SHORT REPORTS

Chronic myeloid leukaemia associated with impairment of hearing

Loss of hearing is a rare complication of chronic myeloid leukaemia.[1 2] We describe the occurrence of varying degrees of impairment of hearing in nine out of 44 Nigerian patients with the disease.

Patients, methods, and results

Chronic myeloid leukaemia was diagnosed in the usual way based on clinical and laboratory findings including total and differential white cell counts. Cytogenetic analysis was not routinely available. The diagnosis of hearing disorders was based on the history given by the patient as well as on findings of routine physical examination. In addition, audiometric studies were performed when indicated, and these were repeated at intervals when possible. In order to evaluate the influence of anaemia and severity of hyperleucocytosis at the time of occurrence of hearing impairment, each patient with an auditory complication of chronic myeloid leukaemia was matched according to age, sex, and state of the disease—that is, whether in a "steady" or accelerated phase—with control patients suffering from the disease but who did not have clinical evidence of a hearing problem. Relevant laboratory data were compared by the usual statistical methods.

Eight of the nine patients with auditory problems were clinically and haematologically in the chronic phase of their disease at the time that the problem occurred. Comparison of the packed cell volumes and white cell counts of these patients (table) with those of the controls showed no significant difference in median packed cell volumes (0·24 *v* 0·33; $p > 0.05$) but a significantly higher median white cell count in the group with impaired hearing ($434{\cdot}0 \times 10^9$/l *v* $257{\cdot}0 \times 10^9$/l; $p < 0.05$). Three of the five patients with moderate hearing impairment who were followed up long enough during chemotherapy showed a remarkable subjective improvement in hearing associated with a reduction in the peripheral white cell count to the range $10{\cdot}0$-$20{\cdot}0 \times 10^9$/l; in the remaining four patients, however (cases 2, 5, 6, 7), profound deafness persisted despite similar satisfactory haematological control.

Comment

We have described auditory disturbances ranging in severity from mild to profound loss of hearing occurring in nine of 44 Nigerian patients with chronic myeloid leukaemia who presented either at an advanced stage or after prolonged lack of control of the disease.

It appears most likely that the uniformly associated high degree of leucocytosis (table) is a major predisposing factor in the pathogenesis of this complication. The role of severe anaemia, which was present in six of our patients (table), is less clear. Hyperleucocytosis may lead to the formation of leucocyte thrombi and failure of the microvasculature,[3] which for unknown reasons manifested in our patients as auditory impairment and also as cerebellar ataxia (case 2), priapism (case 4), and "organic brain syndrome" (case 7). The central role of the physical characteristics of the leucocytes[4] concerned in the leucostasis is underscored by the fact that none of 34 patients with chronic lymphocytic leukaemia who had white cell counts in the same range as our nine patients with chronic myeloid leukaemia manifested any signs of leucostatic syndromes.

Although chronic myeloid leukaemia is largely incurable, its effective control with chemotherapy usually ensures a reasonably good quality of life for about three to five years in most cases.[1 2] Owing to socioeconomic and, in some cases, cultural factors Nigerian patients with chronic myeloid leukaemia present at very late stages of their disease[5] and often are unable to receive regular chemotherapy. Of all the disabilities suffered consequently, loss of hearing appears to be the most distressing to the patient: early diagnosis and effective control of the disease, as in many developed countries, should reduce its occurrence in the future among Nigerians.

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Seroconversion of human T cell lymphotrophic virus III (HTLV-III) in patients with haemophilia: a longitudinal study

Patients with haemophilia are at risk for the acquired immunodeficiency syndrome (AIDS). They have a high prevalence of antibody to human T cell lymphotrophic virus III (HTLV-III) compared with control populations,[1] although few have so far developed AIDS.[2] As part of a surveillance programme on AIDS we studied a group of patients with haemophilia for clinical and immunological features associated with the syndrome.[3] We correlated our findings with the time from onset of HTLV-III infection in each patient, as determined by retrospective antibody studies.

Methods

We studied 30 patients who had received factor VIII treatment within five years. Twenty nine (male) had haemophilia A, and one (female heterozygote) had been treated for postoperative bleeding. One man had

Clinical and laboratory profile of patients with chronic myeloid leukaemia developing various degrees of impairment of hearing

Case No	Age and sex	Packed cell volume*	White cell count ($\times 10^9$/l)*	Platelet count ($\times 10^9$/l)*	Disease phase	Manifestation of vascular stasis
1	50 F	0·19	249·0	Reduced†	Chronic	Partial deafness
2	25 M	0·40	310·0	302·0	Chronic‡	Profound deafness, unsteadiness of gait
3	66 F	0·24	434·0	Reduced†	Chronic‡	Moderate deafness
4	34 M	0·23	470·0	44·0	Chronic	Tinnitus, mild deafness, priapism
5	41 F	0·14	572·0	Normal†	Chronic‡	Profound deafness
6	25 M	0·15	306·0	Normal†	Blastic crisis in relapse‡	Profound deafness
7	42 F	0·43	448·0	650·0	Chronic‡	Profound deafness, psychiatric disorder—organic brain syndrome
8	30 F	0·18	540·0	75·0	Chronic	Dizziness, tinnitus, mild deafness, unsteadiness of gait
9	58 F	0·35	200·0	290·0	Chronic	Tinnitus

*Values at time of presentation with impairment of hearing.
†Counts not done.
‡Deafness occurring after protracted default on follow up.

been tattooed over 10 years previously. No other risk factors for AIDS were present. We determined relative values for T4 and T8 lymphocyte subsets with immunofluorescence, using monoclonal antibodies OKT4 and OKT8. Absolute values were calculated from a count of total lymphocytes on the same day. Stored sera from 1979-84 were tested for HTLV-III antibodies by radioimmunoassay.[1]

Results

The table summarises our results. Five patients had recently developed splenomegaly or lymphadenopathy, and one of these also had mild thrombocytopenia. No opportunistic infection or unexplained loss of weight was noted. A basal cell carcinoma of the face in a 59 year old was recorded.

