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Letters

Contrasting Sex Distribution of Chronic Lymphocytic Leukaemia and Well-differentiated Diffuse Lymphocytic Lymphoma in Ibadan, Nigeria

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DATA FROM the records of the Haematology Department and Cancer Registry of University College Hospital (UCH), Ibadan, Nigeria, show that of 89 patients with chronic lymphocytic leukaemia (CLL) seen between 1971 and 1989, 31 were males and 58 females (1:1.87). Diagnosis in these patients was based on peripheral blood lymphocytosis of 10×10^9/l, with mature-looking lymphocytes constituting at least 40% of the nucleated cells in a bone marrow aspirate film. Numerous basket cells were reported present in the peripheral blood films of most of the patients.

Over 80% of the patients were of low socio-economic class, and were aged 18–75 years, mean 48 (S.D. 14). During the same period, 53 cases of well-differentiated diffuse lymphocytic lymphoma (WDLL) were diagnosed from the histology of lymph-node specimens obtained on biopsy or necropsy. The patients with WDLL included 35 males and 18 females (1.94:1). Their age range was 8–75 years, mean 46 (S.D. 18). Most were also of low socio-economic status. The age and sex distribution of the CLL and WDLL patients is shown in Table 1.

Table 1. Age and sex distribution of patients with CLL and WDLL, at UCH, Ibadan, Nigeria: 1971–1989.

	CLL			WDLL		
Age	M	F	Total	M	F	Total
0–10	0	0	0	2	0	2
11–20	3	1	4	3	2	5
21–30	0	0	0	1	1	2
31–40	6	13	19	1	3	4
41–50	7	21	28	13	7	20
51–60	6	12	18	8	3	11
61–70	7	9	16	3	1	4
71–80	2	2	4	4	1	5
Total	31	58	89	35	18	53

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That females outnumber males among Nigerians with CLL has been noted in previous reports [1–3]. Also, a male preponderance in cases of lymphosarcoma had been observed at UCH [4], which included WDLL [5]. CLL and WDLL are regarded as analogous according to the lymphoma–leukaemia concept [6]. Our patients had the same socio-economic class distribution and modal age group during the period reviewed. It is, however, not clear why they differ in sex distribution. Pregnancy-associated immunodeficiency has contributed to the predominant occurrence of CLL in Nigerian women [2]. It would be interesting to know if this contrasting sex distribution of CLL and WDLL has been observed in other parts of the world, and what might be the contributing factors in a particular environment.

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Colorectal Cancerous Polyps Compared with Benign Adenomas

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SEVERE DYSPLASIA or a focus of carcinoma that extends through the muscularis mucosa but not out of the polyp boundaries, may be found in 5% of adenomatous colorectal polyps [1]. These cancerous polyps are considered an intermediate stage in the transformation of benign adenomas into true cancers. In view of the greater risk for the development of cancer from large or villous adenomas [1–3], we compared the size and histology of 151 cancerous polyps with those of 557 benign adenomas.

All the polyps were resected during colonoscopy and their histology was assessed according to WHO criteria [4]. The cancerous polyps were significantly larger than the benign adenomas: 57% of polyps were larger than 2 cm in diameter compared with 15% of the adenomas ($P < 0.0001$) and 11% of the polyps were smaller than 1 cm in size compared with 52%

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of the adenomas ($P < 0.0001$). There were also significantly more cancerous polyps with villous architecture (11%) than among the benign adenomas (3%) ($P < 0.001$) (χ^2 test).

Our results are in accordance with the assumption that certain features of adenomas are associated with a higher risk for development of the cancerous process. Although large size is one of the main features of cancerous polyps, tiny cancerous polyps may occur [5]. The finding of cancerous polyps certainly allocates the patient into a higher risk group, which means that a closer and more frequent colonoscopic surveillance is necessary.

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Adoptive Immunotherapy of Primary and Metastatic Liver Cancer via Hepatic Artery Catheter

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WE HAVE previously reported the results of adoptive immunotherapy with lymphokine-activated killer (LAK) cells and recombinant interleukin 2 (IL-2) [1, 2] in patients with hepatocellular carcinoma (HCC) [3] which suggested that administration of LAK cells directly into the hepatic artery was more effective and caused less side-effects than systemic administration [3, 4]. All four HCC cases in our study, given small numbers of LAK cells through the hepatic artery in a single dose, showed briefly decreasing serum alphafetoprotein (AFP) levels. This finding prompted us to treat patients with hepatic tumours by AIT via catheters placed into the hepatic artery. Since sustained low blood level of IL-2 has been reported to mediate better proliferation and higher antitumour activity of LAK cells than brief high levels of IL-2 [5], we infused IL-2 (10^6 U per day) through the catheters.

Table 1. Patients' characteristics, response and survival

Case (age/sex)	E	LAK cells ($\times 10^9$)	IL-2 ($\times 10^7$ U)	Size	Responses P.S.*	Survival (mo)
HCC						
1. (63/M)	4	119.0	38.0	PR	4/1	34
2. (21/F)	4	97.0	5.5	PR	4/1	9
3. (68/M)	4	7.5	2.3	NC	1/1	3
4. (34/M)	4	44.8	8.8	PD	2/4	4
5. (64/M)	3	9.6	2.7	NC	1/1	5
Colon						
6. (65/M)	4	14.6	5.2	PD	1/1	6
7. (65/M)	2	57.2	5.5	PD	2/3	7
8. (47/M)	3	54.0	2.4	PD	1/1	6

E = tumour extension in liver measured by area occupied by cancer: 4 = > 60%, 3 = 40–60%, 2 = 20–40% and 1 = < 20%.
PR = partial regression; NC = no change; PD = progressive disease.
*Performance status before/after immunotherapy: 4 = bedridden all day long, 3 = bedridden for more than half the day, 2 = bedridden for less than half the day and 1 = no limitations.

Two out of five patients with HCC had partial tumour regression (Table 1) and tumour sizes and serum AFP levels decreased. However, whilst the patients' general condition improved, tumour growth recommenced as therapy was given intravenously. In case 1 this second growth was suppressed by another course of intra-arterial AIT. Two patients responded to the therapy and lived for as long as 34 and 9 months, respectively, after initiation of adoptive immunotherapy, although they had advanced cancers. These patients had been treated with mitomycin C or 5-fluorouracil more than 1 month before adoptive immunotherapy, although chemotherapy failed to induce tumour regression and caused severe side-effects. Adoptive immunotherapy following chemotherapy is reported to be more effective than adoptive immunotherapy alone in animal models [6, 7] and such combined therapy may be of benefit. Metastatic liver tumours from colonic carcinomas were resistant to adoptive immunotherapy, confirming previous reports [1, 2, 8].

Fever and eosinophilia were less severe side-effects than with systemic adoptive immunotherapy [3]. However, bleeding gastroduodenal ulcers developed in three cases, which probably resulted from continuous administration of IL-2 into the hepatic artery. Thus, intra-arterial LAK cell infusion with continuous intravenous administration of IL-2 may be a better approach.

Many LAK cells are necessary to induce tumour regression [1, 2], but repeated leukaphereses impose great burdens on patients and medical staff. To overcome the problem, a long-term culture method of LAK cells was developed and used in three patients (cases 2, 7 and 8). In this method, half the cells were put aside at harvest, and were further cultured with IL-2. The procedure was repeated several times. This process enabled us to obtain a large number of cells with high LAK activity. Since only three cases have been treated with LAK cells generated by this method, further trials are needed to determine whether such cells can mediate antitumour effects *in vivo*, especially in patients with HCC.

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