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Case Report

Chronic neutrophilic leukaemia-a rare haematological malignancy

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ABSTRACT

Chronic neutrophilic leukaemia is a rare myeloproliferative neoplasm. It requires exhaustive workup and puts a diagnostic challenge to the clinician as well as pathologist. It should be differentiated from chronic myelogenous leukemia and reactive neutrophilia. Prognosis of the disease is poor. Here we report a case presented to us with 4 months of fatigue and fever. Investigation shows leucocytosis with predominant neutrophilia, evaluated and diagnosed as Chronic Neutrophilic Leukaemia (CNL) according to revised WHO criteria.

Keywords: CNL (Chronic Neutrophilic Leukemia)

INTRODUCTION

CNL is an uncommon myeloproliferative neoplasm characterized by sustained mature neutrophilic leucocytosis, hepatosplenomegaly and bone marrow granulocytic hyperplasia.[1]

There is no abnormality in other cell lineages. It is a diagnosis of exclusion of clonal myeloproliferative disorders and reactive neutrophilia. Bone marrow aspiration and biopsy show normal maturation of all cell lineages. Cytogenetics show normal karyotype. It is negative for JAK2 mutation, BCR-ABL translocation and PDGF A and B mutation. CSF3 R mutation is present and included in WHO criteria. Only around 200 cases have been reported worldwide.

World Health Organization (WHO) diagnostic criteria for CNL has been revised recently in 2016.[2] Management of CNL requires cytoreductive therapy. Most commonly used pharmacotherapy is Hydroxyurea.[2] Allogenic bone marrow transplantation has been used for management with variable success. Here we report a case of CNL and the pertinent literature is reviewed.

CASE REPORT

A 33-year-old married Hindu male presented with complains of fatigue for 4 months, low grade fever since last 1month and myalgia from 8days. There was no history of jaundice, weight loss and cough. He consulted to nearby hospital where blood investigations show leucocytosis with predominant neutrophilia. Oral antibiotics has been prescribed for 7days, but symptoms did not relieve and persistent leucocytosis was present. He was referred to our institute for further evaluation and management.

On examination, the patient was conscious, oriented to time, place and person. The pulse rate was 100 beats per minute, the blood pressure 120/78mm Hg, the respiratory rate 18 breaths per minute, and the oxygen saturation 100% (spO2) while he was breathing in ambient air. General physical examination showed palpable spleen 5cm below left costal margin. All other systemic examination was normal.

Blood Investigations revealed (Hemoglobin 13.2gm/dl, total leucocyte counts 78000/cmm, platelet counts

1.48lacs/cmm). Liver and kidney function tests were normal. Blood sugar level was 116mg/dl at the time of admission. Serum Na^+, K^+ and Cl- were 138mmol/l, 4.3mmol/l and 98mmol/l respectively. His serum CPK level was 210U/L and LDH was 2190U/L. Serum procalcitonin was normal. Peripheral blood film (PBF) examination showed leucocytosis with predominant neutrophilia. The morphology of neutrophils was normal with segmented and band form cells present. There was no evidence of myeloblasts and plasma cells in the peripheral blood. Erythrocyte Sedimentation Rate (ESR) was highly raised (118mm) in 1st hour.

Chest-X-ray was normal and USG abdomen showed moderate hepato-spleenomegaly. Blood culture and urine culture were sterile. Leucocyte Alkaline phosphatase (LAP) score was normal. Bone marrow aspiration and biopsy revealed hypercellular marrow with marked neutrophilic proliferation. There was no evidence of myelodysplastic syndrome. Urinary bence john's protein was negative.

BCR - ABL gene not detected by real time PCR. PDGFR A and PDGFR B mutation were also negative. All investigation fulfilled the WHO diagnostic criteria for chronic neutrophilic leukemia and thus diagnosis of chronic neutrophilic leukemia (CNL) was made. CSF3 receptor mutation test could not be done due to financial constraints.

Table 1: WHO diagnostic criteria for CNL (revised in 2016).[6]

Variables	Criteria
PB leucocyte count	>25 x 10^9/l
PB segmented neutrophils	>80%
PB immature granulocytes	<10%
PB blast count	<1%
PB monocyte count	<1x10^9/l
PB increased neutrophils or precursor with dysgranulopoiesis	No
Bone marrow	↑neutrophils, number and % <5% blast Normal neutrophilic maturation Megakaryocytes normal or left shift
BCR- abl1	No
PDGFRA, PDGFRB or fgfr1 mutation or PCM-JAK2	No
CSF 3 R mutation or	Yes
Persistent neutrophilia (at least 3months), splenomegaly, and no identifiable cause of reactive neutrophilia including absence of plasma cell neoplasm	Yes

Treatment with tab hydroxyurea 500mg twice started. Hydration status of the patient was improved. He was symptomatically better within a week. His leucocyte counts were started to decline and after 15days it was completely within normal range.

DISCUSSION

CNL is an uncommon myeloproliferative neoplasm characterized by sustained mature neutrophilic leukocytosis, hepatosplenomegaly and bone marrow granulocytic hyperplasia. In contrast to chronic myeloid leukaemia, the disease primarily involves neutrophilic lineage with persistent proliferation of mature forms of neutrophils.[1] Approximately 200 cases are reported till now in the world. Applying the recently developed WHO diagnostic criteria, could only confirm this diagnosis in fourty cases, indicating a lower rate of occurrence of what is now considered CNL. The median age at diagnosis was 66years (range:15-86) and 56% of all cases were male.[2]

JAK2-V617F Mutation is broadly specific finding for myeloid neoplasia and the main value to date has been primarily to corroborate clonality. Only 5-10% cases of CNL are positive to it.[3] CSF3 receptor mutation is seen in more than 90 percent of chronic neutrophilic leukemia.[4] The majority of patients are asymptomatic at diagnosis, often discovered to have an incidental leukocytosis detected on laboratory testing. Common presenting symptom are fatigue, weight loss, easy bruising, bone pain, night sweats, palpable splenomegaly.[5] Who has revised its diagnostic criteria for CNL in 2016. It includes CSF3 Receptor mutation as a new criterion added.

Management of CNL includes cytoreductive agents, most commonly hydroxyurea. But it has significant side effects like leukopenia, anemia, thrombocytopenia, interstitial pneumonitis and dermatological disturbance.[2,7] The successful use of alpha-interferon has been published in case reports, with durable responses.[8] Allogeneic sibling stem cell transplantation is now being reported in five cases (ages 15, 40, 44, 49, and 60years) in the chronic or accelerated phase or following induction chemotherapy for blast transformation. The median survival was 23.5 months (range:1-106). No information on the use of non-myeloablative, cord blood, or autologous SCT for CNL.[9,10] Ruxolitinib is JAK 1 and 2 inhibitor which is under clinical trial for CNL. The dose of ruxolitinib of 15mg twice daily led to a further decrease in both the white-cell count and the absolute neutrophil count.[11]

CONCLUSION

Chornic neutrophilic leukemia is hematopoeitic malignancy. Patients with persistently raised neutrophilic count should be evaluated for CNL after excluding chronic myelogenous leukemia and reactive neutrophilia.

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