

CASE REPORT

HYPOCELLULAR MYELOYDYSPLASTIC SYNDROME PRESENTING AS MEGALOBLASTIC ANEMIA

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INTRODUCTION

Myelodysplastic Syndromes (MDS) are a heterogeneous group of clonal stem cell disorders which generally occur in older adults but may also affect children. The ineffective hematopoiesis which causes bone marrow failure is accompanied by peripheral blood cytopenia¹. MDS are classified into 5 different morphologic categories according to French-American-British (FAB) classification^{1,2,3}. Hypocellular Myelodysplasia is a less common variant of MDS, characterized by hypocellular marrow in which a small proportion of blasts may be seen usually with occasional blasts in the peripheral blood². We have encountered a distinct young patient of hypocellular MDS presented as megaloblastic anemia and pancytopenia.

CASE REPORT

A 22 years old young male, presented to us in June 2001 with complaints of fever and generalized weakness. He was pale and had very small palpable axillary lymph nodes with no visceromegaly. He was investigated and found to have pancytopenia (Hb= 8.8 gm/dL, TLC= $3.5 \times 10^3/L$, Platelets= $87,000 \times 10^3/L$, MCV= 99 fL, ESR 45 mm, reticulocytes 3.5%). His bone marrow examination was done which revealed moderate megaloblastic anemia with above normal iron stores. He was put on Tab. Folic acid 5 mg bid with Injection Vitamin B₁₂ IM daily, discharged and advised for follow-up in OPD after 2 weeks. He was kept on this treatment for 1 month.

On 10th July, his blood picture was repeated, and again found to have pancytopenia (Hb= 6.6 gm, TLC= $3.5 \times 10^3/L$, Platelets= $37,000 \times 10^3/L$, Reticulocytes= 1.4%). He was again admitted. His Bone marrow examination was repeated and found to have moderate megaloblastic anaemia with dyserythropoietic changes. Trepine biopsy was unsuccessful. He was again sent home and recalled after 1 month.

He came back after 1 month with new complaints of fever along with productive cough. His Chest X-Ray, repeat Blood CP and sputum R/E was done. Sputum examination was found positive for Acid Fast Bacilli along with atypical cavitary infiltrates in the lower zone on a radiograph. He refused bone marrow examination but he had pancytopenia. Considering a possibility of Disseminated Tuberculosis, he was put on Anti-TB drugs along with oral steroids. At this stage, his vitamin B₁₂ and folic acid levels were done, and were found to be within normal range. His Ham's test was also normal and serum Ferritin was increased. CT Scan chest and abdomen were also done which revealed hepatosplenomegaly, and opacities in the right lower lobe of lung posteriorly. To rule out the possibility of lymphoma, lymph node biopsy was done, which was found to have reactive changes only.

Due to hepatosplenomegaly, possibility of aplastic anaemia was ruled out, and because of increased iron stores in bone marrow with negative Ham's test, Paroxysmal nocturnal haemoglobinuria was also not considered. During his stay in the hospital, he was transfused 20 pints of blood and 30 pints of platelets concentrates.

In November 2001, he improved clinically, radiographic findings cleared, but he still had pancytopenia. His bone marrow examination was repeated and his trephine biopsy revealed a Moderately Hypocellular Marrow with dysplastic myelopoiesis and prominent eosinophils and lymphocytes with no evidence of fibrosis.

Diagnosis of Myelodysplasia with Hypocellular Marrow was made. He was also given a trial of anabolic steroids and Cyclosporine-A in adequate doses. But there was no response seen. His blood counts (Hb= 6.3, TLC= $3,000 \times 10^3/L$, Platelets= $11,000 \times 10^3/L$, MCV= 88 fL, Reticulocytes= 0.5%) did not improve. Considering the Hypocellular MDS, he was referred for Bone Marrow Transplantation to England.

DISCUSSION

Megaloblastic anaemia due to vitamin B₁₂ and folate deficiency is a reversible form of ineffective haematopoiesis. MDS is an acquired, irreversible disorder of ineffective haematopoiesis. Megaloblastic anaemia and MDS are generally considered mutually exclusive diagnoses⁴.

Hypocellular MDS is considered a new entity, outside the FAB classification but related to refractory anaemia⁵. It is often difficult to distinguish hypocellular MDS from severe aplastic anaemia because both can present with profoundly hypocellular bone marrows and pancytopenia^{5,6,7,9}. It is important to differentiate between these two diseases for a proper management and prognosis^{5,8,9}.

