INTRODUCTION

Chronic neutrophilic leukaemia (CNL) is an extremely rare myeloproliferative disorder with an erratic and unpredictable clinical course. It presents as a persistent, unexplained leucocytosis with neutrophilic predominance. These neutrophils are mature, segmented polymorphs and band forms. The bone marrow in CNL is hypercellular without any dysplastic features. Patients should have hepatosplenomegaly, elevated leucocyte alkaline phosphatase (LAP) score, absence of Philadelphia chromosome; bcr-abl transcript and no focus of infection in order to diagnose CNL. Associated findings are elevated serum vitamin B12 and uric acid levels. It is necessary to rule out other chronic myeloproliferative disorders like myelogenous leukaemia (CML), atypical chronic myelogenous leukaemia (aCML) and chronic myelomonocytic leukaemia (CMML) by relevant investigations before labeling it as CNL.

Natural history of CNL varies from an indolent course over several months to years, leukaemic transformation (blasts) almost never occurs but the patients continue to deteriorate clinically. However, transformation to acute leukemia has been reported.

Terminal events are usually serious infections or life threatening hemorrhages.

CASE REPORT

A 44 years male presented with excessive sweating since three months with pain in both lower limbs. He was a known case of hypertension on treatment. He had a history of bronchial asthma, malaria, two episodes of jaundice and lichen planus in the past. He had lost about three kilograms in three months. He gave no previous history of tuberculosis, vices or bleeding. Clinical examination revealed pallor, hepatosplenomegaly and subcentimetric axillary lymph nodes. There was no ecchymosis, purpura or evidence of deep vein thrombosis. His older haemograms (CBCs) showed that his leucocyte count had been elevated for the last three months (Haemoglobin and platelet count was normal.) Blood tests done at our center showed: WBC = 33,600/mm³ with Absolute neutrophil count (ANC) = 30.576/mm³, Hb = 13.8 gm%, RBC = 6.13 million/mm³ - microcytic hypochromic, platelets = 1.99 lakh/mm³, S - creatinine = 1.23 mgm% (normal value = 0.5-1.5 mgm%), S - uric acid = 9.7 mgm% (normal value = 2.5-8.0 mgm%), LAP score = 210 (normal value = 25-130), Beta 2 microglobulin = 4447 ng/ml (normal value = 1010-1730 ng/ml), S Vitamin B12 level = 755 pg/ml (normal value = 211-911 pg/ml), S Bilirubin = 1.63 mgm% (normal value 0.3 -1.0 mgm%), S Alkaline phosphatase = 362 mgm% (normal value = 30-120 mgm%), Philadelphia chromosome and Bcr-abl were negative (By FISH). Direct Coomb’s test, Ham’s test and sucrose lysis were negative. Bone marrow studies showed hypercellular marrow with hyperplasia of the myeloid series, no evidence of dysplasia, increase in eosinophilic precursors, suppressed erythroids, megakaryocytes increased in number with occasional clustering and scanty fibrosis. The possibility of any occult infection was ruled out by serial blood cultures, 2D echocardiography, CT abdomen and X-ray chest. The patient was diagnosed to have chronic neutrophilic leukaemia based on the above-mentioned criteria and started on Hydroxyurea, Allopurinol and vitamins. One and a half month later, the patient’s WBC count was 35,000/mm³ with ANC =31,500, Hb=13.2 gm%, platelets = 1,16,000/mm³ i.e. poor response to Hydroxyurea. He also has an elevated serum alkaline phosphatase of 606 mg/dl suggestive of hepatic infiltration by malignant leucocytes.

DISCUSSION

Tuohy reported the first case of CNL in 1920. Only 143
cases have been reported thereafter. Despite extensive research, the pathogenesis and clinical behaviour of CNL has not been completely understood probably due to its rarity.

The neoplastic transformation in CNL occurs at an earlier stage of progenitor cell differentiation than CML as evidenced by the monoclonal human androgen receptor gene assay (HUMARA) pattern in the T cells of the neoplastic clone (which is not seen in CML), and hence it has a poorer prognosis. Parallel tubular granules (PTG) seen in these neutrophils on electronmicroscopy is believed to be pathognomonic of CNL.

Genetic defects inhibit normal neutrophilic apoptosis and functional analysis of these neutrophils suggested normal phagocytosis, increased granule release to immune complexes, decreased bacterial killing and greatly decrease chemotaxis.

Predominantly seen in the older age groups, the mean age of diagnosis is 62 years, though CNL has been reported in patients as young as 15 years. It is known to be familial. Life expectancy in CNL can vary from 6 months to 20 years.

Majority of patients have a normal karyotype though various chromosomal anomalies have been reported such as 11q23 (MLL), 11q14 deletion, trisomy 21 transforming into tetrasomy 21 during blast crisis, trisomy 8, trisomy 9 with partial deletion of long arm of chromosome 20, mosaicism, 46XY + X i.e. gain of an X chromosome during blast crisis, monosomy of chromosome 2.

CNL may be associated with other clonal stem cell disorders like polycythemia, myelomas, myelofibrosis, paraproteinaemias or monoclonal gammopathy of unknown significance (MGUS).

The response to oral chemotherapy is variable, CNL may be altogether refractory to hydroxyurea (as in our case). Busulphan, alpha interferon and imatinib mesylate are the drugs that may be used. Splenectomy and splenic radiation are the other modalities of treatment available. Allogenic bone marrow transplant offers a potential cure especially in younger patients.

Given the fact that blastic transformation is uncommon but the patients continue to deteriorate, the neutrophils must be acquiring a malignant nature over a period of time through mutations not yet understood.

Physicians must not think of CNL as a diagnosis on the first visit unless the patient has serial haemograms (CBCs) of the past to compare and it is established that there is no focus of infection in the body.

REFERENCES
6. Elliott MA, Dewald GW, Tefferi A, Hanson CA. Chronic neutrophilic leukemia (CNL): A clinical, pathologic and