Case series

HAIRY CELL LEUKAEMIA IN A TERTIARY HOSPITAL IN SOUTHERN NIGERIA: 10 YEAR SURVEY

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ABSTRACT

The clinico-pathologic features, incidence and pattern of presentation of patients with the rare hairy cell leukaemia in University of Benin City Teaching Hospital, a major tertiary health centre in Niger Delta region of Nigeria have not been previously documented. All cases that presented from 1993 to 2003 were reviewed and this rare leukaemia constituted 1.5% of all haematological malignancies. Median age at presentation was 40 years. Typical clinical signs of pancytopenia and massive splenomegaly were found. Lymphadenopathy was rare. Normalization of pancytopenia was achieved by splenectomy followed by cytostatic agents but increased susceptibility to infection was not reduced. Four patients received interferon-alpha two patients, cladribine with prednisolone following splenectomy.

KEY WORDS: Hairy cell Leukaemia; Nigeria.

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INTRODUCTION

Hairy cell leukaemia (HCL) haemopathy also known as leukaemic reticuloendotheliosis is a rare type B lymphoid malignancy with distinctive clinical and pathological features. It is a B-lymphoproliferative disorder characterized by pancytopenia, splenomegaly, immunologic abnormalities and morphologically typical neoplastic mononuclear cells in the blood, bone marrow, spleen, liver and other tissues.[1,2] The disease is generally indolent and ultimately fatal in its natural course. Majority of the patients require treatment for life-threatening infections due to pancytopenia or symptomatic splenomegaly.[3] Recently, immunotherapeutic approaches which use monoclonal antibodies have increased the number of therapeutic options for HCL and offer promising salvage strategies for patients who relapse or who are refractory to treatment with purine analogues.[3] In all, an individualized clinical approach is recommended with a role for splenectomy in the patient with cytopenia and a relatively low number of hairy cells in the bone marrow.[4]

A variety of clinical features have been described at diagnosis for HCL, but their exact incidence is not well documented and only a few reports have been recorded from African countries. The aim of this study therefore is to determine the incidence and clinico-pathological profile of this rare group of patients in the Niger Delta region of Nigeria.

PATIENTS AND METHODS

All cases of haematological malignancies seen at the Haematology oncology clinic or admitted to UBTH between 1993 and 2003 were reviewed and cases of HCL identified. This hospital is a major referral center in the Niger Delta of Nigeria. The only practicing haematologists in Edo and Delta states of the Niger Delta region within the period of time functioned in this hospital.

Inclusion Criteria: All patients managed for HCL in the center who had clinical and laboratory

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evidence confirming the diagnosis. All pathologic material was reviewed by an experienced haematopathologist. Diagnosis was established on the presence of characteristic cytological features of hairy cells in either a well-stained (Leishman) peripheral blood film and/or bone marrow aspirates. Trephine biopsy of the spleen or bone marrow for histology was regarded as confirmatory of the diagnosis. Data was sometimes incomplete: patients with the typical clinical findings who did not have either of the above laboratory evidence giving a 70% fulfillment of the inclusion criteria were excluded from this study. Demographic features including the nature of therapy and response were recorded. The Eastern Cooperative Oncology Group (ECOG) scale for measuring performance status (PS) on a scale from 0 to 4 was applied to all patients. Results of complete blood counts were also noted. Anaemia was diagnosed if the haemoglobin concentration was <10g/dl and leucocytopenia if the leucocyte count was $<4.0x10^9/l$. Thrombocytopenia was considered to be present if the platelet count was $<100x10^9/l$.

Response to therapy was indicated by the absence of hairy cells in the peripheral blood film and bone marrow along with improvement of haematological indices, reduction or loss of splenomegaly and lymphadenopathy if previously present as well as improved general well being of the patients.

Statistical methods were analyzed using the Instate Package system version. Results were presented as simple frequencies. Student's t-test or Mann-Whitney test were used for comparing continuous data and Chi-square test with Yates correction when necessary was used for categorical data. The Spearman rank correlation statistics was used to assess relationship between haematological variables and spleen size. All quoted P values were two-sided with significance at 95% probability.

