Chronic Neutrophilic Leukemia: A Rare Case Report

Sharada R. Rane · Maithili M. Kulkarni ·
Shaila C. Puranik

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Abstract Chronic neutrophilic leukemia (CNL) is a rare chronic myeloproliferative disorder characterized by splenomegaly, sustained neutrophilic leukocytosis, raised serum vitamin B12 level and absence of the Philadelphia chromosome and BCR/ABL1 fusion gene. CNL can be distinguished from chronic myelogenous leukemia, leukemoid reaction and myelodysplastic syndrome. We report a case of 45 year old male patient with CNL.

Keyword · Chronic myelogenous leukemia · Chronic neutrophilic leukemia · Leukemoid reaction

Introduction

Chronic neutrophilic leukemia (CNL) is a rare clonal chronic myeloproliferative disorder. The true incidence of CNL is unknown, but only 150 cases have been reported [1]. CNL presents as a sustained mature neutrophilic leukocytosis, the absence of peripheral blood monocytosis, basophilia or eosinophilia and a normal platelet count [2]. The clinical manifestations also include hepatosplenomegaly, elevated leukocyte alkaline phosphatase (LAP), elevated serum vitamin B12 and serum uric acid [3]. Bone

marrow shows granulocytic hyperplasia without evidence of dysplasia or striking reticulin fibrosis. The diagnosis is contingent on thorough initial investigation and follow up to exclude underlying causes of reactive neutrophilia, particularly if evidence of myeloid clonality is lacking [4]. Cytogenetic and molecular analyses are negative for the Philadelphia chromosome and BCR/ABL1 fusion gene [2]. Optimal therapy of CNL remains to be determined. Treatment of CNL consists of therapy with agents such as oral hydroxyurea, busulphan, and 6-thioguanine [3, 5, 6]. The successful use of interferon-alpha has been reported [7]. There is a definite risk of death from either leukemic transformation or progressive refractory neutrophilic leukocytosis [3, 7, 8]. Allogeneic bone marrow transplantation has been reported in one case of CNL [6].

Case Report

45 year male patient was admitted with complaints of generalized weakness, cough with expectoration since 1 month. Patient had pallor, hepatosplenomegaly. Spleen was palpable four cm below left costal margin. Patient had a pneumonic patch on chest X ray. Patient had leukocytosis with count 30,000/cumm. Increase in white blood cells was due to neutrophilia almost exclusively at the segmented and band stage of development. Granulocytes showed toxic granules. Report was given as leukemoid reaction. Culture and sensitivity of sputum was done which showed Methicillin resistant *Staphylococcus aureus* for which a complete course of Vancomycin was done. Fever subsided. Chest X ray was normal after 2 weeks. Follow up peripheral blood smear was done. There was rising leukocytosis with TLC-70,000/cumm with 90 % polymorphs. There was no absolute or relative monocytosis, eosinophilia or

Chronic neutrophilic leukemia is a diagnosis of exclusion and follow up. One should think of this possibility when neutrophilia persists without any underlying cause.

S. R. Rane · M. M. Kulkarni · S. C. Puranik
Pathology Department, BJ Medical College, Pune, India

Present Address:
M. M. Kulkarni (✉)
E 401, Samrajya, Shivirthnagar, Paud Road, Pune, India
e-mail: drmaithili@rediffmail.com

Fig. 1 **a** Peripheral blood smear demonstrating neutrophilia without left shift. (Leishman stain, ×400). **b** Peripheral blood smear demonstrating neutrophilia without left shift. (Leishman stain, ×1000)

basophilia. No blast cells or micromegakaryocytes were seen. No dysplastic features were noted in the granulocytic series (Fig. 1a, b). Platelet count was normal and no hypogranular or large and atypical forms were seen. Hepatosplenomegaly was persistent. Ultrasonography of abdomen did not show any abnormality except for an enlarged liver and spleen. Bone marrow examination was performed. Aspiration was dry tap. Bone marrow biopsy was uniformly hypercellular with packed marrow (Fig. 2). There was granulocytic proliferation. Megakaryocytes were normal. Reticulin stain showed grade 1 fibrosis. There was no significant monocyte or blast population. So we thought of the diagnosis of chronic myeloproliferative disease probably early CML. LAP and Philadelphia chromosome were advised. The LAP score was raised, 368 (Normal 35–100). Philadelphia chromosome and BCR/ABL1 were negative by fluorescent in situ hybridization (FISH) and polymerase chain reaction (PCR). JAK2 was negative which ruled out diagnosis of essential thrombocythemia, myelofibrosis,

Fig. 2 Bone marrow trephine biopsy showing hypercellular marrow. (H and E, ×400)

polycythemia vera. After 1 month peripheral blood smear was repeated. The total leukocyte count was 96,000/cumm with 90 % neutrophils. The immature granulocytes were <5 %. There was no basophilia, no eosinophilia. Platelets count was normal. So we thought of the diagnosis of CNL. Serum vitamin B12 was markedly raised (>2,000 pg/ml). With this history, investigations and tincture of time, diagnosis of CNL was made after excluding other causes of neutrophilia. Hydroxyurea was started to control blood counts. After 1 month of therapy the total leukocyte count was reduced to 20,000/cumm, but platelet count was reduced to 40,000/cumm. So the dose of hydroxyurea was reduced. The total count was again raised. Patient developed respiratory infection and succumbed to death after 3 months of diagnosis.

Discussion

CNL is a rare hematological disorder which must be distinguished from leukemoid reaction, chronic myelogenous leukemia, and its variants, other chronic myeloproliferative disorders and myelodysplastic syndromes. The causes of neutrophilia are varied such as infections, chronic inflammatory conditions and occult malignancy. After excluding all other causes, hematological causes should be considered. In our patient there was no evidence of infection and underlying malignancy was also excluded with absence of symptoms and signs as well as normal radiological findings. Patient had hepatosplenomegaly and grade I reticulin fibrosis. Total leukocyte count was rising even after complete course of antibiotics and in the absence of fever. The peripheral blood smear in CNL shows mature neutrophilia, while that of a leukemoid reaction can be left shifted, so leukemoid reaction was ruled out. Chronic myelogenous

leukemia can present with neutrophilia and presence of Philadelphia chromosome should be tested for. Neutrophilic chronic myelogenous leukemia usually has a lower white cell count, lower circulating immature granulocytes, milder anemia, less prominent splenomegaly, normal LAP score and a lower propensity for acute transformation [9]. In our case BCR/ABL fusion gene was negative by both FISH and PCR. The LAP score was elevated. So diagnosis of chronic myelogenous leukemia was ruled out. Myelodysplastic syndrome can sometimes be associated with neutrophilia. In our case there were no dysplastic features in any of the cell lines. Also significant organomegaly is unlikely to occur in myelodysplastic syndromes [10]. Thus CNL is a diagnosis of exclusion.

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