Megaloblastic anemia is an anemia that results from inhibition of DNA synthesis during red blood cell production. Children usually present with generalized weakness, fatigue, failure to thrive, or irritability. Diagnosis is usually based on complete blood count and peripheral smear, which may show macroovalocytes, hyper segmented neutrophils, reticulocytopenia and a raised mean corpuscular volume (MCV >100 fl). In advanced cases, pancytopenia may be seen. Here, we report a 15-year-old female child who presented with high grade fever and vomiting. Her initial blood picture revealed severe anemia with normal MCV and decreased total leucocyte count. The child had persistent pancytopenia for which vitamin B12 levels were evaluated, and it was found to be decreased. Megaloblastic anemia is an important cause of cytopenias, but to best of our knowledge, there are not many studies quoting its incidence.

Keywords: Anemia, Megaloblastic, Pancytopenia, Vitamin B12

INTRODUCTION

Megaloblastic anemia is characterized by ineffective erythropoiesis with premature death of cells, a decreased output of red blood cells (RBCs) from bone marrow, and consequently anemia. Megaloblastic anemia is suspected in anemic patients with macrocytic indices (mean corpuscular volume [MCV] >100 fl). The earliest change is the development of macrocytosis and elevated MCV without anemia. Diagnosis is usually based on complete blood count (CBC) and peripheral smear, which may show macroovalocytes, hyper segmented neutrophils, reticulocytopenia. In advanced cases, neutropenia and thrombocytopenia develop simulating aplastic anemia or leukemia. Megaloblastic anemia is an important cause of cytopenias, but to best of our knowledge, there are not many studies quoting its incidence.

CASE REPORT

A 15-year-old female child was brought to the emergency department of Chalmeda Anand Rao institute of Medical Sciences, Karimnagar which is a tertiary care centre that caters 3 districts of Northern Telangana with high grade, continuous fever with chills and rigors and vomiting 2-3 episodes daily which were non projectile, non-bilious in nature, since 10 days. There is no history suggestive of acute respiratory tract infection and urinary tract infection. There is no history of rash, diarrhoea, pain abdomen and bleeding manifestations. No history of headache and head injury. On general examination, severe pallor and icterus were noted. On gastrointestinal system examination, mild splenomegaly was noted. On clinical grounds, malaria was suspected, and antimalarial treatment started. Hematological investigations revealed severe anemia (Hemoglobin (Hb) - 4.7 g%, RBC - 1.6 million/mm³), total leucocyte count (TLC) - <2000/mm³, differential leucocyte count not possible due to low count, platelets 1.5 lakhs/mm³. Her RBC indices were as follows: Reticulocyte count <0.5%, MCV - 88 fl, mean corpuscular hemoglobin: 28 pg and mean corpuscular Hb concentration - 32%. Peripheral smear showed microscopic RBCs with many schistocytes and target cells. No hemoparasites were seen. Widal test and malaria rapid diagnostic test were negative. After transfusing 1 unit of B+ compatible packed RBCs, her blood picture was as follows: Hb - 7.2 g%, TLC - 2000/mm³ and platelets - 1.43 lakhs/mm³. Before transfusion, blood samples were sent for iron profile and Hb electrophoresis. Electrophoresis report was normal. Iron profile was in favour of anemia of chronic disease with increased serum ferritin (177.1 ng/ml), normal serum iron (104.3 mcg/dl), decreased total iron-binding capacity.
capacity (88 mcg/dl), decreased transferrin (61/mcgg/dl) and increased iron saturation (118%). Two days post-transfusion, her blood picture revealed pancytopenia. So again 1 unit compatible whole blood was transfused. Even then, pancytopeny persisted with a mild increase in Hb levels, platelets 4000/mm$^3$, TLC 1000/mm$^3$. Due to persistent pancytopenia, vitamin B12 levels were ordered which came out to be 97 pg/ml ($N_1 = 160-1300$ pg/ml). To know bone marrow status and for confirmation of megaloblastic anemia, bone marrow aspiration was done. Simultaneously, a repeat peripheral smear was sent. Bone marrow aspiration revealed hypercellular marrow with M:E ratio of 1:4, erythroid hyperplasia with megalonormoblastic reaction, megaloblastic leucopoiesis mainly in myelocytes and metamyelocytes confirming the diagnosis of megaloblastic anemia. Peripheral smear also showed macrovalocytes. She was started on injection vitamin B12 1000 mcg/day/IM. After receiving vitamin B12 injection for 4 days, there was improvement in the blood picture with Hb - 7.6 g%, TLC - 1100/mm$^3$ and platelets - 1.03 lakhs/mm$^3$. With this history, clinical examination, investigations and response to vitamin B12 injections, we strongly considered the diagnosis of megaloblastic anemia.

