Case Report

An Association Between Hypoplastic Myelodysplastic Syndrome and T-Prolymphocytic Leukaemia

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ABSTRACT

Myelodysplastic syndrome (MDS) represents one of the most challenging health-related problems in the elderly, characterized by dysplastic morphology in the bone marrow in association with ineffective hematopoiesis. Hypoplastic MDS (h-MDS) accounts for 12–17% of all patients with MDS and has yet to be shown to alter the disease course or prognosis. The concept that T-cell-mediated autoimmunity contributes to bone marrow failure in MDS has been widely accepted due to hematologic improvement after immunosuppressive therapy. T-cell expansion is known to occur in these patients, but development of chronic T-cell disorders, especially T-prolymphocytic leukemia (PLL) in a hypocellular MDS is extremely rare, which has an aggressive course. The possible explanation for the association between the two disorders is that T-PLL might arise from a clonally arranged MDS stem cell. We report a unique case of h-MDS with non-progressive pancytopenia and severe hypocellular marrow for 2 years, followed by T-PLL within few months.

Keywords: Chronic T-cell disorders, hypoplastic MDS, T-PLL

INTRODUCTION

Myelodysplastic syndromes (MDSs) represent a group of clonal hematological disorders characterized by progressive cytopenia reflecting defects in erythroid, myeloid and megakaryocytic maturation.[1] Anemia, neutropenia and thrombocytopenia, separated or in combination, despite a hyper- or normocellular marrow define MDS.[2] Hypoplastic MDS (h-MDS) accounts for 12–17% of all patients with MDS.[3] Clonality studies of mature blood cells and immature progenitors suggest that a myeloid–lymphoid stem cell might be the principal target for clonal transformation at least in a major part of MDS.[4] An association between MDS and autoimmune disorders and with chronic T-cell disorders like large granular lymphocytic leukemia (LGL) has been recognized and is suggestive of an abnormal functioning immune system in MDS.[4] Lymphoproliferative disorders, especially T-prolymphocytic leukemia (PLL) developing in an h-MDS patient, is extremely rare and has an aggressive course. We are reporting a unique case of T-PLL developing in h-MDS, and this is probably the first case report in the literature.

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CASE REPORT

A 45-year-old male was admitted with generalized weakness, palpitation, gradual weight loss and frequent syncopal attacks for more than 2 years. On examination, the patient was afebrile, had severe pallor and mild splenomegaly was present. Previous reports showed progressive pancytopenia and hypocellular marrow since 2 years. The iron profile was: serum iron – 115.50 μg/dL, total iron binding capacity – 324.20 μg/dL, %transferrin saturation – 35.63%, ferritin – 177.10 ng/mL and markedly elevated B12 levels (>2000 pg/mL). Hemoglobin was 3.9 gm%, total leukocyte count was 2100 cells/cumm, platelet count was 70,000 cells/cumm and reticulocyte count was 0.8% at the time of admission. Pancytopenia [Figure 1a] was persistent on every visit and the peripheral smear showed normocytic and macrocytic RBCs, leukopenia, hypogranular and pseudo Pelger-Huet neutrophils [Figure 1b and 1c],

which were characteristic with relative lymphocytosis and no blasts in the peripheral smear; the platelet count was reduced. The bone marrow aspiration smears and cell block preparation showed severe hypocellularity (<20% for his age) [Figure 1d]. Sparse erythroid cells with dyserythropoiesis [Figure 2a and 2b], minimal dysmyelopoietic (hypogranular and hyposegmented myeloid cells – 10%) and dysmegakaryopoietic (hypolobated and micromegakaryocytes [Figure 2c and 2d] features were evident with blasts <5% and absence of fibrosis in biopsy sections. Cytogenetic analysis could not yield any result due to inadequate cellularity at this stage. CD34 immunostaining revealed sparse precursors. The possibility of aplastic anemia and hypoplastic acute myeloid leukaemia (h-AML) were ruled out. Hams Test and HIV-I and II were negative. A diagnosis of primary H-MDS was made in the absence of chemotherapy and radiotherapy. The patient was transfusion dependent and later started on Thalidomide. On follow-up within few months, because of persistent pancytopenia, the patient was subjected for repeat bone marrow study, where the smear and section showed cellular marrow with diffuse infiltrate of mature lymphocytes (60%) [Figure 3a and b] with no evidence of improved hematopoiesis. The karyotype showed no abnormalities. The neoplastic cells showed a mature T-cell immunophenotype, CD3+, CD4+, CD5+, CD7+ and CD8+, and Tdt-, CD20-, CD23-, CD79a-, CD34-, Bcl2- and CyclinD1-, and was diagnosed as T-PLL. The patient was deteriorating and succumbed to death within a month of diagnosis.

