (1.96%)	2(3.92%)	3(5.88%)
>5Years to10 Years	2(3.92%)	4(7.85%)	6(11.77%)
>10Years to14 Years	15(29.41%)	22(43.14%)	37(72.55%)
	20(39.21%)	31(60.79%)	51(100%)

Clinical findings of patients with megaloblastic anemia are listed in TABLE -2. Pallor was present in 44 cases . 38 cases presented with fever and 7 presented with bleeding manifestations. Bleeding was mainly seen in the skin and subcutaneous tissues. Splenomegaly was present in 16 cases. The platelet counts obtained from Analyser were confirmed by peripheral blood smear examination. Cases with macrocytic blood picture on smear examination were subjected to bone marrow examination to confirm diagnosis of megaloblastic anemia. The diagnosis of megaloblastic anemia was established on the basis of megaloblastic bone marrow. Adequate iron stores ruled out concomitant iron deficiency. There were no neurological deficits in any of the children studied.MCV levels done on 24 patients showed levels of more than 100fl in 8 patients and serum vitamin B 12 assay done on 34 patients showed levels of less than 187ng/l in 16 patients.

. The commonest clinical presentations were pallor and fever .Irritability , anorexia, weight loss and generalised weakness were the other clinical presentations.

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Table=2: Clinical Features (n=51)

Clinical Features	**No. of Cases**	**%age**
Pallor	44	86.27%
Fever	38	74.50%
Bleeding Manifestations	7	13.72%
Splenomegaly	16	31.37%
Palor+Splenomegaly+Bleeding manifestations	5	9.80%

Note: Multiple findings were present in more than one patients

Table=3: Hematological Features (Cytopenias) (n=51)

Hematological features	**No. of Cases**	**%age**
Anaemia	16	31.38%
Anaemia+Leucopenia	03	5.88%
Anaemia+Thrombocytopenia	14	27.45%
Anaemia+Thrombocytopenia+Leucopenia	18	35.29%

Macrocytic anemia and bicytopenia were observed in peripheral smear examination of 17 patients (33.33 %)

The median Hb was 10 grams/dl with severe anemia noted in 36 patients(70.60%) (Table-IV)

Table-IV. SEVERITY OF ANAEMIA (n=51)

Anaemia	**Haemoglobin %age**	**No of Patients**
Mild	10 to 12 gm%	7(13.72%)
Moderate.	8 t0 10 gm %	8(15.68%)
Severe	<8 gm %	36(70.60%)

DISCUSSION

All megaloblastic anemias are characterised by ineffective erythropoesis, a term that describes active erythropoesis with premature death of cells, a decreased output of RBC s from bone marrow and consequently anemia [(20).] Megaloblastic anemia is an anemia that results from inhibition of DNA synthesis in RBC production. When DNA synthesis is impaired, cell cycle cannot progress from growth stage to mitotic stage. This results in continued cell growth without division which causes nuclear –cytoplasmic asynchrony and presents as macrocytosis. Thus megaloblastic anemia is a distinct type of anemia characterised by macrocytic RBC and typical morphological changes in RBC precursors[(25).] The precursors are larger than cells of same stage and maturation. Megaloblastic anemia presents with protean manifestations- children usually present

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with generalised weakness, fatigue ,failure to thrive or irritability. Other common findings include pallor ,glossitis, vomiting,hemorrahages etc [20].

The common age of presentation in our study was between age of 10 to 14 years(72.54 %). In other studies megaloblastic anemia is reported to occur in older age groups with an equal sex ratio or male preponderance[3,9,4]. Clinical examination of cases in our study showed pallor in 44 cases(86.24 %).Other studies found 98.8% - 100% of patients presenting with pallor [10,11,17].Fever was seen in 74.50 % of patients in our study, the commonest cause being infection to which the patient is much more susceptible in this disease due to impaired intracellular killing of ingested bacteria by neutrophils and macrophages [6,2,1].Bleeding was noted in 13.72 % of patients of our study ;it could be most likely due to thrombocytopenia. An earlier study documented bleeding in 17 -20% of patients in megaloblastic anemia [20,6,2]. Thrombocytopenia is believed to be due to impaired DNA synthesis resulting in ineffective erythropoesis [2]

Pallor was present in 44 patients of our study. It is explainable on the basis of decreased life span of RBC s and to premature destruction of developing megaloblasts in the marrow.[2]. Bicytopenia was noted by Meghann et al to be in 44.8%, which is more compared to the present study[23]. An earlier series reported incidence of pancytopenia in 43,8% and bicytopenia in 80.5% cases.[2] The varying results could be due to difference in duration of anemia which is proportional to development of cytopenia .It is generally believed that as severity of anemia increases thrombocytopenia develops followed by neutropenia.[2] .

In our study females outnumbered males and pallor was the commonest clinical presentation. Megaloblastic anemia was the commonest cause of pancytopenia (35.2%) in children below 14 yrs which is comparable to the finding of Bhatnagar et.al [14]. Similar findings(43 to 72%) have been reported by other authors [12,17,18]. Anemia and thrombocytopenia was seen in 27.45 % of patients In other studies thrombocytopenia ranged from 9.9%to 37 % [1,15,18,20].

As the closest differential diagnosis of this condition is aplastic anemia and both may have presence of macrocytes in PBF ,it poses a difficulty in distinction between the two in the absence of macro-ovalocytes and hypersegmented neutrophils.[22,7]. The etiology and the pathogenesis of the heterogenous group of disorders under megaloblastic anemia share common characteristics like-

*Large cells with an arrest in nuclear maturation.

*Nuclear maturation is immature relative to cytoplasmic maturity

Hence these cells that can be seen in bone marrow aspirates and in peripheral smears have been called megaloblasts. These abnormalities due to impaired DNA synthesis and to a lesser extent RNA and protein synthesis are apparent in the rapidly dividing cells such as blood cells and gastrointestinal cells. The clinical course could be acute or chronic and can have varied spectrum of severe anemia , pancytopenia and gastrointestinal dysfunction [5,19,21]

Megaloblastic anemia was predominantly diagnosed by bone marrow and vit B12 assay ,where emphasis has to be laid on Vit B12 assay in order to standardize diagnostic options among various hospital settings .It also adds the advantage of less expertise, easy to perform process and decreased risk of infection.[26].

We are of the opinion that regular reporting of common diseases like Megaloblastic anemia and its varied presentations in various age groups ,guides child care physicians in early detection of the disease .Megaloblastic anemia is a preventable and treatable cause of progressive neurological disease in children with poor reporting of wide range of clinical presentations and distribution among various age groups.

CONCLUSION

Megaloblastic anemia can present with varied clinical manifestations. On the basis of observations made in this study it is concluded that in any anemia strong suspicion of Megaloblastic anemia should be made by Paediatricians to improve the clinical outcome. The most common presenting complaints in megaloblastic anemia due to vit B12 deficiency are anorexia ,generalized weakness and irritability manifesting clinically as pallor and hematologically as macrocytic anemia and bicytopenia. Regular reports of common presentations in various age groups keep the Pediatrician vigilant for the early detection. Being a rapidly correctable disorder, early detection and prompt notification can be very helpful and a simple , cheap and easy procedure like bone marrow examination can be really helpful . A complete blood count with red cell indices, examination of PBF , bone marrow examination and vitamin assay are sufficient to make a definite diagnosis of megaloblastic anemia. Long term followup and diet councelling should be done . The fortification of diet to prevent megaloblastic anemia needs to be taken up as a national public health issue .This study described the varied presentations of disease in children and degree of the disease among various age groups.

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