Case Report-VI

Chronic Neutrophilic Leukemia : A Case Report and Review of Literature

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ABSTRACT

We report a case of chronic neutrophilic leukemia, a rare clonal myeloproliferative disorder. The relevant literature is reviewed.

INTRODUCTION

Chronic Neutrophilic leukemia is a clonal myeloproliferative disorder characterized by persistent mature neutrophilia. It is a relatively rare neoplasm, which has been accepted recently as a distinct entity by the World Health Organization (WHO) classification of haemopoietic malignancies. We report here a case of chronic neutrophilic leukemia and the pertinent literature is reviewed.

CASE REPORT

54-year-old male presented with history of fatigue of 2 months duration. There was no history of fever or bleeding manifestations. He was evaluated outside and detected to have high white cell counts and referred to our institute to rule out leukemia. Clinical examination revealed enlarged firm, liver-3cm in size and spleen-4cm below the left costal margin. There was no peripheral lymph node enlargement or bleeding manifestations. Patient had no gum hypertrophy and systemic examination was within normal limits. Investigations Blood Hb-14.5g%, WBC $32x10^9$/L, platelet count- $320x10^9$/L differential: N_{85} L_9 E_4 B_2. The absolute neutrophil count was $27.2x10^9$/L. The neutrophils were of normal morphology with segmented and band forms also being present. There were no myeloblasts present in the peripheral blood. ESR-25 mm in the first hour. Biochemistry revealed hyperuricemia with serum uric acid of 10.5mg/dl. Renal function tests and liver function tests were normal. Bone marrow aspiration revealed hypercellular marrow with marked neutrophilic proliferation. There was no evidence of myeloma or myelodysplastic syndrome. Neutrophilic alkaline phosphatase was elevated. Conventional cytogenetics revealed normal karyotype. Philadelphia (Ph) chromosome was not demonstrated. Polymerase chain reaction (PCR) for bcr-abl was negative.

Investigation done for any evidence of chronic infection or occult malignancy were negative. A possible diagnosis of chronic neutrophilic leukemia was made and the patient was placed on follow-up. Three months later as the WBC had risen to $45x10^9$cells/L he was started on hydroxyurea.[7] Patient achieved hematological response by 6 months with normalization of white cell count and disappearance of hepatosplenomegaly. Patient has now completed 2 years of follow-up and continues to be in haematologic remission on hydroxyurea.

DISCUSSION

Chronic neutrophilic leukemia has been reported as a rare entity characterized by

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persistent mature neutrophilia in association with hepatosplenomegaly, elevated serum B 12 levels, hyperuricaemia and raised alkaline phosphatase. There should be no dysplasia or striking reticulin fibrosis. These together with absence of basophilia, monocytosis and absence of bcr-abl transcript define the disease.[1,2] WHO classification of haematopoeitic malignancies has identified chronic neutophilic leukemia as a distinct entity.[3] Tuohy reported the first case of chronic neutrophilic leukemia in 1920.[4] Tanzer et al introduced the term chronic neutrophilic leukemia in 1964.[5]

Chronic neutrophilic leukemia is a disease of elderly with a mean age of diagnosis of 62 years. Overall median survival is 30 months, with a 5-year survival of 28%. Most patients are not anaemic or thrombocytopenic at presentation but have peripheral leucocytosis with mean leucocyte count of $54x10^9$ cells/L with predominant segmented and band cells. Metamyelocytes, myeloctes and nucleated red cells were infrequent and myeloblasts are rarely present. Serum vitamin B12 and uric acid levels are usually increased and they have high neutrophilic alkaline phosphatase. Bone marrow biopsies reveal hypercellular marrow with marked neutrophilic proliferation with no unusual distribution pattern. Cytogenetic abnormalities are seen in 37% of cases. Trisomy 8, trisomy 21 and deletions 20 are the most common. Familial occurrence of chronic neutrophilic leukemia has also been reported.[6] Transformation to acute leukemia is common and seen in 20% of patients.[7] Death is usually due to cerebral haemorrhage, blastic transformation or fulminant infection .[8,9,10]

Differential diagnoses are usually causes of chronic neutrophilia. Underlying malignancy, infection, inflammation, or drug induced leukemoid reaction has to be ruled out. The presence of multiple myeloma indicates a secondary plasma cell associated neutrophilia. Chronic myeloid leukemia can present with neutrophilia and presence of Philadelphia chromosome have to be tested for. Neutrophilic CML usually has a lower white cell count, lower circulating immature granulocytes, milder anaemia, less prominent splenomegaly, normal neutrophil alkaline phosphatase and a lower propensity for acute transformation. Chronic neutrophilia can also occur as a component of myelodysplastic syndrome.

Light and electron microscopy studies of neutrophilic from a chronic neutrophilic leukemia patient do not reveal any differences from normal mature neutrophils. However functional characterization shows marked differences. The cells are less viable and bactericidal activity is less. The total content of lysosome and β glucorinidase activity is also decreased.[11] No definite recommendations are available for the treatment of these patients. Previously treatment like splenic radiotherapy or Splenectomy was aimed at relieving symptoms. Oral chemotherapy including hydroxyurea and busulphan has been used to control hyperleucocytosis.[12] Alpha interferon therapy similar to CML has also been tried.[13] In younger individuals allogeneic transplantation has been tried for attainment of remission.

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