<table>
<thead>
<tr>
<th>Hb levels</th>
<th>TLC</th>
<th>Platelets</th>
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<tbody>
<tr>
<td>At the time of admission</td>
<td>4.7 g%</td>
<td>&lt;2000/mm$^3$ DLC not possible due to low count</td>
</tr>
<tr>
<td>After 1 unit packed RBCs transfusion</td>
<td>7.2 g%</td>
<td>2000/mm$^3$</td>
</tr>
<tr>
<td>Two days post transfusion</td>
<td>5.7 g%</td>
<td>1000/mm$^3$</td>
</tr>
<tr>
<td>After 1 unit whole blood transfusion</td>
<td>7.4 g%</td>
<td>1000/mm$^3$</td>
</tr>
<tr>
<td>After 4 days of vitamin B12 IM injections</td>
<td>7.6 g%</td>
<td>1100/mm$^3$</td>
</tr>
</tbody>
</table>

DISCUSSION

Deficiency of vitamin B12 and folate most commonly results in megaloblastic anemia. All megaloblastic anemias are characterized by ineffective erythropoiesis, a kinetic term that describes active erythropoiesis with premature death of cells, a decreased output of RBCs from bone marrow, and consequently anemia.$^{1,4}$

Megaloblastic anemia is a distinct type of anemia characterized by macrocytic RBCs and typical morphological changes in RBC precursors. The precursors are larger than the cells of same stage and maturation and exhibit disparity in nuclear cytoptasmic maturation. Myeloid and platelet precursors are also affected, and giant metamyelocytes and neutrophil bands are often present in bone marrow.

Children usually present with generalized weakness, fatigue, failure to thrive, or irritability. Other common findings include pallor, glossitis, vomiting, diarrhea, icterus, paraesthesias, hypotonia, seizures, tremors, developmental regression, neuropsychiatric changes, hemorrhages etc.$^{1,5}$

Megaloblastic anemia is suspected in anemic patients with macrocytic indices (MCV >100 fl). Diagnosis is usually based on CBC and peripheral smear which may show macrovalocytes, hyper segmented neutrophils, reticulocytopenia. The earliest change is the development of macrocytosis and elevated MCV without anemia. In advanced cases, neutropenia and thrombocytopenia can occur, simulating aplastic anemia or leukemia.

In the present case, the child’s RBC indices were within normal limits. Serum iron studies were not in favor of iron deficiency anemia. It is suggestive of anemia of chronic disease. All 3 cell lines were decreased. Icterus, not an infrequent feature in this disease was noticed, in this case. It is explainable on the basis of decreased life span of RBCs and to premature destruction of developing megaloblasts in the marrow.$^6$

Megaloblastic anemia is an important cause of cytopenias (pancytopenia and bicytopenia), but to the best of our knowledge, there are not many studies quoting its incidence. An earlier series reported an incidence of pancytopenia in 43.8% and bicytopenia in 80.55% cases.$^{5,8}$

The varying results in the two series could be due to the difference in the duration of anemia, which is proportional to the development of cytopenias. It is generally believed that as the severity of anemia increases, thrombocytopenia develops followed by neutropenia.$^{5,7,8}$

CONCLUSION

Megaloblastic anemia is an important cause of anemia in childhood. Megaloblastic anemia should be strongly suspected in all children having bicytopenia and pancytopenia. Megaloblastic anemia is generally suspected in children having anemia with raised MCV. However in this child who presented with anemia and normal MCV, vitamin B12 deficiency was suspected based on pancytopenia with anemia, and it was confirmed by bone marrow aspiration. So whenever a child presents with pancytopenia, treatable conditions like nutritional (vitamin B12) deficiencies shouldn’t be ignored.

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