Chronic lymphocytic leukaemia: A review of 7 cases from University Hospital, Kuala Lumpur

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Summary

Chronic lymphocytic leukaemia (CLL) is rare locally. Seven CLL patients which constituted 0.9% of the total 747 cases of leukaemic patients were diagnosed over a 5 year period. They had similar haematological profiles as Western patients though most of them had advanced disease at presentation. Treatment of CLL patients was palliative and should be reserved for symptomatic patients and/or patients with progressive disease.

Key Words: Chronic lymphocytic leukaemia, Malaysian patients, Patient characteristics, Management.

Introduction

Chronic lymphocytic leukaemia (CLL) is a haematological malignancy characterised by clonal proliferation and accumulation of relatively mature-looking lymphocytes. CLL is the commonest leukaemia in USA and Europe, accounting for approximately 30% of all cases, but is extremely rare in the Orient.[1] This paper reviewed 7 CLL seen in a referral centre for haematological disorders.

Patients and Methods

Chronic lymphocytic leukaemia (CLL) was diagnosed by the criteria proposed for protocol studies in CLL[2] which included peripheral blood lymphocytosis more than 15000/uL on two examinations at least two weeks apart with morphologically well differentiated small lymphocytes, and a marrow lymphocytosis exceeding 40% of non erythroid nucleated cells. The clinical and laboratory data of 7 patients who fulfilled the diagnostic criteria from 1984-8 were reviewed. Over the same study period, a total of 747 cases of leukaemias (Department registry) were diagnosed.

Results

Biodata: All 7 patients were Chinese with 5 males and 2 females. All except one patient were above 50 years of age.

Clinical features: The diagnosis of CLL was made ''incidentally'' in 3 patients when they presented with unrelated problems. Two patients complained of glandular enlargement while two others had symptoms related to anaemia at presentation. Only one patient had no detectable physical signs while 5 patients had generalised lymphadenopathy and splenomegaly was detected in 4 patients (Table I).

Haematological data: Anaemia was detected in 2 patients while thrombocytopenia was present in one patient. Extreme lymphocytosis (>40,000/uL) was noted in 4 patients (Table II). A typical CLL blood film i.e. lymphocytosis with many 'smudge' cells was present in 5 patients (Fig.1). Bone marrow aspirates were done on 6 patients and showed lymphocytosis (>40%) in all patients. Four patients had concurrent trephine biopsy and all showed diffuse interstitial pattern of lymphocytic infiltration (Fig.2).

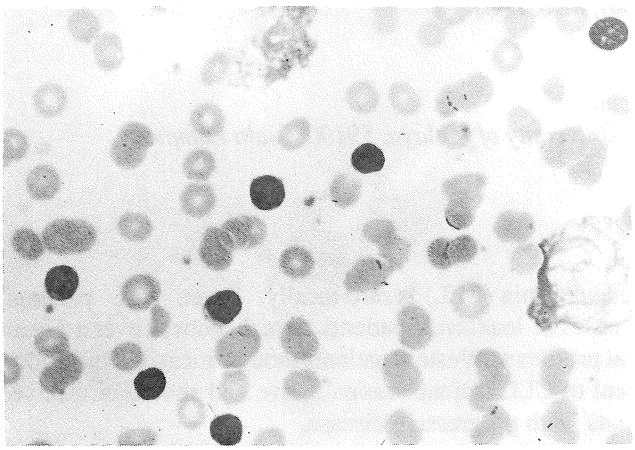

Figure 1. Peripheral blood film of case no.2. Male, Chinese, 62, presenting with bilateral inguinal swelling, Hb = 9g/dl, Twbc = $20x10^9$ (80% lymphocytes) showing increased number of mature-looking lymphocytes with characteristic 'smudge' cells. MGG x 400.

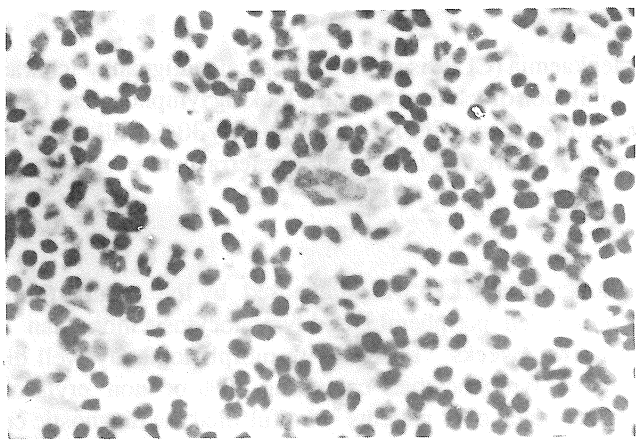

Figure 2. Trephine biopsy showing diffuse interstitial pattern of lymphocytic infiltration. H&E x 200.