RESULTS

There were 401 patients with haematological malignancies managed in UBTH within the study period. A total of six patients were diagnosed with HCL over 10 years based on the cytological-clinical criteria representing 1.5% of all haematologic malignancies. This gives 0.6 cases/year. Since UBTH is the only referral center serving Edo state with haematologists, we may assume that practically all identified cases of HCL and indeed all leukaemias from neighboring state will be referred to UBTH. Using the 1991 National Population Census figure for Edo state, which is 3,259,184, the calculated incidence of HCL will be 0.18/million/year. Male patients (n=5) outnumbered females (n=1) with an overall median age of 40 years (range, 39-50 years). Average duration of symptoms before presentation was 6months (range, 0-60months).

Table-I: shows the clinical features at diagnosis. Main presenting symptoms were due to anaemia (weakness and fatigue), abdominal swelling in six cases (100%) and splenic discomfort in 6 cases (100%) with complaints

Table-I: Baseline characteristics and main clinical features of HCL patients at the time of diagnosis.

Biologic variables	*n*	*%*
Incidence	6	1.5
Sex (M:F)	5:1	83.3:16.7
Age (years)		
<30	0	0
31-40	4	66.7
>40	2	33.3
Presenting features		
Weakness and fatigue	6	100
Abdominal swelling	6	100
Splenic discomfort/pain	6	100
Fever	4	66.7
Weight loss	3	50.0
Nausea and vomiting	3	50.0
Bleeding diasthesis	2	33.3
Signs		
Spleen palpable		
1-10cm	1	16.7
11-20cm	1	16.7
>20cm	4	66.7
Liver palpable	4	66.7
Lymphadenopathy	1	16.7
Performance status		
0-1	2	33.3
2-4	4	66.7
Bone marrow biopsy		
Focal	2	33.3
Diffuse	4	66.7
Incidental diagnosis	0	0

attributable to massive splenic enlargement were also encountered. Pain was generally moderate in intensity, often pleuritic in nature. Presence of fever (>38°C) was recorded in 66.7% of the patients with three of them having associated mycobacterial infections. Weight loss was usually mild to moderate and almost always related to anorexia with nausea and vomiting and early satiety in association with prominent splenomegaly. The least common presentation was bleeding from the mucous membrane in two patients (33.3%). Spleen was massively enlarged (>20cm; range, 14-24cm) in most of our patients with pallor forming the commonest physical finding. Pain attributable to splenic pathology revealed that spleen size was greater in patients with a history of fatigue / weakness. Only one patient (16.7%) presented with enlarged lymph nodes (axillary and inguinal). There was no incidental diagnosis and four of the patients (66.7%) presented with the worst performance status (2-4) as assessed according to the ECOG scale.

Haematological findings (Table-II) at the time of diagnosis revealed pancytopenia while three cases had leucocytosis. Five patients (83.3%) presented with severe anaemia with haemoglobin level less than the mean of 9.8g / dl and two cases with thrombocytopenia ($100x10^9$ / l). Comparing the haematological values at diagnosis and six months post therapy revealed a lower median leucocyte count (P=0.0043), insignificant increase in platelet count (P=0.24) and a higher haemoglobin level (P=0.36). Typical pattern of bone marrow involvement in HCL was characterized by focal (33.3%) as well as diffuse (66.7%) mononuclear cell infiltration with individual nuclei of hairy cells infiltrating between the marrow fat cells. Most of the patients displayed megaloblastoid erythropoiesis. Lymph node biopsies were rarely documented.

Table-II: Hematological findings of HCL patients post therapy

Parameter	*Diagnosis (Mean±SD)*	*Post therapy (Mean±SD)*	*P value*
Haemoglobin (g / dl)	9.8±1.2	11.4±1.16	0.360
Total leucocyte count ($x10^9$ / l)	22±15.4	6.5±1.9	0.004
Platelet count ($x10^9$ / l)	103±108	112±117	0.240

Table-III: Relationship between spleen size and haematological parameters

Parameters	**r*	*P value*
Haemoglobin and spleen size	0.98	0.0007
Leucocyte count and spleen size	0.92	0.009
Platelet count and spleen size	0.95	0.004

*r = correlation coefficient

Table-III: revealed the relationship between the spleen size and haematological parameters. Leucocyte counts at diagnosis showed a significant correlation with spleen size (r = 0.92, p=0.009). Also, the spleen size at presentation showed a significant negative correlation with haemoglobin level (r = -0.98, p=0.0007) and platelet count (r = -0.95, p=0.004).