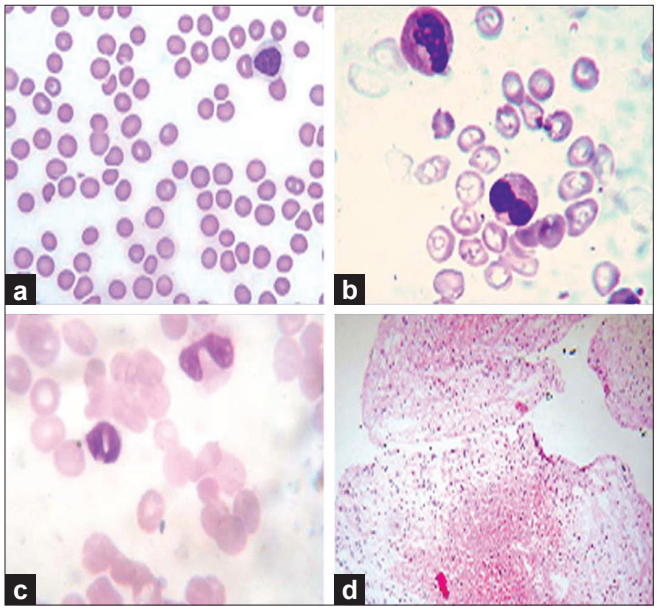

Figure 1: (a) Pancytopenia peripheral smear. (b, c) Pelger-Heut anamoly. Peripheral smear. (d) Hypocellular marrow–cell block preparation H and E, 10×

DISCUSSION

The h-MDS variant is not incorporated in the WHO classification of MDS. The challenge on diagnosis is to distinguish those cases from aplastic anemia.[5] The diagnosis may be difficult in h-MDS if the aspirate is so sparsely cellular as to preclude cytogenetic studies. Significant clonal cytogenetic abnormalities are present in only half of all MDS cases, and full karyotype analysis, which requires cells in metaphase, may not be possible because cells may be scarce or senescent.[6] We encountered similar problems when there was hypocellular marrow, but later, when diagnosed as T-PLL, the marrow culture showed a normal karyotype. There is growing scientific evidence supporting the hypothesis that cytogenetic abnormalities are not the initiating clonal event but are acquired during disease progression.[4]

H-MDS has yet to be shown to alter the disease course or prognosis, but some studies suggest benefit from

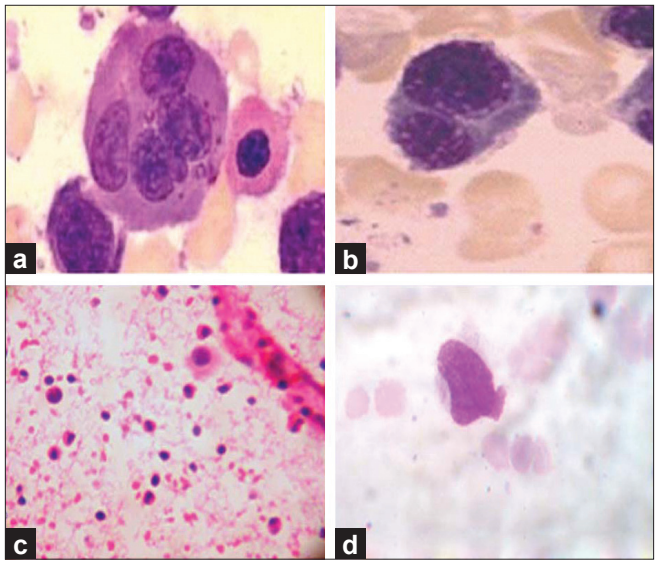

Figure 2: (a) Dyserythropoiesis with multinucleation in BMA. (b) Binucleated form. (c) Dysmegakaryopoiesis–cell block H and E, 40×. (d) dysmegakaryopoiesis BMA

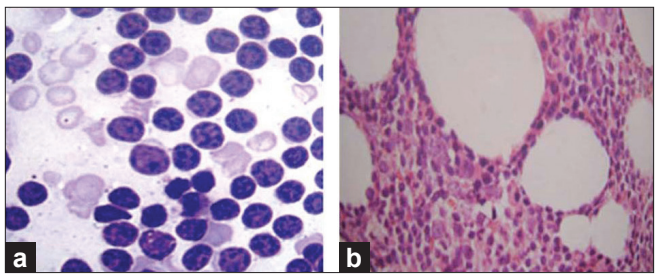

Figure 3: (a) Lymphoid infiltrate in BMA. (b) Lymphoid infiltrate in BMB (H and E, 40×)

immunosuppressive therapeutics.[5] It is presently unknown whether h-MDS patients have a preceding, but unrecognised, phase of excessive apoptosis insufficiently compensated by hyperproliferation, or whether their disease is more related to aplastic anemia. Several years ago, *in vitro* studies have proven that autologous cytotoxic T-lymphocytes can exert an inhibitory effect on MDS myelopoiesis. An association between MDS and autoimmune disorders and with chronic T-cell disorders like LGL has been recognized and is suggestive of an abnormal functioning immune system in MDS.[4] But, occurrence of T-PLL in h-MDS is extremely rare and, possibly, this is the first case in the literature.

T-PLL/CLL accounts for less than 1% of all lymphoproliferative disorders. Lymphadenopathy and splenomegaly are uncommonly found in these patients.[7] The disease has an aggressive course. The immunophenotype is that of mature T-cell, which is usually CD4+ but, occasionally, can be CD8+, which was evident in our case. Expression of CD7 helps to distinguish it from other CLPDs, like Sezary syndrome and adult T-cell leukemia/lymphoma.[8] To conclude, the finding of activated and clonal T-cell population in MDS is further argument for the use of immunosuppression to treat the cytopenias of MDS.

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