Case Report

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Lenalidomide-Induced Cure for a Patient with Lower-Risk Myelodysplastic Syndrome (MDS) and Transfusion-Dependent Anemia. A Case Report

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ABSTRACT

Lenalidomide is the preferred treatment for patients with lower-risk MDS and transfusion-dependent anemia. Lenalidomide is not considered a cure for MDS but it has proven to be an effective treatment for lower-risk MDS. We present a patient with lower-risk MDS and transfusion-dependent anemia who not only responded well to lenalidomide therapy but has been transfusion-independent for over 6 years since her treatment with lenalidomide was stopped. Her blood erythrocyte count (hemoglobin level) has been normal since and we consider this to be the first report of a case with MDS being cured by lenalidomide therapy.

Keywords: Myelodysplastic Syndrome; Lenalidomide; Transfusion-Dependent Anemia

Introduction

Myelodysplastic syndromes (MDS) are a diverse group of hematological disorders that affect the blood and bone marrow [1,2]. One subgroup in this syndrome is the lower-risk MDS with transfusion-dependent anemia [3]. The median life expectancy in this group of disorder is typically between 3-10 years with most studies indicating a median survival closer to the lower end of that range due to the increased risk of complications associated with regular blood transfusion, and iron overload; however, individual cases can vary significantly based on different factors like genetic mutations, comorbidities and overall health condition [3]. MDS treatment is usually decided according to the risk classification. The goal of therapy in lower-risk MDS is to improve cytopenia, reduce transfusion requirements, improve quality of life, prolong overall survival, and maybe reduce the risk of progression to leukemia [3]. Different medications have been tried in MDS, however, no effective treatment has yet been established. Prednisone, G-CSF, erythropoiesis-stimulating agents such as epoetin alfa or luspatercept, lenalidomide, and hypomethylating agents either singly or in combinations have been tried with some success to meet the above-stated goals but not as a cure [4-8]. We present the first documented case of a lower-risk, transfusion-dependent MDS that appears to have been cured in the patient after a conventional dose of lenalidomide therapy.

Case Report

We report a patient with transfusion-dependent lower-risk MDS who responded well to lenalidomide. The patient became transfusion-independent after five years of therapy with lenalidomide and has been transfusion independent ever since her treatment was stopped seven years ago. The patient, is a 75-year-old African American female who was referred to our hospital for the evaluation and management of transfusion-dependent anemia. The patient had no major complaints except for being tired and generalized weakness. Her physical examination was unremarkable except for pallor. Her

laboratory investigations revealed: WBC 3.9 X 10^9/L, hemoglobin 7.8 g/dl, with a slightly raised MCV at 106.0 fl and slightly raised MCH at 32.0 pg and a platelet count of 248 X 10^9/L. Neutrophils were 59%, lymphocytes 10% monocytes 9% and bands 18%, myelocytes 2%, and metamyelocytes 2%. Her ESR was raised to 50 mm/hr. Her serum iron was normal at 66 mcg/dl, iron binding capacity was slightly low at 241 mcg/dl, ferriin was high at 2360 and erythropoietin level was high at 47.1 milliunit/ml. Her B12 level was normal at 414 pg/ml, and folic acid level was > 24 ng/ml. Her complete metabolic profile was normal. Her stool occult blood test X3 was negative and a colonoscopy and esophagogastroduodenoscopy did not reveal any source of bleeding. A bone marrow aspirate and biopsy revealed moderate to markedly cellular marrow (Figure 1) with trilineage hyperplasia and maturational abnormalities. Megakaryocytes were adequate in number. Many of the megakaryocytes were small and hypo-lobated (Figure 2). Red cell maturation was megaloblastic. Erythroid maturation showed mild to moderate dyserythropoiesis (Figure 3), and some of the neutrophil series showed dysgranulopoiesis (hypo and hyper lobulation, hypo granulation) (Figure 4). The ME ratio was about 3:1. Myeloblasts were not increased. Iron stain on the aspirate smear showed increased iron stores (Figure 5) with many sideroblasts (Figure 5 inset) but no obvious ringed sideroblasts. The morphologic features were most consistent with a diagnosis of MDS (refractory anemia). Flow cytometry was negative. Despite best efforts, it was not possible to complete the cytogenetic studies on the bone marrow cells. Karyotype analysis of only three metaphase cells, revealed a normal 46, XX cell, a 45, XX-14 cell, and a 46, XX del (17p) cell. With only a limited number of cells available for analysis, one could not rule out the possibility that a subpopulation of cells went undetected in the study. Her JAK–2 mutations, and BCR–ABL translocation were negative. She was started on prednisone 10 mg by mouth daily for three months to which she failed to respond and continued to require repeated blood transfusions. She was then switched to lenalidomide 10 mg by mouth daily for 28 days. She responded well to lenalidomide therapy and her blood transfusion requirement fell substantially. About two years after the start of lenalidomide therapy she became transfusion-independent and her blood counts returned to normal. Her treatment was continued for six more years when her therapy was abruptly stopped due to the refusal by the insurance carrier to pay for her medication. It is now 12 years that she has been clinically and hematologically stable without requiring any other therapy or blood transfusion.