Details of patients with haemophilia 1979-84

Case No	Age (years)	Pretreatment factor VIII coagulant activity (%)	1979		1980		1981		1982		1983		1984		Lymphocyte count (× 10⁹/l)		Ratio T4:T8 (normal range 1·5-4·1)	Special findings
			a	b	a	b	a	b	a	b	a	b	a	b	T4*	T8†		
1	23	2					+		+	+	+	+			0·88	0·74	1·2	
2	29	1				−	+		+		+		+		1·2	0·63	1·9	Splenomegaly and lymphadenopathy (1984)
3	23	3						+	+	+	+	+	+		1·6	1·2	1·6	
4	23	1				−		+	+	+	+	+	+		0·77	0·18	2·15	Factor VIII inhibitor
5	59	1		−					+	+		+			0·27	0·52	0·55	Basal cell carcinoma (1983)
6	43	1					−		+		+	+	+		1·64	0·59	2·8	
7	39	1		−		−			+	+		+	+		0·48	0·1	4·8	
8	24	1		−		−		−	+		+		+		0·64	0·9	0·72	
9	18	1		−					−	+	+		+		0·9	0·62	1·43	Splenomegaly (1984)
10	44	1		−				−			+		+					
11	47	1		−					−		+	+			0·28	0·25	1·1	Lymphadenopathy, mild thrombocytopenia (1984)
12	30	1		−				−			+		+		0·2	0·17	1·21	
13	39	1				−		−	−			+			0·38	0·14	2·8	Factor VIII inhibitor positive for hepatitis B surface antigen
14	15	2		−		−				−			+		1·4	0·84	1·67	
15	27	1		−				−		−			+		0·64	0·67	0·96	Lymphadenopathy (1984)
16	16	1											+		0·66	0·26	2·5	Lymphadenopathy (1984), positive for hepatitis B surface antigen
17	33	2		−				−		−			+	+	0·49	0·58	0·85	Factor VIII inhibitor, positive for hepatitis B surface antigen
18	50	1							−			−	+		1·02	0·48	2·2	
19	8	1				−			−		−	−	+		1·18	0·84	1·41	
20	23	3				−		−	−			−	−	+	0·6	0·24	2·48	
21	39	1											−	−	0·88	0·54	1·6	Positive for hepatitis B surface antigen
22	36	1		−				−		−		−	−		0·88	0·76	1·17	
23	29	1										−			1·3	0·46	2·81	
24	24	1										−		−				
25	41	4											−		1·1	0·58	1·87	
26	54	4											−	−	0·37	0·34	1·07	Positive for hepatitis B surface antigen
27	58	9							−					−	0·7	0·51	1·21	
28	19	15									−				1·1	0·34	3·2	
29	63	25									−			−	0·56	0·23	2·48	Fatal haematemesis (1984)
30	50	50											−	−	2·4	1·3	1·93	Female heterozygote

a = serum January-June; b = serum July-December. *Normal range 1·05 (SD 0·35) × 10⁹/l. †Normal range 0·57 (SD 0·20) × 10⁹/l.

Seven patients had T4 lymphocyte counts of less than 0·5 × 10⁹/l, with clinical findings in only one. Twenty had detectable HTLV-III antibodies at the most recent date of testing. The earliest positive result was detected in January 1981. Thereafter roughly 15% of our subjects seroconverted each year until 1984. Seroconversion could be dated often to within six months, but no coincidental acute illness identified. No patient with detectable antibody became seronegative in later samples. All five patients with clinical findings were seropositive, and depletion of T4 was associated with anti-HTLV-III in six out of seven cases. No overall difference in distribution of T4 and T8 lymphocyte counts existed between seropositive and seronegative groups, and no association was noted between the time after seroconversion and the presence of clinical or immunological abnormalities.

Comment

British patients with haemophilia, like Americans, have been exposed to HTLV-III for at least four years.[4] Most of our seropositive patients had had large amounts of factor VIII treatment, predominantly commercial concentrate from the United States, often over 50 000 units/year of factor VIII activity. Four patients who seroconverted during 1984, however, had had little treatment, including one man who had used only 3250 units during 1983, all from the same batch of commercial concentrate. Five patients had used only products from the National Health Service over five years, and all were seronegative, in keeping with the low prevalence of anti-HTLV-III in British blood donors.[1]

To what extent should we inform these patients about their antibody state without causing anxiety? For example, four patients who were seropositive for four years had normal T4 lymphocyte counts and would probably not develop AIDS, although recently detected lymphadenopathy and splenomegaly in one suggests caution. Lymphadenopathy and splenomegaly in patients with haemophilia, however, may have causes other than AIDS. Unfortunately we failed to identify features that might help distinguish between self limiting HTLV-III infection and infection leading to AIDS or a carrier state. Urgency is underlined by the recent report of transmission of AIDS from a patient with haemophilia to his child via his spouse.[5] A genetic or additional acquired factor may be proved necessary for the development of AIDS from HTLV-III infection. Until then, patients with haemophilia who are seronegative from exposure to the virus must be protected and those who have already been infected monitored.

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