Case report

Low dose melphalan is a treatment option in elderly patients with high risk myelodysplastic syndrome or secondary acute myeloblastic leukaemia

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Abstract—We present the case of a 71 year-old man with secondary acute myeloblastic leukemia, who was successfully treated with low dose melphalan plus Epo plus G-CSF. We treated the patient with 2 mg of melphalan once a day orally, G-CSF 5 mg/kg 3 times a week and Epo 10,000 ui subcutaneously 3 times a week until the maximum response was obtained. Complete remission was achieved after 16 weeks of continuous treatment. Treatment-related toxicity was not significant. We recommend the use of low dose melphalan in elderly patients with high risk MDS as a treatment option.

Key words: Myelodysplastic syndrome; MDS; refractory anemia; blasts; RAEB; RAEB-t; secondary leukemia; AML-MDS; melphalan treatment.

INTRODUCTION

Myelodysplastic syndromes (MDSs) are a heterogeneous group of bone marrow clonal disorders with unfavorable outcome, for which there is no effective treatment yet. Ineffective haematopoiesis and maturation defects are the dominant features of MDSs [1, 2]. The FAB classification of MDS subtypes relies on the morphologic characteristics and the percentage of immature cells in the bone marrow and the peripheral blood [2]. High risk MDSs include refractory anaemia with excess of
blasts (RAEB) which accounts for 30–35% of MDS cases with a median survival of 6–12 months and RAEB in transformation (RAEB-t) which accounts for about 25% of cases of MDS and is associated with a median survival of 9 months or less [3–12].

A variety of therapeutic options, ranging from supportive care to allogeneic stem cell transplantation, are under consideration for MDS. However, the median survival of less than 9 months in high risk MDS patients, underlines the necessity for new drug regimens. Additionally, high risk MDS patients are mostly elderly with poor tolerance to intensive chemotherapy regimens, rendering the excessive toxicity of most of the effective drug combination regimens a major concern. There is clearly a need to develop new therapeutic agents or strategies for the treatment of MDS.

Low dose melphalan has been shown to induce remissions in elderly patients with RAEB, RAEB-t [13, 14] or secondary to MDS acute myeloblastic leukemia (SAML) [14]. We present a case of SAML to MDS (RAEB-t) which was treated successfully with low dose melphalan with minor treatment-associated toxicity.

**CASE REPORT**

A 71 year-old male presented in January 2000 with pancytopenia, which was incidentally found in a routine complete blood count. His medication was digitalis and 100 mg acetylsalicylic acid orally once a day because of atrial fibrillation. His family history was unremarkable. The patient complained only of weakness and fatigue. On physical examination the patient was pale with small petechiae on the lower limbs. A mild systolic cardiac murmur was audible at the apex. The liver was palpable 2 cm below the right costal margin. No splenomegaly or lymphadenopathy were present.

Laboratory tests revealed: WBC $2.2 \times 10^9 / l$ (neutrophils 18%, lymphocytes 68%, monocytes 7%, eosinophils 4% and blasts 3%), Ht 29.6%, Hb 10.3 g/dl, MCV 106 fl, MCH 37 pg, MCHC 35 g/dl and PLT $50 \times 10^9 / l$. Reticulocyte count was low and serum iron, ferritin, vitamin B$_{12}$ and folic acid levels were normal. Autoimmune serology was negative. Serologic tests for hepatitis B, C virus, HIV-I, HIV-II, EBV and CMV proved negative. Bone marrow aspirates showed a normocellular marrow with about 25% blast cell infiltration. The blast cells were CD34 and CD17 positive. The bone marrow karyotype was normal. The diagnosis of MDS (RAEB-t type) according to FAB classification or SAML with multilineage dysplasia according to the updated WHO classification was made [2, 15].

Treatment by low dose of aracytin (ara-C) was initiated. In February 2000 the patient received ara-C 20 mg subcutaneously (s.c.) for 10 consecutive days every third week, in association with EPO 10.000 ui s.c. every other day. Therapy resulted in a 50% increase of the neutrophils and platelets count, while the haemoglobin levels rase less than 3 gr/dl, but the blood transfusion rate was 50% decreased. The partial remission lasted for about 5 months. In July 2000 the haemoglobin level dropped and the patient was transfused with 7 units of packed red cells.