Four of the patients had splenectomy and interferon-alpha, $3x10^6$ U weekly for an average of four months while the remaining patients had cladribine, 0.07mg / kg / day by continuous infusion, over a seven-day period. Partial remission was recorded in all the interferon-treated and one cladribine patient while complete remission was observed in the other cladribine-treated patient.

DISCUSSION

Hairy cell leukaemia (HCL) is a well-recognized entity among the B lymphoid disorders. With the wide variability in its clinical and haematologic manifestations, several subtypes of HCL such as leucopenic and non leucopenic subtypes and subtypes with and without massive splenomegaly have been proposed.[5] Newer therapeutic options such as purine analogues have been adopted with minimal toxicity. However, these different chemotherapies failed to demonstrate sustained benefit, as the best treatment protocol for HCL has not yet been identified. Prime objective of treatment was normalization of the blood counts since pancytopenia is the main cause of complications. In addition, splenectomy is still indicated

in the treatment of young patients with significant splenomegaly and only minimal bone marrow involvement since it presumably alleviates the pancytopenic effect of hypersplenism by removing the site of leukaemic cell proliferation.[6] Interferon-alpha has been reported to benefit HCL patients with active disease, whether or not they had undergone prior splenectomy and is known to induce partial response of relatively short duration.

HCL accounted for approximately 1.5% of all haematological malignancies; an incidence of 0.18/million/year. This is in contrast with the mean incidence of 4.7/million/year in a well defined population of Iceland.[7] the higher incidence in some of the geographic regions probably reflects the better and earlier detection technique of the disease. That only six cases of HCL were confirmed within the 10-year period of study reflects the rarity of the disease. The incidence of HCL in Chinese (0.035/100,000 population per year) has also been reported to be much lower than in Western series,[8,9] but this is about two times the incidence in this report. Median age of 40 years at presentation was slightly lower when compared to the Caucasians.[10] Male predominance is similar to that in the western world probably depicting an occupational association.[11] This may be due to the fact that males are more exposed to environmental pollution as they are the breadwinners especially in the Niger Delta region of Nigeria, with petrochemical industries and gas flare sites where all the patients came from. However, no association has been found between HCL and employment in a job exposed to benzene or ionizing radiation in another study.[12,13]

The clinical and laboratory features of our patients are similar to previous reports in the diaspora.[8] The main clinical features at diagnosis associated with pancytopenia were anaemia symptoms, abdominal swelling and splenic discomfort/pain. Anaemia probably resulted from infiltration/reduced bone marrow production, megaloblastoid marrow and splenic pooling. The patients were moderately neutropenic and monocytopenic and the presence of infections did not run its normal course. Three of the patients (50%) had associated mycobacterial infections for which they were treated while two patients (33.3%) presented with bleeding diathesis with platelet count below $100x10^9$/l. Alpha-IFN treatment with splenectomy showed a significant response with normalization of the haematological parameters, though only the leucocyte count was statistically significant ($p=0.004$).This was similar to another study carried out in Illinois, USA.[14] Haematological complications of pancytopenia are due not only to the enlarged spleen causing hypersplenism but probably also due to the hairy cells in the bone marrow inducing cytokine-mediated suppression of haematopoiesis.[15] Several investigators have suggested that the stimulating cytokines are produced by the malignant B cells themselves, indicating an autocrine growth regulation.[15]

Main physical sign was massive splenomegaly (66.7%), a measure of tumor load,[16] and hepatomegaly (66.7%). This measure of tumor load with massive spleen in HCL was confirmed in this study with the presence of a significant positive relationship between white cell count and splenic size ($r=0.92$; $p=0.009$). Presence of massive spleen in HCL patients confers a less favorable prognosis and probably reflects the advanced stage of the disease.[17] Involvement of splenomegaly leads to secondary consumption of red cells, platelets and neutrophils as well as other complications of an enlarged spleen, including infarction-or-rarely rupture.[2] Also, a low hairy cell index at diagnosis has been reported to correlate favorably with a good haematological response.[18] Only one patient (16.7%) had lymphadenopathy which has been reported to be rare.

In conclusion, six cases of the rare HCL were seen over a 10-year period in a tertiary hospital in Southern Nigeria giving an incidence of 0.18/million/year, which is lower than what is reported in other series where it is also rare. Normalization of pancytopenia was achieved with the cytotoxic drugs but cure did not occur.

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