Staging: Using Binet's staging[3] (Table III), 4 patients were in stage C, 2 patients in stage B and only one patient was in stage A.
Immunological studies: Immunoglobulins assays done on 6 patients showed low level of IgG in 2 patients while 3 of them had normal levels. One patient had polycloincreases in IgG and IgA. No paraprotein was present in any patient.
Treatment: Six patients were given systemic chemotherapy in view of progressive and symptomatic disease. Intermittent 2 weekly courses of chlorambucil (0.1 mg/kg/d) were given with 2 weeks rest between courses. Steroids were given concurrently if there were cytopenias. Three patients had complete responses (i.e. clinical resolution of signs and restoration of normal blood counts) after 2 courses of treatment. One patient developed profound neutropenia and treatment was stopped. He died of hepatic failure of unknown cause after being followed up for 3 years. Two other patients died within a month after treatment due to unrelated causes namely acute myocardial infarction and septic osteomyelitis after fixation of fracture neck of femur respectively. One patient was being followed up regularly without treatment as he was asymptomatic and had stable disease.

Discussion

The rarity of CLL in the tropics was highlighted as early as 1944[4] Thereafter similar observations were reported from Japan[5] and India[6]. Wells and Lau reported 3 CLL patients out of 203 cases of leukaemia diagnosed between 1949 to 1958 in Singapore. In our study, the 7 CLL cases accounted for only 0.7% of the total 747 cases of leukaemia diagnosed in the hospital over a 5 year period. Our patients were mainly from the elderly age group with a male preponderence similar to the western CLL patients[7].

The diagnosis of CLL can usually be made by careful review of clinical data and results of haematological investigations including a blood count, peripheral blood morphology and bone marrow examination. The typical blood film with many 'smudge' cells and presence of lymphocytosis consisting of mature looking lymphocytes is highly suggestive of CLL[8]. Bone marrow examination including both marrow aspirates and trephine biopsies should be done for all CLL patients. In addition to its diagnostic values, the histological pattern of lymphocytic infiltrate shown on the trephine biopsy is of prognostic importance. Our 4 patients who had trephine biopsy done showed diffuse interstitial pattern of lymphocytic infiltration which denoted a poorer prognosis.[9] Hypogammaglobulinemia was detected in 2 out of the 6 patients studied. None of our patients had recurrent infections though one patient died of a single documented episode of osteomyelitis. Most of our patients were in advanced stage of disease probably due to late presentations and/or lack of awareness of this rare disease hence resulting in delay in diagnosis. Four of the referred cases were diagnosed erroneously as lymphoma in 3 patients and acute lymphoblastic leukaemia in one patient after initial haematological investigations.

The treatment of CLL patients is generally reserved for patients who are symptomatic of the disease or have progressive disease. Patients with early or static disease should not be given systemic cytotoxic as to date no survival advantage has been documented.[10] Six of our patients were given systemic chemotherapy with intermittent dose of chlorambucil and steroid was added whenever there was cytopenia. Three patients were able to tolerate the treatment without any unacceptable toxicity but one patient developed neutropenia which necessitated drug stoppage. All 3 patients had gratifying clinical and haematological remissions. The result of the treatment could not be assessed in 2 other patients as they died of unrelated causes soon after treatment was started. Though more intensive multiple drug regimens such as COP

Table 1 : Clinical Data of the seven CLL Patients

No.	Age/Sex	Race	Presenting Complaint	Clinical Signs	Binet's Staging	Chemotherapy	Response	Follow up duration (month)	Current Status
1	74/M	Chinese	Chest pain	None	A	No	-	30	Well
2	62/M	Chinese	Bilateral inguinal swelling	• Splenomegaly (7 cm) generalised lymphadenopathy	B	Yes	Complete	40	Well
3	72/M	Chinese	Inability to walk (fracture neck of right femur)	• Splenomegaly (5cm) • Generalised lymphadenopathy	C	Yes	Cannot be assessed	1	Died of osteo-myelitis
4	88/F	Chinese	Symptoms of anaemia	• Generalised lymphadenopathy	C	Yes	Complete	3	Well
5	56/M	Chinese	Chest pain (unstable angina)	• .Generalised lymphadenopathy • Hepatosplenomegaly	C	Yes	Cannot be assessed	1	Died of AMI.
6	45/M	Chinese	Symptoms of anaemia	• Hepatosplenomegaly	C	Yes	Treatment stopped because of neutropenia	48	Died of hepatic failure
7	59/M	Chinese	Bilateral neck swelling	• Generalised lymphadenopathy	B	Yes	Complete	6	Well

(cyclophosphamide, vincristine, prednisolone) or modified CHOP (cyclophosphamide, adriamycin, vincristine and prednisolone) have been used in some centres[11,12] there is no convincing evidence that survival is prolonged despite higher initial response rates. Hence chlorambucil remains the primary standard therapy for CLL patients who are symptomatic or have progressive disease.

Table 2 : BINET'S STAGING

STAGE	
A	<3 Lymphoid areas * involved
B	>3 Lymphoid areas involved
C	Hb < 10 g/dl+
	Platelet < 100 x 10 9/L +
	Regardless of lymphoid areas involved

*A lymphoid area includes liver, or spleen or a single group of nodes e.g. neck, axillae, groins.

+Anaemia and thrombocytopenia excluded caused by a definite autoimmune process.

Table 3: BLOOD COUNTS AT PRESENTATION

		Number of Patients
Hb (g/dl)	<10	2
	⩾10	5
Lymphocytes(x10^9/L)	>4	0
	4-<15	2
	15-<40	1
	⩾ 40	4
Platelets (x10^9/L)		
	<100	1
	⩾100	6

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