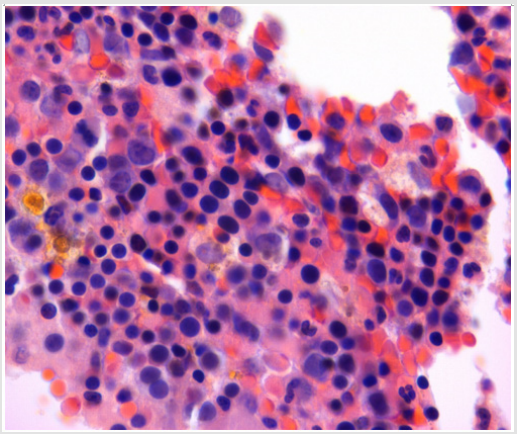

Figure 1: Bone marrow biopsy section showing hypercellular marrow.

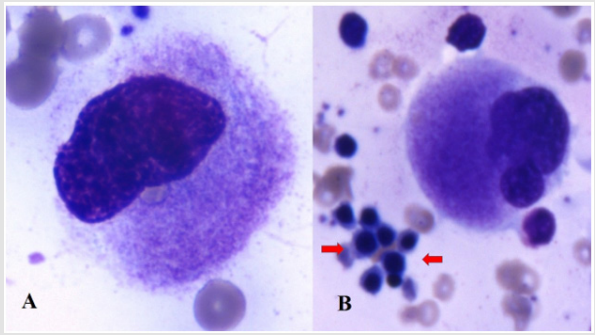

Figure 2: Bone marrow aspirate smear showing dysplastic megakaryocytes.
(A) Mono and
(B) Bi-nucleated megakaryocytes. Note an erythroid clusters in Figure 2-B (arrows).

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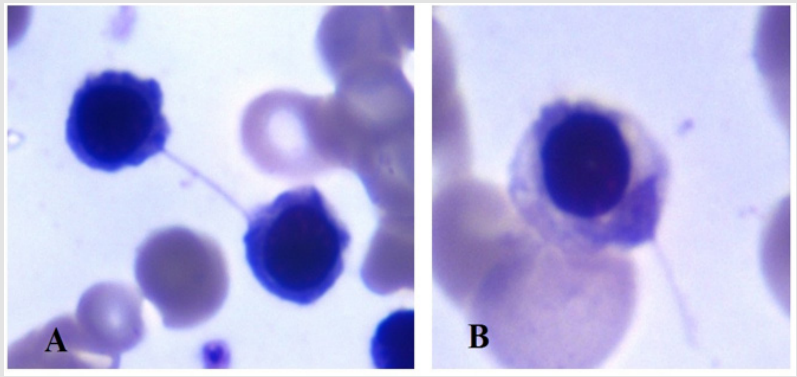

Figure 3: Bone marrow aspirate smear showing dysplastic changes in erythroid precursors.
(A) Inter-cytoplasmic bridging,
(B) Nuclear cytoplasmic maturation asynchrony.