Our patient presented in an evolving state of the disease, with atypical manifestations. Initially he was found to have pancytopenia and megaloblastic anaemia for which he was advised therapeutic doses of vitamin B₁₂ and folic acid. But there were no signs of improvement and repeat bone marrow examination showed dysplastic changes. At this stage, normal serum vitamin levels were seen. At that stage, possibility of refractory anaemia with MDS was considered. It is well known that in MDS and refractory anaemia, patients do not improve with vitamin therapy². We also considered lymphoma, because he had palpable axillary and inguinal lymph nodes and bone marrow lymphocytosis. Initially these lymph nodes were very small for a proper biopsy. CT scan abdomen was ordered to look for other lymph nodes in the abdomen, but it was negative. Splenomegaly was an incidental finding, biopsy of lymph node showed reactive changes.

Patient took anti-tuberculous drugs because of the cavitary lesions in the lungs, but he persistently showed a picture of refractory anaemia. Bone marrow aspiration and trephine biopsy were repeated in November 2001 to re-evaluate the case. He was then found to have myelodysplasia and hypocellular marrow with prominent lymphocytes and eosinophils with no evidence of fibrosis. This patient at an age of 22 years had a very atypical picture of hypocellular MDS.

Mostly the patients with hypocellular MDS are older¹. These patients usually present with symptoms of anaemia and thrombocytopenia. Peripheral blood picture shows anaemia with occasional poikilocytosis, anisocytosis and often macrocytes; granulocytopenia with hypogranular or agranular neutrophils with poorly condensed chromatin and Pelger-Huet anomaly with hyposegmented nuclei; thrombocytopenia, occasionally giant platelets or hypogranular platelets, low or normal reticulocyte count, raised or normal MCV (mean corpuscular volume) and occasionally a small proportion of blasts may be seen. Bone marrow has ineffective haematopoiesis with dysplasia in one or more cell lineages. Marrow cellularity is usually normal or increased for the patient's age. Trephine is always hypocellular with no fibrosis³. The histologic evaluation of a trephine bone marrow biopsy is of critical importance for the evaluation of fibrotic or hypocellular MDS since these patterns are not reflected by the cytological examination. The combined cytological and histological diagnosis of bone marrow and peripheral blood is a reliable tool for the initial diagnosis of MDS¹. These patients also have chromosomal abnormalities³.

Treatment of hypocellular MDS is allogenic Bone Marrow Transplantation. It has been mentioned that there is a role of anabolic steroids and immunomodulatory drugs like cyclosporine-A as well³. But this treatment needs more detailed grand scale studies.

REFERENCES

1. Schmitt-Graeff A, Mattern D, Kohler H, Hezel J, Lubbert M. Myelodysplastic syndromes (MDS). Aspects of haematopathologic diagnosis. *Pathologie* 2000;21(1):1-15.
 2. Gordon-Smith EC. Aplastic anaemia. In: Weatherall DJ, Ledinghim JG, Warrell DA. *Oxford textbook of Medicine*. 3rd ed. Oxford: Oxford University Press;1996:3447.
 3. Malaspina CH, O'Reilly JR. Myelodysplastic syndromes. In: Fauci AS, Braunwald E, Wilson DJ, Martin BJ, Kasper, Hauser SL, eds. *Harrison's Principles of Internal Medicine*. 14th ed. New York: McGraw-Hill; 1998:678.
 4. Drabick JJ, Davis BJ, Byrd JC. Concurrent pernicious anaemia and myelodysplastic syndrome. *Ann Hematol* 2001;80(4):243-5.
 5. Lorand-Metze I, Meira DG, Lima CS, Vassallo J, Metzke K. The differential diagnosis between aplastic anaemia and hypocellular myelodysplasia in patients with pancytopenia. *Haematologica* 1999;84(6):564-5.
 6. Barrett J, Saunthararajah Y, Molldrem J. Myelodysplastic syndrome and aplastic anaemia: distinct entities or diseases linked by a common pathophysiology? *Semin Hematol* 2000;37(1):15-29.
 7. Elghetany MT, Hudnall SD, Gardner FH. Peripheral blood picture in primary hypocellular refractory anaemia and idiopathic acquired aplastic anaemia: an additional tool for differential diagnosis. *Haematologica* 1997;82(1):21-4.
 8. Varma N, Varma S, Marwaha N, Garewal G. Aplastic anaemia versus hypocellular myelodysplastic syndrome. *Indian J Cancer* 1995;32(3):110-5.
 9. Toyama K, Ohyashiki K, Yoshida Y, Abe T, Asano S, Hirai H, et al. Clinical and cytogenetic findings of myelodysplastic syndromes showing hypocellular bone marrow or minimal dysplasia, in comparison with typical myelodysplastic syndromes. *Int J Hematol* 1993;58(1-2):53-61.
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