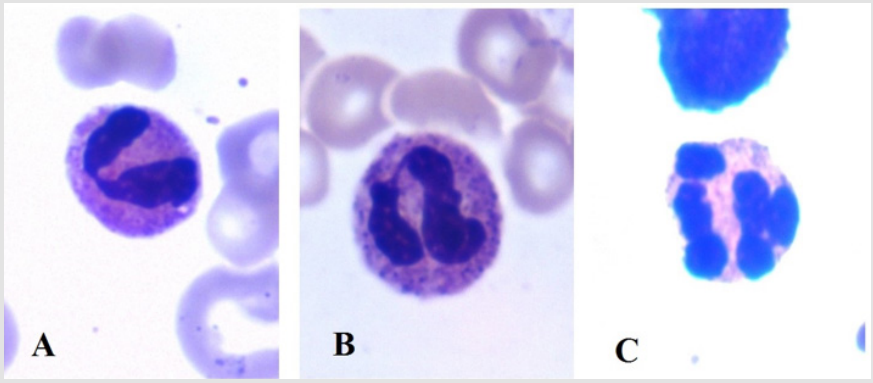

Figure 4: Bone marrow aspirate smear showing dysplastic changes in granuloid precursors.
(A) A pseudo-Pelger-Huet anomaly,
(B) Bi-lobed, and
(C) Multi-lobed nuclei.

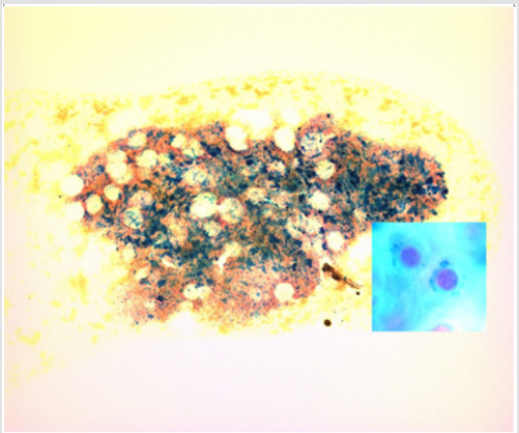

Figure 5: Bone marrow aspirate spicule showing increased iron store (Prussian blue stain). The inset shows two sideroblasts.

Discussion

Lenalidomide is an oral immunomodulatory agent with potent antitumor activity. It was first approved by the US Food and Drug Administration to treat patients with low-and intermediate- risk MDS with deletion 5q chromosomal abnormality [9]. It is also active in other malignancies, such as multiple myeloma and relapsed or refractory mantle cell lymphoma [10,11]. Although the international prognostic scoring systems have divided MDS into two large groups as low or high-risk [12] but the highly heterogeneous nature of MDS complicates the treatment of this disease. For the majority of MDS patients, the therapeutic approach is based on IPSS [13] or revised IPSS stratification. The only curative treatment option actually comes with allogeneic hematopoietic stem cell transplantation (AHSTC). This treatment is suitable only for a limited number of "fit" patients [3]. For the majority of patients, the preferred treatment methods are generally non-invasive options due to their age, comorbidities, etc. Almost all of the available treatment options ranging from erythroid maturation agents, steroids, growth factors, lenalidomide, and hypomethylating agents are used to correct cytopenias, improve quality of life, and if possible, to prevent disease progression rather than any curative intent except for AHSCT. Lenalidomide has proven to be a good choice with a treatment success of up to 70% in patients with transfusion-dependent anemia [14,15].

The treatment of our patient with lenalidomide was initially started with the hope of managing her condition conservatively and reducing the frequency of blood transfusions. Interestingly, following two years of treatment she became completely transfusion independent but her treatment was continued for six more years because of the fear of the recurrence of her disease. Eight years into the treatment her treatment was suddenly stopped due to the reluctance of the insurance provider to pay for her medication. This turned out to be a blessing in disguise as the patient has remained transfusion independent for the last six years. She is now alive 14 years after her initial diagnosis and six years without any treatment. According to current literature, a patient with cancer is considered to be cured when the patient has been in complete remission for a significant period, is no longer on treatment, and has no greater chance of dying from the disease than the general population. It also means that there are no signs of cancer and it is not expected to come back. We believe our patient fulfills this criterion. We also believe that this is perhaps one of the first and longest surviving patients with a diagnosis of MDS who we believe has been cured by lenalidomide therapy.

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